Therapeutic Approaches for Platelet Disorders

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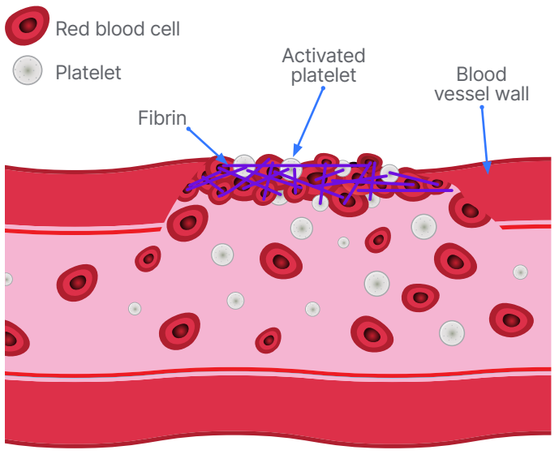
Introduction

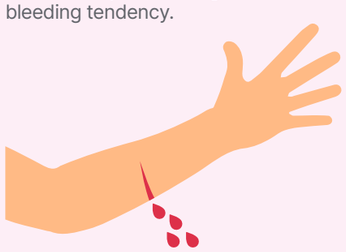
- Blood consists of many types of cells, such as white blood cells, red blood cells, and platelets.
- When a blood vessel breaks, platelets will localise to the site of injury and trigger a coagulation cascade. During this, an enzyme, thrombin, cleaves fibrinogen into fibrin monomers, which then polymerise together to form the blood clot.



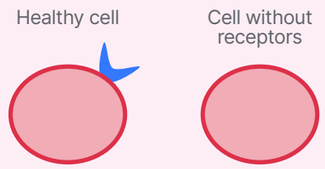
- Platelet disorders refer to either the surplus, deficiency, or dysfunction of platelets. Symptoms can include excessive bruising, prolonged bleeding, fatigue, chest pain, and vomiting.

Types of Platelet Disorders[1]

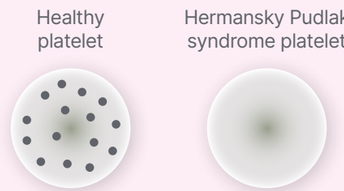
Bernard-Soulier disease: characterised by dysfunction of the glycoprotein Ib-IX-V complex, leading to increased bleeding tendency.



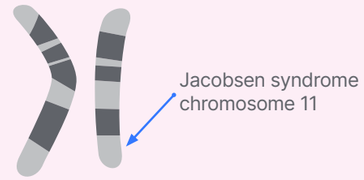
Glanzmann's thrombasthenia: an inherited platelet disorder caused by a deficiency or dysfunction of the glycoprotein IIb/IIIa receptor, resulting in impaired platelet aggregation and increased bleeding tendency.



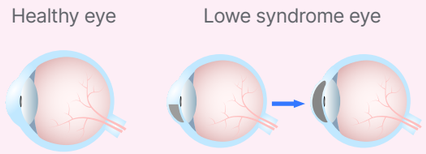
Hermansky Pudlak syndrome: characterised by oculocutaneous albinism, and other systemic manifestations, caused by defects in the biogenesis of platelet granules and lysosome-related organelles.



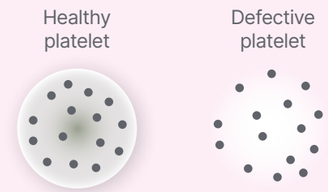
Jacobsen syndrome: a rare chromosomal disorder characterised by multiple physical and developmental abnormalities, including heart defects, intellectual disability, and thrombocytopenia, caused by a deletion in the long arm of chromosome 11.



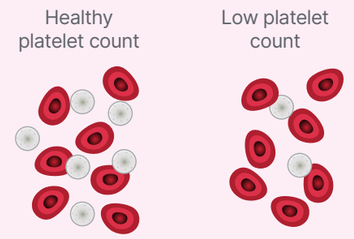
Lowe syndrome: a rare X-linked genetic disorder characterised by congenital cataracts, intellectual disability, and kidney abnormalities, which can include thrombocytopenia, caused by mutations in the *OCRL* gene.



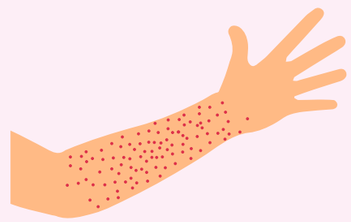
Platelet release and storage pool defects: a group of disorders characterised by abnormal storage or release of platelet granules, leading to impaired platelet function and increased bleeding tendency.



TAR syndrome: a rare congenital disorder characterised by thrombocytopenia, which is low platelet count, and bilateral absence or hypoplasia of the radius bone in the forearm.



TTP: characterised by microvascular thrombosis, resulting in thrombocytopenia, haemolytic anaemia, and organ damage, often caused by a deficiency of the ADAMTS13 enzyme.

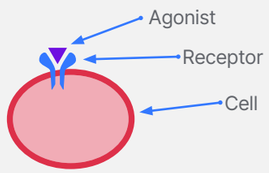


Examples of Drugs: FDA Approval Timeline[4-5]

- **1986** — Tranexamic acid (antifibrinolytic agent)
- **1991** — Ticolopidine (antiplatelet agent)
- **1994** — Abciximab (antiplatelet agent)
- **1997** — Clopidiogrel (antiplatelet agent)
- **1998** — Eptifibatide (anti-coagulant agent)
- **1998** — Tirofiban (antiplatelet agent)
- **2008** — Romiplostim (TPO-RA)
- **2009** — Prasugrel (antiplatelet agent)

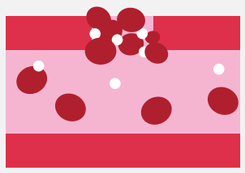
Innovative Therapies[2,3]

TPO-RA stimulate the production of platelets in the bone marrow and are used to treat thrombocytopenia, including ITP and myelodysplastic syndromes.

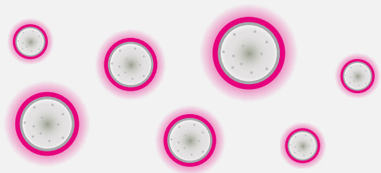


Result: increased platelet production

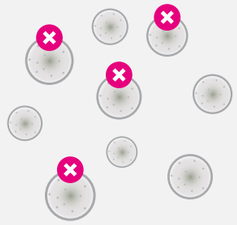
Antifibrinolytic agents, such as tranexamic acid, help reduce bleeding by stabilising blood clots and preventing their breakdown.



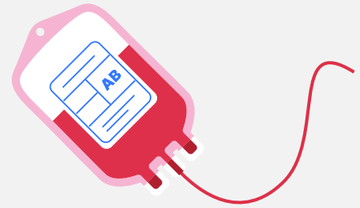
Immunosuppressive therapy may be used in cases of immune-mediated platelet disorders like ITP; for which medications that suppress the immune system, such as corticosteroids, immunoglobulins, or immunosuppressants, may be prescribed to reduce platelet destruction.



Anticoagulants or antiplatelet agents are used to prevent blood clots in conditions associated with platelet hyperactivity or increased thrombotic risk.



Platelet transfusions may be necessary to increase the platelet count quickly in cases of severe thrombocytopenia or active bleeding. However, transfusions are typically reserved for emergencies or when other treatments are ineffective due to potential risks and complications associated with transfusions.



Abbreviations:

ITP: immune thrombocytopenic purpura; TAR: thrombocytopenia with absent radius; TPO-RA: thrombopoietin receptor agonists; TTP: thrombotic thrombocytopenic purpura.

References

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