Physiology

Platelets, Hemostasis, and Bleeding Disorders

م.د. أحمد تركي هاني
MBChB. MSc. PhD.

Hemostasis Overview

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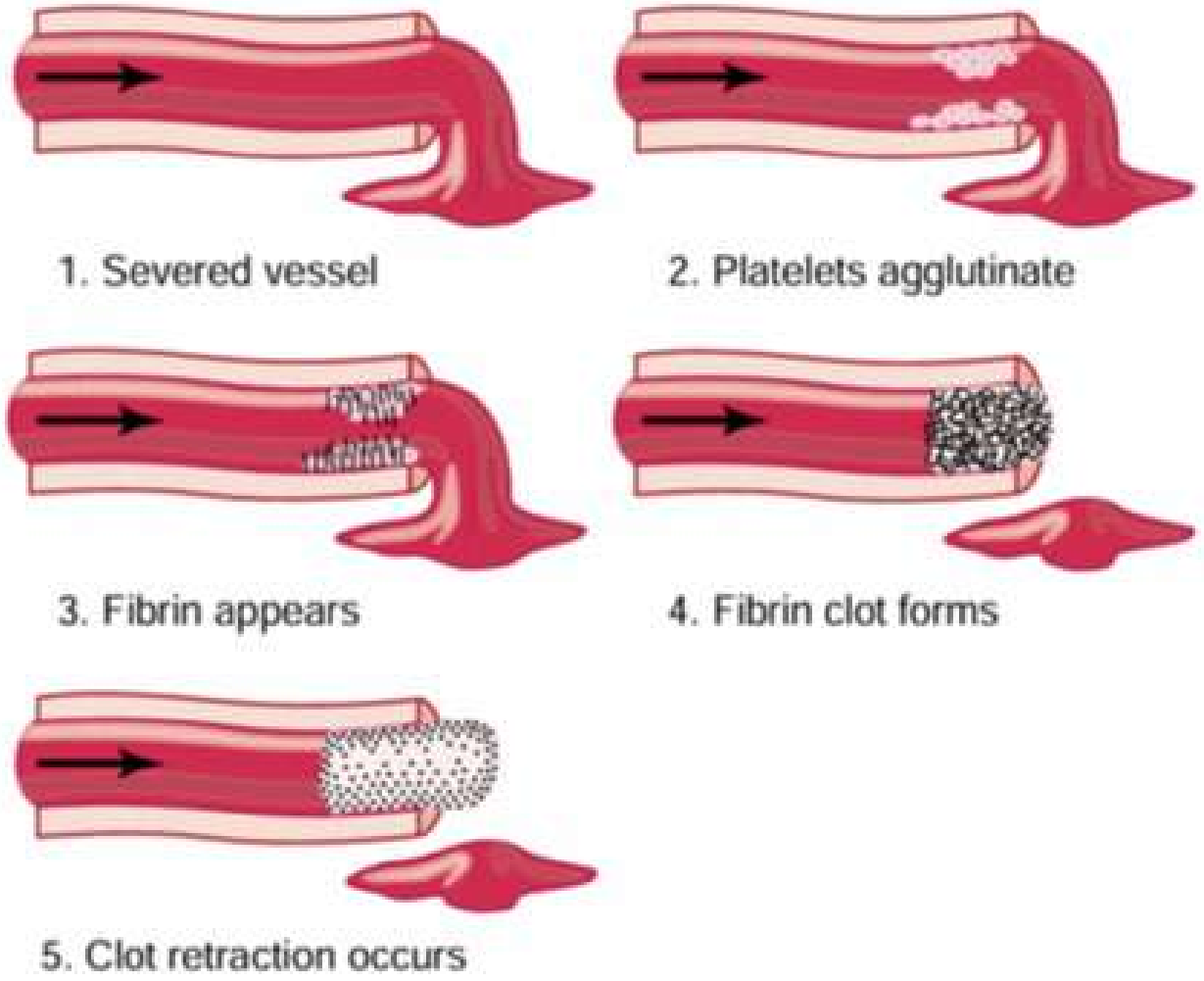
MBChB. MSc. PhD.



Clotting process in a traumatized blood vessel.

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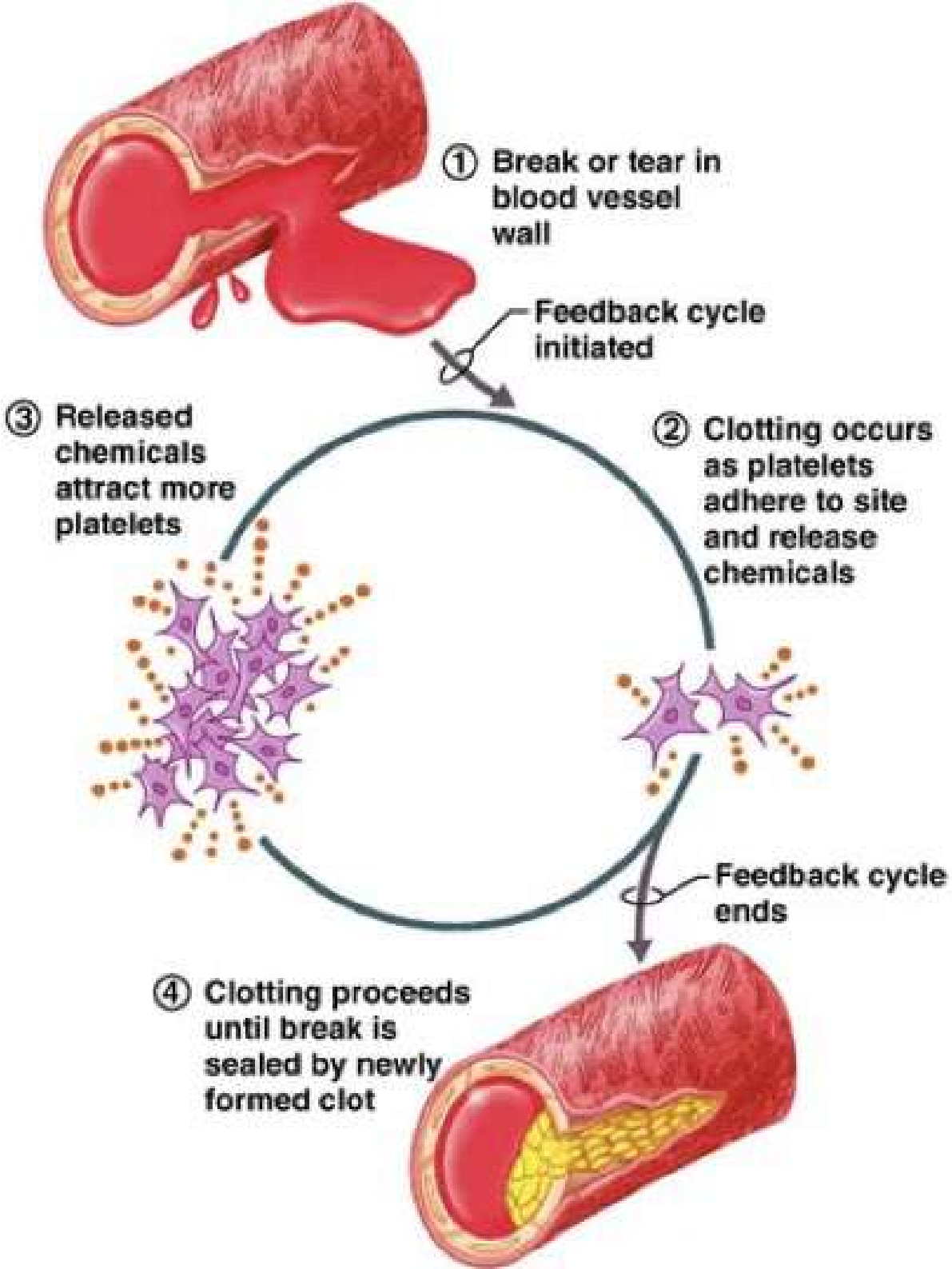
Blood clotting

Positive Feedback:



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Hemostasis:

All physiological processes that prevent and stop bleeding in case of blood vessel injuries.

Three Major Steps:

1. **Vascular Spasm**: Vasoconstriction at injury site
2. **Primary Hemostasis**:

- Platelet plug formation

3. **Secondary Hemostasis**:

- Coagulation cascade → Fibrin clot formation

End Result: Stable fibrin-platelet clot sealing the vessel

Platelets + Fibrin =
Clot formation

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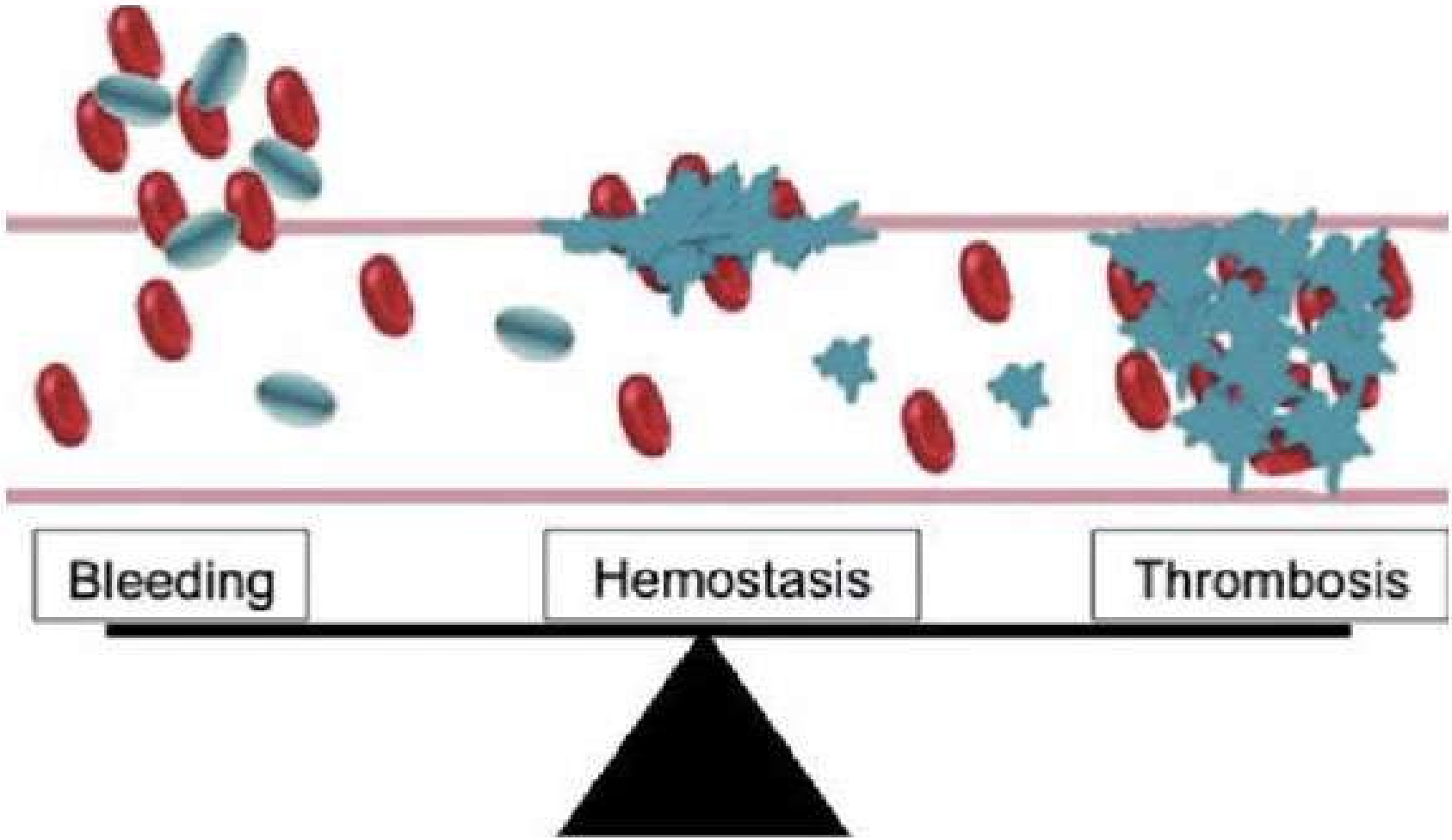

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Platelet Formation (Thrombopoiesis)

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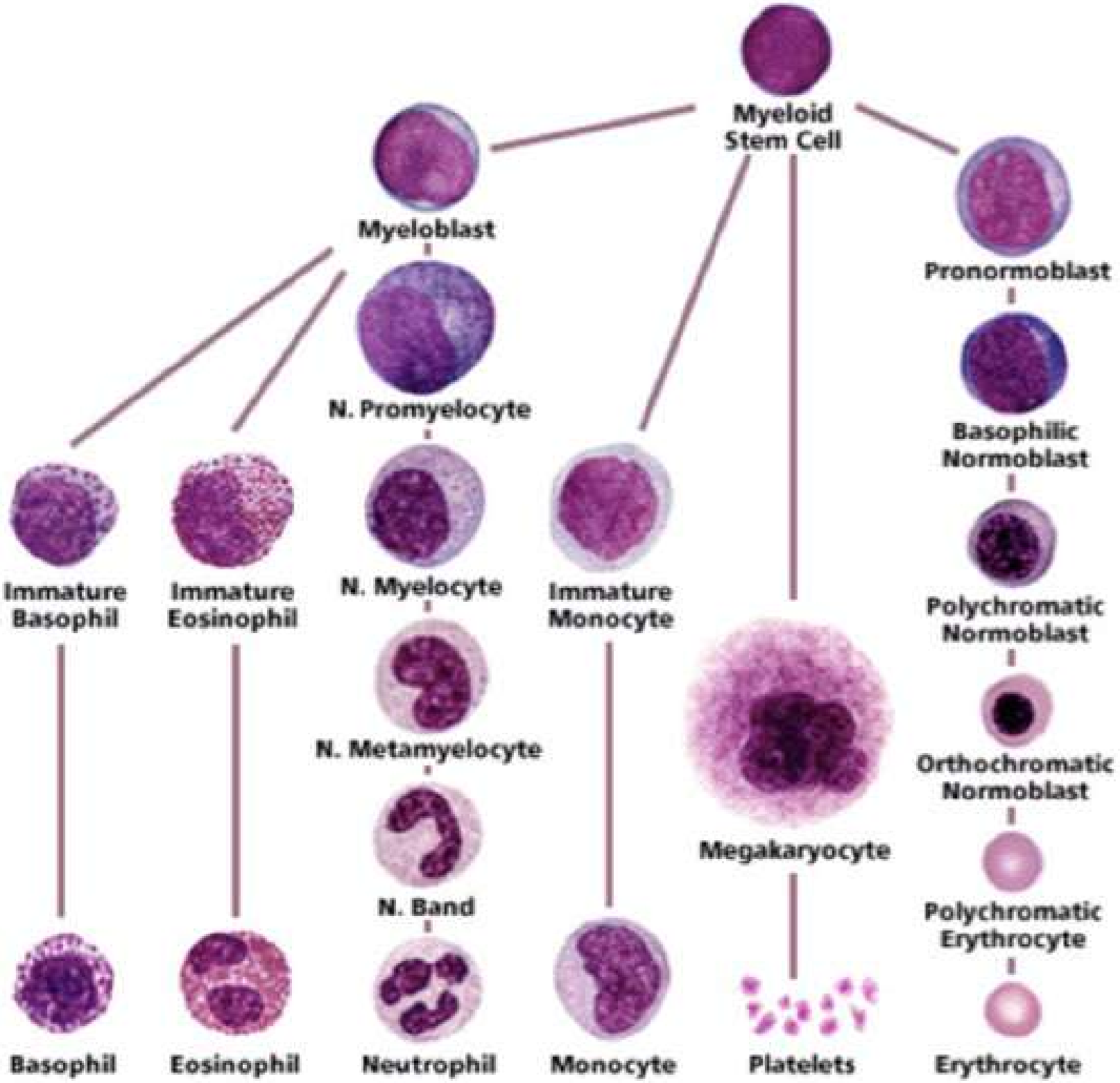

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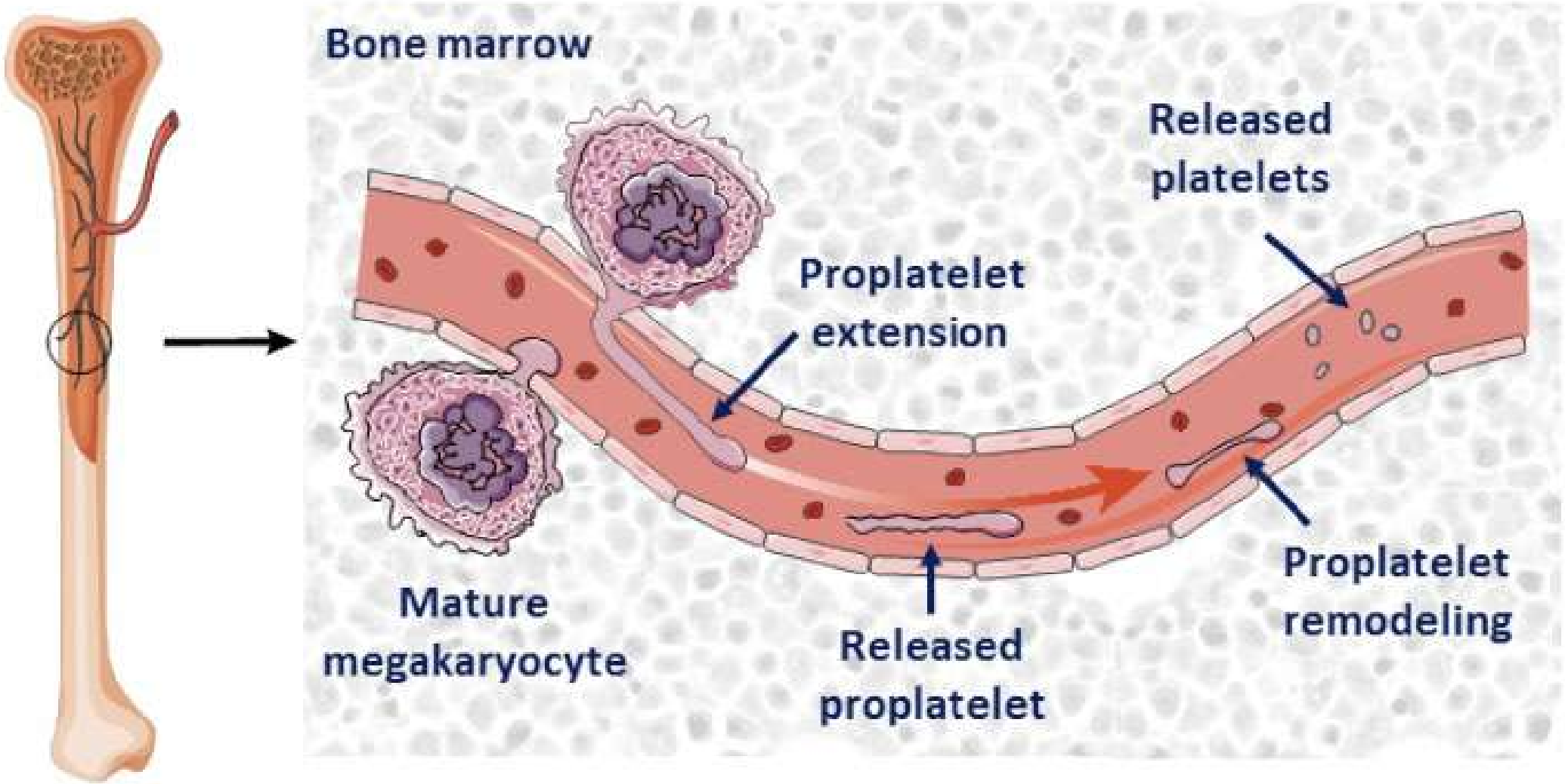
Thrombopoiesis:

Production of thrombocytes (platelets) by megakaryocytes in the bone marrow.



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• **Origin**: Hematopoietic stem cells → Myeloid lineage → Megakaryocytes

• **Regulation**:

• Thrombopoietin (TPO): Main regulator, produced by liver & kidneys

• **Process**:

• Megakaryocytes extend cytoplasmic processes (proplatelets) into bone marrow sinusoids

• Platelets bud off from proplatelets

• **Lifespan**: 7–10 days

• **Clearance**: By spleen and liver

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Functions of Platelets

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MBChB. MSc. PhD.

Primary Hemostasis:

- Adhesion to exposed collagen (via vWF)
- Activation and shape change
- Secretion of granules (ADP, thromboxane A2)
- Aggregation (GpIIb/IIIa binding fibrinogen)

Support for Coagulation:

- Provide phospholipid surface for coagulation cascade

Other Roles:

- Inflammation and immune modulation
- Angiogenesis and wound healing

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Coagulation Cascade

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Secondary Hemostasis:

Activation (a) of Coagulation cascade via (Extrinsic/Intrinsic) pathway = formation of fibrin

- **Intrinsic Pathway**: Initiated by contact activation
- **Extrinsic Pathway**: Triggered by tissue factor
- **Common Pathway**: Factor X → Xa → Thrombin → Fibrin
- Amplification and feedback mechanisms by thrombin

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MBChB. MSc. PhD.

Anticoagulants (Physiological)

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Endogenous Anticoagulants:

- Antithrombin III: Inhibits thrombin, Factor Xa
- Protein C & S: Inactivate Factors Va and VIIIa
- Tissue Factor Pathway Inhibitor (TFPI): Inhibits extrinsic pathway
- Fibrinolysis:
- Plasminogen → Plasmin (via tPA)
- Plasmin breaks down fibrin clot

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MBChB. MSc. PhD.

Clinical Anticoagulants

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- Heparin: Activates antithrombin III
- Warfarin: Inhibits Vitamin K-dependent factors (II, VII, IX, X)
- tPA (Alteplase): Clot dissolution in stroke, MI

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MBChB. MSc. PhD.

Bleeding Disorders

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MBChB. MSc. PhD.

- Normal platelets Count: 150,000–400,000/μL
- **Thrombocytopenia**: <150,000/μL
- Causes: bone marrow failure, autoimmune (ITP), infections, drugs
- **Thrombocytosis**: >400,000/μL
- Causes: myeloproliferative disorders, inflammation (reactive)

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Purpura

- Definition: Purple discolorations due to small vessel bleeding
- Types:
- Thrombocytopenic: e.g., ITP (immune thrombocytopenia purpura)
- Non-thrombocytopenic: e.g., vascular fragility (scurvy, steroids)

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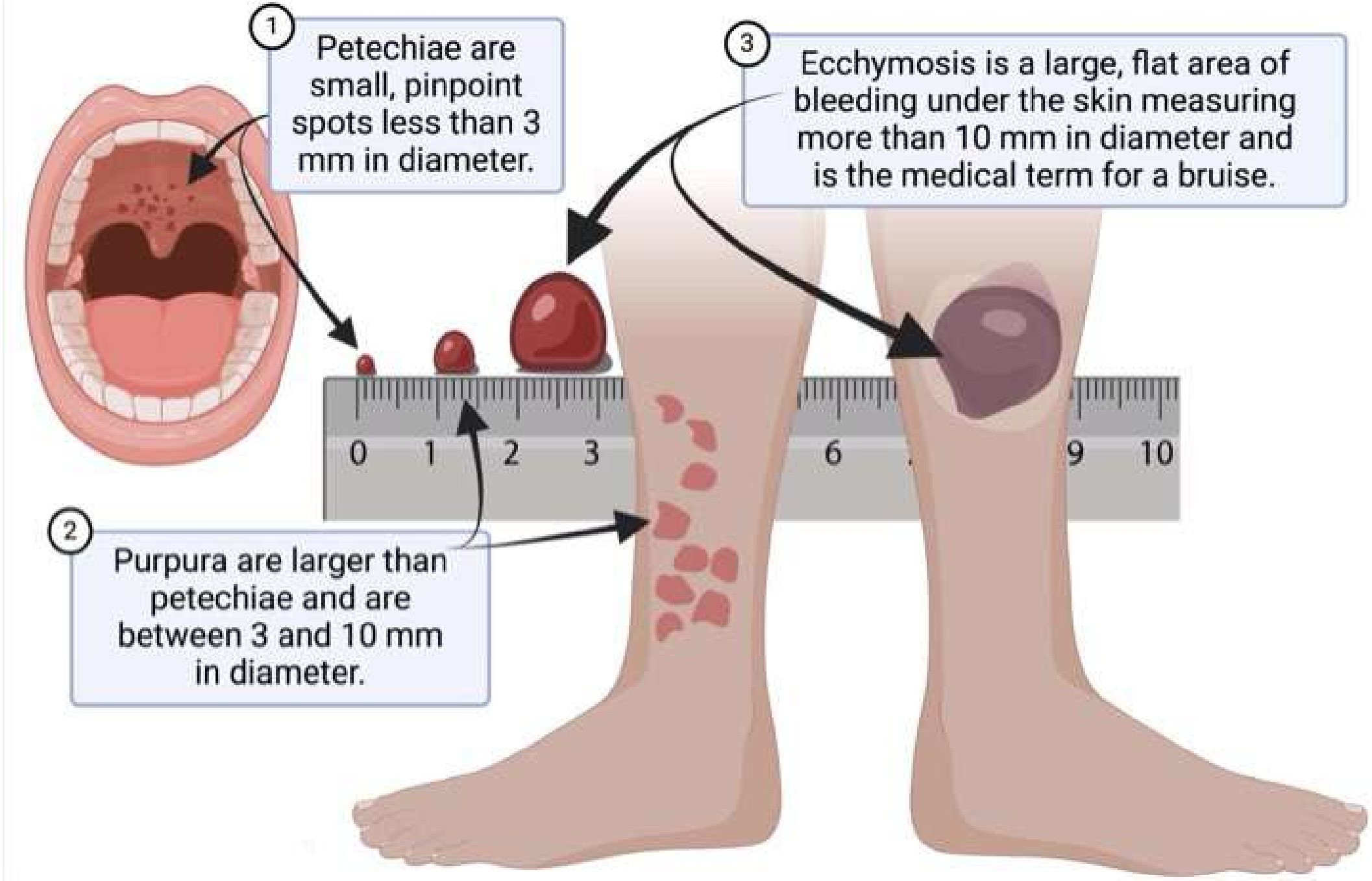

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Hemophilia

- Type A: Factor VIII deficiency
- Type B: Factor IX deficiency
- Inheritance: X-linked recessive

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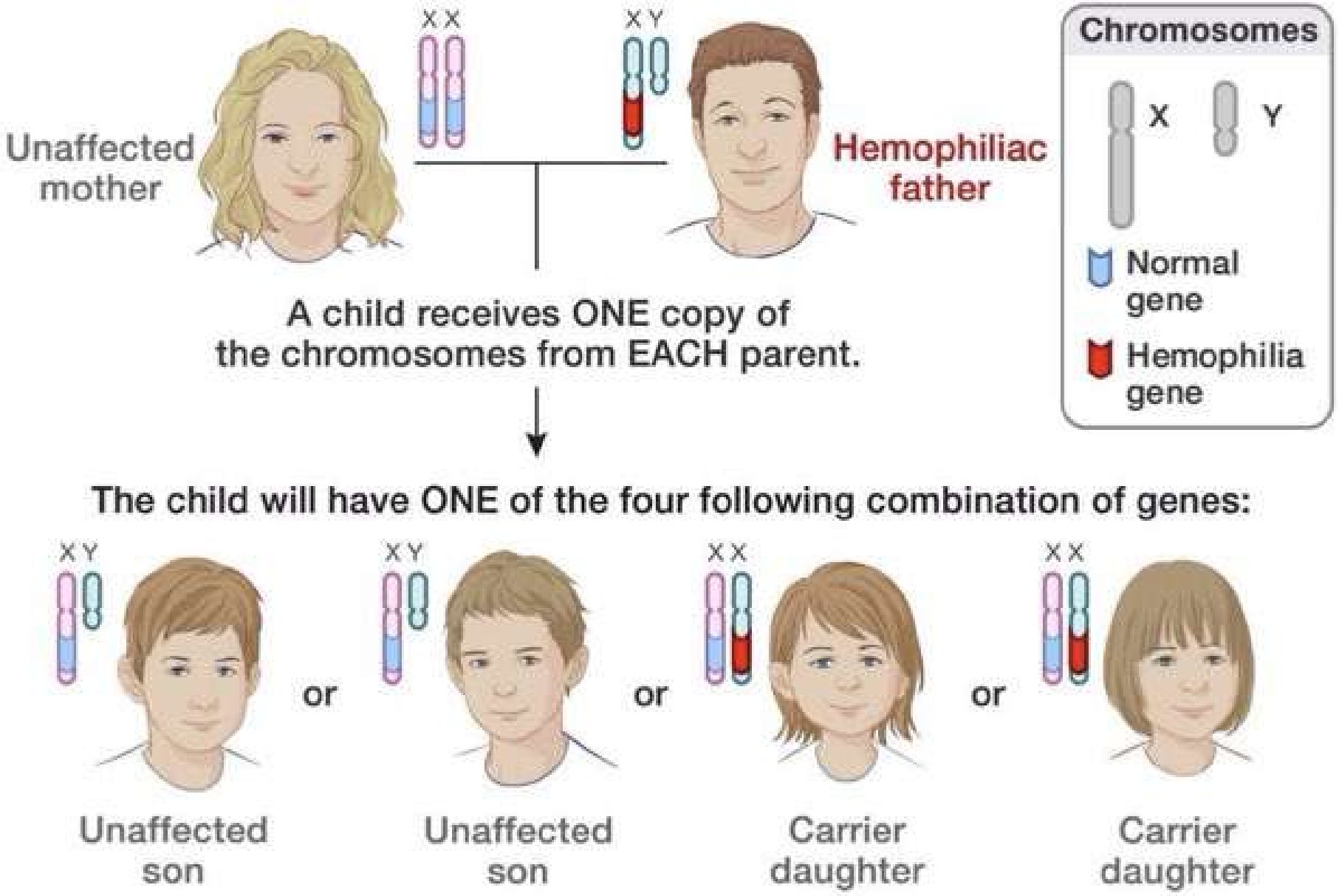

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Hemophilia

- Clinical Features:
- Deep tissue bleeds, hemarthroses
- Lab Findings: Increased aPTT, normal PT/platelets
- Treatment: Factor replacement therapy

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Summary

- Platelets are essential for primary hemostasis and coagulation support
- Hemostasis involves a cascade of tightly regulated events
- Bleeding disorders (hemophilia, purpura) arise from defects in coagulation or platelets
- Understanding mechanisms guides effective treatment

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