THROMBOPOIESIS

The development of platelets in the bone marrow is called **thrombopoiesis** or ***thrombocytopoiesis***. Platelets are the smallest formed elements of blood. They are anuclear fragments of **megakaryocytes**. Megakaryocytes are the ***giant cells*** in the bone marrow.

Mature Megakaryocytes

These are the **largest cells** in bone marrow.

Megakaryocyte has **large nucleus**, which is polyploid (**Polyploid bone marrow cells**). The cells are still **bigger in size** (more than 25 to 50 µm). Platelets are formed in the bone marrow by a process of fragmentation of the cytoplasm of megakaryocytes

Platelets:

Megakaryocytes form platelets by **pinching off bits of cytoplasm** and **extruding them into the circulation**. On average, each megakaryocyte produces about **2000 to 3000 platelets**.
Normally, platelet production per day is about 35,000 to 45,000 per microliter of blood.

Life History

Platelets survive in circulation for about **8–12 days**.

Spleen plays an important role in destruction of platelets.
Therefore, **platelet count increases after splenectomy** and **decreases in splenomegaly.**

Structure

Platelets are small, anucleate cell fragments adapted to participate in hemostasis. By their membrane properties they adhere to damaged blood vessels and aggregate with each other. Though the cells are small, platelets have **developed cellular structures**

Properties of Platelets

Platelets have **three unique properties**: **adhesion, aggregation, and activation & release**.

Adhesion:

Platelets easily adhere to the damaged vascular endothelium. This is called **platelet adhesion**.
Platelets have the tendency to stick to the exposed collagen of the injured vessel wall. Adhesion is **facilitated by von Willebrand factor**.

Role of Membrane Proteins: **von Willebrand factor** (vWF) mediates adhesion of platelets to subendothelium via GpIb on the surface of platelets.

Aggregation

Platelets not only stick to the injured vessel wall but also to each other. The property of platelets to **stick to each other** is called platelet aggregation.

Fibrinogen and GpIIb-IIIa mainly promote aggregation of platelet to each other
Also, **thrombin, ADP and PAF** promote platelet aggregation.

Activation & Release (Secretion)

Platelets are activated when they bind to collagen or to each other.
The activation is facilitated by **thrombin and ADP.**

Platelets normally circulate as round to oval disc like structures. With activation platelets undergo shape-change i.e. they become more spherical and form **pseudopodia**.
The activated platelets change their shape and discharge their granular contents. The discharge of the granular content to the exterior through open canalicular system is called **platelet release**.
The **release reaction** (secretion) is facilitated by chemicals released from platelet granules.

Functions of Platelets

1. Temporary hemostasis: Platelets prevent bleeding by forming plugs at the site of injury (**temporary hemostatic plug**). Platelets also promote vasoconstriction by producing serotonin that helps in hemostasis.
2. Blood coagulation: Platelets contribute to blood coagulation by releasing platelet factor 4, and synthesizing clotting factor V and XI.
3. Clot retraction: Platelets promote clot retraction, which is essential for stabilization of clot.
4. Thrombolysis: Platelet controls fibrinolysis.
5. Phagocytosis: Platelets phagocytose smaller molecules like immune complexes and viruses.
6. Storage and transport: Platelets synthesize, secrete and transport many chemical substances
7. Vascular growth: Platelets help in growth of vascular endothelium by secreting platelet–derived growth factor (**PDGF**). PDGF is also produced by macrophages and endothelial cells.

Normal Count & Variations

Normal count of platelet is 1.5–4 lakhs/mm3 of blood.

Thrombocytopenia is defined as the **platelet count less than 1.5 lakhs/mm3 of blood.**
CRITICAL COUNT: However, significant bleeding occurs when platelet count decreases below 50,000/mm3 of blood. Therefore, platelet count below 50,000/mm3 of blood is called **critical count**.

Spontaneous haemorrhagic tendency becomes clinically evident only after severe depletion of the platelet count to level below 20,000/μl

Thrombocytopenia may result from 4 main groups of causes:
Impaired platelet production, Accelerated platelet destruction, Splenic sequestration, Dilutional loss.

Thrombocytosis: Increased platelet count above 4 Lakhs/mm3 of blood
Thrombocytosis commonly occurs in polycythemia vera, chronic myeloid leukemia, iron deficiency anemia, splenectomy, chronic infection, surgery and following acute hemorrhage.

CLOT RETRACTION
If platelets are present in the clot in a test tube, within minutes to hours, the clot contracts, extruding a very large fraction of serum is called **clot retraction**.

The **platelet filopodia** extends into fibrin clot and **fibrin strands tug with filopodia**. Thus, shrinkage of platelet with contraction of filopodia causes ***internalization of fibrin*** that causes clot retraction.