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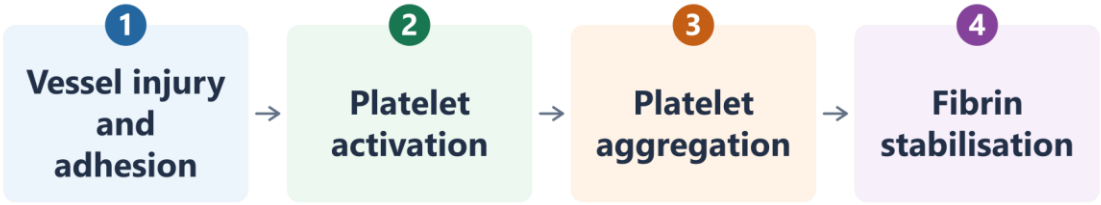
Pathology - Topic 20 - Hemorrhagic disorders

Normal Haemostasis

- **Haemostasis** stops blood loss from an injured vessel while keeping blood fluid elsewhere.

A Localised Response to Vessel Injury

- It depends on the vessel wall, platelets, coagulation proteins, natural anticoagulants and fibrinolysis.



1. Vascular Constriction and Platelet Adhesion

- A damaged vessel constricts, reducing local blood flow while a platelet plug begins to form.
- Exposed subendothelial material binds von Willebrand factor, which links collagen to platelet GPIb-containing receptors.
    - This adhesion is particularly important under high shear stress.

2. Platelet Activation and Aggregation

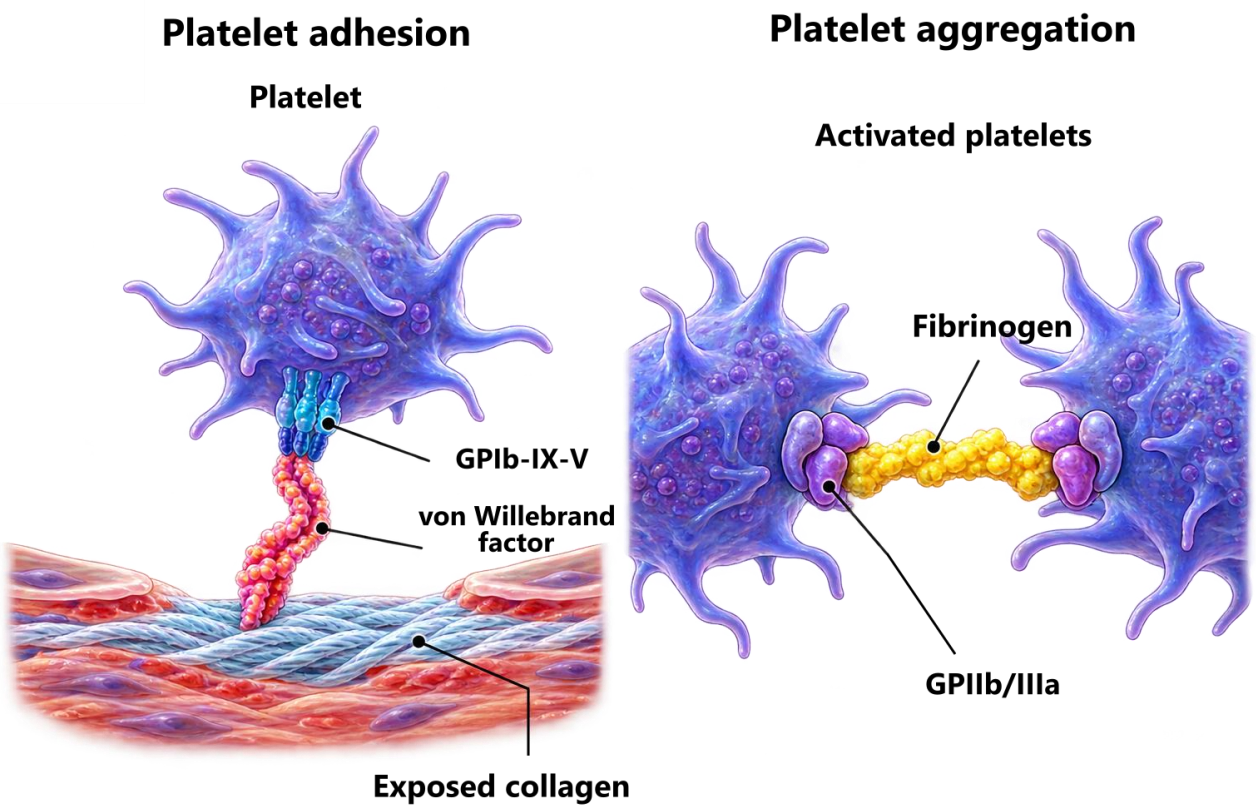
A. Platelet Activation

- Adherent platelets change shape and release substances that recruit and activate additional platelets.
- ADP and thromboxane A2 help amplify the response.

B. Platelet Aggregation

- Activated GPIIb/IIIa receptors bind fibrinogen, which bridges platelets and produces aggregation.
- The resulting primary platelet plug is initially fragile.

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Platelet adhesion and aggregation depend on different receptor–protein interactions

3. Coagulation and Fibrin Stabilisation

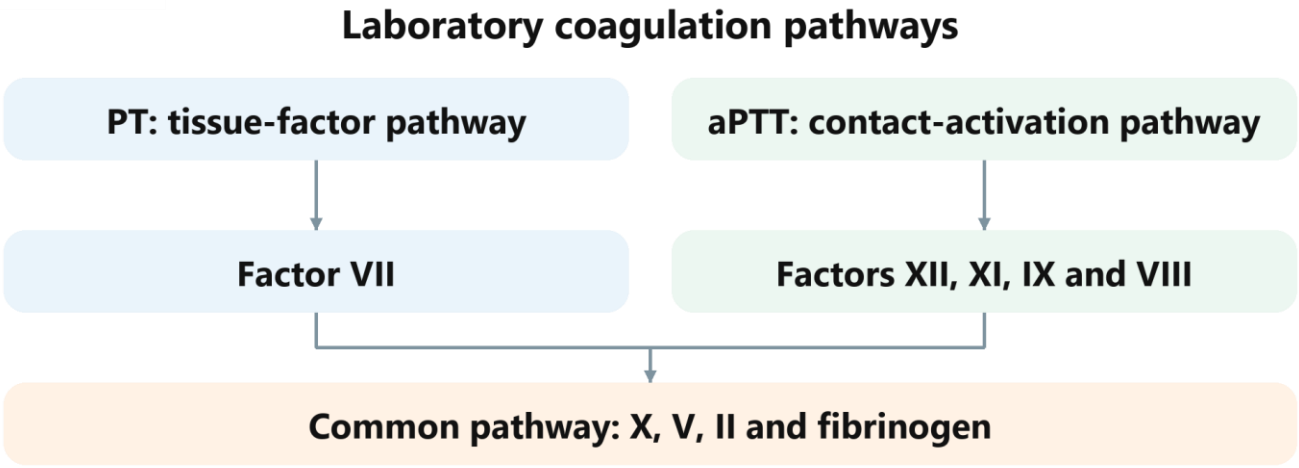
- Tissue factor exposure initiates coagulation reactions that generate factor Xa and then thrombin.
- Thrombin converts fibrinogen to fibrin and amplifies platelet and coagulation-factor activation.
- Factor XIII cross-links fibrin and stabilises the clot.
    - The traditional intrinsic and extrinsic pathways help explain laboratory tests, but haemostasis in the body occurs on interacting cell surfaces.

4. Restriction and Removal of the Clot

- Intact endothelium, antithrombin, the protein C system and tissue factor pathway inhibitor restrain coagulation.
- Plasmin breaks down fibrin as healing proceeds.
    - D-dimer is produced when cross-linked fibrin is degraded and therefore indicates fibrin formation and breakdown, not one specific disease.

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The Coagulation Pathways and Their Laboratory Tests



Laboratory grouping; factor XII deficiency need not cause bleeding

PT and aPTT assess different entry pathways and a shared common pathway

Screening Coagulation Tests

- The laboratory **PT** assesses the tissue-factor pathway and common pathway, including factors VII, X, V, II and fibrinogen.
- The **aPTT** assesses the contact-activation and common pathways, including factors XII, XI, IX, VIII, X, V, II and fibrinogen.
- A prolonged aPTT from factor XII deficiency need not indicate a clinical bleeding tendency.

Natural Anticoagulants and Fibrinolysis

- Antithrombin inhibits thrombin and factor Xa, while activated protein C with protein S inactivates factors Va and VIIIa.
- Tissue plasminogen activator promotes plasmin formation on fibrin and contributes to clot removal.

Clinical Patterns of Bleeding

- Platelet or vessel-wall disorders commonly cause petechiae, purpura and bleeding from skin or mucosal surfaces.
    - Nosebleeds, gum bleeding and heavy menstrual bleeding are characteristic examples.
- Coagulation-factor defects more often cause deep muscle haematomas, joint bleeding and delayed bleeding after injury.
    - These patterns overlap, so history and examination direct rather than replace testing.
- Ask about childhood bleeding, surgery, dental extraction, childbirth, medicines and family history.
    - A negative family history does not exclude a new mutation or an acquired bleeding disorder.

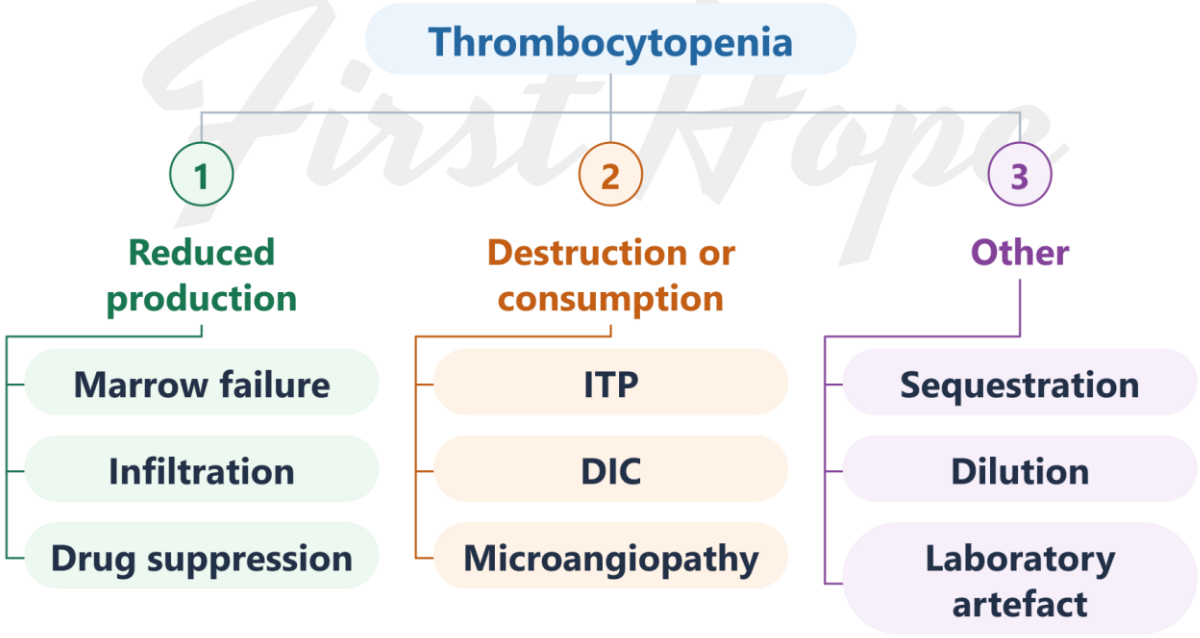
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Vessel-Wall Disorders

- Vessel-wall disorders cause bleeding through vascular injury or fragility rather than a primary platelet or coagulation-factor defect.
- Small-vessel inflammation, fragile connective tissue and nutritional defects can cause bleeding despite a normal platelet count.
- Vitamin C deficiency impairs collagen support and can produce perifollicular bleeding, gum changes and poor wound healing.
- Steroid-related or age-related skin fragility can cause easy bruising, while inherited connective-tissue disorders can increase vessel fragility.
- Hereditary haemorrhagic telangiectasia produces abnormal vascular connections and recurrent bleeding.
    - Normal screening clotting times do not exclude a vascular cause.

Thrombocytopenia

- Thrombocytopenia is a platelet count below the appropriate reference range.



Mechanisms of a Reduced Platelet Count

1. Reduced Production

- Marrow failure, leukaemia, infiltration, severe nutritional deficiency and cytotoxic medicines can reduce platelet production.
    - Other blood-cell lines may also be low when the marrow is broadly affected.

2. Increased Destruction or Consumption

- Immune thrombocytopenia, drug-dependent antibodies, DIC and thrombotic microangiopathies can lower the count through different mechanisms.

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- A low platelet count therefore does not mean that every patient has immune thrombocytopenia.

3. Sequestration, Dilution and Artefact

Sequestration and Dilution

- An enlarged spleen can sequester platelets, while massive fluid or red-cell replacement can dilute them.

Pseudothrombocytopenia

- EDTA-associated clumping can produce **pseudothrombocytopenia** on an automated analyser.
- Review the film and obtain an appropriate repeat specimen before diagnosing disease from a clumped sample.

Immune Thrombocytopenia

- **ITP** is an immune disorder with increased platelet destruction and often impaired platelet production.

Platelet Destruction and Clinical Features

- Antibodies and immune cells affect platelet glycoproteins and megakaryocytes, with splenic removal playing an important role.
- The usual pattern is otherwise unexplained isolated thrombocytopenia, often with petechiae, bruising or mucosal bleeding.
- ITP may be primary or secondary to autoimmune disease, selected infections or lymphoid disorders.
  - Children may develop an acute post-infectious pattern, while adult disease can persist.

Diagnostic Threshold and Duration Categories

- The conventional diagnostic threshold for ITP is a platelet count **below 100 × 10^9/L**, after alternative causes of thrombocytopenia have been excluded.

1. Newly Diagnosed ITP

- Newly diagnosed ITP has been present for **less than three months**.

2. Persistent ITP

- Persistent ITP lasts **three to twelve months** from diagnosis.

3. Chronic ITP

- Chronic ITP continues for **more than twelve months**.

Laboratory Findings and Exclusion of Mimics

- The platelet count is low, and the smear may show larger young platelets.

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