Lecture 7 : Platelets

■ INTRODUCTION

Platelets or thrombocytes are the formed elements of blood. Platelets are small colorless, non-nucleated and moderately refractive bodies. These formed elements of blood are considered to be the fragments of cytoplasm.

Size of Platelets

Diameter : 2.5 μ (2 to 4 μ)
Volume : 7.5 cu μ (7 to 8 cu μ).

Shape of Platelets

Normally, platelets are of several shapes, viz. spherical or rod-shaped and become oval or disk-shaped when inactivated. Sometimes, the platelets have dumbbell shape, comma shape, cigar shape or any other unusual shape.

■ STRUCTURE AND COMPOSITION

Platelet is constituted by:

1. Cell membrane or surface membrane
2. Microtubules
3. Cytoplasm.

■ CELL MEMBRANE

Cell membrane of platelet is 6 nm thick. Extensive invagination of cell membrane forms an open **canalicular system** (Fig. 1). This canalicular system is a delicate tunnel system through which the platelet granules extrude their contents.

Cell membrane of platelet contains lipids in the form of phospholipids, cholesterol and glycolipids, carbohydrates as glycocalyx and glycoproteins and proteins. Of these substances, glycoproteins and phospholipids are functionally important.

Glycoproteins

Glycoproteins prevent the adherence of platelets to normal endothelium, but accelerate the adherence of platelets to collagen and damaged endothelium in ruptured blood vessels. Glycoproteins also form the receptors for adenosine diphosphate (ADP) and thrombin.

Phospholipids

Phospholipids accelerate the clotting reactions. The phospholipids form the precursors of thromboxane A_2 and other prostaglandin-related substances.

■ MICROTUBULES

Microtubules form a ring around cytoplasm below the cell membrane. Microtubules are made up of polymerized proteins called **tubulin.** These tubules provide structural support for the inactivated platelets to maintain the disk-like shape.

■ CYTOPLASM

Cytoplasm of platelets contains the cellular organelles, Golgi apparatus, endoplasmic reticulum, mitochondria, microtubule, microvessels, filaments and granules.

Cytoplasm also contains some chemical substances such as proteins, enzymes, hormonal substances, etc.

Proteins

1. *Contractile proteins*
   i. Actin and myosin: Contractile proteins, which are responsible for contraction of platelets.
   ii. Thrombosthenin: Third contractile protein, which is responsible for clot retraction.
2. *von Willebrand factor:* Responsible for adherence of platelets and regulation of plasma level of factor VIII.
3. *Fibrin-stabilizing factor:* A clotting factor.
4. *Platelet-derived growth factor (PDGF):* Responsible for repair of damaged blood vessels and wound healing. It is a potent mytogen (chemical agent that promotes mitosis) for smooth muscle fibers of blood vessels.
5. *Platelet-activating factor (PAF):* Causes aggregation of platelets during the injury of blood vessels, resulting in prevention of excess loss of blood.
6. *Vitronectin (serum spreading factor):* Promotes adhesion of platelets and spreading of tissue cells in culture.
7. *Thrombospondin:* Inhibits angiogenesis (formation of new blood vessels from pre-existing vessels).

Enzymes

1. Adensosine triphosphatase (ATPase)
2. Enzymes necessary for synthesis of prostaglandins.

Hormonal Substances

1. Adrenaline
2. 5-hydroxytryptamine (5-HT; serotonin)
3. Histamine.

Other Chemical Substances

1. Glycogen
2. Substances like blood group antigens
3. Inorganic substances such as calcium, copper, magnesium and iron.

Platelet Granules

Granules present in cytoplasm of platelets are of two types:

1. Alpha granules
2. Dense granules.

Substances present in these granules are given in Table 1.

Alpha granules

Alpha granules contain:

1. Clotting factors – fibrinogen, V and XIII
2. Platelet-derived growth factor
3. Vascular endothelial growth factor (VEGF)
4. Basic fibroblast growth factor (FGF)
5. Endostatin
6. Thrombospondin.

Dense granules

Dense granules contain:

1. Nucleotides
2. Serotonin
3. Phospholipid
4. Calcium
5. Lysosomes.

■ NORMAL COUNT AND VARIATIONS

Normal platelet count is 2,50,000/cu mm of blood. It ranges between 2,00,000 and 4,00,000/cu mm of blood.

■ PHYSIOLOGICAL VARIATIONS

1. *Age:* Platelets are less in infants (1,50,000 to 2,00,000/cu mm) and reaches normal level at 3rd month after birth.
2. *Sex:* There is no difference in the platelet count between males and females. In females, it is reduced during menstruation.
3. *High altitude:* Platelet count increases.
4. *After meals:* After taking food, the platelet count increases.

TABLE 1: Substances present in platelet granules

Alpha granules	Dense granules
Clotting factors: fibrinogen, V and XIII Platelet-derived growth factor Vascular endothelial growth factor Basic fibroblast growth factor Endostatin Thrombospondin	Nucleotides Serotonin Phospholipid Calcium Lysosomes

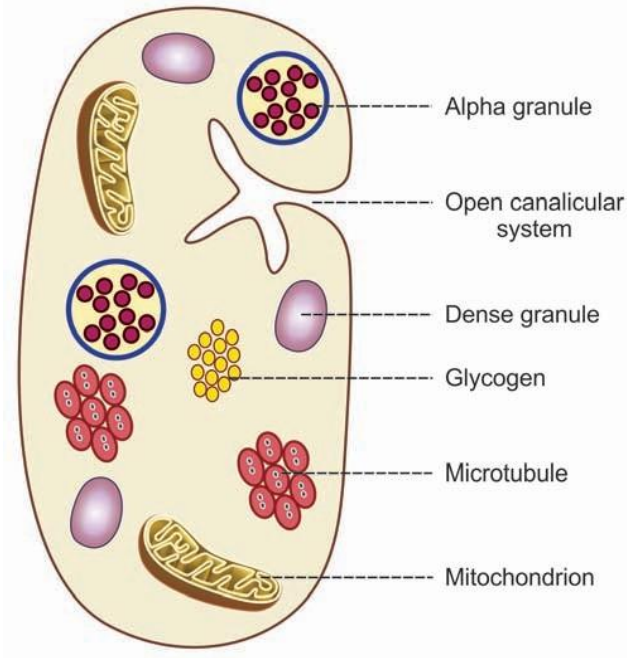

FIGURE 1: Platelet under electron microscope

■ PATHOLOGICAL VARIATIONS

Refer applied physiology of this chapter.

■ PROPERTIES OF PLATELETS

Platelets have three important properties (three 'A's):

1. Adhesiveness
2. Aggregation
3. Agglutination.

■ ADHESIVENESS

Adhesiveness is the property of sticking to a rough surface. During injury of blood vessel, endothelium is damaged and the subendothelial collagen is exposed. While coming in contact with collagen, platelets are activated and adhere to collagen. Adhesion of platelets involves interaction between **von Willebrand factor** secreted by damaged endothelium and a receptor protein called glycoprotein Ib situated on the surface of platelet membrane. Other factors which accelerate adhesiveness are collagen, thrombin, ADP, Thromboxane A_2, calcium ions, P-selectin and vitronectin.

■ AGGREGATION (GROUPING OF PLATELETS)

Aggregation is the grouping of platelets. Adhesion is followed by activation of more number of platelets by substances released from dense granules of platelets.

During activation, the platelets change their shape with elongation of long filamentous pseudopodia which are called processes or filopodia (Fig. 18.2).

Filopodia help the platelets aggregate together. Activation and aggregation of platelets is accelerated by ADP, thromboxane A_2 and platelet-activating factor (PTA: cytokine secreted by neutrophils and monocytes;).

■ AGGLUTINATION

Agglutination is the clumping together of platelets. Aggregated platelets are agglutinated by the actions of some platelet agglutinins and platelet-activating factor.

■ FUNCTIONS OF PLATELETS

Normally, platelets are inactive and execute their actions only when activated. Activated platelets immediately release many substances. This process is known as platelet release reaction. Functions of platelets are carried out by these substances.

Functions of platelets are:

■ 1. ROLE IN BLOOD CLOTTING

Platelets are responsible for the formation of intrinsic prothrombin activator. This substance is responsible for the onset of blood clotting.

■ 2. ROLE IN CLOT RETRACTION

In the blood clot, blood cells including platelets are entrapped in between the fibrin threads. Cytoplasm of platelets contains the **contractile proteins,** namely actin, myosin and thrombosthenin, which are responsible for clot retraction.

■ 3. ROLE IN PREVENTION OF BLOOD LOSS (HEMOSTASIS)

Platelets accelerate the hemostasis by three ways:

i. Platelets secrete 5-HT, which causes the constriction of blood vessels.
ii. Due to the adhesive property, the platelets seal the damage in blood vessels like capillaries.
iii. By formation of temporary plug, the platelets seal the damage in blood vessels.

■ 4. ROLE IN REPAIR OF RUPTURED BLOOD VESSEL

Platelet-derived growth factor (PDGF) formed in cytoplasm of platelets is useful for the repair of the endothelium and other structures of the ruptured blood vessels.

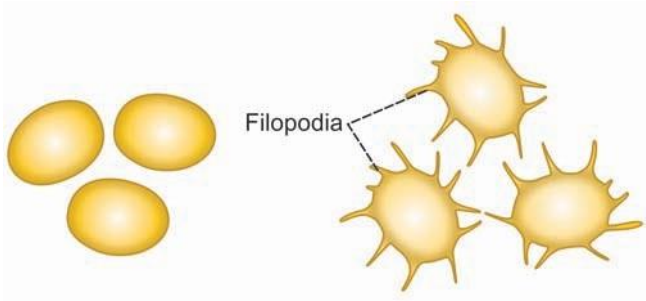

FIGURE 2: A. Inactive platelets. **B.** Activated platelets.

■ 5. ROLE IN DEFENSE MECHANISM

By the property of agglutination, platelets encircle the foreign bodies and destroy them.

■ ACTIVATORS AND INHIBITORS OF PLATELETS

■ ACTIVATORS OF PLATELETS

1. Collagen, which is exposed during damage of blood vessels
2. von Willebrand factor
3. Thromboxane A_2
4. Platelet-activating factor
5. Thrombin
6. ADP
7. Calcium ions
8. P-selectin: Cell adhesion molecule secreted from endothelial cells
9. Convulxin: Purified protein from snake venom.

■ INHIBITORS OF PLATELETS

1. Nitric oxide
2. Clotting factors: II, IX, X, XI and XII
3. Prostacyclin
4. Nucleotidases which breakdown the ADP.

■ DEVELOPMENT OF PLATELETS

Platelets are formed from bone marrow. Pluripotent stem cell gives rise to the colony forming unit-megakaryocyte (CFU-M). This develops into megakaryocyte. Cytoplasm of megakaryocyte form **pseudopodium.** A portion of pseudopodium is detached to form platelet, which enters the circulation (Fig. 10.2).

Production of platelets is influenced by colony-stimulating factors and **thrombopoietin.** Colony-stimulating factors are secreted by monocytes and T lymphocytes. Thrombopoietin is a glycoprotein like erythropoietin. It is secreted by liver and kidneys.

■ LIFESPAN AND FATE OF PLATELETS

Average lifespan of platelets is 10 days. It varies between 8 and 11 days. Platelets are destroyed by tissue macrophage system in spleen. So, **splenomegaly** (enlargement of spleen) decreases platelet count and **splenectomy** (removal of spleen) increases platelet count.

■ APPLIED PHYSIOLOGY – PLATELET DISORDERS

Platelet disorders occur because of pathological variation in platelet count and dysfunction of platelets.

Platelet disorders are:

1. Thrombocytopenia
2. Thrombocytosis
3. Thrombocythemia
4. Glanzmann's thrombasthenia.

1. *Thrombocytopenia*

Decrease in platelet count is called thrombocytopenia. It leads to thrombocytopenic purpura.

Thrombocytopenia occurs in the following conditions:

i. Acute infections
ii. Acute leukemia
iii. Aplastic and pernicious anemia
iv. Chickenpox
v. Smallpox
vi. Splenomegaly
vii. Scarlet fever
viii. Typhoid
ix. Tuberculosis
x. Purpura
xi. Gaucher's disease.

2. *Thrombocytosis*

Increase in platelet count is called thrombocytosis.

Thrombocytosis occurs in the following conditions:

i. Allergic conditions
ii. Asphyxia
iii. Hemorrhage
iv. Bone fractures
v. Surgical operations
vi. Splenectomy
vii. Rheumatic fever
viii. Trauma (wound or injury or damage caused by external force).

3. *Thrombocythemia*

Thrombocythemia is the condition with persistent and abnormal increase in platelet count. Thrombocythemia occurs in the following conditions:

i. Carcinoma
ii. Chronic leukemia
iii. Hodgkin's disease.

4. *Glanzmann's Thrombasthenia*

Glanzmann's thrombasthenia is an inherited hemorrhagic disorder, caused by structural or functional abnormality of platelets. It leads to **thrombasthenic purpura** (Chapter 20). However, the platelet count is normal. It is characterized by normal clotting time, normal or prolonged bleeding time but defective clot retraction.