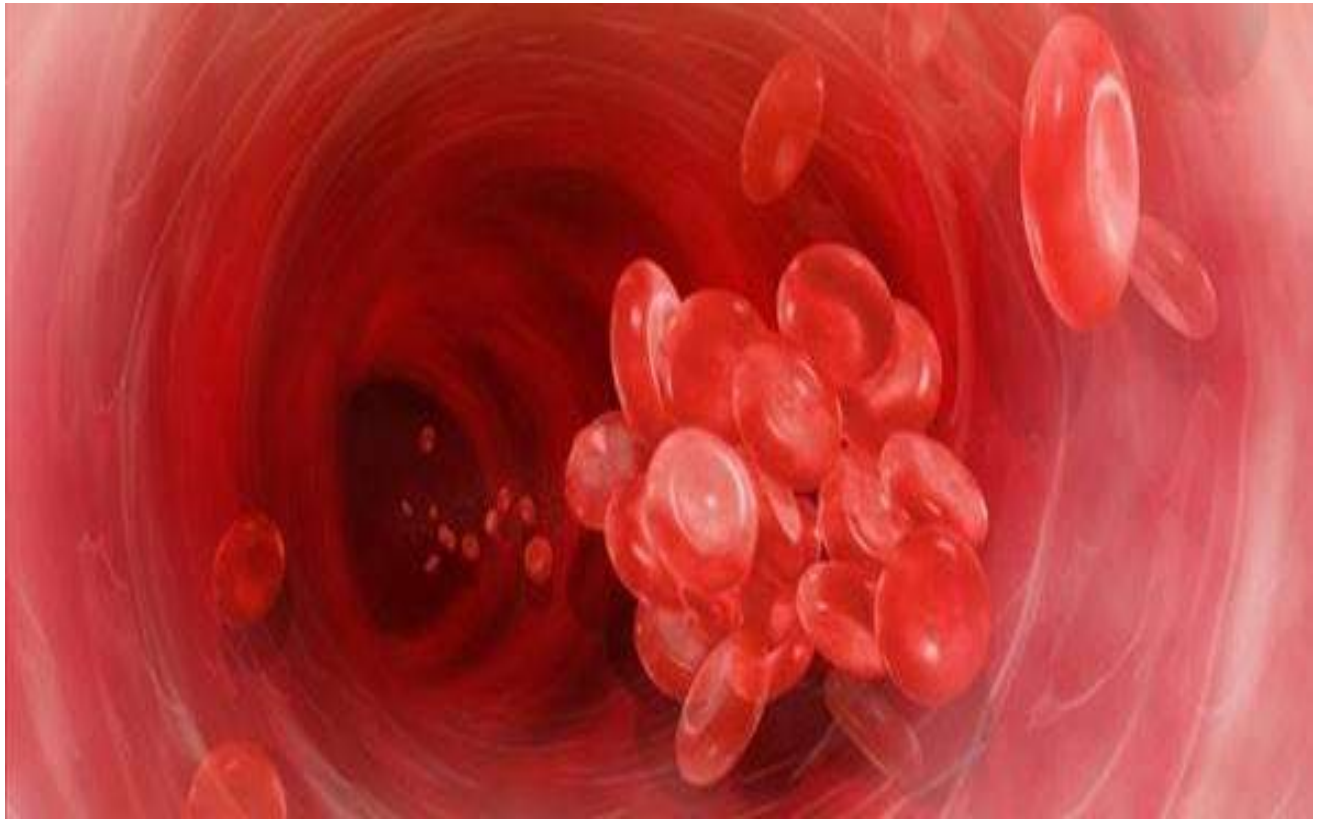
THE CIRCULATORY SYSTEM: BLOOD



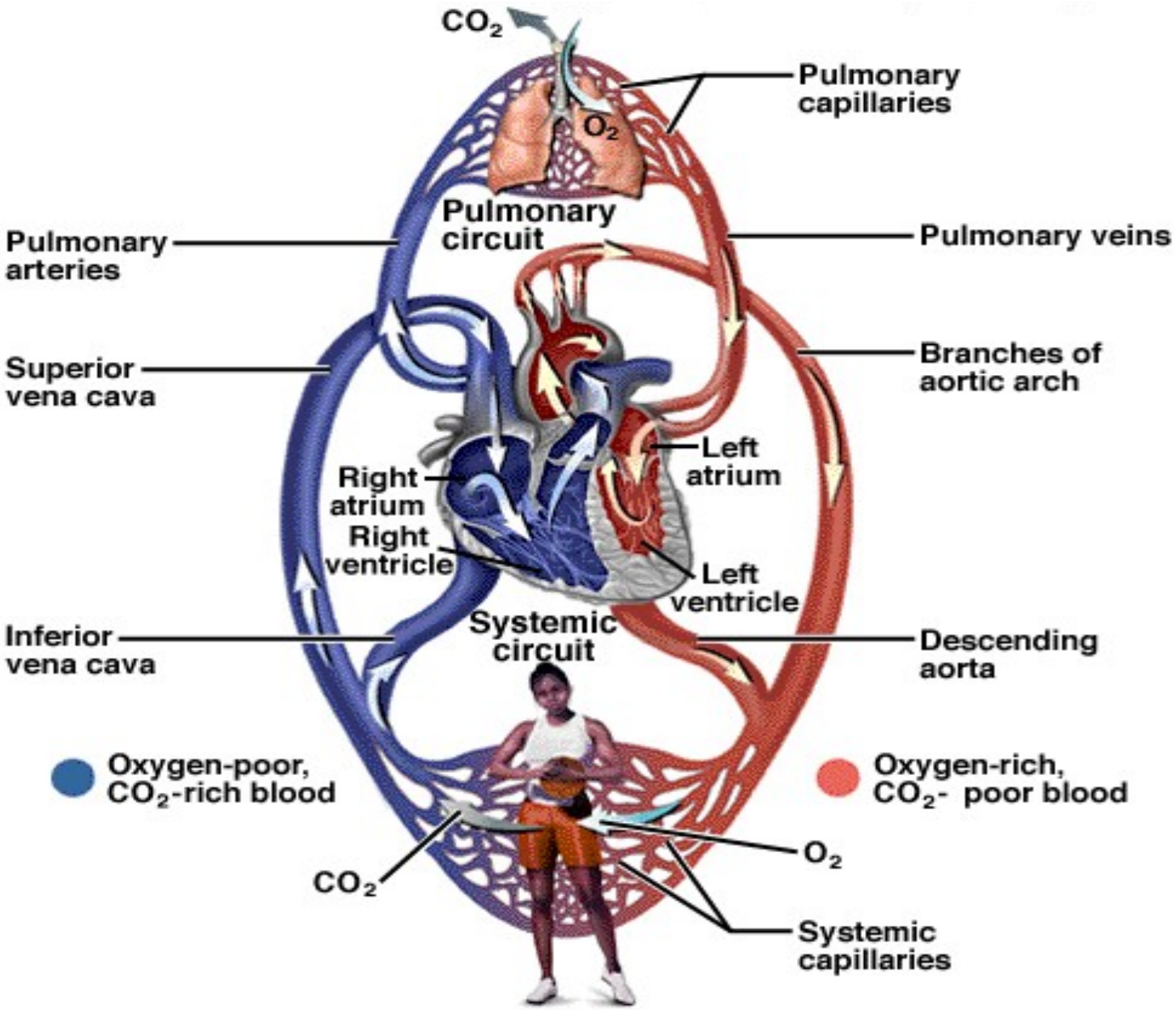
BLOOD FACTS

- Approximately 8% of an adult's body weight is made up of blood.
- Females have around 4-5 litres, while males have around 5-6 litres. This difference is mainly due to the differences in body size between men and women.
- Its mean temperature is 38 degrees Celcius.
- It has a pH of 7.35-7.45, making it slightly basic (less than 7 is considered acidic).
- Whole blood is about 4.5-5.5 times as viscous as water, indicating that it is more resistant to flow than water. This viscosity is vital to the function of blood because if blood flows too easily or with too much resistance, it can strain the heart and lead to severe cardiovascular problems.
- Blood in the arteries is a brighter red than blood in the veins because of the higher levels of oxygen found in the arteries.
- An artificial substitute for human blood has not been found.

The circulatory system is composed of:

- The blood (the circulating material)
- The heart (pump)
- Blood vessels (conduit)

The circulatory system



Primary Functions of the Circulatory System

Transportation

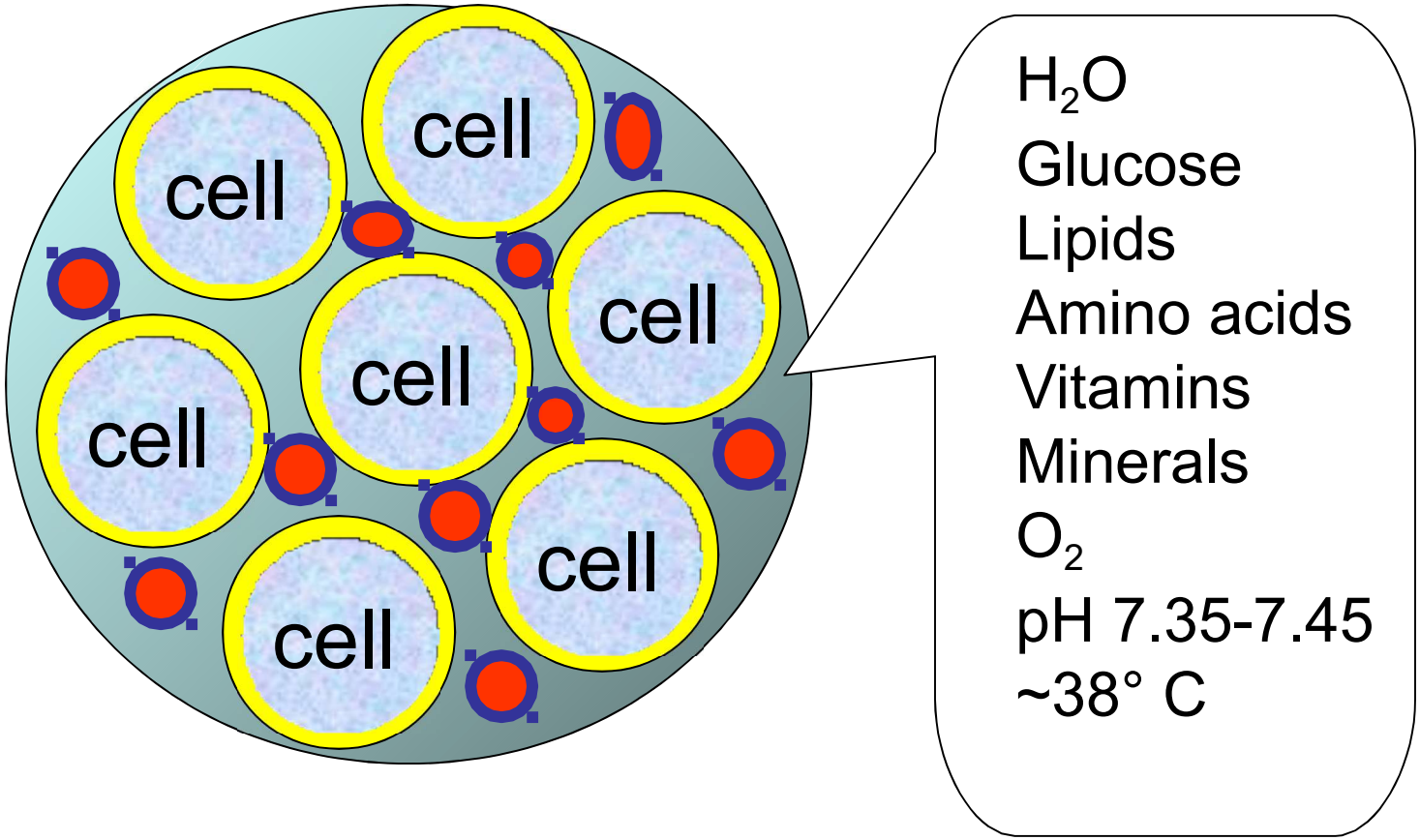
- **Oxygen**
- **Nutrition**
- **Hormones**
- **Clotting factors**
- **Protective substances**

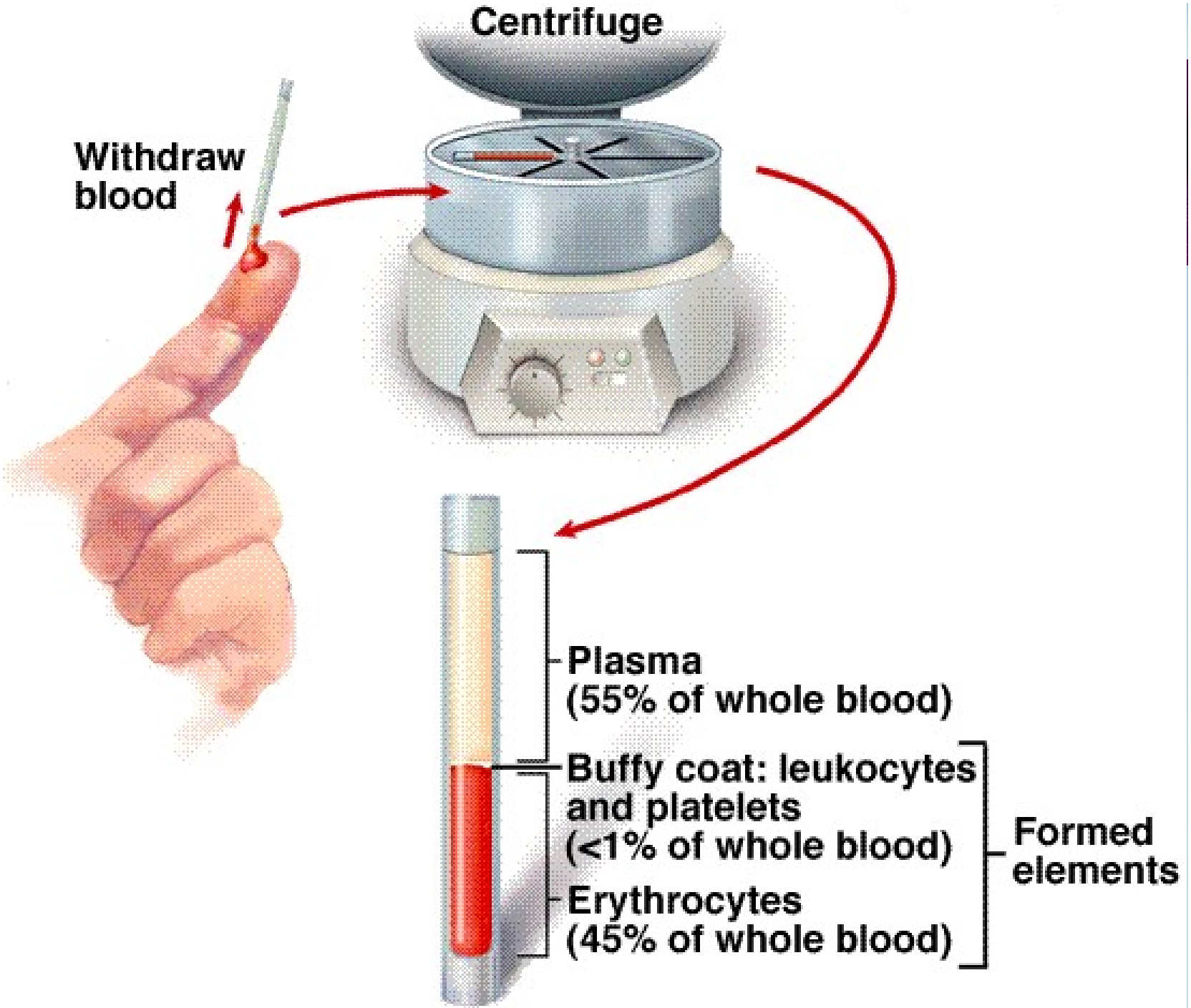
- Collect waste products from tissue cells and deliver to special organs (kidney, lung) for disposal

Primary Functions of the Circulatory System

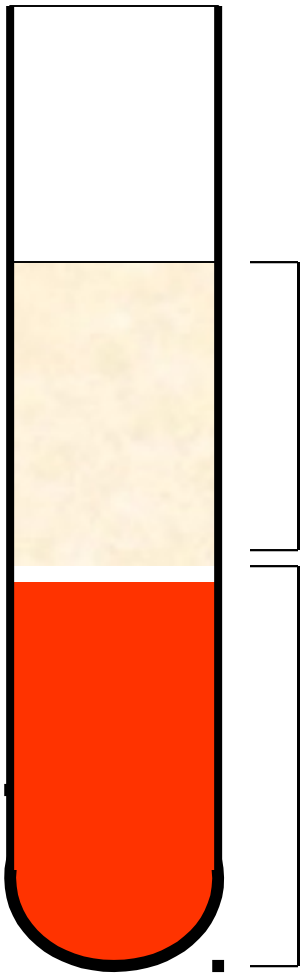
Protection

- Special components of the blood patrol the whole body and fight against invaded microorganisms and cancerous cells.




Centrifuge
Withdraw blood
Plasma (55% of whole blood)
Buffy coat: leukocytes and platelets (<1% of whole blood)
Erythrocytes (45% of whole blood)
Formed elements

Composition of the Blood



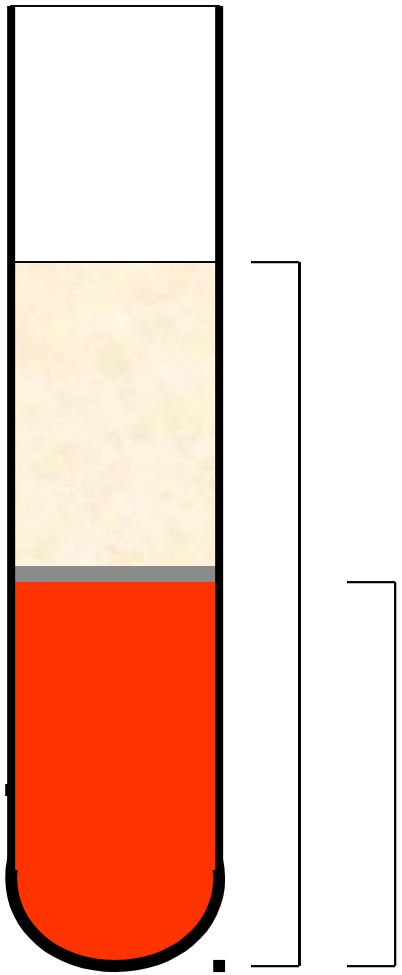
1) Plasma

2) The Formed Elements
(blood cells/cell fragments)

General Properties of Whole Blood

- Fraction of body weight **8%**
- Volume **Female: 4-5 L**
  Male: 5-6 L
- temperature **38° C (100.4° F)**
- pH **7.35 - 7.45**
- Viscosity (relative to water) **Whole blood: 4.5-5.5**
  plasma: 2.0
- Osmolarity **280-300 mOsm/L**
- Mean salinity (mainly NaCl) **0.85%**

Hematocrit



RBCs as percent of total blood volume

100%

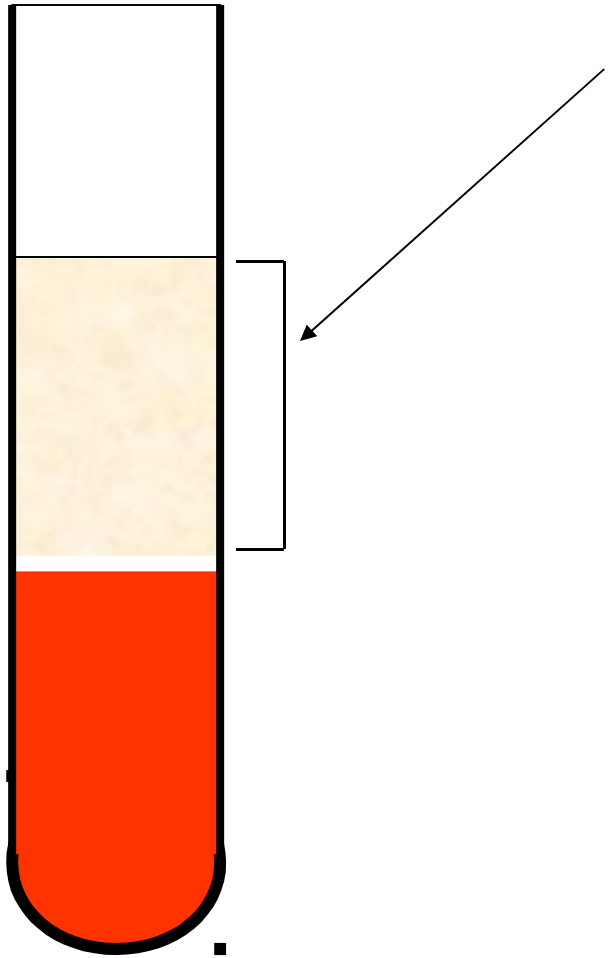
- Female: **37%-48%**
- male: **45%-52%**

General Properties of Whole Blood

- **Hemoglobin**
- **Female:** 12-16 g/100 ml
- **male:** 13-18 g/100 ml

- **Mean RBC count**
- **Female:** 4.8 million/μl
- **male:** 5.4 million/μl
- **Platelet counts** 130,000-360,000/μl
- ***Total WBC counts*** 4,000-11,000/μl

Plasma



Composition of Plasma

Water	92% by weight
Proteins	Total 6-9 g/100 ml
Albumin	60% of total plasma protein
Globulin	36% of total plasma protein
Fibrinogen	4% of total plasma protein
Enzymes of diagnostic value	trace
Glucose (dextrose)	70-110 mg/100 ml
Amino acid	33-51 mg/100 ml
Lactic acid	6-16 mg/100 ml

Composition of Plasma (continued)

Total lipid	450-850 mg/100 ml
Cholesterol	120-220 mg/100 ml
Fatty acids	190-420 mg/100 ml
High-density lipoprotein (HDL)	30-80 mg/100 ml
Low-density lipoprotein (LDL)	62-185 mg/100 ml
Neutral Fats (triglycerides)	40-150 mg/100 ml
Phospholipids	6-12 mg/100 ml

Composition of Plasma (continued)

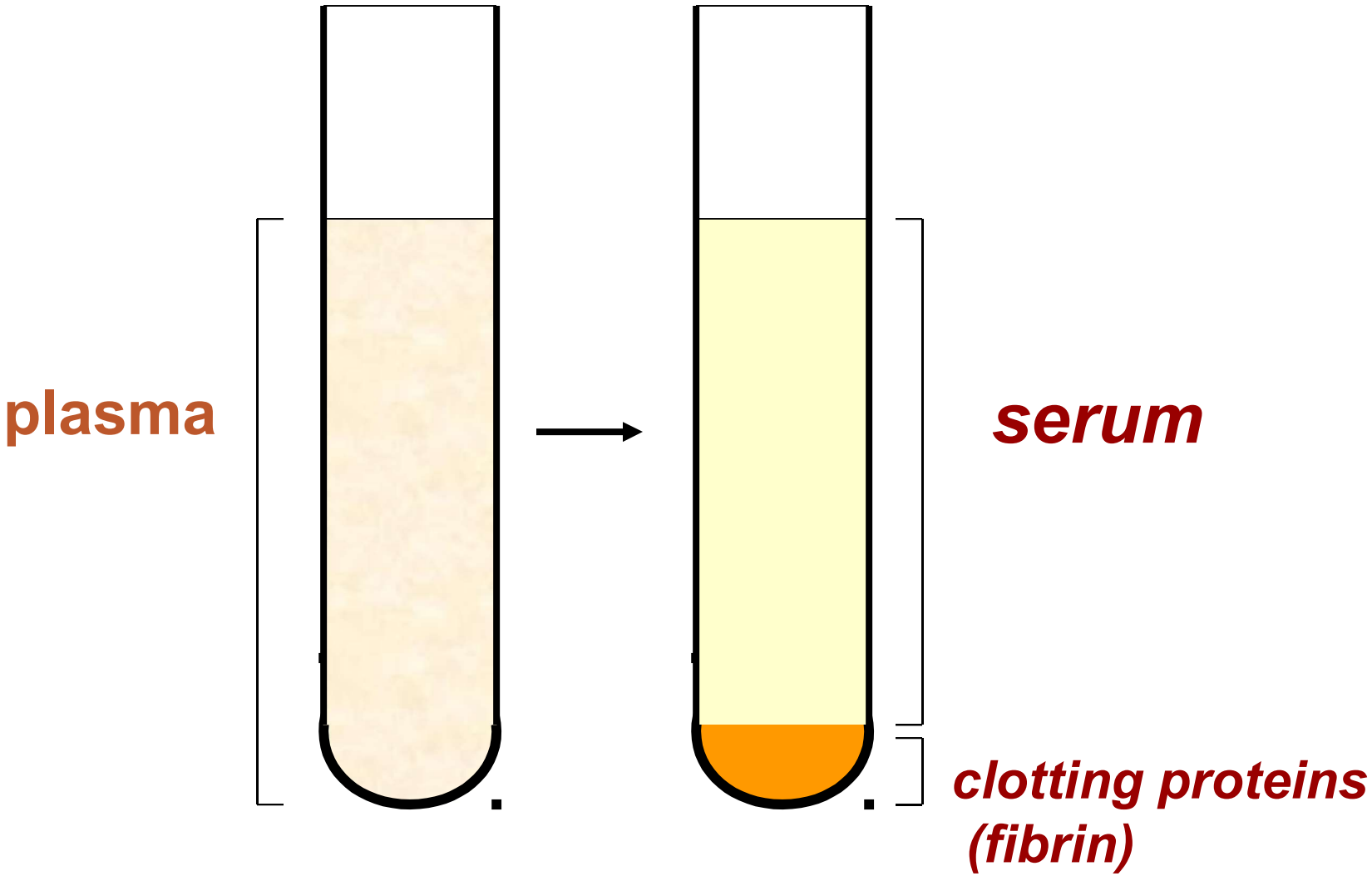
Iron	50-150 μg/100 ml
Vitamins (A, B, C, D, E, K)	Trace amount
Electrolytes	
Sodium	135-145 mEq/L
Potassium	3.5-5.0 mEq/L
Magnesium	1.3-2.1 mEq/L
Calcium	9.2-10.4 mEq/L
Chloride	90-106 mEq/L
Bicarbonate	23.1-26.7 mEq/L
Phosphate	1.4-2.7 mEq/L
Sulfate	0.6-1.2 mEq/L

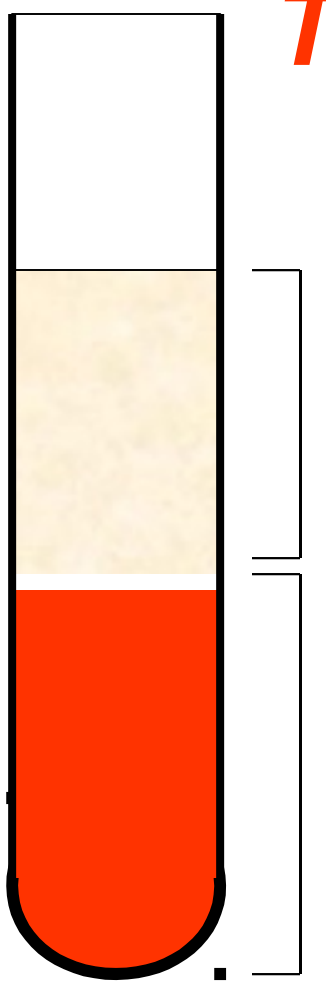
Composition of Plasma (continued)

Nitrogenous Wastes

Ammonia	0.02-0.09 mg/100 ml
Urea	8-25 mg/100 ml
Creatine	0.2-0.8 mg/100 ml
Creatinine	0.6-1.5 mg/100 ml
Uric acid	1.5-8.0 mg/100 ml
Bilirubin	0-1.0 mg/100 ml

Respiratory gases (O_2, CO_2, and N_2)

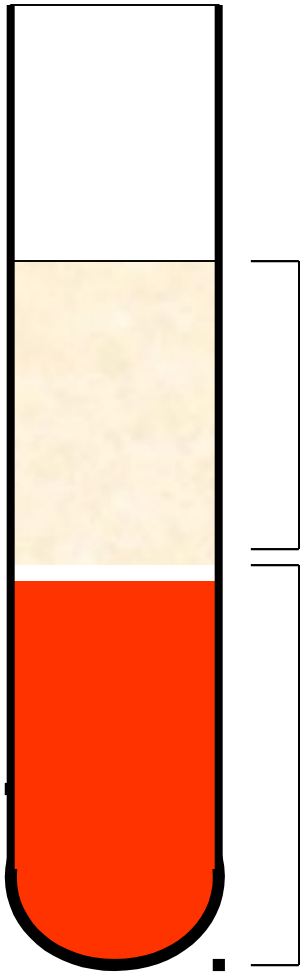

plasma
serum
clotting proteins
(fibrin)



The Formed Elements

(Blood Cells)

Formed elements include:



Erythrocytes (red blood cells, RBCs)

Platelets (cellular fragments)

Leukocytes (white blood cells, WBCs)

Granulocytes

Neutrophils

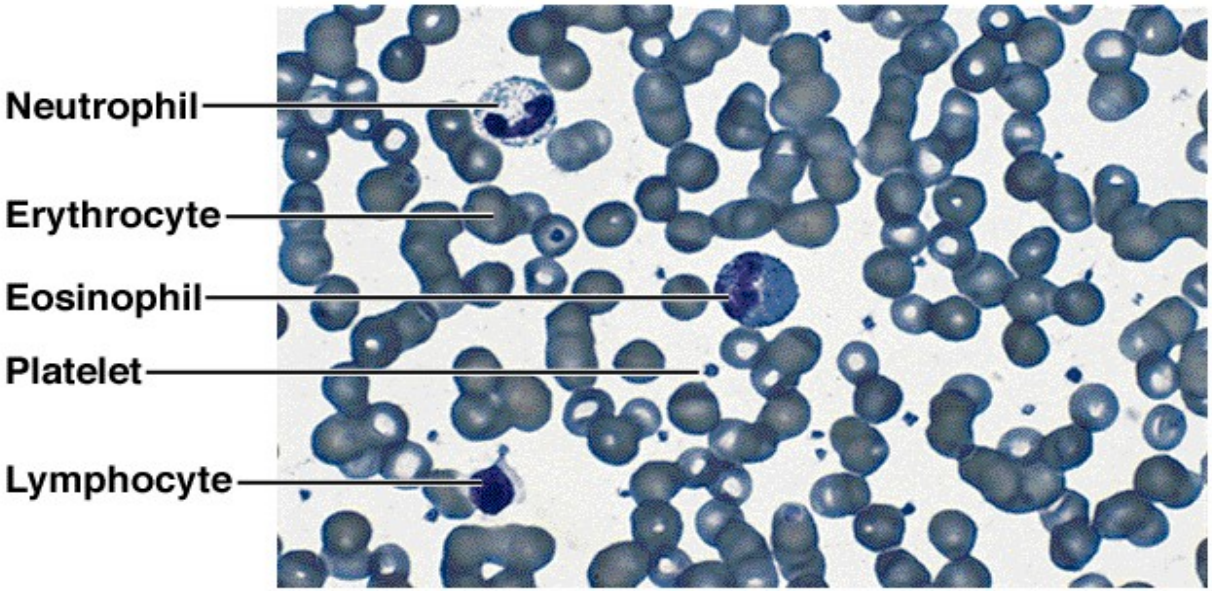
Eosinophils Basophils

Agranulocytes

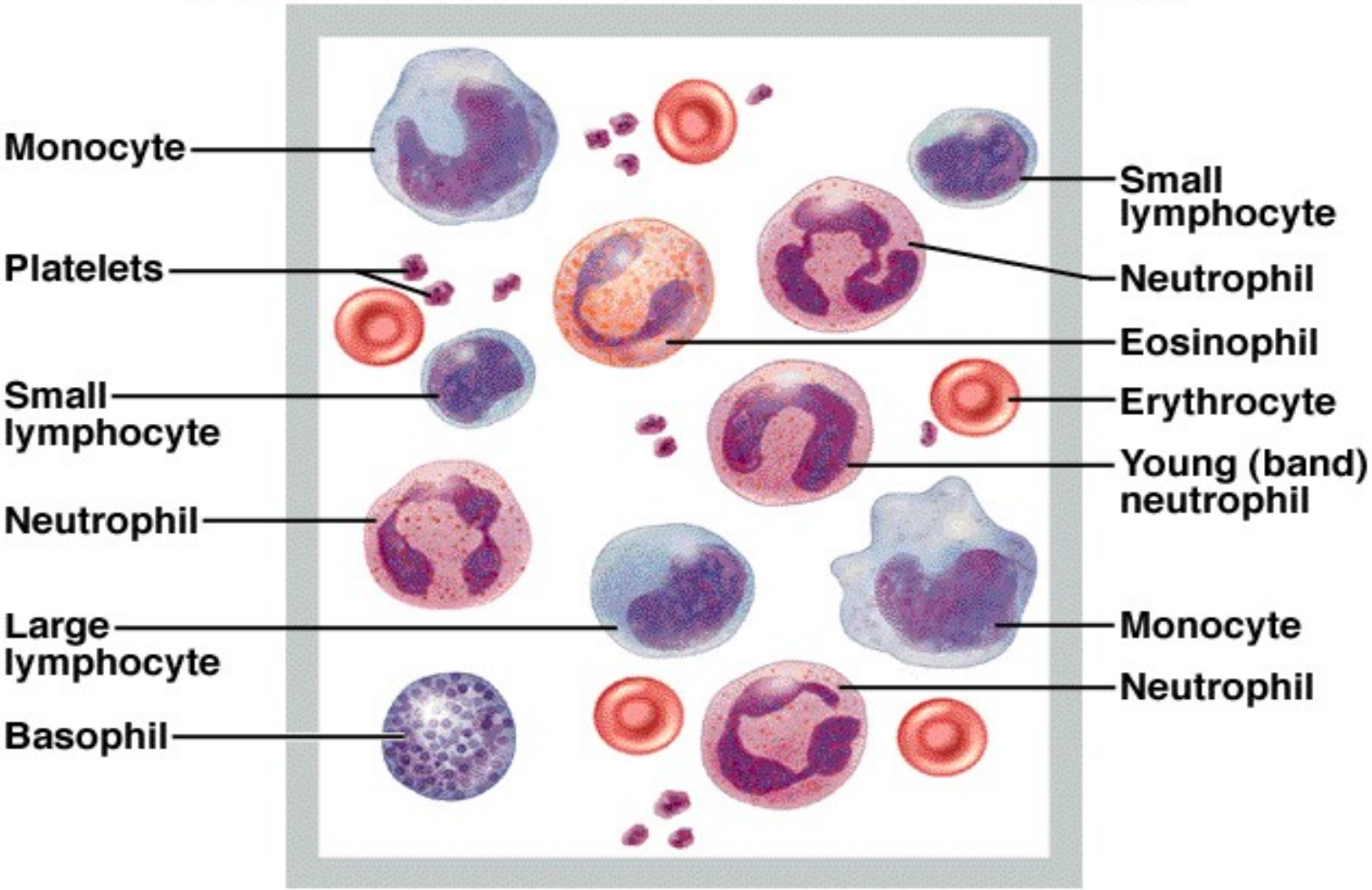
Lymphocytes

Monocytes

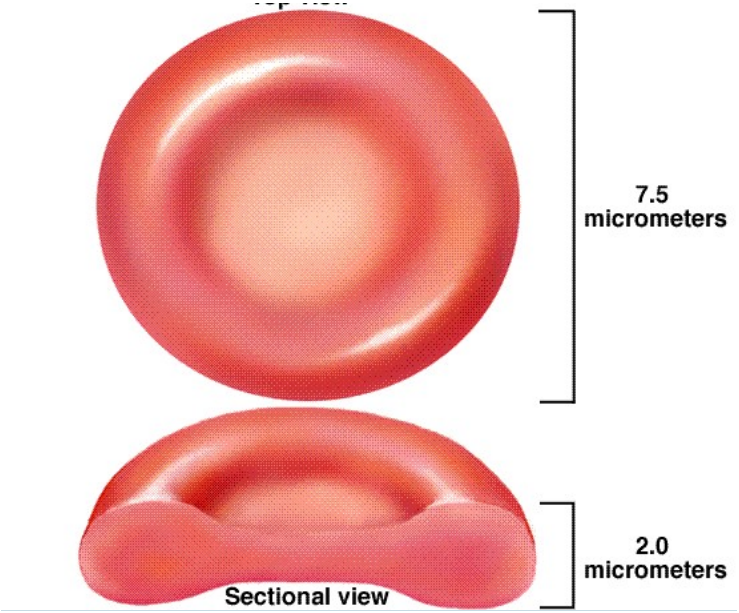
Normal Blood Smear



Formed Elements of Blood



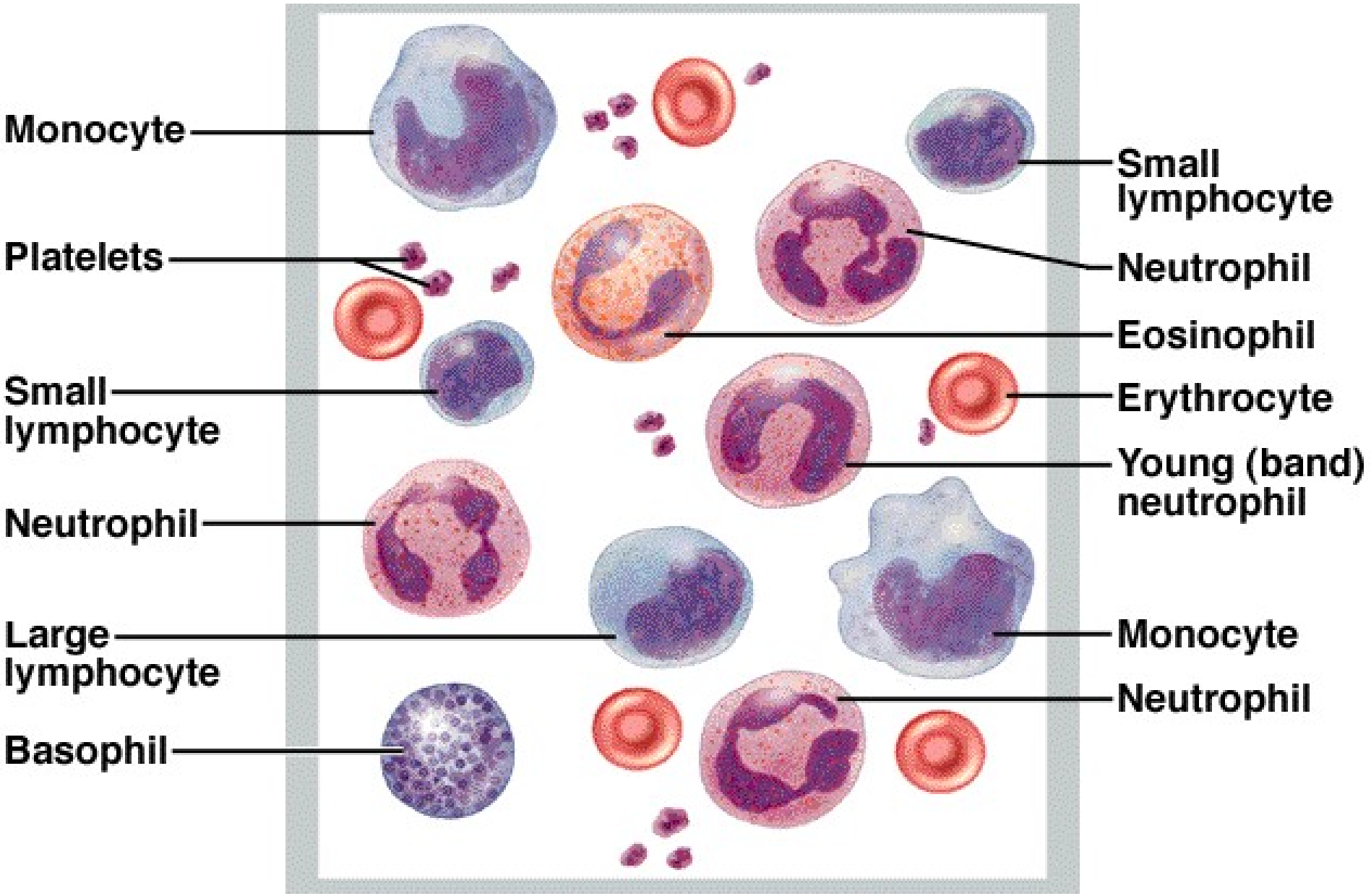
Erythrocytes (Red Blood Cells, RBCs)



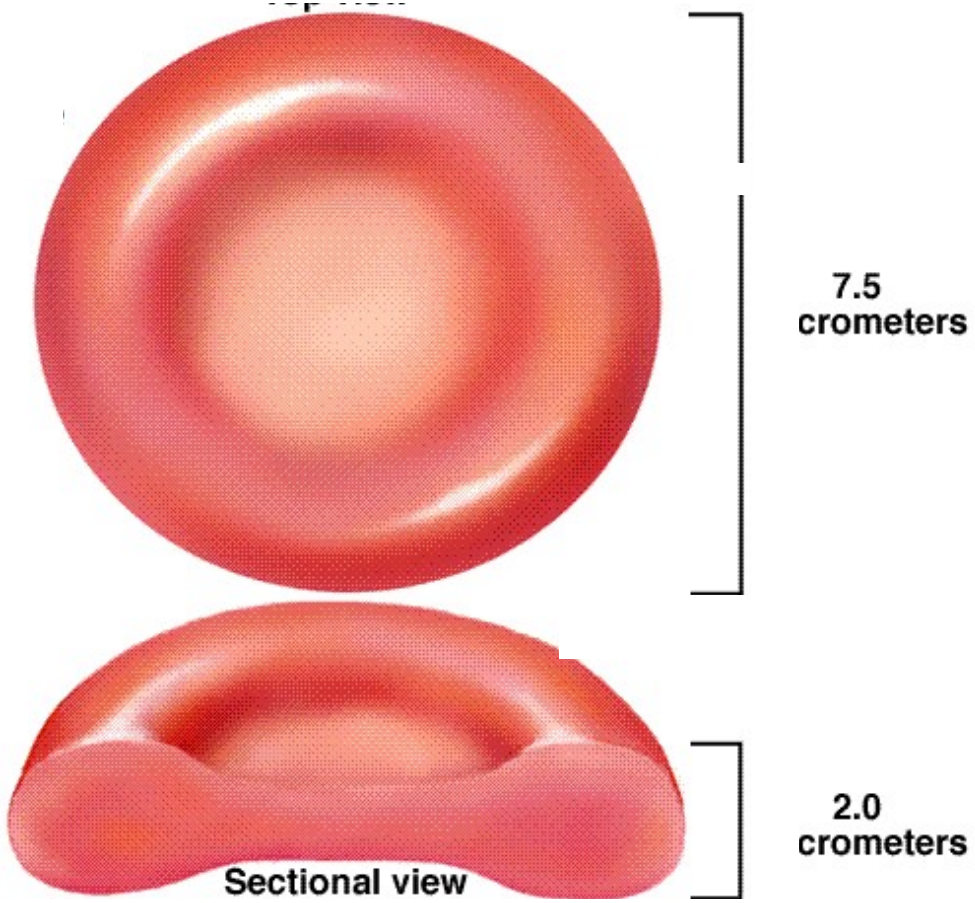
Appearance:

- ***biconcave disc*** shape, which is suited for gas exchange. The shape is flexible so that RBCs can pass though the smallest blood vessels, i.e., capillaries.

Erythrocytes are smaller than Leukocytes.



Erythrocytes (Red Blood Cells, RBCs)



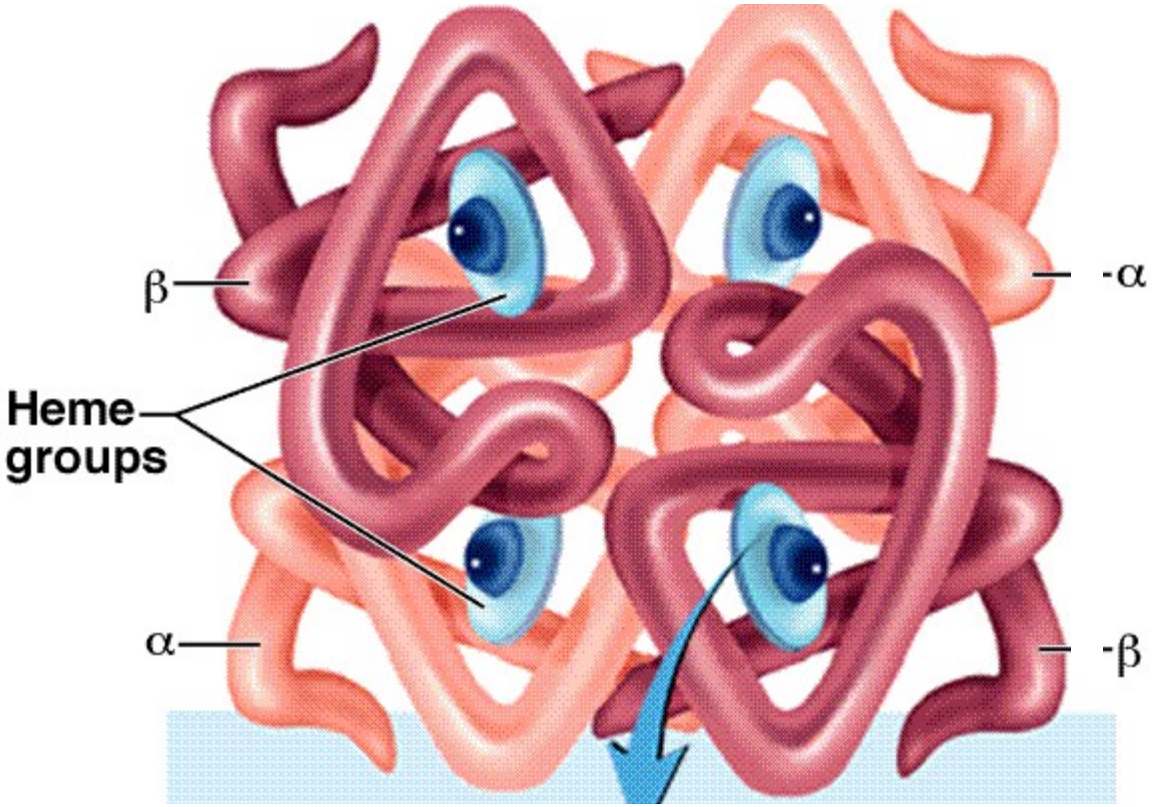
Structure:

-Primary cell content is *hemoglobin*, the protein that binds oxygen and carbon dioxide.

- no nucleus nor mitochondria

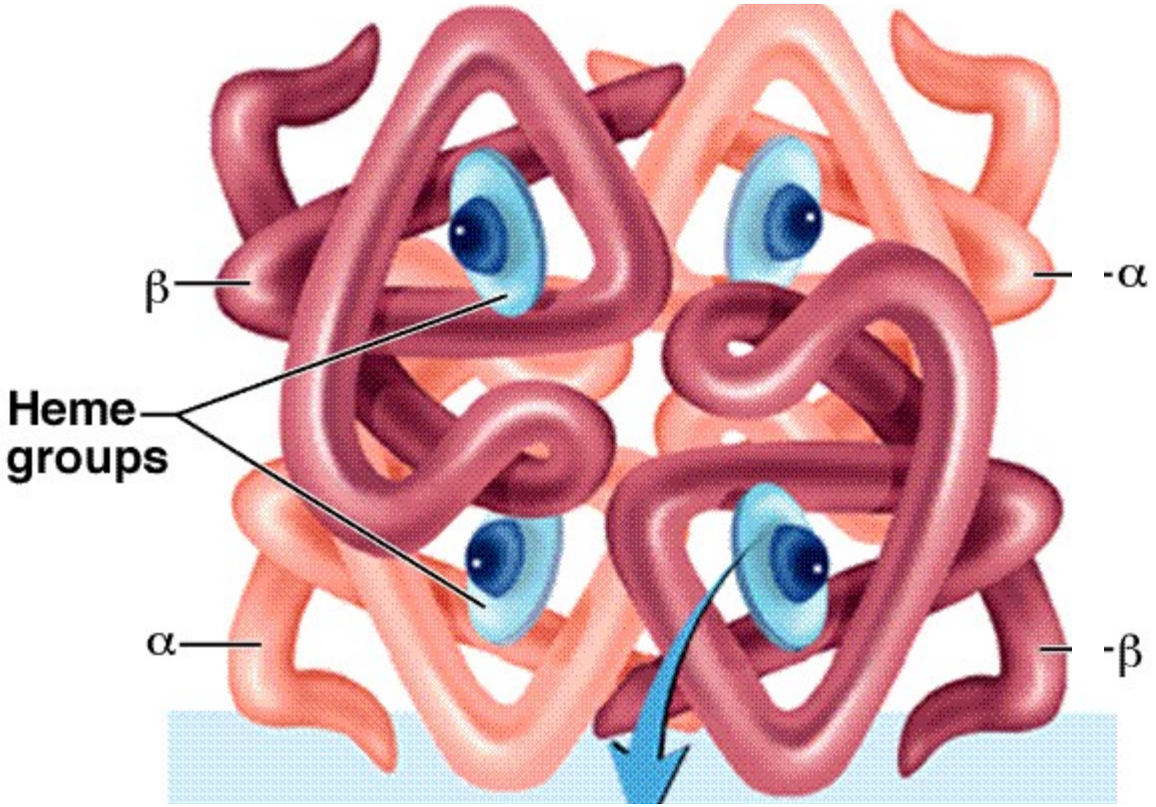
Hemoglobin consists of :

globin and *heme* pigment



Globin

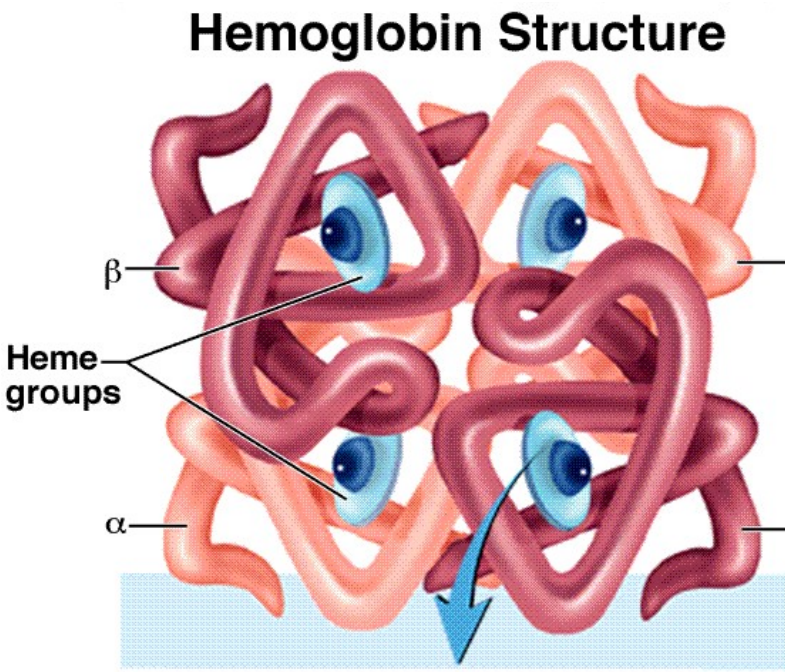
- Consists of two α and two β subunits
- Each subunit binds to a heme group

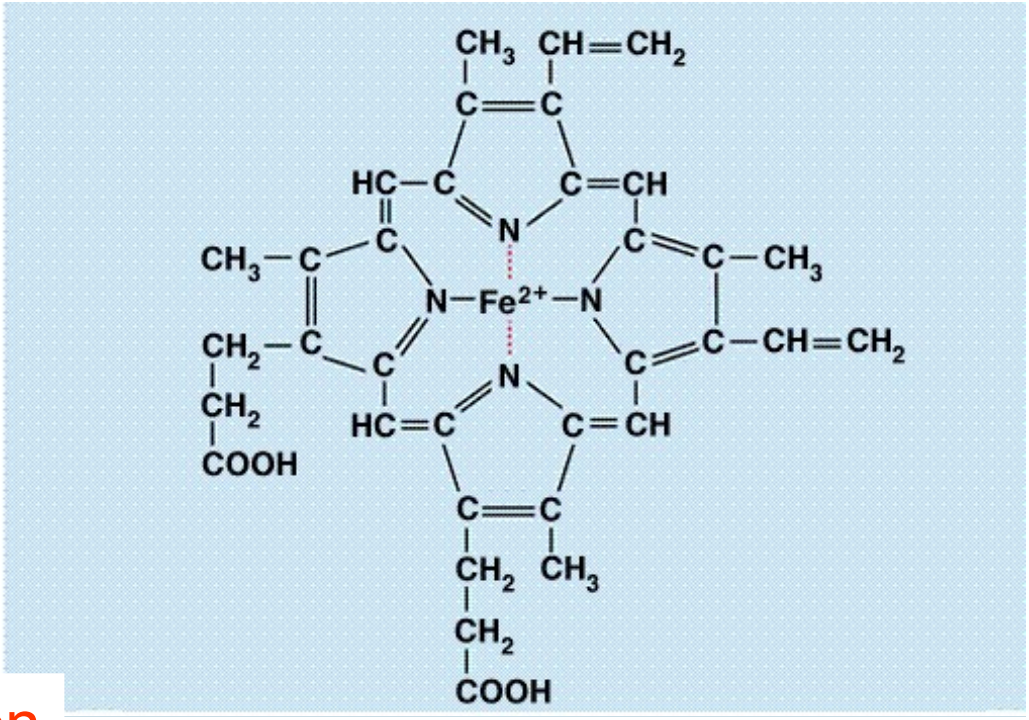


Heme Groups

Each heme group bears an atom of iron, which binds reversibly with one molecule of oxygen

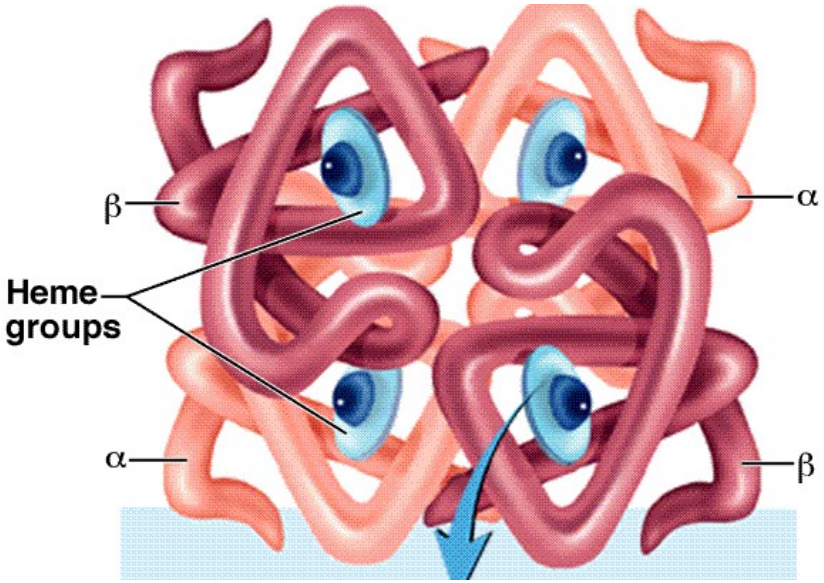
Heme Group Structure





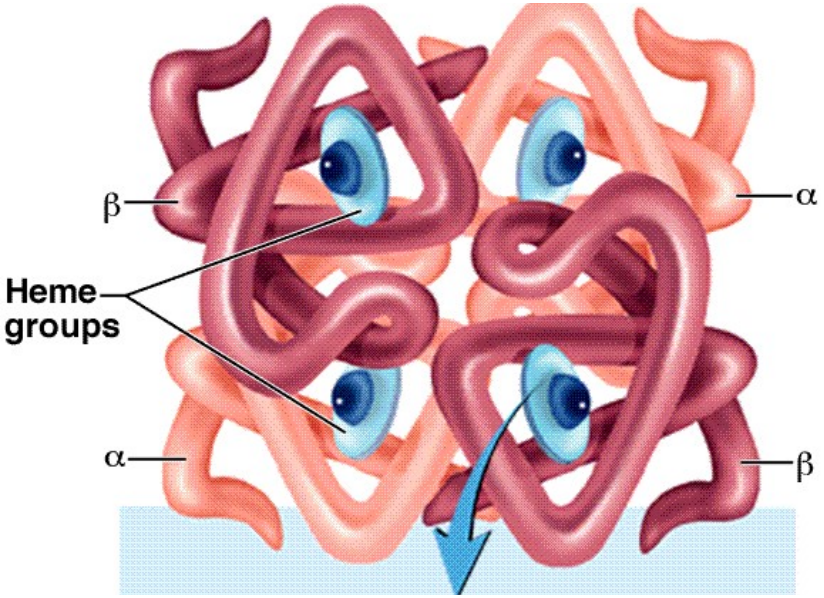
carry four molecules of oxygen

Carbon monoxide competes with oxygen for heme binding with a much higher affinity.



Problem: deoxygenate hemoglobin

Treatment: hyperbaric oxygen chamber



Oxyhemoglobin

-bound with oxygen

-red

Deoxyhemoglobin

-free of oxygen

-dark red.

Carbaminohemoglobin

20% of carbon dioxide in the blood binds to the **globin** part of hemoglobin, which is called ***carbamino- hemoglobin***.

Functions of Erythrocytes

1) Primary Function

Transport oxygen from the lung to tissue cells and carbon dioxide from tissue cells to the lung

2) Buffer blood pH

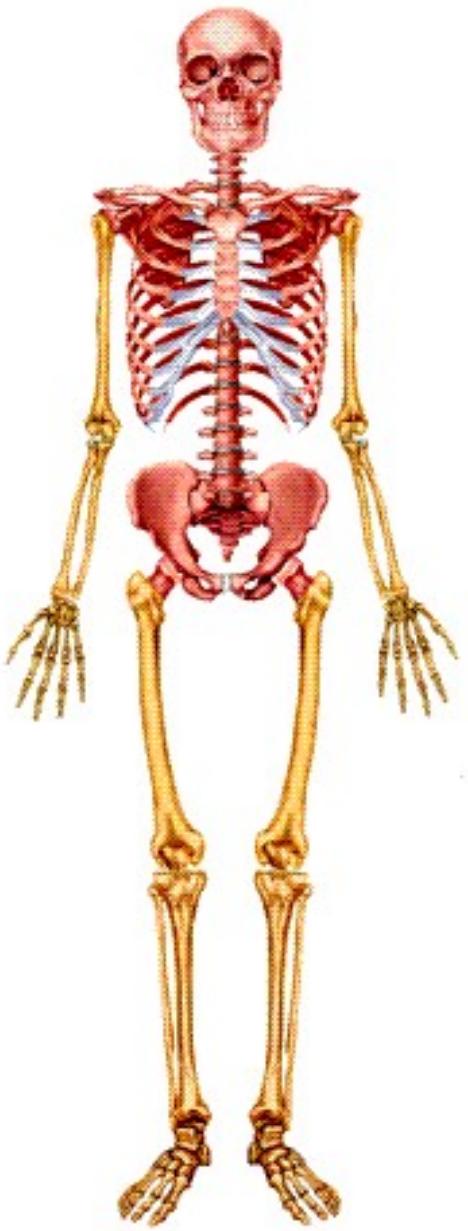
Production of Erythrocytes

Hematopoiesis
refers to whole blood cell production.

Erythropoiesis
refers specifically to red blood cell production.

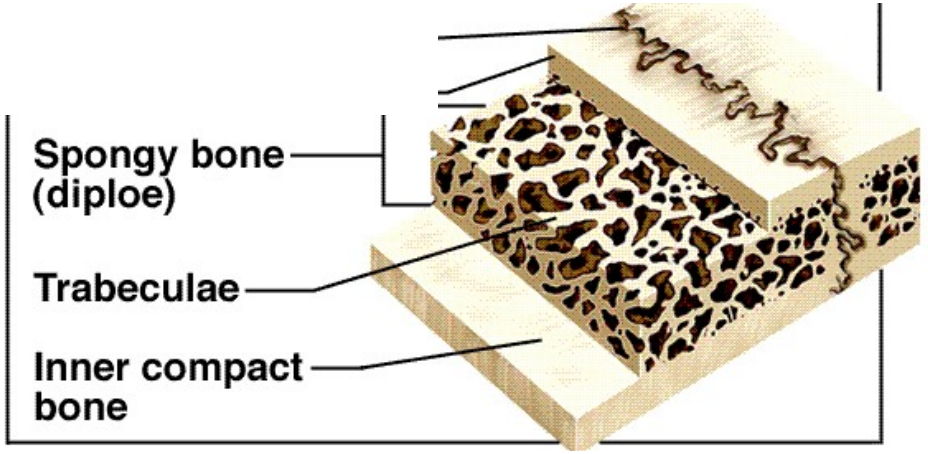
All blood cells, including red and white, are produced in ***red bone marrow***.

On average, one ounce, or 100 billion blood cells, are made each day.

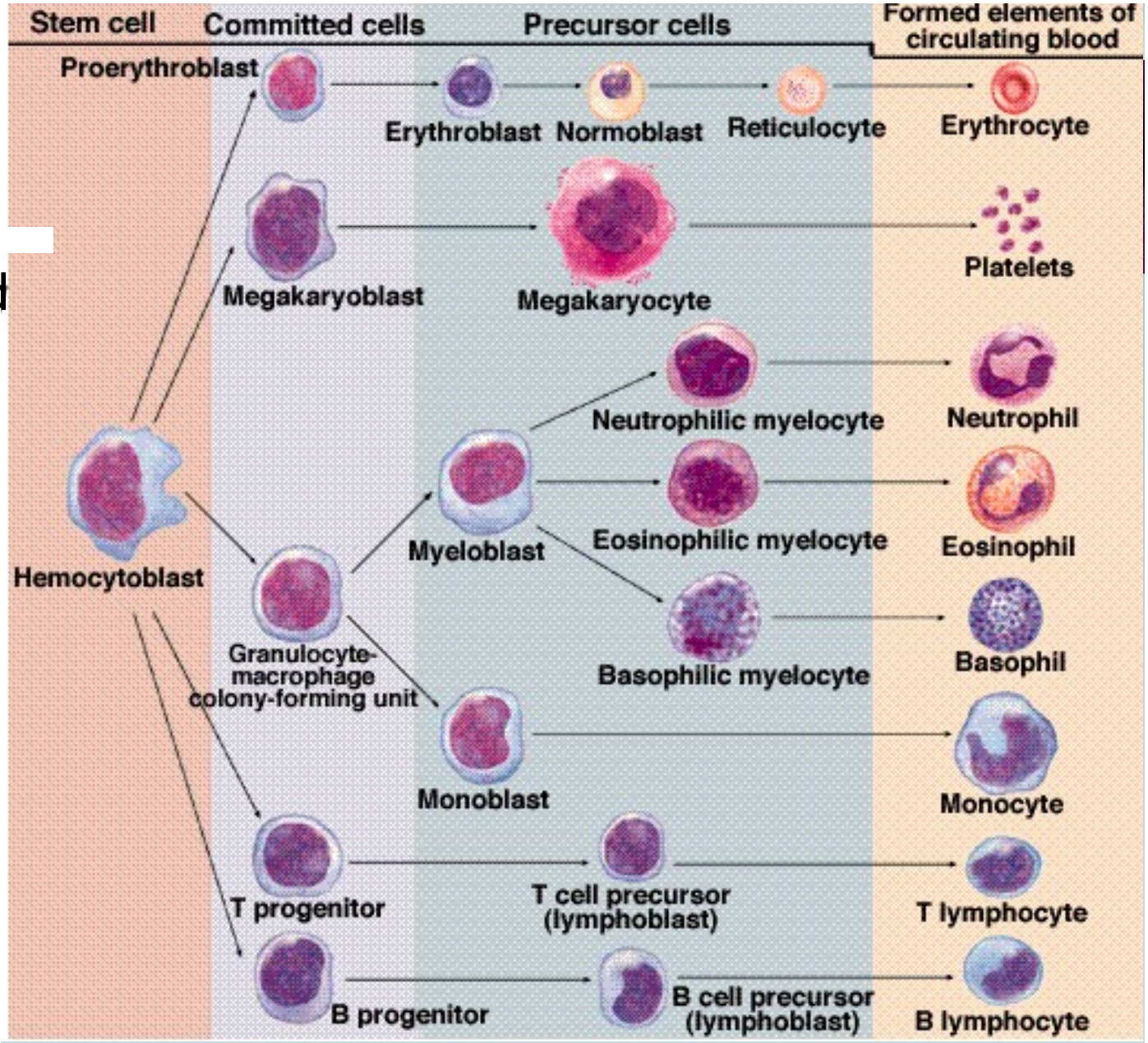


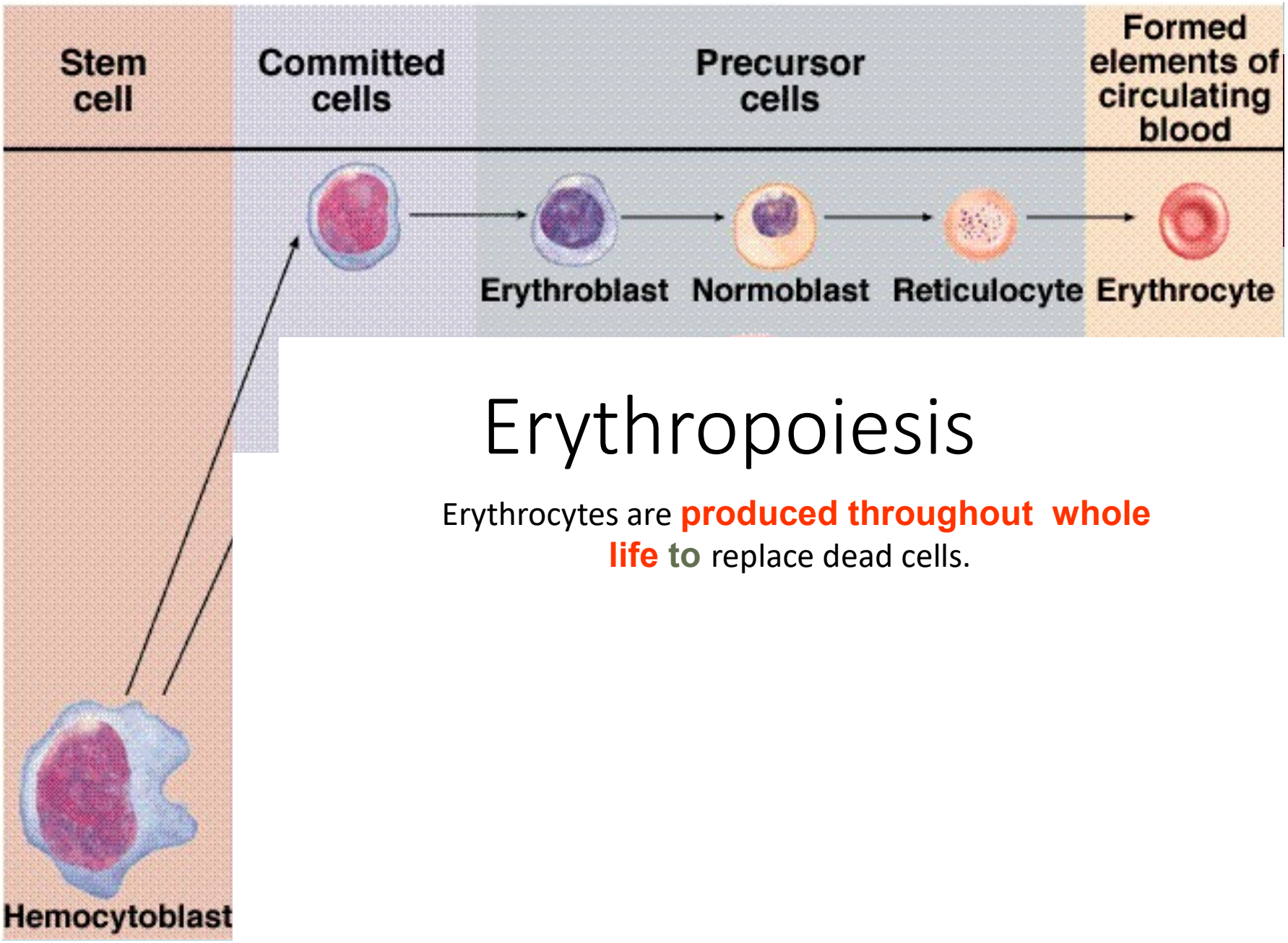
Hematopoiesis

-The **red bone marrow** is a network of reticular connective tissue that borders on wide blood capillaries called blood sinusoids. As hemocytoblasts mature, they migrate through the thin walls of the sinusoids to enter the blood.



All of blood cells including red and white arise from the same type of stem cell, the ***hematopoietic stem cell*** or ***hemocytoblast***





Erythropoiesis

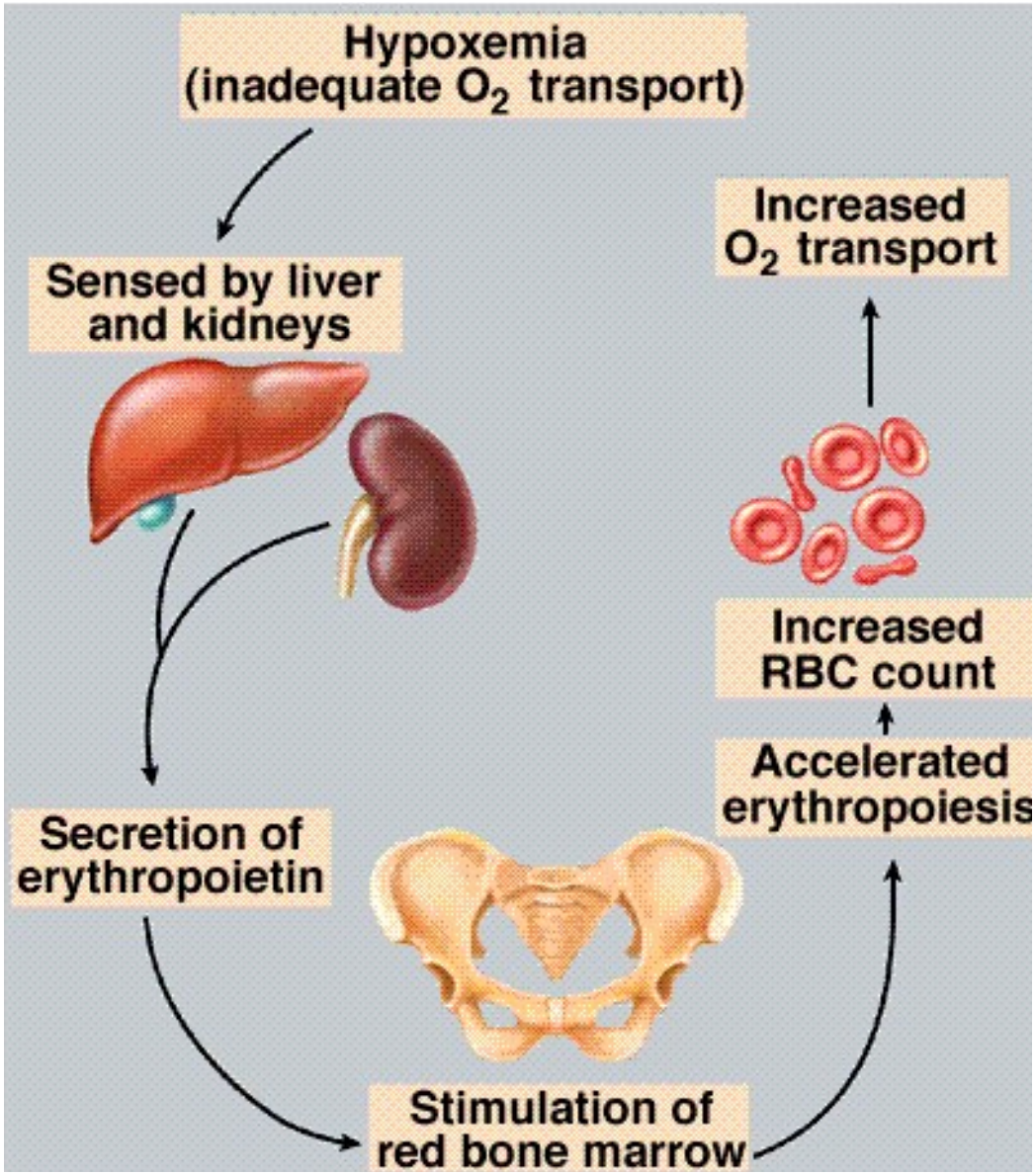
Erythrocytes are **produced throughout whole life to** replace dead cells.

Feedback Regulation of Erythropoiesis

- regulated by renal oxygen content.

- ***Erythropoietin,*** a glycoprotein hormone, is produced by renal cells in response to a decreased renal blood O2 content.

- Erythropoietin stimulates erythrocyte production in the red bone marrow.



A drop in renal blood oxygen level can result from:

1) reduced numbers of red blood cells due to hemorrhage or excess RBC destruction.

2) reduced availability of oxygen to the blood, as might occur at high altitudes or during pneumonia.

3) increased demands for oxygen (common in those who are engaged in aerobic exercise).

Ways to increase Red Blood Cell Count in Sports

Legal

raise RBC count by training athletes at high altitude

Illegal

use *erythropoietin, androgen,* or their analogs

Dietary Requirements for Erythropoiesis

Iron vitamin B12 folic acid

More important to women due to the loss of blood during menstruation

Erythrocyte Disorders

Anemia

is a condition in which the blood has an abnormally low oxygen-carrying capacity.

Common causes of anemia include:

1) an insufficient number of red blood cells

2) decreased hemoglobin content

3) abnormal hemoglobin

Two such examples are ***Thalassemias*** and ***Sickle-cell anemia***, which are caused by genetic defects.

Erythrocyte Disorders - 2

Polycythemia

is an abnormal excess of erythrocytes that increases the viscosity of the blood, causing it to sludge or flow sluggishly.

Common causes of polycythemia include:

1)Bone marrow cancer

2)A response to reduced availability of oxygen as at high altitudes

Human Blood Groups

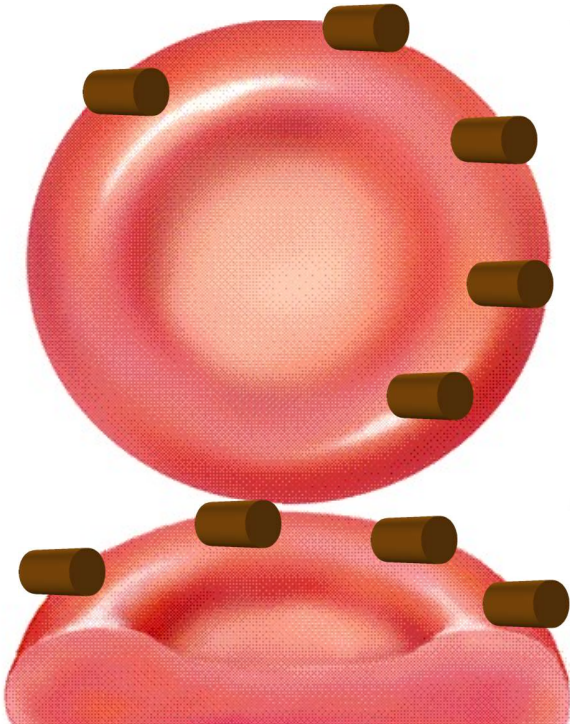
Human Blood Groups

-were learned from tragedies (death) caused by mismatch during transfusion in ancient time.

-ABO blood types were identified in 1900 by Karl Landstein (1930 Nobel laureate).

-Other blood types were identified later.

***Blood type* is determined by**



Agglutinogens

- are specific glycoproteins on red blood cell membranes.
- All RBCs in an individual carry the same specific type of agglutinogens.

ABO Blood Groups

Type A: RBCs carry agglutinogen A.

Type B: RBCs carry agglutinogen B.

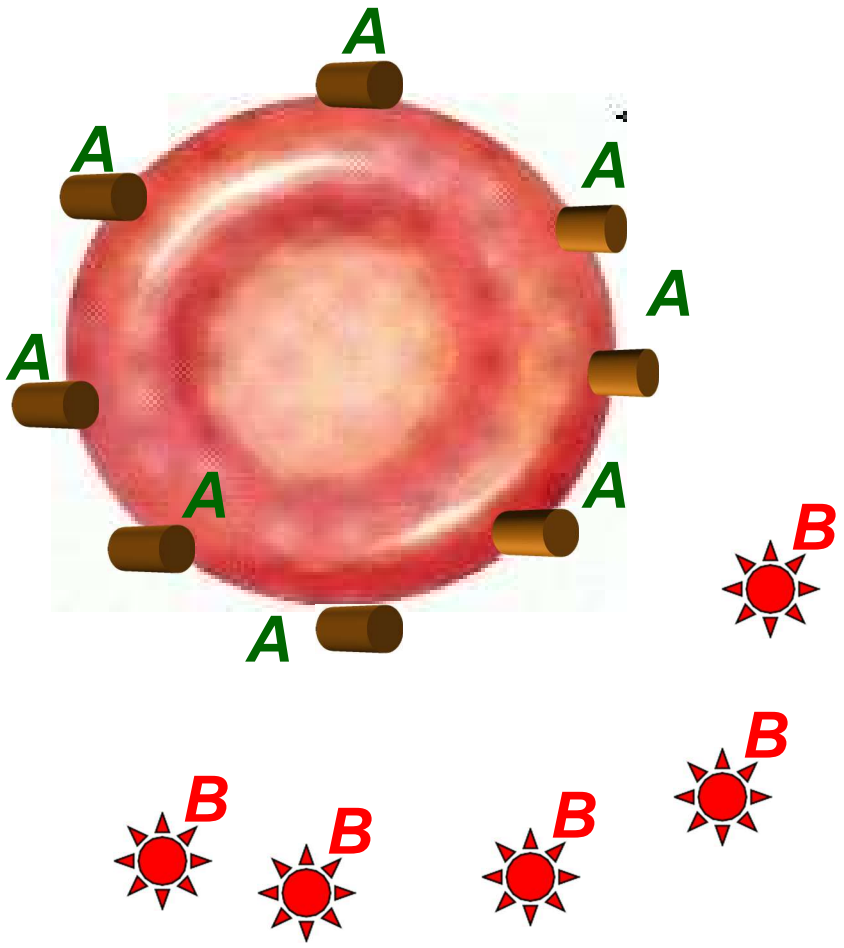
Type O: RBCs carry no A nor B agglutinogens.

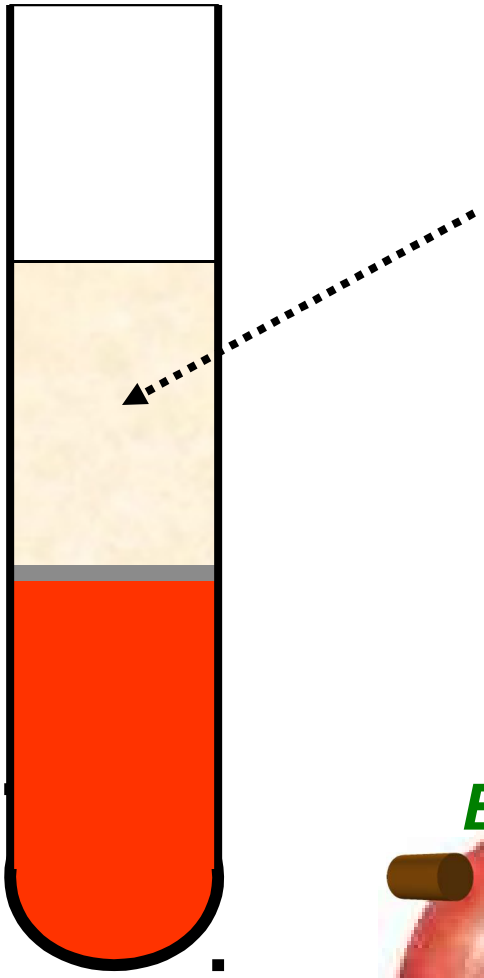
Type AB: RBCs carry both A and B agglutinogens.

Type A blood

- RBCs carry type ***A agglutinogens***.

- Plasma contain preformed antibodies, ***Agglutinin B***, against B agglutinogens.

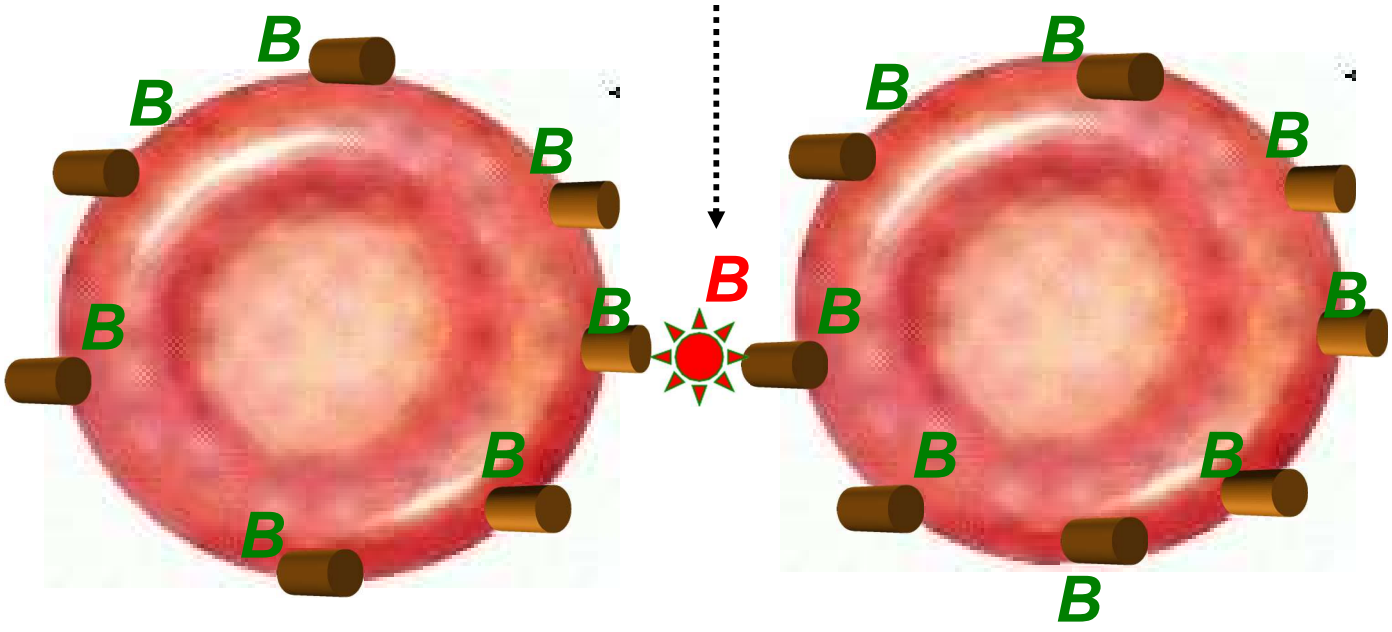




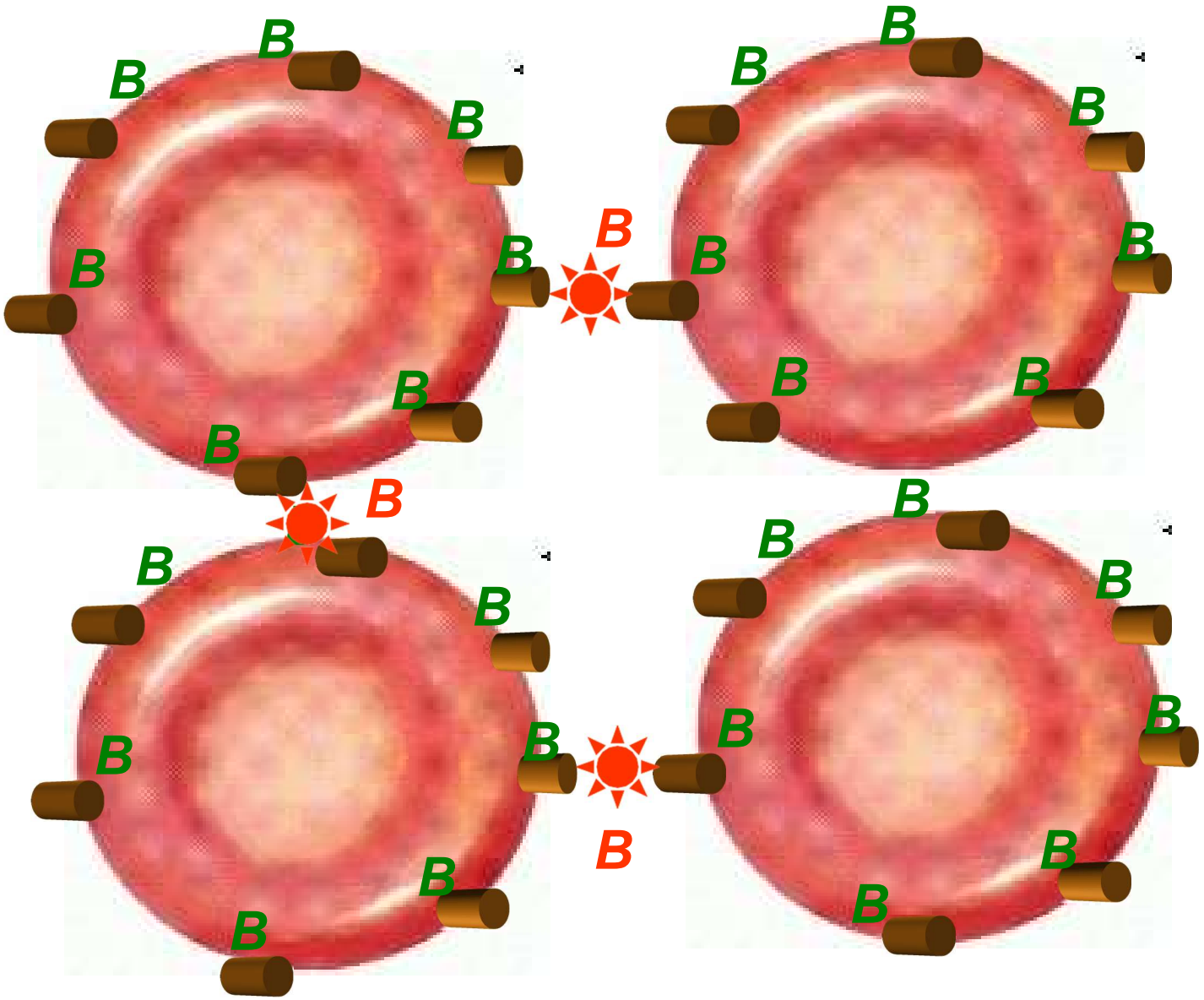
Agglutinins

- are preformed antibodies in plasma
- bind to agglutinogens that are not carried by host RBCs
- cause agglutination --- aggregation and lysis of incompatible RBCs.

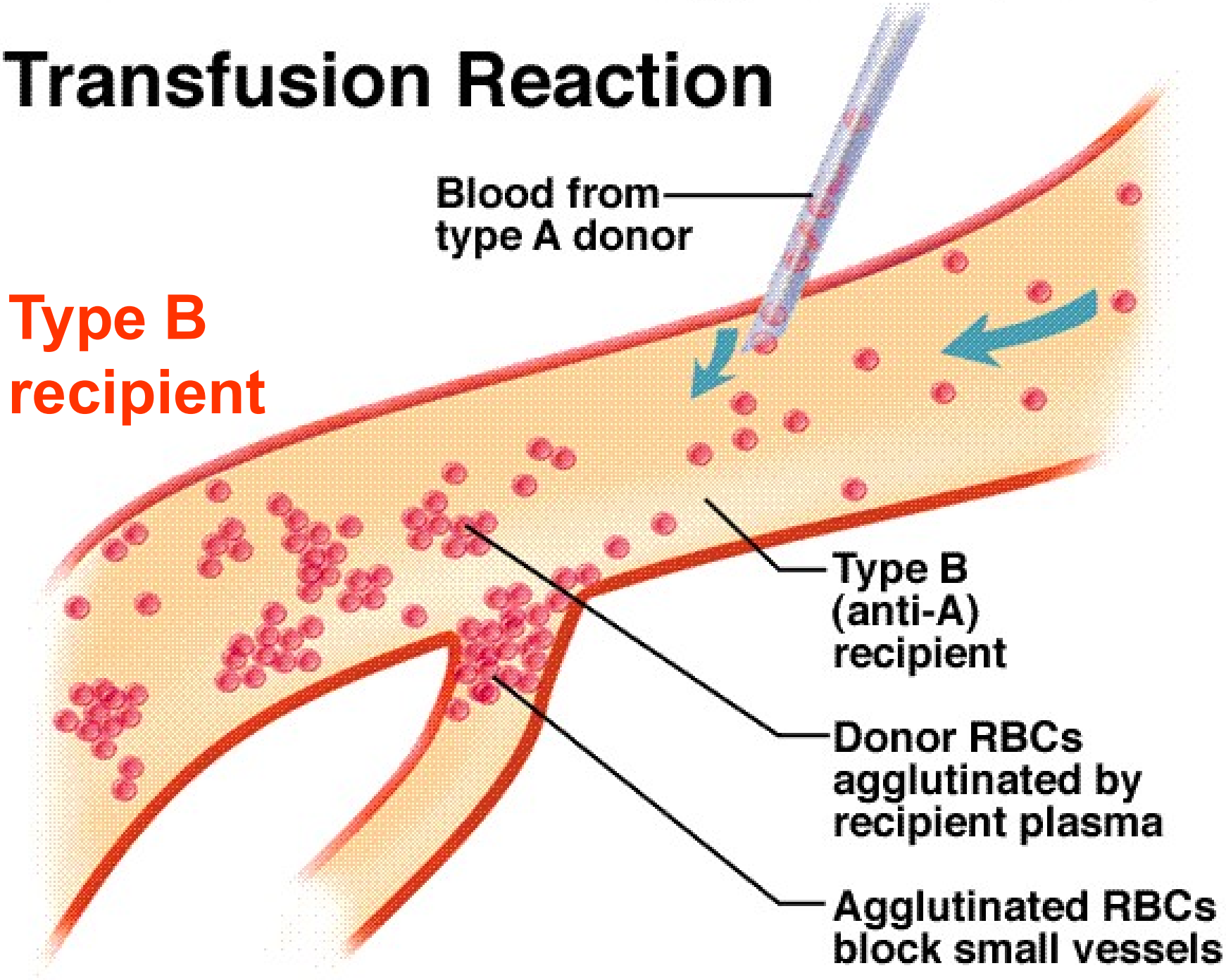
Agglutinin B



Mix *Type A plasma* with *Type B RBCs*



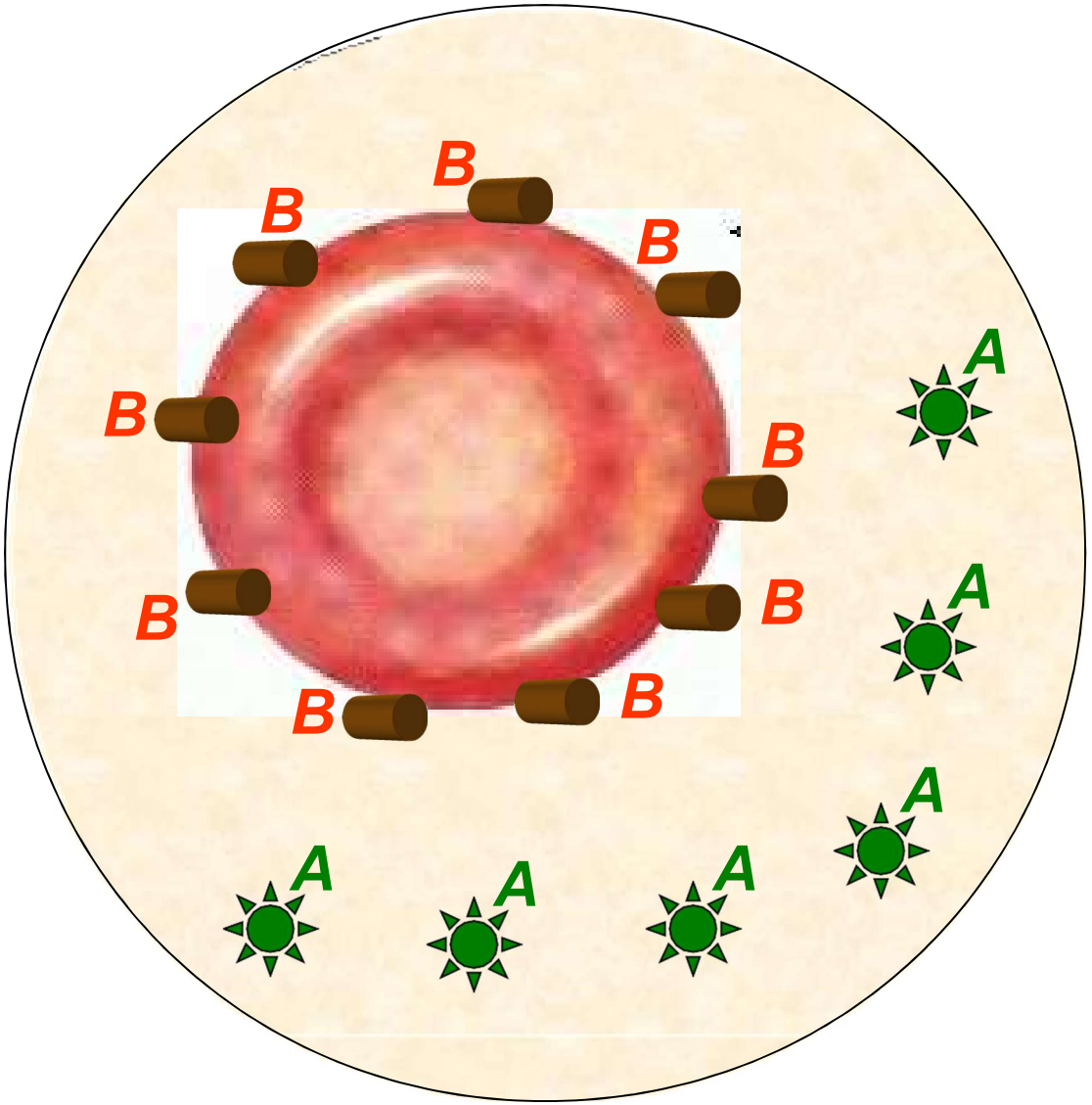
Transfusion Reaction



Type B blood

-RBCs carry type ***B agglutinogens***.

- Plasma contain agglutinin against ***A agglutinogens***.

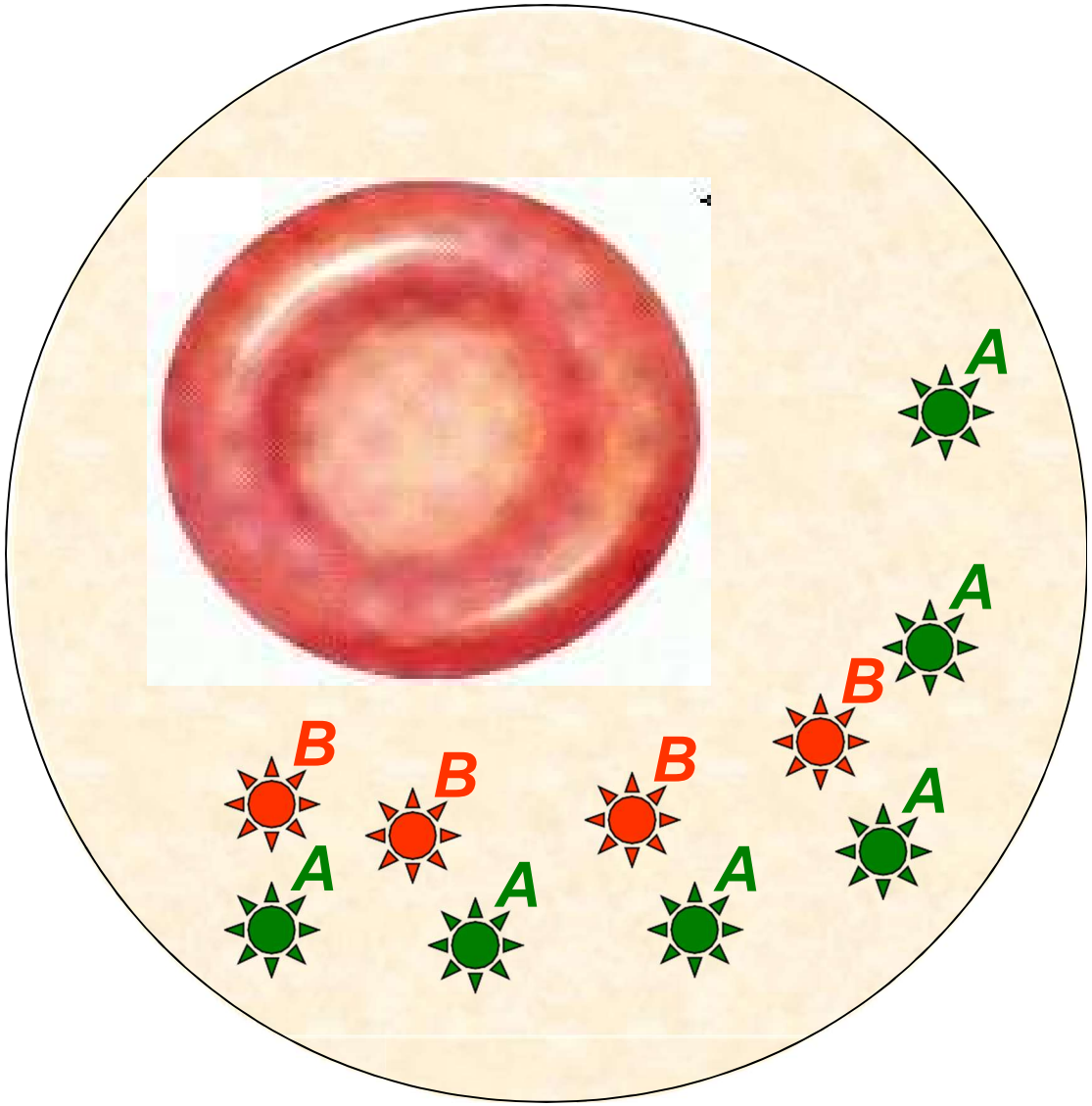


Type O blood

-RBCs carry neither type A nor type B agglutinogens.

-Plasma contain agglutinin against both ***A*** and ***B*** ***agglutinogens.***

- The person can accept only type O blood transfusion.



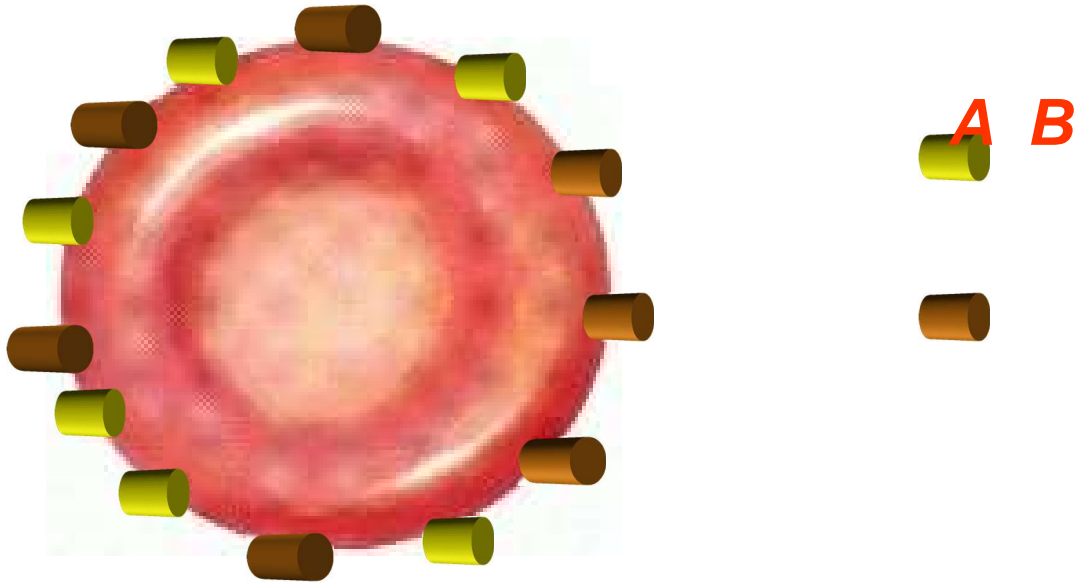
Type AB blood

Agglutinogen(s) ?

Agglutinin(s) ?

Type AB blood

Agglutinogen(s): **A and B**



Agglutinin(s) ? **No A nor B**

Summary of ABO Blood Groups

Blood Type	Agglutinogen (on RBC)	Agglutinin (in Plasma)
A	A	B
B	B	A
O		A & B
AB	A & B	

Blood Type Match

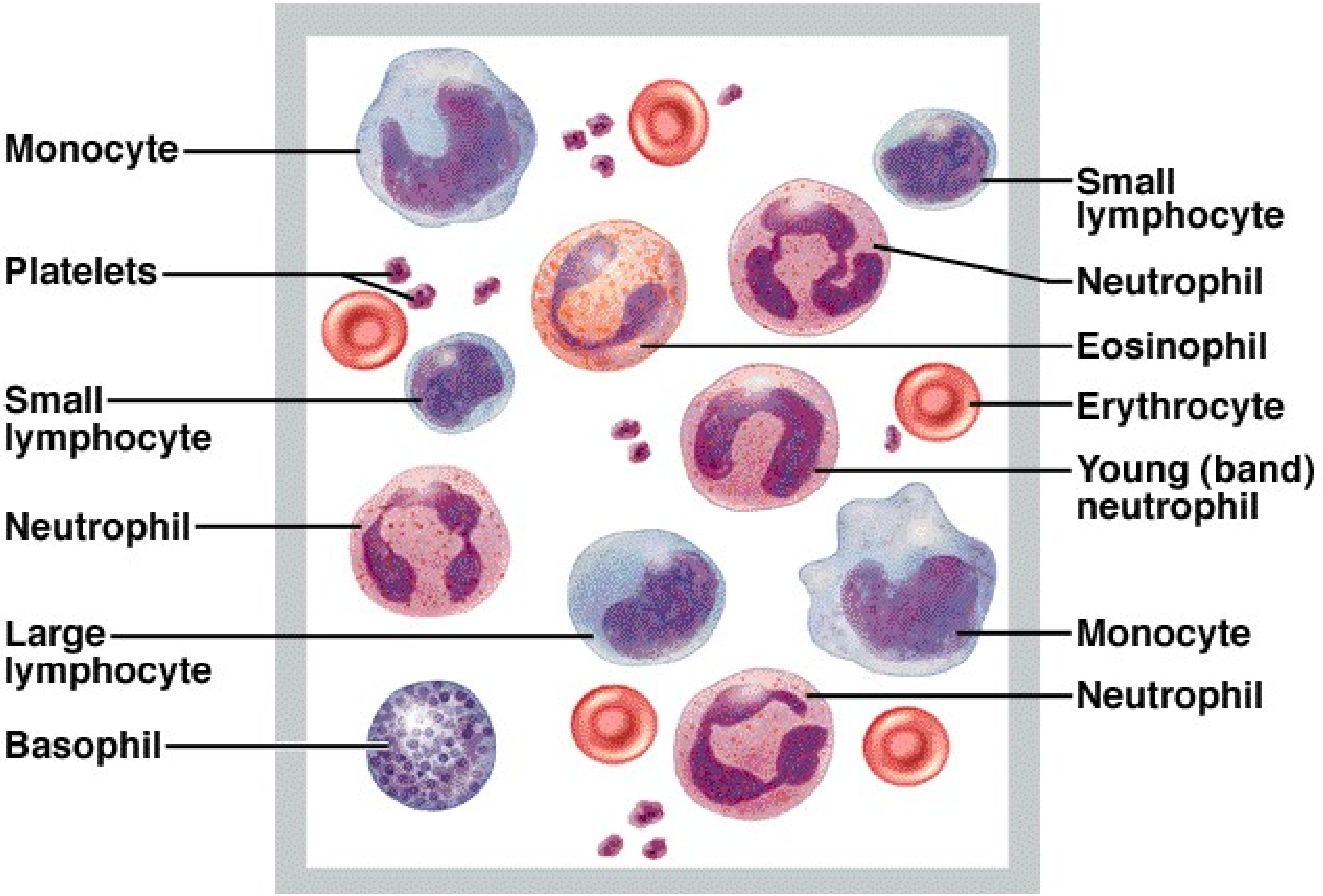
R \ D	A	B	O	AB
A	Yes	No	Yes?	No
B	No	Yes	Yes?	No
O	No	No	Yes	No
AB	Yes?	Yes?	Yes?	Yes

Leukocytes (White Cells)

Leukocytes are grouped into two major categories:

Granulocytes
-contain specialized membrane-bound cytoplasmic granules
-include ***neutrophils, eosinophils,*** and ***basophils.***

Agranulocytes
-lack obvious granules
-include ***lymphocytes*** and ***monocytes***


Monocyte
Platelets
Small lymphocyte
Neutrophil
Large lymphocyte
Basophil
Small lymphocyte
Neutrophil
Eosinophil
Erythrocyte
Young (band) neutrophil
Monocyte
Neutrophil

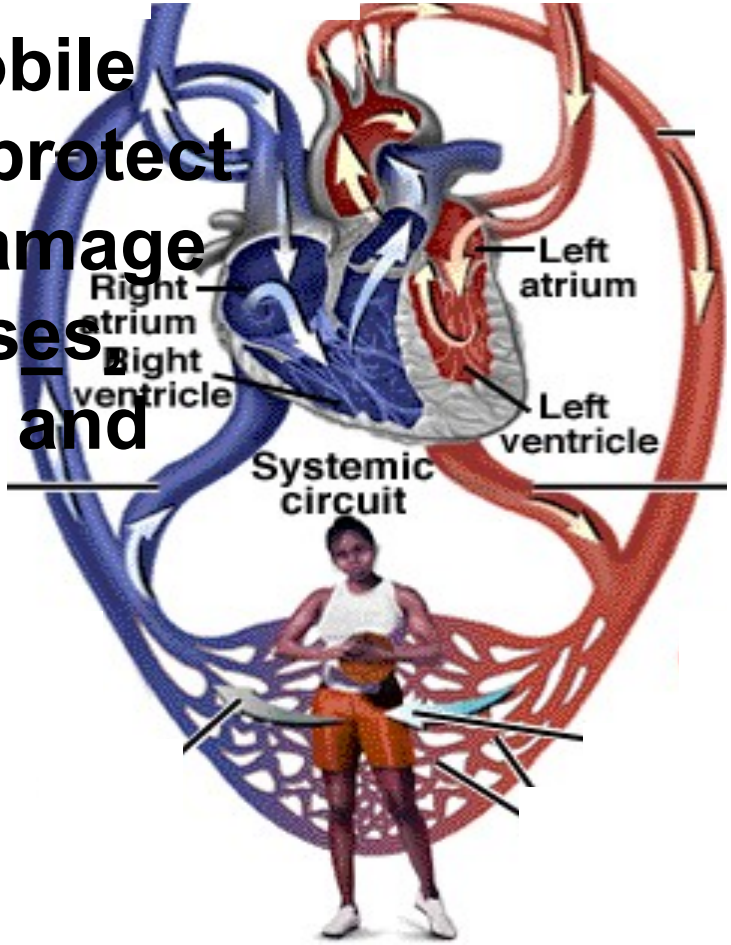
Leukocytes (WBCs) Count

4,000-11,000 / μL

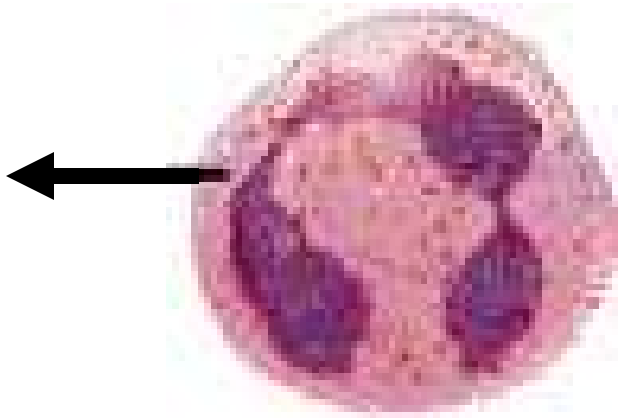
Function of Leukocytes:

defense against diseases

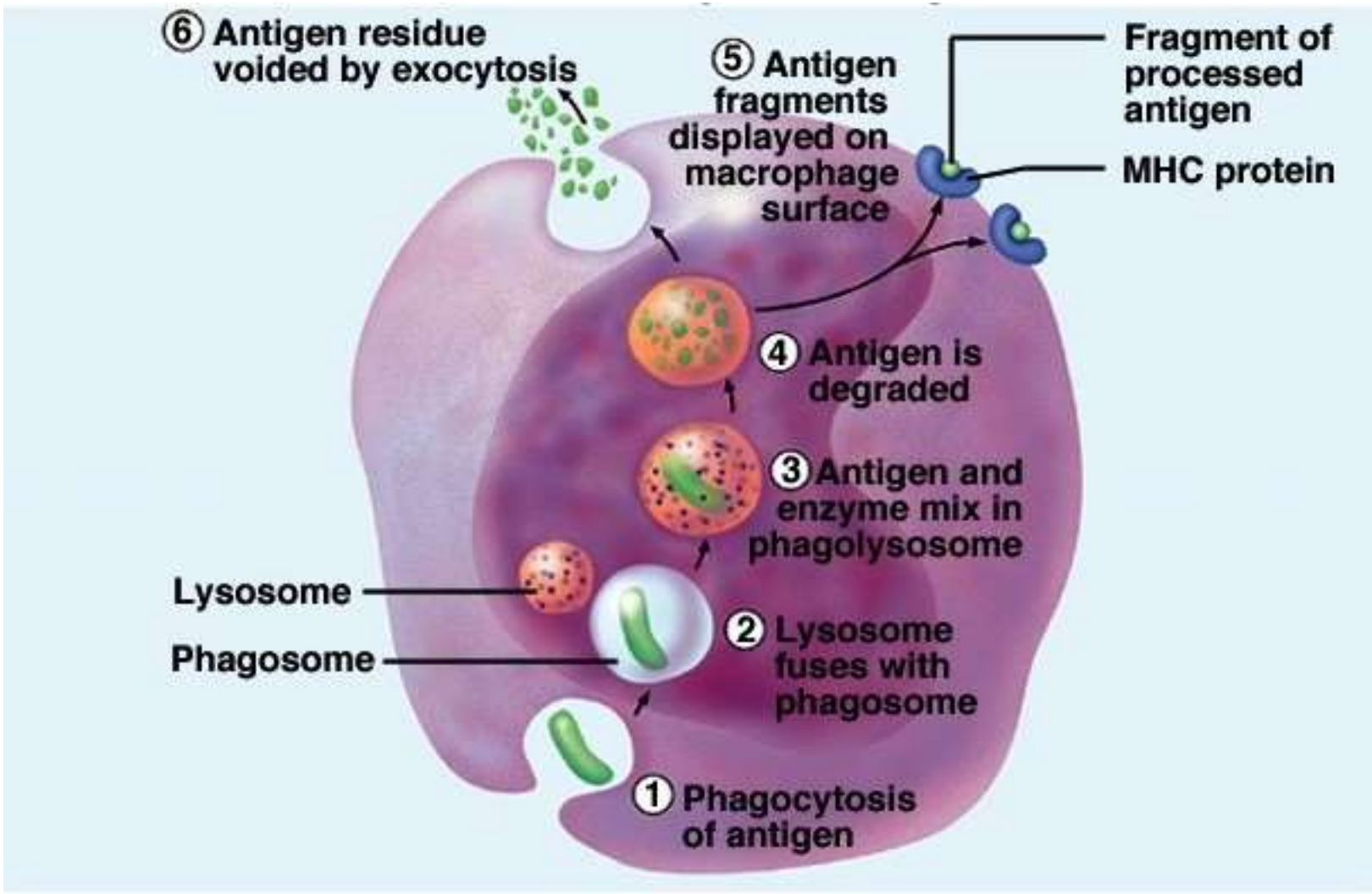
Leukocytes form a mobile army that helps protect the body from damage by bacteria, viruses, parasites, toxins and tumor cells.

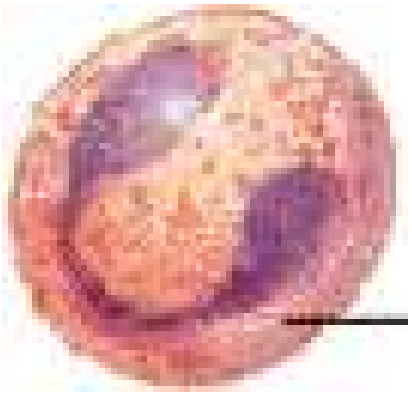


Neutrophils



- 40%-70% WBCs
- Nucleus multilobed
- Duration of development: 6-9 days
- Life Span: 6 hours to a few days
- Function: phagocytize bacteria

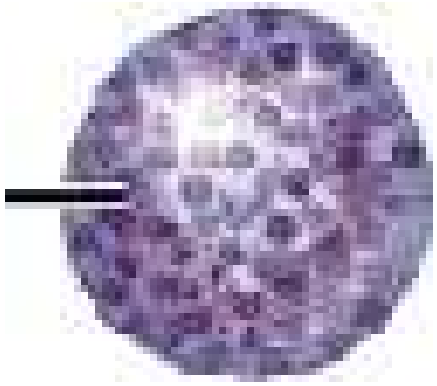

⑥ Antigen residue voided by exocytosis
⑤ Antigen fragments displayed on macrophage surface
Fragment of processed antigen
MHC protein
④ Antigen is degraded
③ Antigen and enzyme mix in phagolysosome
Lysosome
Phagosome
② Lysosome fuses with phagosome
① Phagocytosis of antigen



Eosinophils

- 1%-4% WBCs
- Nucleus bilobed
- Development:6-9 days
- Life Span: 8-12 days
- Function:
  1) Kill parasitic worms
  2) destroy antigen-antibody complexes
  3) inactivate some inflammatory chemical of allergy

Basophils

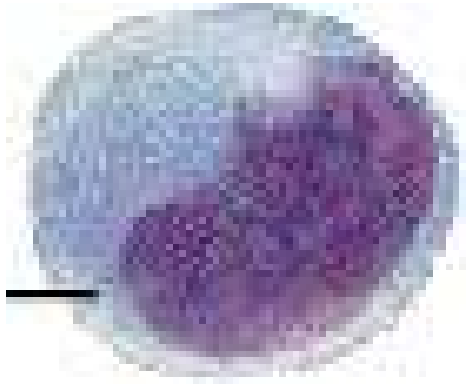


- 0.5% WBCs
- Nucleus lobed
- Development: 3-7 days
- Life Span: a few hours to a few days
- Function:

  1)Release histamine and other mediators of inflammation

  2)contain heparin, an anticoagulant

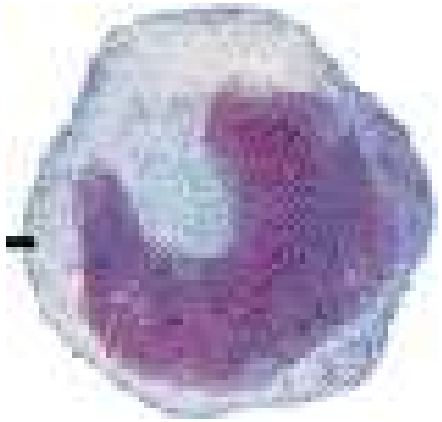
Lymphocytes



- T cells and B cells
- 20%-45% WBCs
- Nucleus spherical or indented
- Development: days to weeks
- Life Span: hours to years
- Function

Mount immune response by direct cell attack (T cells) or via antibodies (B cells)

Monocytes –



- 4%-8% WBCs
- Nucleus U-shaped
- Development: 2-3 days
- Life Span: months
- Function:

  Phagocytosis

  develop into ***macrophages*** in tissues

HEMOSTASIS

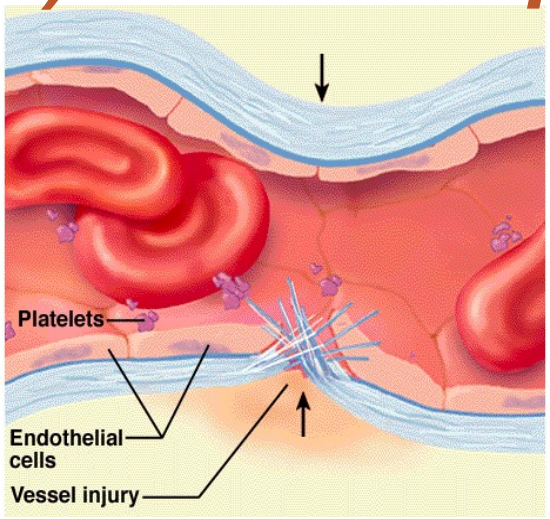
Hemostasis refers to the stoppage of bleeding.

Hemostatsis = Homeostasis

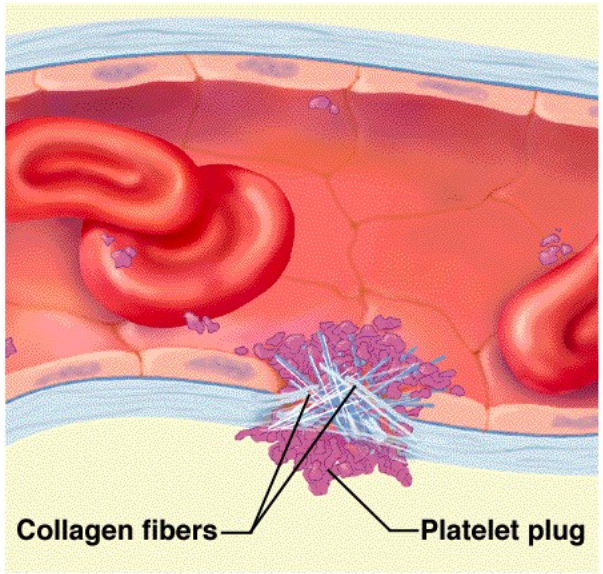
Maintaining balance

Three phases occur in rapid sequence.

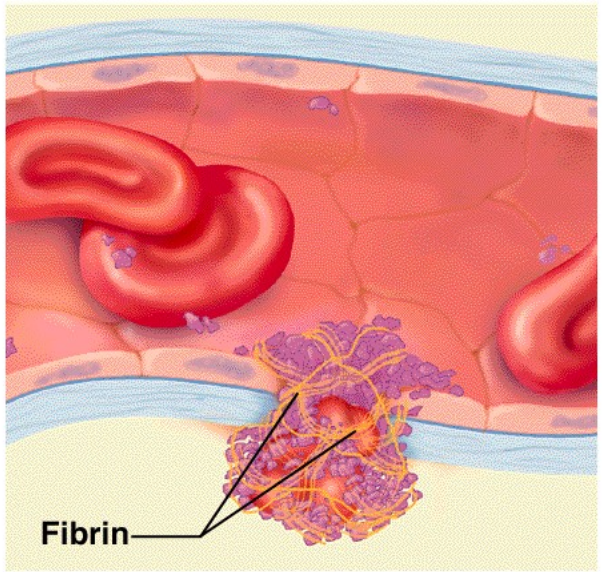
1) vascular spa



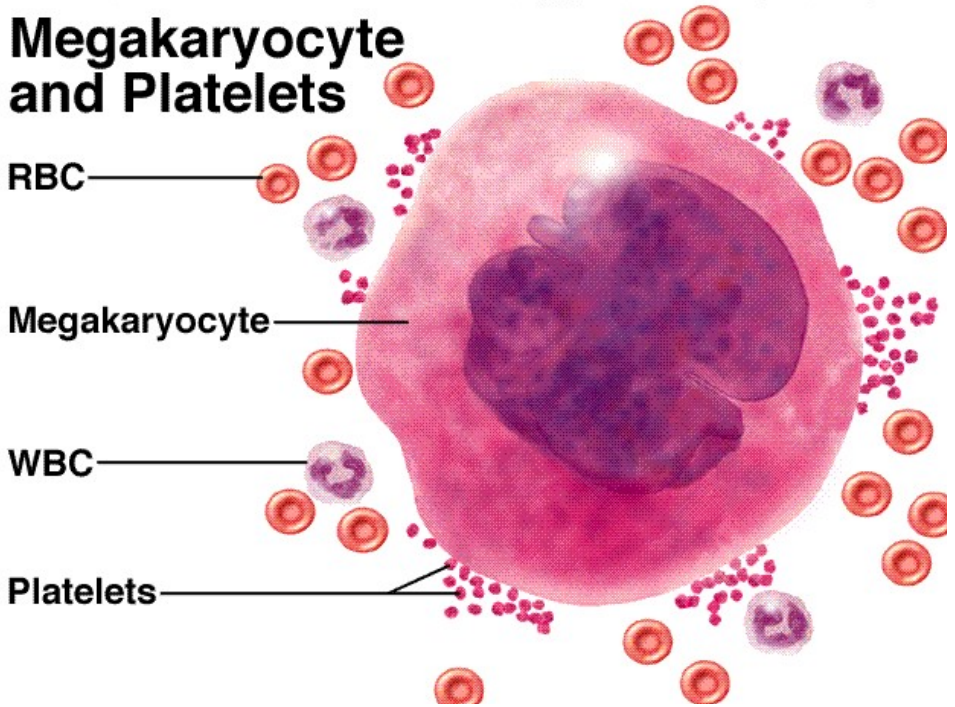
2) platelet plug formation



3) blood clotting / coagulation



Platelets



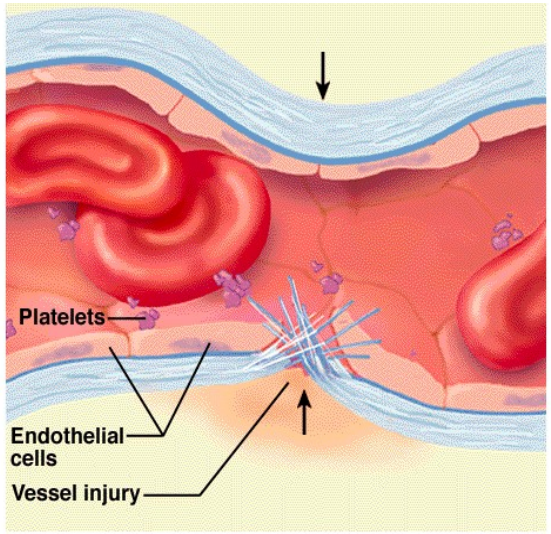
Platelets are not cells but cytoplasmic fragments of extraordinarily large (up to 60 μm in diameter) cells called ***megakaryocytes***.

Normal Platelet Count: 130,000 – 400,000/μl

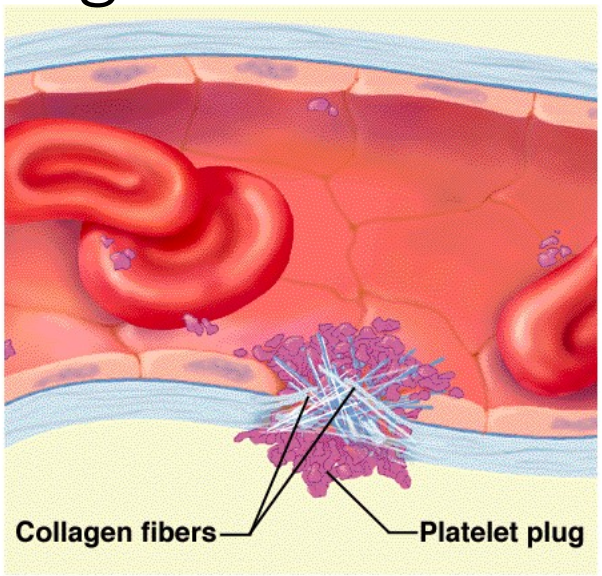
Function of Platelets

1) Secrete vasoconstrictors that cause vascular spasms in broken vessels

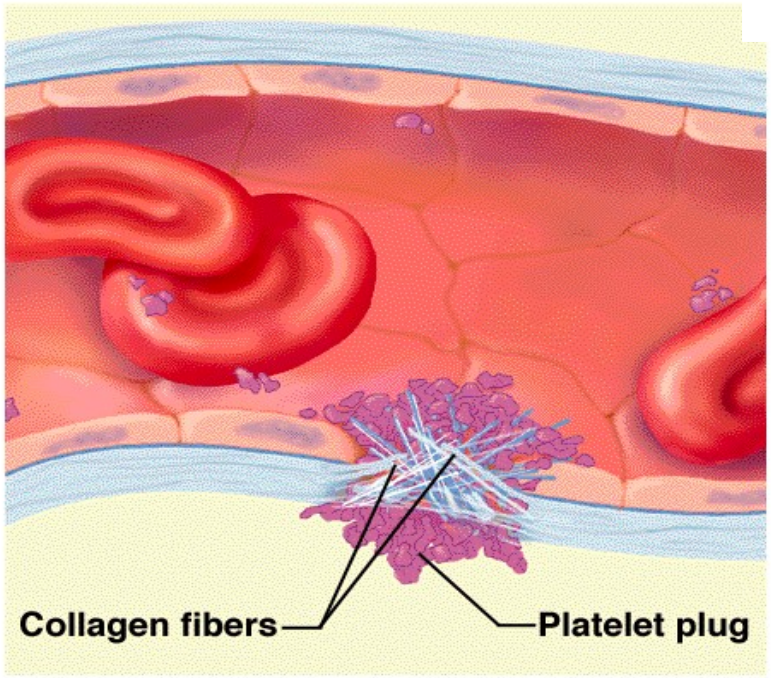
vascular spasms



2) Form temporary platelet plugs to stop bleeding

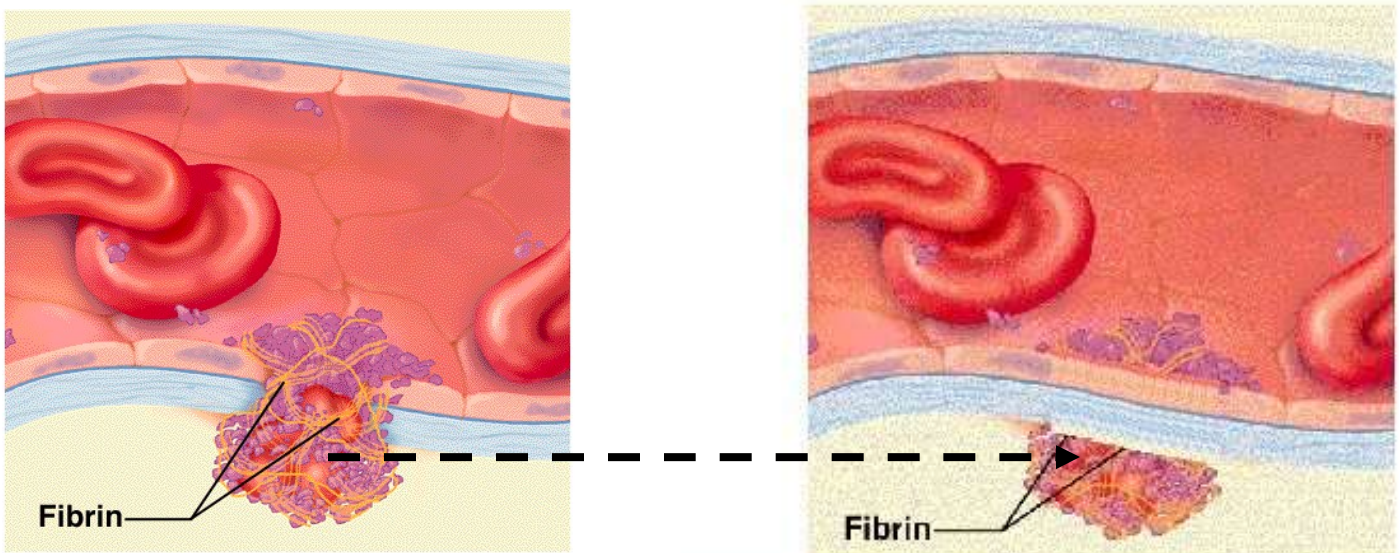


3) Secrete chemicals that attract neutrophils and **monocytes to sites of inflammation**



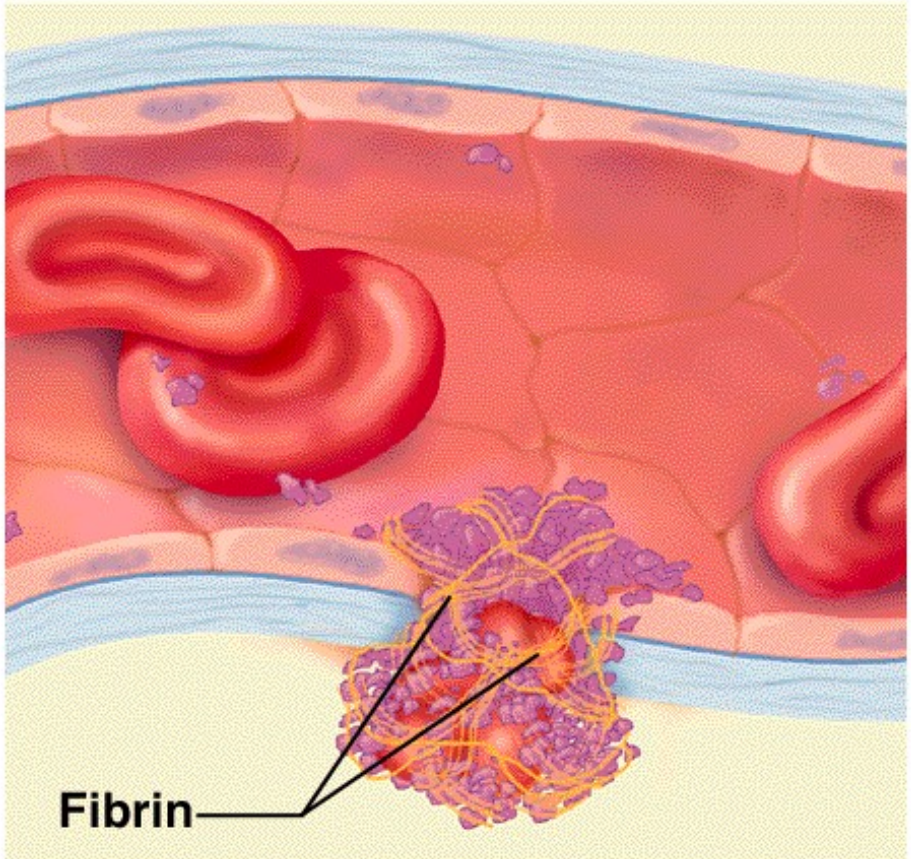
4) Secrete growth factors that stimulate mitosis in fibroblasts and smooth muscle and help maintain the linings of blood vessels

5) Dissolve blood clots that have outlast their usefulness



Coagulation (Clotting)

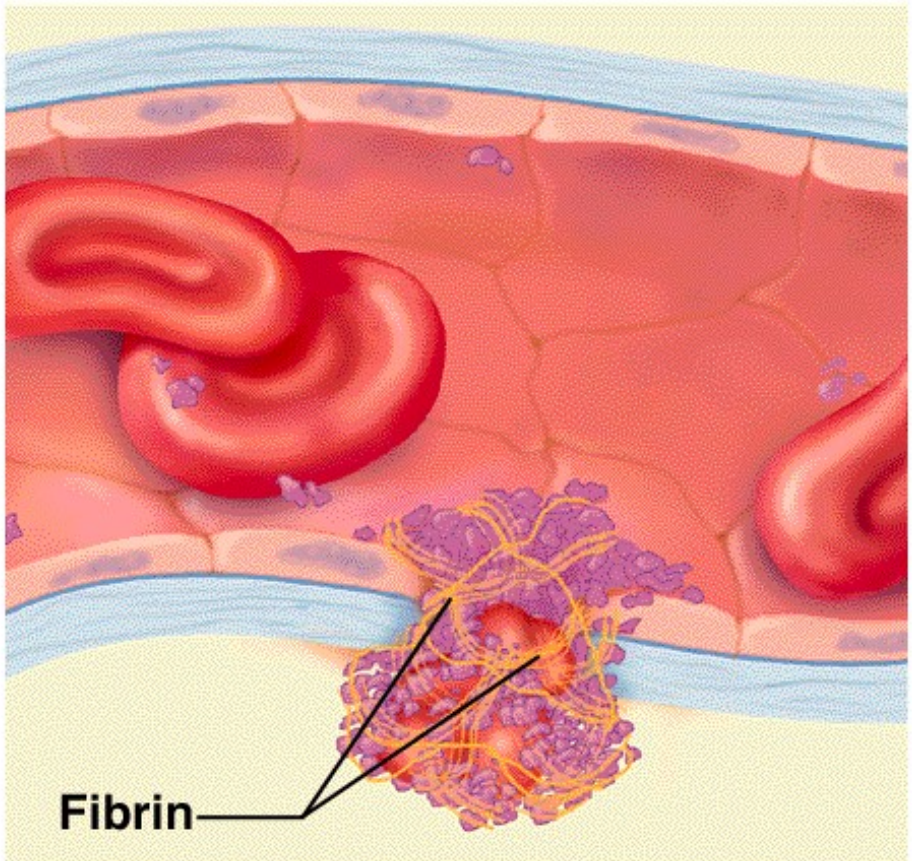
- Many clotting factors in plasma are involved in clotting.
- These factors are inactive in the blood.
- They are activated when:
  1) blood vessel is broken, or
  2) blood flow slows down.



- The sequential activation (reaction cascade) of the clotting factors finally leads to the formation of ***fibrin meshwork***.

-

Bloo d cells are trapped in fibrin meshwork to form a hard clot.



Coagulation Disorders

Thrombosis is the abnormal clotting of blood in an unbroken vessel.

Thrombus is a clot that attaches to the wall of blood vessel.

Embolus is a clot that comes off the wall of blood vessel and travel in the blood stream.

Embolism is the blockage of blood flow by an embolus that lodges in a small blood vessel.

Infarction refers to cell death that results from embolism. Infarction is responsible for most strokes and heart attacks.

Bleeding Disorders

Thrombocytopenia

-the number of circulating platelets is deficient (<50,000/μl)

-causes spontaneous bleeding from small blood vessels all over the body

Deficiency of clotting factors due to ***impaired liver function***

Hemophilias

Hereditary bleeding disorders due to deficiency of clotting factors