Lec 14: Platelets: Count, Function, Structure, Disorders, and Diagnosis

Introduction to Platelets:

Platelets, also known as thrombocytes, are small, anucleate cell fragments derived from megakaryocytes in the bone marrow. They play a crucial role in hemostasis (blood clotting), wound healing, and immune responses.

Platelet Count :

1. Normal Range of platelets of blood 150_400/µL
2. Below 150,000/µL = Thrombocytopenia (low platelets)
3. Above 450,000/µL = Thrombocytosis (high platelets)

Factors Affecting Platelet Count

1. Age & Gender: Slight variations occur naturally.
2. Medications: Chemotherapy, heparin, aspirin, etc.
3. Infections & Diseases: Viral infections, leukemia, liver disease, etc.

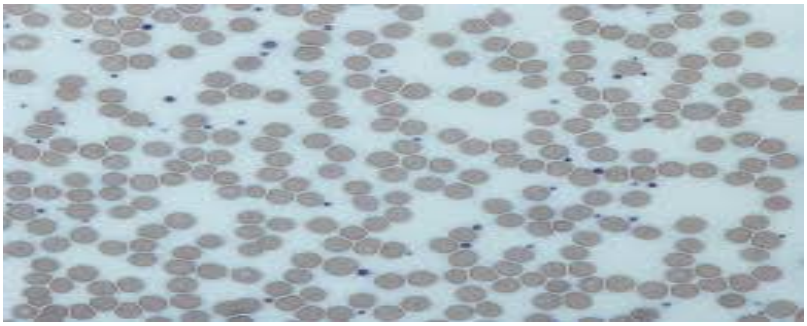
Platelet Structure:

1. Size: 2–4 µm in diameter
2. Lifespan: ~7–10 days
3. Shape: Disc-shaped when inactive, but form pseudopodia upon activation

Components:

1. Plasma membrane: Contains glycoproteins (GPIIb/IIIa) that mediate adhesion.
2. Cytoplasm: Rich in granules and organelles.
3. Granules:

a. Alpha granules: Contain clotting factors, von Willebrand factor (vWF), fibrinogen.
b. Dense granules: Contain serotonin, ADP, calcium, and ATP (promote aggregation.(



Platelet Function:

Platelets are critical for hemostasis and other functions:

A. Hemostasis (Clot Formation)

1. Adhesion – Platelets adhere to exposed collagen at the injury site via von Willebrand factor (vWF).
2. Activation – Platelets change shape, release granules, and express surface receptors.
3. Aggregation – Platelets stick together using fibrinogen and form a plug.
4. Coagulation Cascade Support – Platelets provide a surface for clotting factors.
5. Clot Retraction & Resolution – Platelets contract to stabilize the clot and aid in healing.

B. Other Functions

1. Wound Healing – Release growth factors like PDGF (platelet-derived growth factor).
2. Immune Response – Platelets interact with immune cells to fight infections.

Platelet Disorders:

Platelets are essential for blood clotting and immune functions. Disorders related to platelets can lead to bleeding (thrombocytopenia) or excessive clotting (thrombocytosis). Early diagnosis and appropriate treatment are critical to managing these conditions effectively.

A. Thrombocytopenia (Low Platelets)
B. (Thrombocytosis (High Platelets)
C. Platelet Function Disorders

A.Thrombocytopenia causes:

1. Bone marrow failure (leukemia, aplastic anemia)
2. Increased destruction (ITP, DIC, heparin-induced thrombocytopenia(
3. Sequestration (hypersplenism)
4. Immune Thrombocytopenic Purpura (ITP): Autoimmune destruction of platelets
5. Disseminated Intravascular Coagulation (DIC): Widespread clotting and bleeding

• Symptoms: Easy bruising, petechiae, prolonged bleeding

B. Thrombocytosis causes:

1. Primary: Essential thrombocythemia (bone marrow disorder(
2. Secondary: Infection, inflammation, cancer

• Symptoms: Increased clotting risk, stroke, or bleeding

C. Platelet Function Disorders: Examples:

• Bernard-Soulier Syndrome: Deficiency of GPIb (platelet adhesion defect)

• Glanzmann's Thrombasthenia: Deficiency of GPIIb/IIIa (platelet aggregation defect(

Diagnosis of Platelet Disorders

A. Complete Blood Count (CBC): Determines platelet count (thrombocytopenia vs. thrombocytosis).

B. Peripheral Blood Smear: Examines platelet morphology (size, shape, granules.(

C. Platelet Function Tests:

• Bleeding Time: Evaluates platelet plug formation.

• Platelet Aggregometry: Measures response to agonists like ADP, epinephrine.

• Flow Cytometry: Detects glycoprotein deficiencies.

D. Bone Marrow Biopsy :Assesses platelet production abnormalities.

Treatment Approaches

a. Thrombocytopenia:
   Corticosteroids, IVIG (for ITP)
   Platelet transfusion (if severe)
b. Thrombocytosis:
   Aspirin (to reduce clotting risk)
   Hydroxyurea (for essential thrombocythemia)
c. Platelet Function Disorders:
   Desmopressin (for mild disorders)
   Platelet transfusion (for severe bleeding)

Lec15 : Introduction to Hemostasis, Clotting Factors, and Related Disorders

Hemostasis is the physiological process that prevents excessive blood loss after injury while maintaining blood fluidity within the vessels. It involves platelets, clotting factors, and blood vessels, ensuring a balance between clot formation and clot dissolution.

Phases of Hemostasis

1.Vascular Spasm (Vasoconstriction)

- Immediate reflex contraction of blood vessels to reduce blood loss.
- Mediated by endothelin and thromboxane A2 (TXA2).

2.Primary Hemostasis (Platelet Plug Formation)

- Platelets adhere to the exposed collagen via von Willebrand Factor (vWF.(
- Platelets activate, release granules (ADP, TXA2), and aggregate using fibrinogen.

3.Secondary Hemostasis (Coagulation Cascade)

- Formation of a stable fibrin clot via the coagulation cascade.

4.Clot Retraction & Fibrinolysis (Clot Resolution)

- Clot contracts via actin-myosin in platelets.
- Plasmin dissolves the clot to restore blood flow.

Clotting Factors and the Coagulation Cascade:

The coagulation cascade consists of a series of enzymatic reactions that ultimately form a fibrin clot. It occurs via three pathways:

A. The Three Coagulation Pathways

1.Intrinsic Pathway (Contact Activation Pathway)

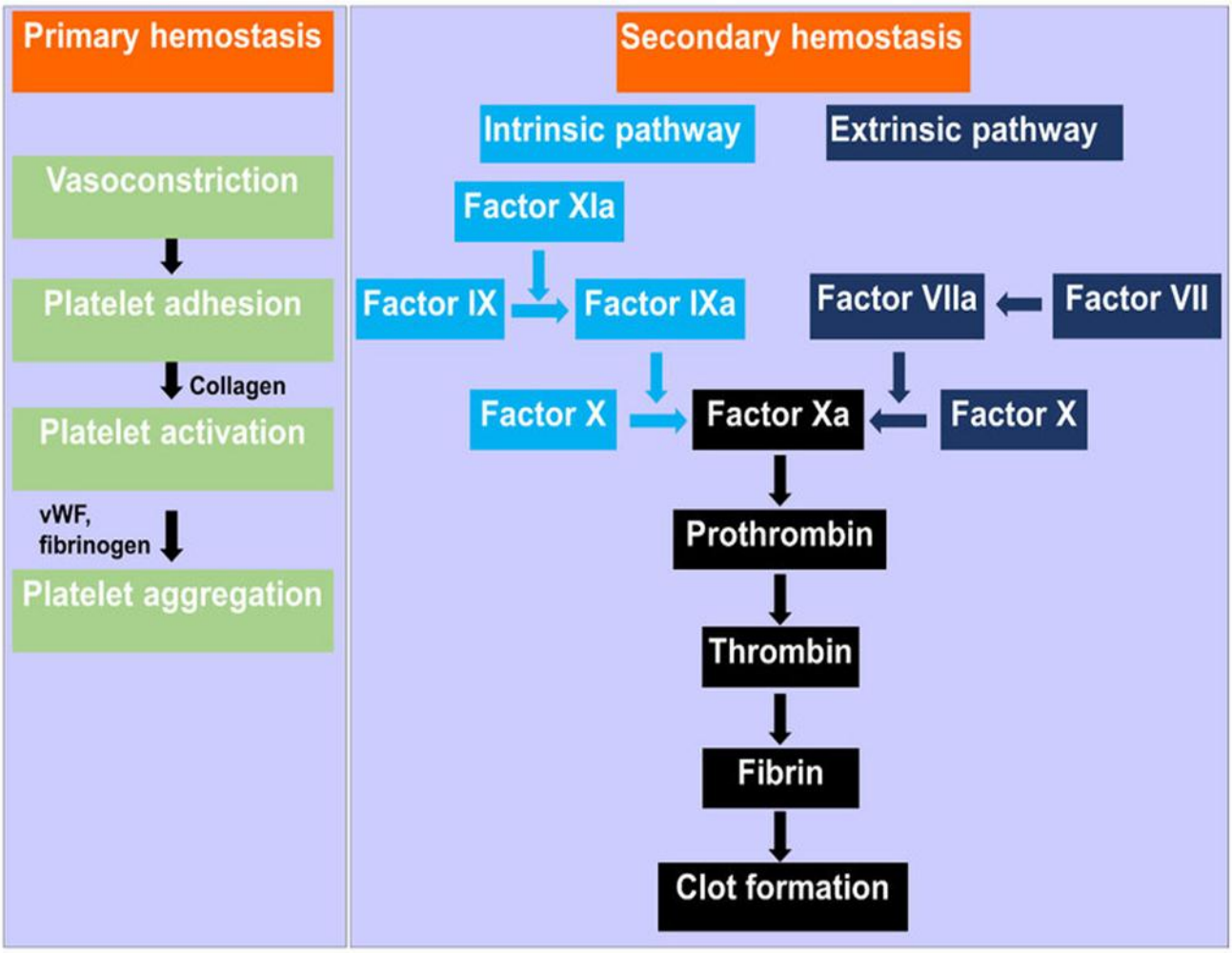
- Triggered by exposure to negatively charged surfaces (e.g., collagen).
- Factors involved: XII → XI → IX → VIII → X
- Tested using Activated Partial Thromboplastin Time (aPTT)

2.Extrinsic Pathway (Tissue Factor Pathway)

- Activated by tissue factor (TF) release from injured cells.
- Factors involved: VII → X
- Tested using Prothrombin Time (PT/INR)

3.Common Pathway (Final Clot Formation)

- Factor X activates prothrombin (Factor II) to thrombin (Factor IIa).
- Thrombin converts fibrinogen (Factor I) to fibrin (Factor Ia).
- Factor XIII stabilizes the fibrin clot.



B.Key Coagulation Factors & Their Roles

Factor	Name	Function
I	Fibrinogen	fibrin clot
II	Prothrombin	Converts to thrombin
III	Tissue Factor	Activates extrinsic pathway
IV	Calcium	Required for clotting
V	Labile Factor	Cofactor for Factor X
VII	Stable Factor	Activates Factor X (extrinsic)
VIII	Anti-hemophilic A	Cofactor for Factor IX (intrinsic)
IX	Anti-hemophilic B	Activates Factor X (intrinsic)
X	Stuart-Prower Factor	Activates prothrombin
XI	Plasma Thromboplastin	Antecedent Activates Factor IX
XII	Hageman Factor	Activates intrinsic pathway
XIII	Fibrin-Stabilizing Factor	Cross-links fibrin

Disorders of Hemostasis: Disorders affecting hemostasis can lead to

A. **excessive bleeding (hemorrhagic disorders)**
B. **excessive clotting (thrombotic disorders).**

A. Hemorrhagic Disorders (Bleeding Disorders)

1.Hemophilia (Deficiency of clotting factors):

• Hemophilia A: Factor VIII deficiency.

• Hemophilia B: Factor IX deficiency.

• Symptoms: Prolonged bleeding, hemarthrosis (joint bleeding.(

2.Von Willebrand Disease (vWD):

• Deficiency of von Willebrand Factor, leading to platelet dysfunction.

• Symptoms: Easy bruising, nosebleeds, menorrhagia.

3.Disseminated Intravascular Coagulation (DIC):

• Widespread clotting followed by bleeding due to depletion of clotting factors.

• Causes: Sepsis, trauma, malignancy, obstetric complications.

• Lab findings: ↑ PT, ↑ aPTT, ↓ platelets, ↓ fibrinogen, ↑ D-dimer.

4.Liver Disease & Vitamin K Deficiency: The liver synthesizes most clotting factors.

• Vitamin K is required for Factors II, VII, IX, X production.

B. Thrombotic Disorders (Excessive Clotting)

1.Deep Vein Thrombosis (DVT) & Pulmonary Embolism (PE)

• Formation of clots in deep veins, which may embolize to the lungs.

• Risk factors: Immobility, surgery, pregnancy, cancer, Factor V Leiden mutation.

2.Factor V Leiden Mutation : Mutation makes Factor V resistant to inactivation by Protein C, leading to hypercoagulability.

3.Antiphospholipid Syndrome (APS): Autoimmune disorder causing recurrent clots and pregnancy loss

4.Protein C, Protein S , or Antithrombin III Deficiency:

• These natural anticoagulants help prevent excessive clotting.

•Deficiencies increase thrombosis risk.

Diagnostic Tests for Hemostasis Disorders

A. Screening Tests

a. Complete Blood Count (CBC): Checks platelet count.
b. Prothrombin Time (PT/INR): Assesses extrinsic pathway (Factor VII.(
c. Activated Partial Thromboplastin Time (aPTT): Assesses intrinsic pathway (Factors VIII, IX, XI, XII.(
d. Thrombin Time (TT): Assesses fibrin formation.

B. Specialized Tests

a. Mixing Studies: Differentiate factor deficiency vs. inhibitor.
b. D-Dimer Test: Elevated in DIC, DVT, and PE.
c. Factor Assays: Measure levels of specific clotting factors.
d. Von Willebrand Panel: Tests vWF antigen and function.

Treatment Approaches

A. Hemorrhagic Disorders

• Hemophilia: Factor replacement therapy (Factor VIII or IX infusions)

• Von Willebrand Disease: Desmopressin (DDAVP) to increase vWF.

• DIC: Treat the underlying cause; FFP (fresh frozen plasma) & platelets if severe bleeding.

B. Thrombotic Disorders

• DVT/PE: Anticoagulants (heparin, warfarin, DOACs).

• Factor V Leiden & APS: Long-term anticoagulation therapy.

• Protein C/S Deficiency: Heparin followed by warfarin therapy.