

Lect. No.6

Blood Physiology

Prof. Dr. Nader Abo-Tubikh

Mazaya University College

Department of Medical Lab Technology

Blood

Definition:

Blood is essentially a two-phase specialized fluid consisting of formed **cellular elements** suspended in a liquid medium, **plasma**.

Functions of Blood

1. Transport of dissolved substances
2. Regulation of pH and ions
3. Restriction of fluid losses at injury sites
4. Defense against toxins and pathogens
5. Stabilization of body temperature

General Characteristics of Blood

- 38°C (100.4°F) is normal temperature
- High viscosity
- Slightly alkaline pH (7.35–7.45)

Blood Volume

- Blood volume (liters) = 7% of body weight (kilograms):
 - adult male: 5 to 6 liters
 - adult female: 4 to 5 liters
- Plasma makes up 50–60% of blood volume.
- More than 90% of plasma is water

Blood Components

The formed elements

- 1. Red cells (erythrocytes)*
- 2. White cells (leukocytes)*
- 3. Platelets*

If a blood sample is centrifuged in a tube, the cellular elements will settle to the bottom. The **red cells** will lie on the bottom of the tube, and will occupy **40-45%** of the total volume of blood. The **white cells**, being less dense, will settle on top of the red cells, and will occupy about **5%** of blood volume.

The volume of red blood cells present in blood is referred to as the **hematocrit**.

The number of red blood cells per unit volume of blood is called **blood count** (normally 5-6 million cells/microliter).

Blood Components

Plasma

- The remaining **50-55%** of blood volume is contributed by the **plasma**.
- Is similar to, and exchanges fluids with, interstitial fluid
- Is matrix of formed elements
- Blood plasma contains a variety of plasma proteins (e.g., albumin, globulin), electrolytes, hormones, enzymes, and blood gases.

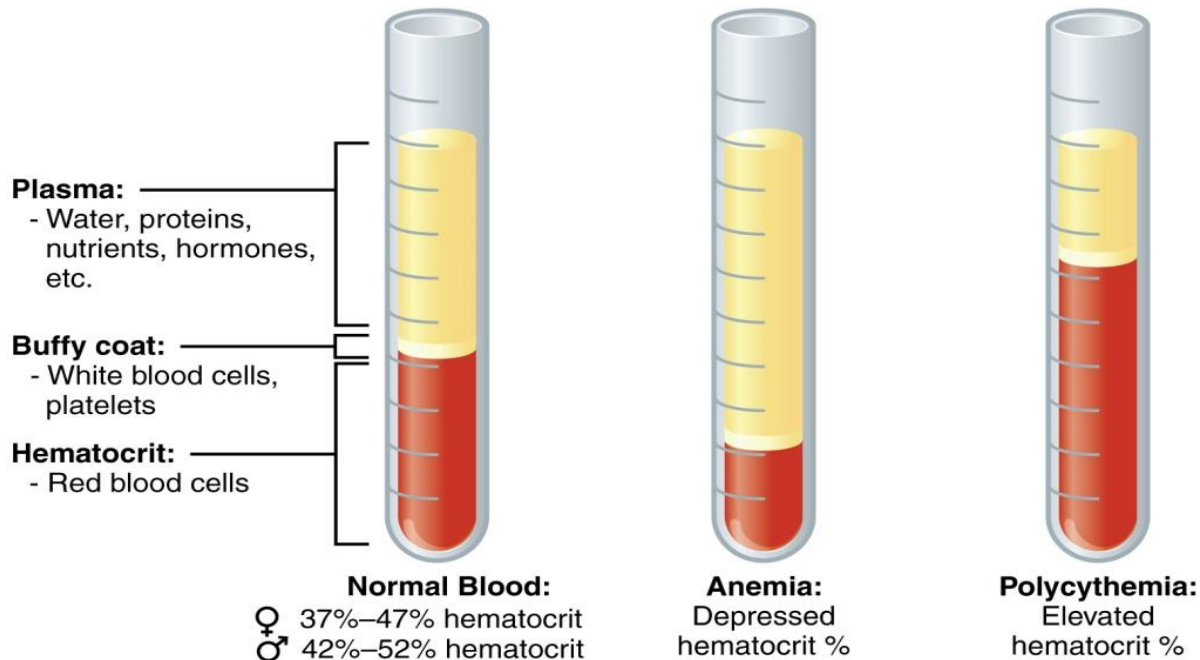
Fractionation

Process of separating whole blood for **clinical analysis**: into plasma and formed elements

Too few red blood cells = anemia

Hematocrit or hemoglobin levels are below normal is caused by several conditions

Too many red blood cells = polycythemia



(a)

Functions of Blood cells

1. **Red blood cells (RBCs) or erythrocytes:**
 - transport oxygen
2. **White blood cells (WBCs) or leukocytes:**
 - part of the immune system
3. **Platelets:**
 - cell fragments involved in clotting

Hemopoiesis

- Process of producing formed elements
- By myeloid and lymphoid stem cells

Functions of Plasma Proteins

- **Albumins** (60%)
- Transport substances:
 - fatty acids
 - thyroid hormones
 - steroid hormones
- **Globulins** (35%)
 1. **Antibodies**, also called **immunoglobulins**
 2. **Transport globulins** (small molecules):
 - hormone-binding proteins
 - metalloproteins
 - apolipoproteins (**lipoproteins**)
 - steroid-binding proteins
- **Fibrinogen** (4%)
- Molecules form clots
- Produce long, insoluble strands of **fibrin**

Functions of Plasma Proteins

- **Serum**

Liquid part of a blood sample in which dissolved fibrinogen has converted to solid fibrin.

- **Other Plasma Proteins** (1% of plasma):

Changing quantities of specialized plasma proteins such as enzymes, hormones, and prohormones.

- **Origin of Plasma Proteins**

- 90% made in liver.
- Antibodies made by plasma cells.
- Peptide hormones made by endocrine organs

Red Blood Cells (RBC)

RBC's make up 99.9% of blood's formed elements.

Lifespan of RBC's: Live for about 120 days.

- **RBC count:**

The number of RBCs in 1 microliter whole blood:

- Male: 4.5–6.3 million
- Female: 4.–5.5 million

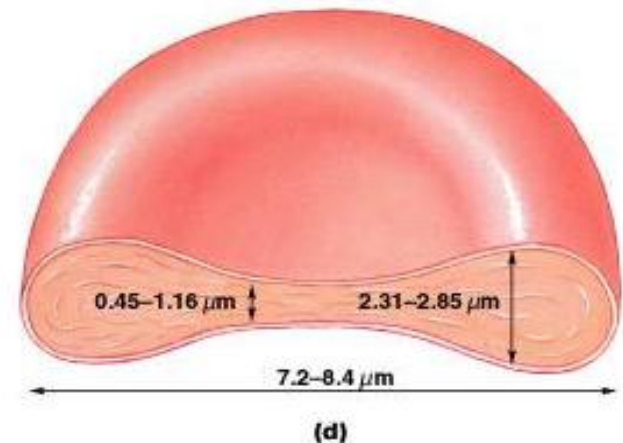
- **Hematocrit (packed cell volume, PCV):**

Percentage of RBCs in centrifuged whole blood

- male: 4–52
- female: 3–47

RBC Structure

- Small and highly specialized disc
- Thin in middle and thicker at edge
- Lack nuclei, mitochondria, and riboso



Importance of RBC Shape and Size

1. High surface-to-volume ratio:
 - quickly absorbs and releases oxygen
2. Discs form stacks:
 - smoothes flow through narrow blood vessels
3. Discs bend and flex entering small capillaries:
 - 7.8 μm RBC passes through 4 μm capillary

Hemoglobin (Hb)

- Protein molecule, transports respiratory gases
- Normal hemoglobin (adult male): 14–18 g/dl whole blood
- **Fetal Hemoglobin**: Strong form of hemoglobin found in embryos
Takes oxygen from mother's hemoglobin

Complex quaternary structure

Four globular protein subunits each with 1 molecule of **heme** .

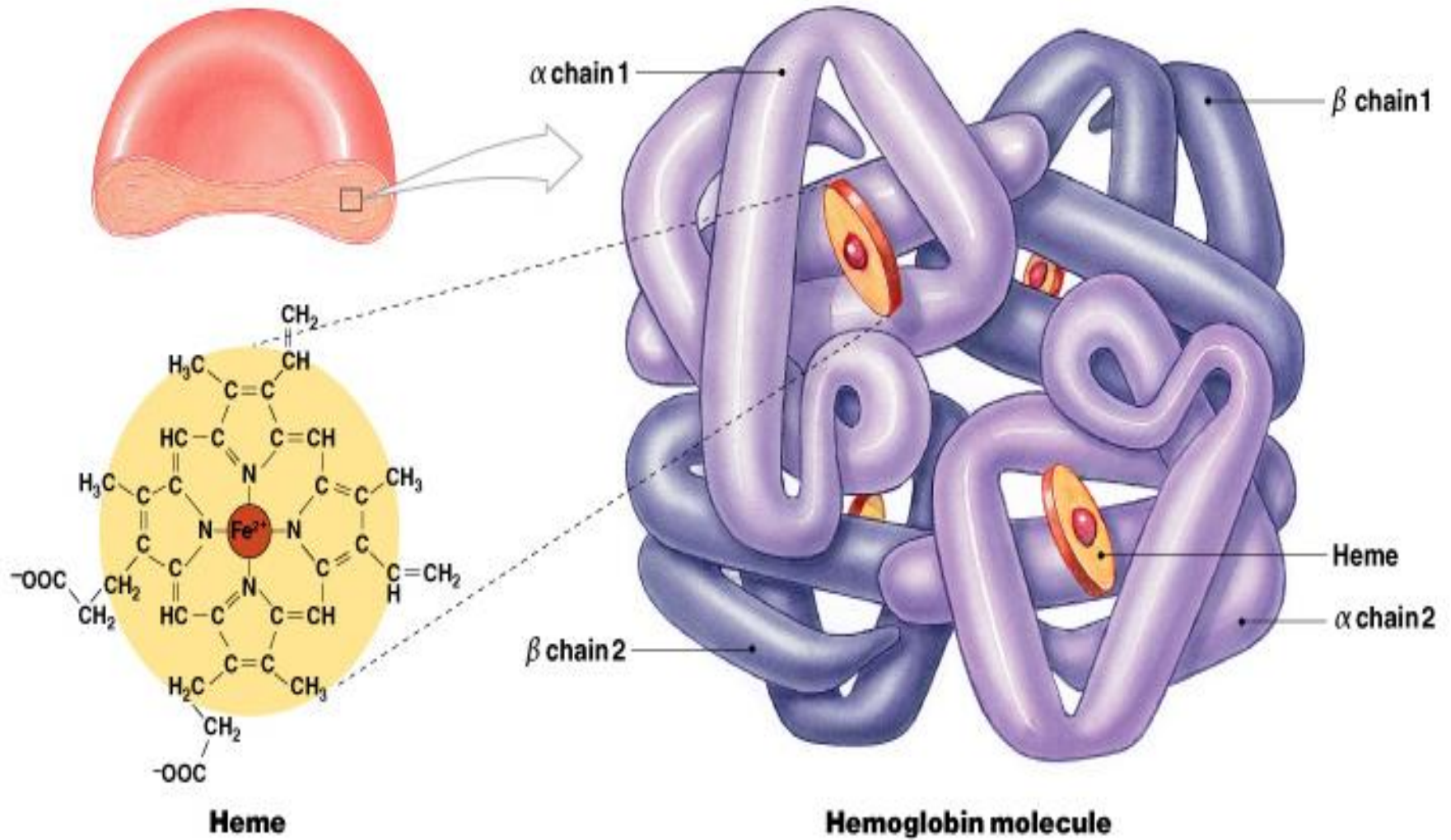
Each heme contains 1 iron ion.

Iron ions easily associate with oxygen (**oxyhemoglobin**) or dissociate from oxygen (**deoxyhemoglobin**).

Carbaminohemoglobin

With low oxygen (peripheral capillaries): hemoglobin releases oxygen
binds carbon dioxide and carries it to lungs

Hemoglobin



Recycling RBCs

- 1% of circulating RBCs wear out per day (about 3 million RBCs per second).
- Macrophages of liver, spleen, and bone marrow:
 - monitor RBCs
 - engulf RBCs before membranes rupture (**hemolyze**)
- **Diagnosing Disorders**
- **Hemoglobinuria:**
 - hemoglobin breakdown products in urine due to excess hemolysis in blood stream
- **Hematuria:**
 - whole red blood cells in urine due to kidney or tissue damage

Hemoglobin Recycling

- Phagocytes break hemoglobin into components:
 - globular proteins to amino acids.
 - heme to biliverdin
 - Biliverdin (green) is converted to bilirubin (yellow)
 - Bilirubin is excreted by liver (bile)
 - jaundice is caused by bilirubin buildup
 - Bilirubin converted by intestinal bacteria to urobilins and stercobilins which account for the yellow brown to brown color of stool.
 - Iron: To transport proteins (transferrin)
 - To storage proteins (ferritin and hemosiderin)

RBC Maturation

Stages of RBC Maturation

Myeloid stem cell

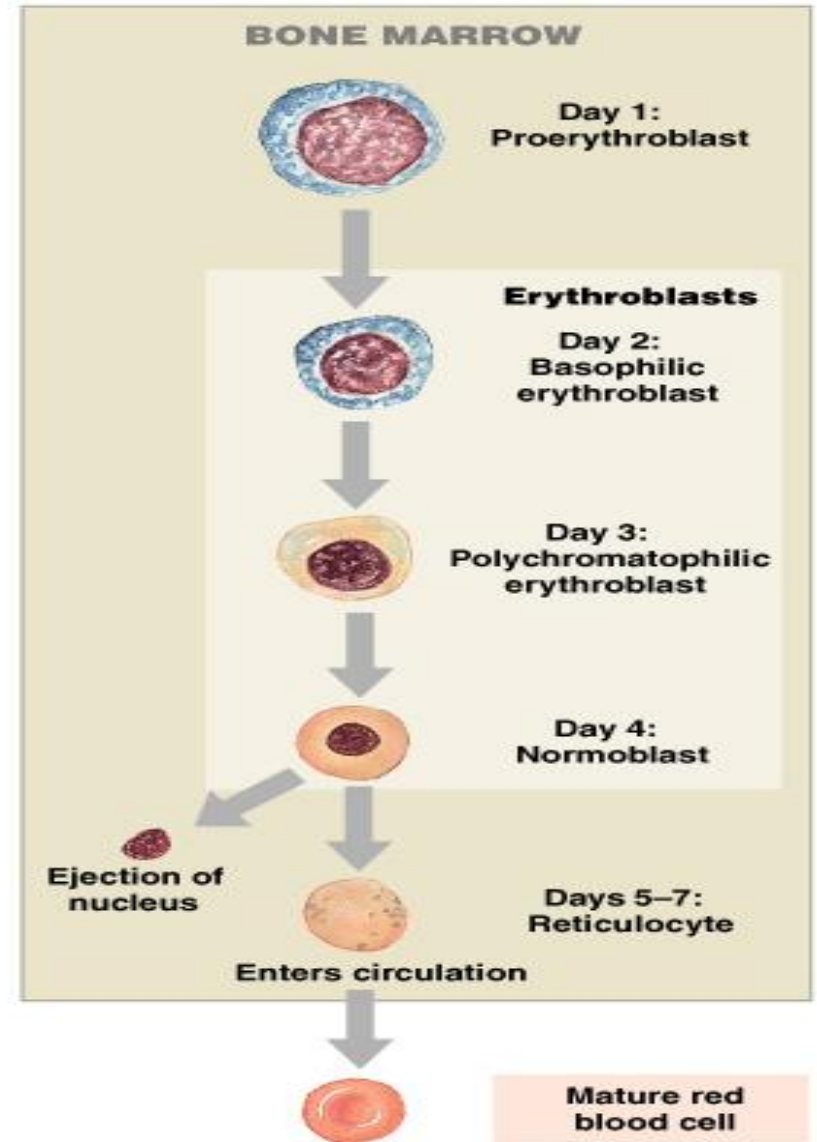
Proerythroblast

Erythroblasts

Normoblast

Reticulocyte

Mature RBC



Erythropoiesis

Red blood cell formation occurs only in red bone marrow (**myeloid tissue**). Stem cells mature to become RBCs.

Building red blood cells requires the following **components**:
amino acids, iron, vitamins B₁₂, B₆, and folic acid

Pernicious Anemia

Low RBC production due to unavailability of **vitamin B₁₂**. **Absorption of vit. B₁₂** needs intrinsic factor produced by the parietal cells in the gastric glands of the stomach.

Hemocytoblasts

- Stem cells in bone marrow divide to produce:
 - **myeloid stem cells**: become RBCs, some WBCs
 - **lymphoid stem cells**: become lymphocytes

Stimulating Hormones

- **Erythropoietin (EPO)** (Also called **erythropoiesis-stimulating hormone**):
 - secreted when oxygen in peripheral tissues is low (**hypoxia**)
 - due to disease or high altitude

RBC Tests

TABLE 19-1 RBC Tests and Related Terminology

Test	Determines	Terms Associated with Abnormal Values	
		Elevated	Depressed
Hematocrit (Hct)	Percentage of formed elements in whole blood Normal = 37–54	Polycythemia (may reflect erythrocytosis or leukocytosis)	Anemia
Reticulocyte count (Retic.)	Percentage of circulating reticulocytes Normal = 0.8%	Reticulocytosis	
Hemoglobin concentration (Hb)	Concentration of hemoglobin in blood Normal = 12–18 g/dl		Anemia
RBC count	Number of RBCs per μl of whole blood Normal = 4.2–6.3 million/ μl	Erythrocytosis/polycythemia	Anemia
Mean corpuscular volume (MCV)	Average volume of single RBC Normal = 82–101 μm^3 (normocytic)	Macrocytic	Microcytic
Mean corpuscular hemoglobin concentration (MCHC)	Average amount of Hb in one RBC Normal = 27–34 $\text{pg}/\mu\text{l}$ (normochromic)	Hyperchromic	Hypochromic

Blood Typing

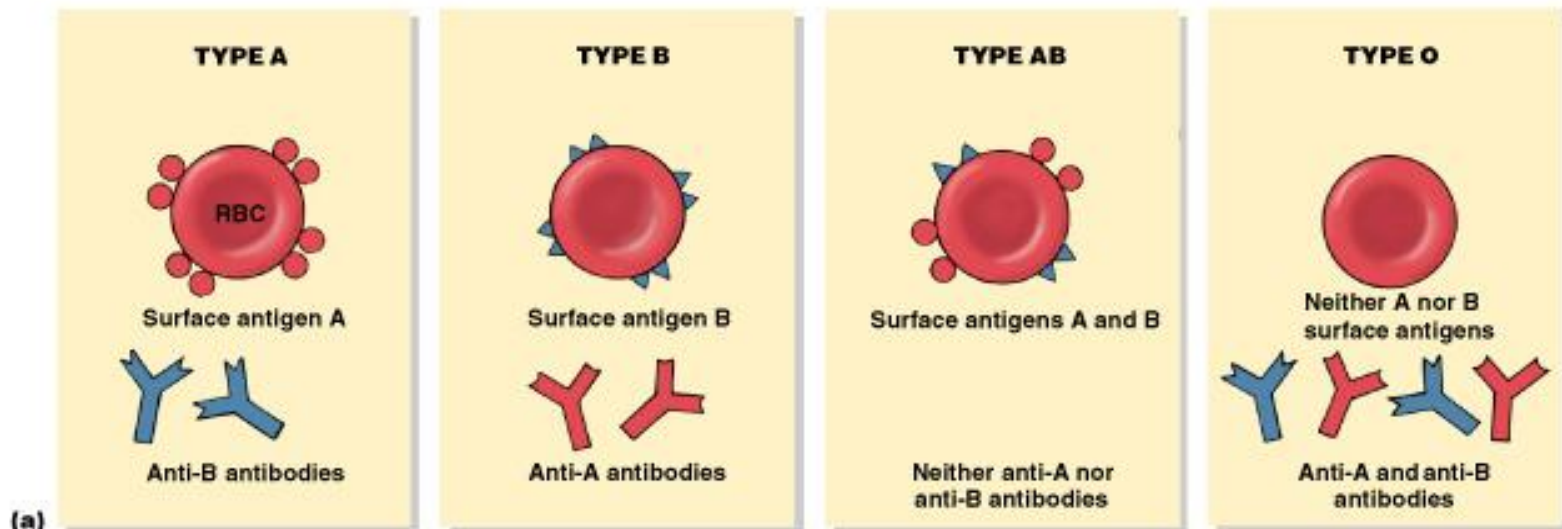
Surface Antigens: Are cell surface proteins that identify cells to immune system. Normal cells are ignored and foreign cells attacked.

Blood Types: Are genetically determined by presence or absence of RBC surface antigens **A**, **B**, **Rh**.

Agglutinogens

- Antigens on surface of RBCs
- Screened by immune system
- Plasma antibodies attack (**agglutinate**) foreign antigens

4 Basic Blood Types

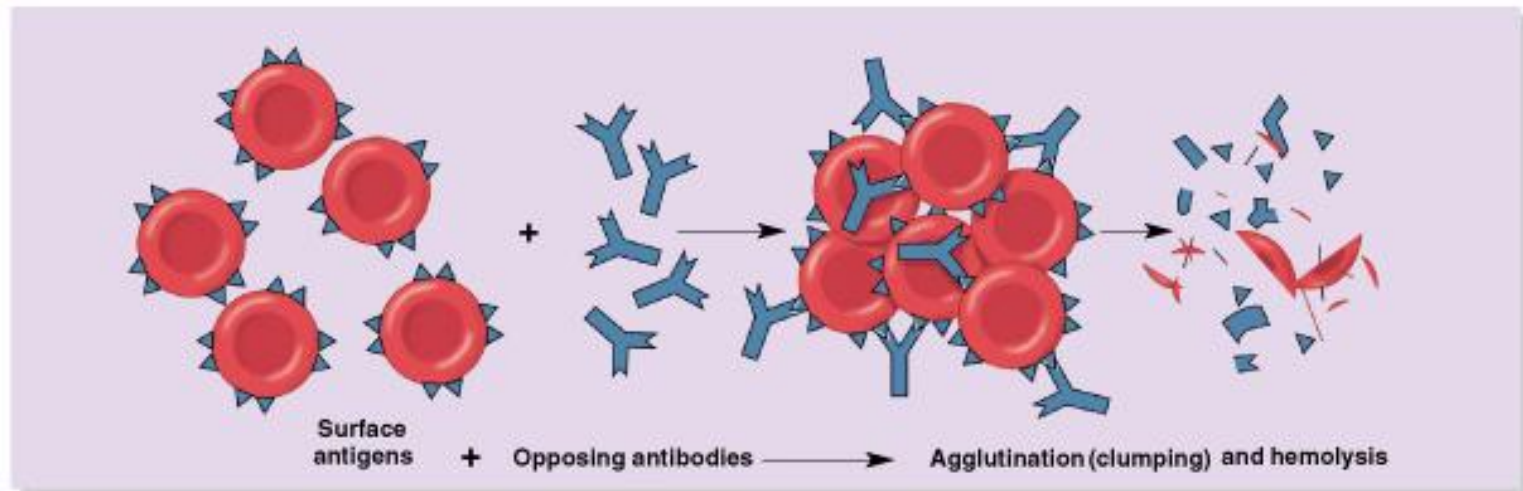


The Rh Factor

- Also called **D antigen**
- Either **Rh positive** (Rh^+) or **Rh negative** (Rh^-)
- Only **sensitized** Rh^- blood has anti-Rh antibodies

















Cross-Reaction

- Also called **transfusion reaction**
- Plasma antibody meets its specific surface antigen
- Blood will agglutinate and hemolyze
- If donor and recipient blood types not compatible



Blood Type Test

Determines blood type and compatibility

Blood sample	Anti-A	Anti-B	Anti-D	Blood type
				A ⁺
				B ⁺
				AB ⁺
				O ⁻

Cross-Match Test

Performed on donor and recipient blood for compatibility

Without cross-match, type O⁻ is universal donor

White Blood Cells (WBCs)

- Also called **leukocytes**
- Do not have hemoglobin
- Have nuclei and other organelles
- Small numbers in blood: 6000 to 9000 per microliter

Functions of WBCs

- Defend against pathogens
- Remove toxins and wastes
- Attack abnormal cells

WBC Movement

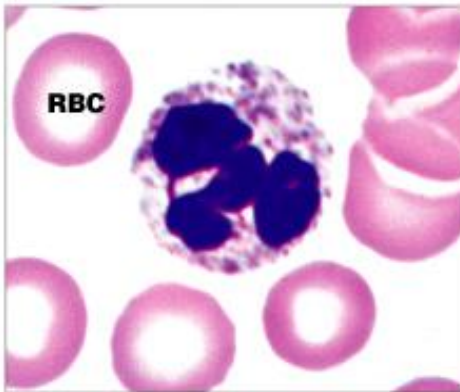
- Most WBCs in:
 - connective tissue proper
 - lymphatic system organs

Circulating WBCs

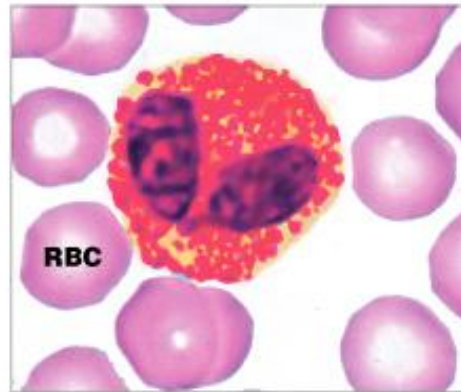
1. Migrate out of bloodstream
2. Have amoeboid movement
3. Attracted to chemical stimuli (**positive chemotaxis**)
4. Some are phagocytic: neutrophils, eosinophils, and monocytes

Types of WBCs

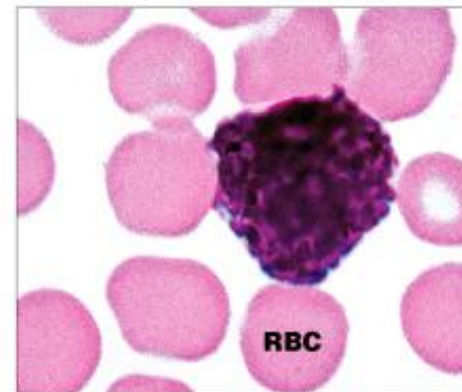
1. Neutrophils
2. Eosinophils
3. Basophils
4. Monocytes
5. Lymphocytes



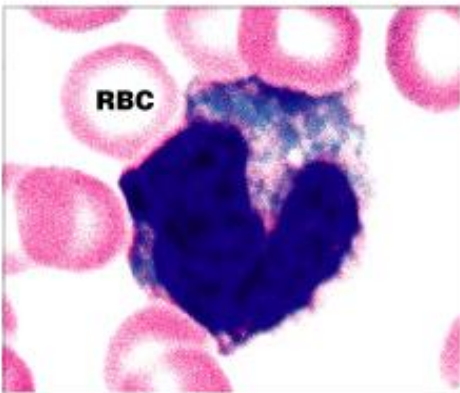
(a) Neutrophil



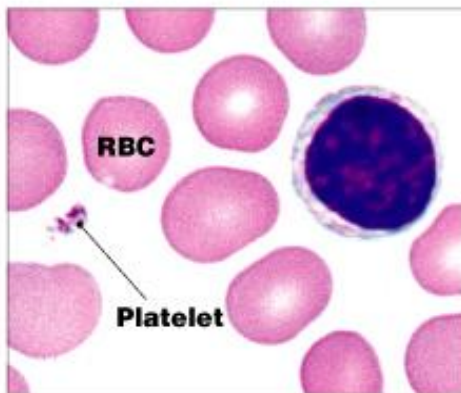
(b) Eosinophil



(c) Basophil



(d) Monocyte



(e) Lymphocyte

Neutrophils

- Also called **polymorphonuclear leukocytes**
- 50–70% of circulating WBCs
- Pale cytoplasm granules with:
 - lysosomal enzymes
 - bactericides (hydrogen peroxide and superoxide)

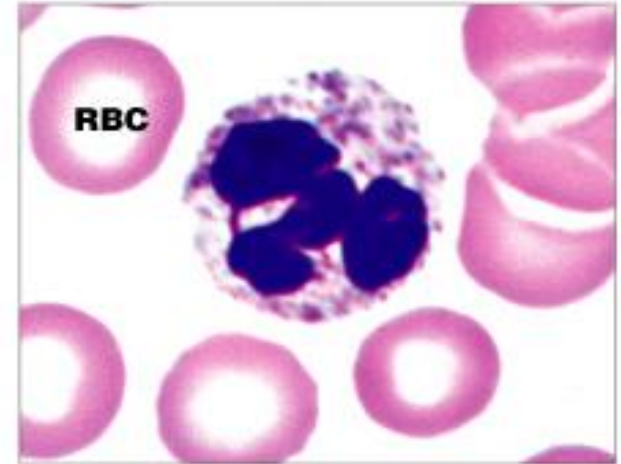
Neutrophil Action

- Very active, first to attack bacteria
- Engulf pathogens
- Digest pathogens
- Release prostaglandins and leukotrienes
- Form pus

Degranulation: Removing granules from cytoplasm

Defensins:

- peptides from lysosomes
- attack pathogen membranes



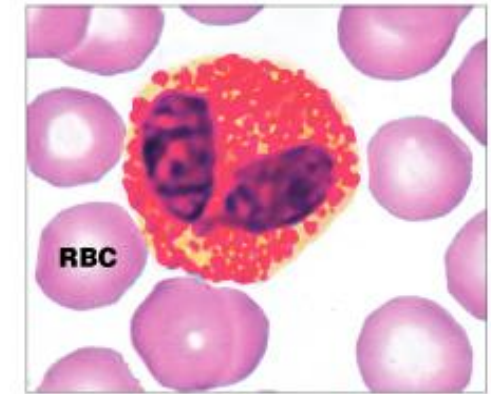
(a) Neutrophil

Eosinophils

- Also called **acidophils**
- 2–4% of circulating WBCs
- Attack large parasites
- Excrete toxic compounds:
 - nitric oxide
 - cytotoxic enzymes

Eosinophil Actions

- Are sensitive to allergens
- Control inflammation with enzymes that counteract inflammatory effects of neutrophils and mast cells.



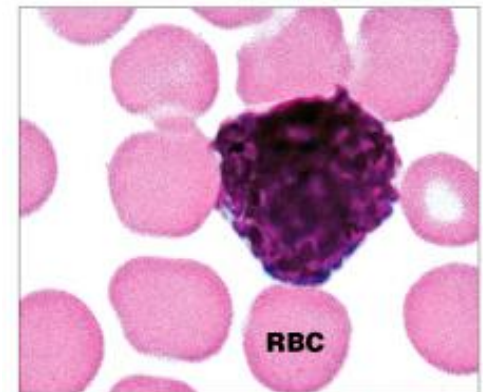
(b) Eosinophil

Basophils

- Are less than 1% of circulating WBCs
- Are small
- Accumulate in damaged tissue

Basophil Actions

- Release **histamine**: dilates blood vessels
- Release **heparin**: prevents blood clotting



(c) Basophil

Monocytes

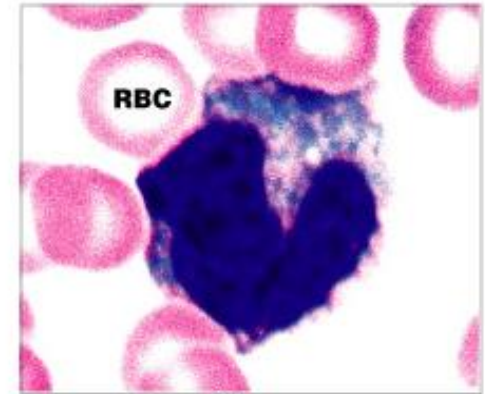
- 2–8% of circulating WBCs
- Are large and spherical
- Enter peripheral tissues and become macrophages

Macrophage Actions

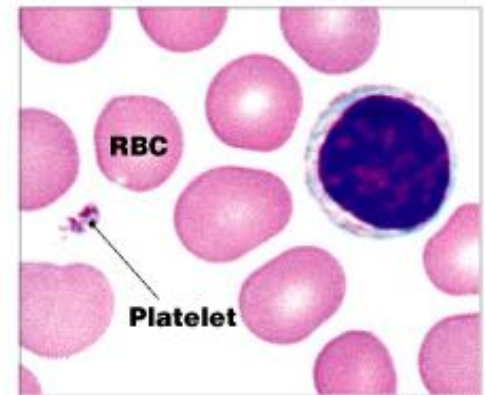
- Engulf large particles and pathogens
- Secrete substances that attract immune system cells and fibroblasts to injured area.

Lymphocytes

- 20–30% of circulating WBCs
- Are larger than RBCs
- Migrate in and out of blood
- Mostly in connective tissues and lymphatic organs
- **Lymphocyte Actions**
- Are part of the body's **specific defense** system



(d) Monocyte



(e) Lymphocyte

3 Classes of Lymphocytes

1. T cells

- Cell-mediated immunity
- Attack foreign cells directly

2. B cells

- Humoral immunity
- Differentiate into **plasma cells** (activated B cells that secrete antibodies).
- Synthesize antibodies

3. Natural killer (NK) cells

Detect and destroy abnormal tissue cells (cancers).

The **Differential Count** of Circulating WBCs

- Detects changes in WBC populations
- Infections, inflammation, and allergic reactions

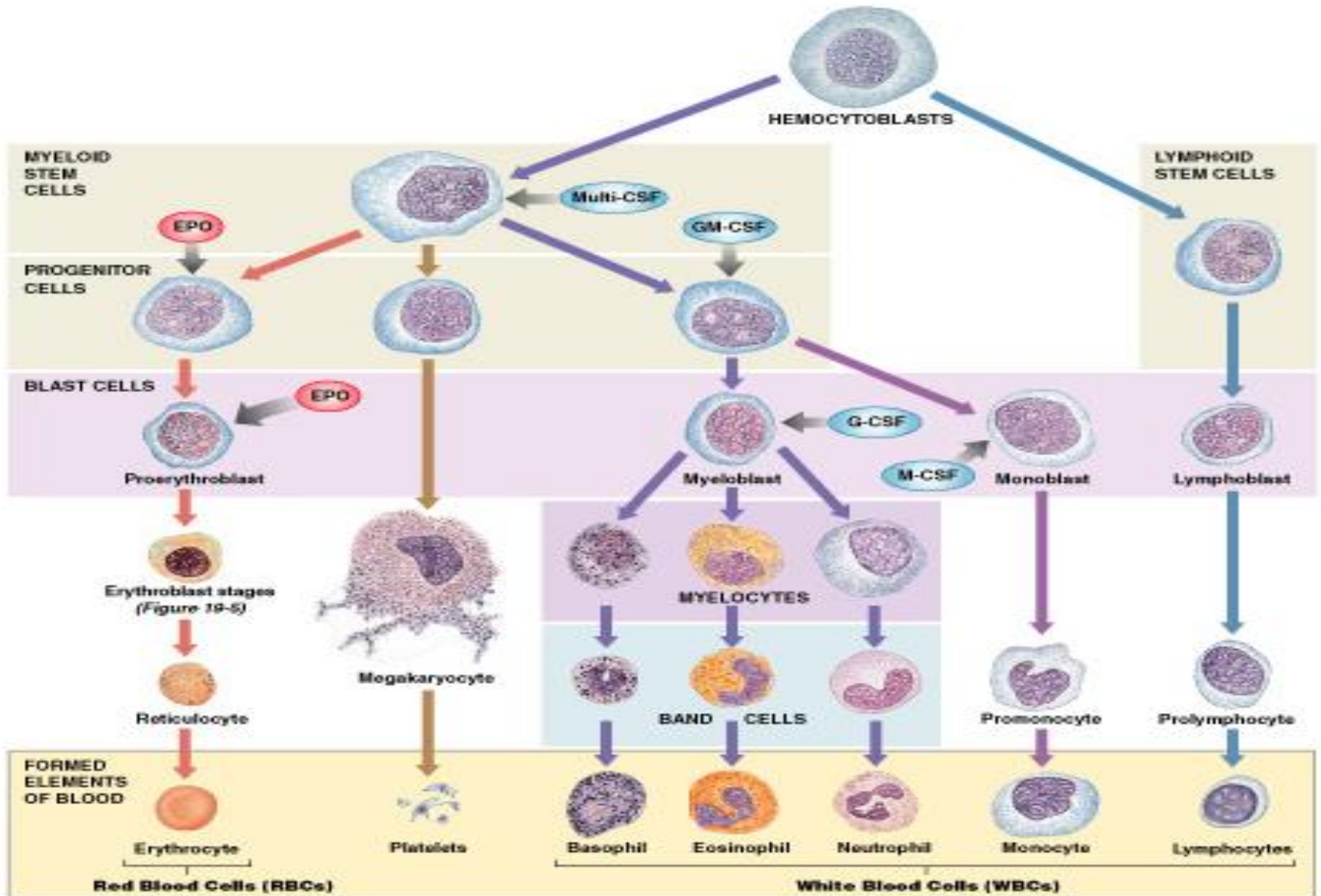
WBC Disorders

- **Leukopenia:** abnormally low WBC count
- **Leukocytosis:** abnormally high WBC count
- **Leukemia:** extremely high WBC count

KEY CONCEPT

- RBCs outnumber WBCs 1000:1
- WBCs defend against infection, foreign cells, or toxins
- WBCs clean up and repair damaged tissues

WBC Production



WBC Production

- All blood cells originate from hemocytoblasts which produce myeloid stem cells and lymphoid stem cells.

Myeloid Stem Cells

Differentiate into **progenitor cells**:

which produce all WBCs except lymphocytes

Lymphoid stem cells

Produce **Lymphocytes**

Lymphopoiesis: The production of lymphocytes

Some lymphoid stem cells migrate to peripheral **lymphoid tissues** (thymus, spleen, lymph nodes) and also produce lymphocytes

WBC Development

- WBCs, except **monocytes** develop fully in **bone marrow**
- **Monocytes** develop into **macrophages** in **peripheral tissues**.

Four Colony Stimulating Factors (CSFs)

- Hormones that regulate blood cell populations:
 1. **M-CSF**: Stimulates monocyte production
 2. **G-CSF**: Stimulates granulocyte production
(neutrophils, eosinophils, and basophils)
 3. **GM-CSF**: Stimulates granulocyte and monocyte production
 4. **Multi-CSF**: Accelerates production of granulocytes, monocytes, platelets, and RBCs

Platelets

- Cell fragments involved in human clotting system
- Nonmammalian vertebrates have **thrombocytes** (nucleated cells)
- **Platelet Circulation**
- Circulates for 9–12 days
- Are removed by spleen
- 2/3 are reserved for emergencies.
- **Platelet Counts**
- 150,000 to 500,000 per microliter
- **Thrombocytopenia:**
 - abnormally low platelet count
- **Thrombocytosis:**
 - abnormally high platelet count

Platelets Functions

1. Release important clotting chemicals
2. Temporarily patch damaged vessel walls
3. Actively contract tissue after clot formation

Platelet Production

Also called **thrombocytopoiesis**: occurs in bone marrow

Megakaryocytes

- Giant cells
- Manufacture platelets from cytoplasm.

Hormonal Controls

- Thrombopoietin (TPO)
- Interleukin-6 (IL-6)
- Multi-CSF

Hemostasis

- The cessation of bleeding:

1. Vascular phase
2. Platelet phase
3. Coagulation phase

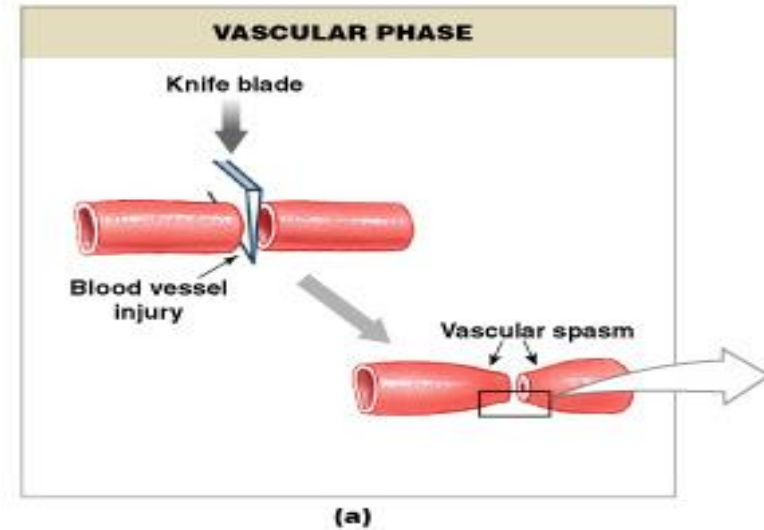
The Vascular Phase

- A cut triggers **vascular spasm**
- 30-minute contraction
- 1. Endothelial cells contract:
expose basal lamina to bloodstream
- 2. Endothelial cells release:

- chemical factors: ADP, tissue factor, and prostacyclin
- local hormones: **endothelins**
- stimulate smooth muscle contraction and cell division

3. Endothelial cell membranes become “sticky”:

- seal off blood flow

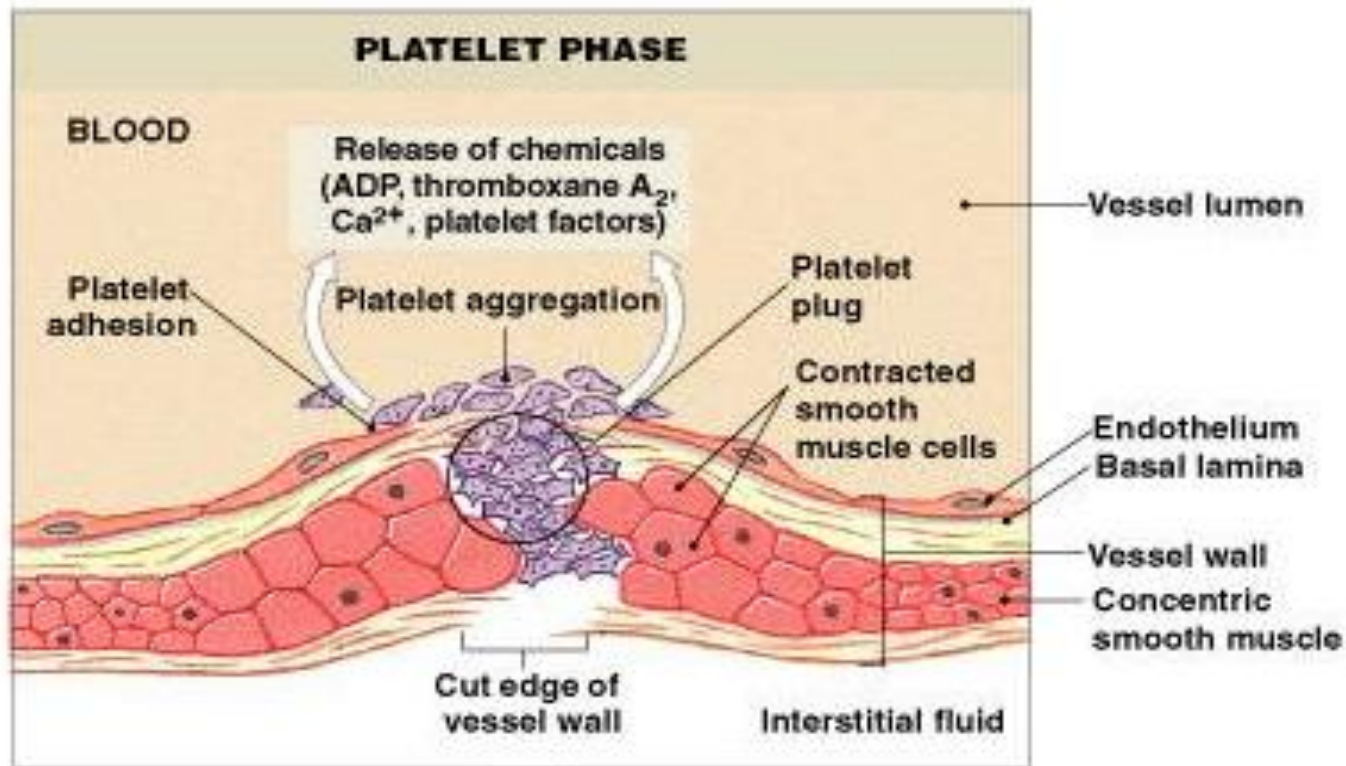


The Platelet Phase

Begins within 15 seconds after injury

Steps of Platelet Phase:

1. Platelet adhesion (attachment):
 - to sticky endothelial surfaces
 - to basal laminae
 - to exposed collagen fibers
2. Platelet aggregation stick together forms platelet plug closes small breaks



(b)

Activated Platelets Release Clotting Compounds

Adenosine diphosphate (ADP)

Thromboxane A₂ and serotonin

Clotting factors

Platelet-derived growth factor (PDGF)

Calcium ions

Platelet Plug: Size Restriction

- **Prostacyclin:**

- released by endothelial cells
- inhibits platelet aggregation

- **Inhibitory compounds:**

- released by other white blood cells

The Coagulation Phase

- It begins 30 sec after injury
- Blood clotting (**coagulation**):
 - Involves a series of steps
 - converts circulating **fibrinogen** into insoluble **fibrin**

Blood Clot : Fibrin network covers platelet plug, traps blood cells and seals off the area.

Clotting Factors (Also called **procoagulants**)

Proteins or ions in plasma Required for normal clotting.

Bleeding Time : Normally, a small puncture wound stops bleeding in 1–4 minutes

Clotting: Area Restriction

1. Anticoagulants (plasma proteins):
 - antithrombin-III
 - alpha-2-macroglobulin
2. Heparin
3. Protein C –stimulates formation an enzyme that breaks down fibrin strands.
4. Prostacyclin also inhibits platelet aggregation

Calcium ions (Ca^{2+}) and vitamin K are both essential to the clotting process

Clot Retraction After clot has formed: Platelets contract and pull torn area together. This takes 30–60 minutes

Fibrinolysis: Slow process of dissolving clot using thrombin and tissue plasminogen activator (t-PA).

Activate plasminogen produces plasmin which digests fibrin strands.