

Review Article

Platelets and Preservation: An Update Review of Challenges for a Resource-Limited Setting

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Abstract

Platelets are small anucleate cytoplasmic fragments derived from bone marrow megakaryocytes under the influence of thrombopoietin. They play essential roles in primary haemostasis by adhering, activating, and aggregating at sites of vascular injury while providing a phospholipid surface for secondary coagulation. Beyond haemostasis, platelets contribute to inflammation, immunity, angiogenesis, and tissue repair through the release of bioactive mediators. Platelet transfusion is indicated for severe thrombocytopenia, platelet dysfunction, and bleeding disorders. Platelet concentrates, prepared from whole blood or apheresis, require stringent storage conditions to maintain viability. However, their preparation and preservation remain challenging in resource-limited settings because of inadequate infrastructure, equipment, funding, and quality assurance systems, emphasizing the need for improved transfusion services.

1. Introduction

Platelets, also known as thrombocytes, are small, anucleate cytoplasmic fragments derived from bone marrow megakaryocytes and circulate in the blood for approximately 7–10 days [1–4]. They are indispensable for primary haemostasis, responding to vascular injury through adhesion, activation, secretion, and aggregation to form a platelet plug [5–8]. In addition, platelets support secondary haemostasis by providing a phospholipid surface for the assembly of coagulation complexes, thrombin generation, and fibrin formation [9–12]. Their biological activities extend beyond haemostasis to include inflammation, innate immunity, angiogenesis, wound healing, vascular integrity, and tissue repair [13–17]. The normal adult platelet count is generally $150\text{--}450 \times 10^9/\text{L}$, although laboratory reference intervals may vary [1, 2, 18]. Platelet abnormalities may be quantitative, involving thrombocytopenia or thrombocytosis, or qualitative, involving impaired adhesion, secretion, activation, or aggregation [5, 19–21]. These abnormalities can produce clinically significant bleeding or contribute to thrombosis, depending on their underlying mechanisms and clinical context [6, 9, 22]. Platelet assessment is therefore essential in haematology, clinical laboratory science, surgery, oncology, and transfusion medicine [1, 2, 23]. Platelet transfusion provides temporary haemostatic support for selected patients with severe thrombocytopenia or clinically significant platelet dysfunction [24–27]. However, transfusion decisions must balance the anticipated clinical benefit against risks such as bacterial contamination, febrile and allergic reactions, alloimmunization, and transfusion-associated circulatory complications [24, 28–30]. The preparation, storage, and distribution of platelet concentrates consequently require rigorous quality management, validated procedures, and appropriate clinical indications [28, 31, 32].

2. Synthesis, Structure and Functions

Platelet production, or thrombopoiesis, begins with haematopoietic stem cells that differentiate through progenitor stages into megakaryocytes within the bone marrow [3, 4, 33]. Thrombopoietin, produced predominantly by the liver, is the principal regulator of megakaryocyte development and platelet production [34, 35]. Its interaction with the c-Mpl receptor activates signalling pathways that support megakaryocyte proliferation, maturation, and platelet release [34–36]. Other cytokines and growth factors, including interleukin-6 and interleukin-11, can influence thrombopoiesis under particular physiological and pathological conditions [35, 37]. During maturation, megakaryocytes undergo endomitosis, resulting in polyploid cells with extensive cytoplasm and a complex internal membrane system [3, 4, 33]. Mature megakaryocytes develop proplatelet extensions that project into bone marrow sinusoids, where platelet-sized fragments are released into the circulation [3, 33, 38]. Cytoskeletal reorganization, microtubule assembly, membrane remodelling, and intracellular transport contribute to this process [38–40]. Platelets may also be released from megakaryocytes in the pulmonary circulation, although the relative contribution of this mechanism to normal human platelet production remains an area of investigation [39, 41]. Circulating platelets are approximately 2–3 μm in diameter and usually have a discoid shape maintained by their cytoskeleton [1, 2, 42]. Although they lack a nucleus, platelets contain mitochondria, messenger RNA, ribosomes, signalling proteins, membrane receptors, and secretory organelles that enable them to respond rapidly to vascular injury [2, 42, 43]. Their plasma membrane contains glycoprotein receptors, including the glycoprotein Ib-IX-V complex and integrin $\alpha\text{IIb}\beta_3$, also known as GPIIb/IIIa [5, 6, 44]. These receptors have complementary roles in platelet adhesion, activation, and aggregation [6, 44, 45]. The GPIb-IX-V complex mediates platelet attachment to von Willebrand factor, particularly under conditions of high shear stress, while glycoprotein VI and integrin $\alpha_2\beta_1$ contribute to platelet interactions with exposed collagen [6, 44, 46]. Following adhesion, intracellular signalling activates platelets and promotes the release of granule contents and the expression of activated $\alpha\text{IIb}\beta_3$ integrins [5, 6, 45]. Fibrinogen and other adhesive ligands then bridge adjacent platelets, facilitating aggregation and formation of the primary haemostatic plug [5, 9, 45]. Platelets contain an open canalicular system that facilitates membrane exchange and secretion, as well as a dense tubular system involved in calcium regulation and signalling [2, 42, 47]. Their α -granules store adhesive proteins, growth factors, chemokines, and inflammatory mediators; dense granules contain adenosine diphosphate, calcium, and serotonin; and lysosomal granules contain hydrolytic enzymes [2, 47, 48]. These organelles support platelet recruitment, secretion, clot stabilization, and communication with surrounding cells [47–49]. Platelet activation is initiated by several agonists, including collagen, thrombin, thromboxane A_2 , and adenosine diphosphate [5, 9, 50]. Receptor-mediated signalling increases intracellular calcium, stimulates granule secretion, promotes shape change, and activates integrin $\alpha\text{IIb}\beta_3$ [5, 50, 51]. Activated platelets also expose phosphatidylserine on their outer membrane, providing a surface for the assembly of coagulation complexes and facilitating thrombin generation [9–12, 51]. Thrombin converts fibrinogen to fibrin, which reinforces the platelet plug and produces a more stable haemostatic clot [9–12]. Platelets also participate in clot retraction through interactions between their cytoskeleton and the fibrin network [9, 42, 52]. Following haemostasis, platelet-derived growth factors and other mediators influence endothelial repair, angiogenesis, and tissue regeneration [14–16, 48]. However, excessive platelet activation can promote arterial thrombosis and contribute to the pathogenesis of myocardial infarction, ischaemic stroke, and peripheral arterial disease [22, 53, 54]. Beyond haemostasis, platelets interact with neutrophils, monocytes, lymphocytes, endothelial cells, and microorganisms [13, 17, 55]. They release cytokines and chemokines, express immune-related receptors, and contribute to leukocyte recruitment and inflammatory signalling [13, 17, 55, 56]. Platelets can support host defence against certain pathogens, but platelet-immune interactions may also aggravate inflammatory injury in sepsis and other disorders [13, 17, 56]. Their physiological importance therefore reflects a balance between haemostasis, immune surveillance, inflammation, and vascular homeostasis [13–17]. Platelet lifespan is regulated by production, survival, and clearance mechanisms involving the liver and spleen [1, 2, 57]. Desialylation and recognition by hepatic clearance receptors contribute to the removal of aged platelets, while immune-mediated destruction can accelerate platelet clearance in pathological conditions [57, 58]. Understanding these mechanisms is important when interpreting thrombocytopenia, evaluating platelet turnover, and determining the likely response to platelet transfusion [19, 20, 57].

3. Indications for Platelet Transfusion

Platelet transfusion is used to prevent or treat bleeding in patients with severe thrombocytopenia, clinically significant platelet dysfunction, or selected conditions associated with impaired primary haemostasis [24–27, 59]. Common indications include chemotherapy-induced thrombocytopenia, acute leukaemia, aplastic anaemia, myelodysplastic syndromes, bone marrow failure, and selected cases of disseminated intravascular coagulation [24–27, 59]. The decision to transfuse should consider the platelet count, bleeding severity, underlying diagnosis, planned procedures, concurrent coagulation abnormalities, and overall clinical condition [24–27, 60]. Prophylactic platelet transfusion is commonly recommended when the platelet count is below $10 \times 10^9/\text{L}$ in clinically stable patients with hypoproliferative thrombocytopenia [24–27, 59]. This threshold is intended to reduce the risk of spontaneous bleeding in appropriately selected patients and should not be applied indiscriminately to every cause of thrombocytopenia [24, 25, 59]. Clinical instability, fever, active bleeding, sepsis, and other factors may alter the assessment of bleeding risk and the need for transfusion [25–27, 60]. For invasive procedures, the appropriate platelet threshold depends on the procedure, anatomical site, urgency, and associated bleeding risk [24–27, 60]. Major surgery and procedures involving critical anatomical sites may require higher platelet counts than lower-risk procedures [24, 26, 60]. The latest international recommendations also emphasize procedure-specific thresholds and avoidance of unnecessary transfusions when the expected clinical benefit is limited [59, 60]. Clinical teams should therefore use current national or institutional guidelines rather than rely on a single universal platelet threshold [24, 27, 59]. Therapeutic platelet transfusion is indicated for clinically significant bleeding when thrombocytopenia or platelet dysfunction contributes to impaired haemostasis [24–27]. In these situations, the urgency, dose, and monitoring strategy depend on bleeding severity, anatomical location, laboratory findings, and response to treatment [25–27, 59]. Platelet transfusion may also be required in selected patients with inherited platelet function disorders undergoing surgery or experiencing major haemorrhage [24, 26, 61]. Some conditions require special consideration. In immune thrombocytopenia, transfused platelets may be rapidly destroyed by circulating antibodies; transfusion is therefore generally reserved for life-threatening bleeding and used alongside disease-directed treatment [26, 27, 61]. In thrombotic thrombocytopenic purpura, platelet transfusion is generally avoided unless life-threatening bleeding or another exceptional indication justifies its use because the disorder involves pathological platelet-rich microvascular thrombosis [26, 61, 62]. In disseminated intravascular coagulation, transfusion decisions should be guided by bleeding, procedural requirements, platelet counts, and the underlying cause of the

coagulopathy [24–27, 62]. Platelet transfusion is not without risk. Adverse effects include febrile non-haemolytic and allergic reactions, bacterial sepsis, transfusion-associated circulatory overload, and alloimmunization against platelet or human leukocyte antigens [28–30, 63]. Repeated transfusions may result in platelet refractoriness, characterized by inadequate post-transfusion platelet count increments [63, 64]. This may result from immune causes, such as HLA antibodies, or non-immune causes, including fever, infection, bleeding, disseminated intravascular coagulation, and splenic sequestration [63, 64]. Appropriate patient assessment, component selection, and post-transfusion monitoring are therefore essential [24, 28, 63].

4. Platelet Concentrate

Platelet concentrates are blood components prepared from whole-blood donations or collected by apheresis for the prevention and treatment of bleeding caused by thrombocytopenia or platelet dysfunction [24, 28, 31]. Whole-blood-derived platelet concentrates may be prepared using platelet-rich plasma or buffy-coat methods, depending on the blood service's equipment and processing procedures [28, 31, 65]. Apheresis collection uses specialized equipment to separate platelets from a donor's blood and return the remaining components to the donor [28, 31, 65]. Apheresis platelets typically provide an adult therapeutic dose from a single donor, whereas equivalent doses of whole-blood-derived platelets may require pooling components from several donations [28, 31, 65]. Product selection depends on clinical need, availability, donor exposure considerations, compatibility, and local blood-service capacity [24, 28, 31]. A standard adult dose generally increases the platelet count, but the magnitude of the increment varies with the platelet dose, recipient blood volume, ongoing bleeding, infection, immune-mediated destruction, and splenic sequestration [24, 25, 64]. Platelet concentrates are generally stored at 20–24°C with continuous gentle agitation under validated blood-bank conditions [28, 31, 66]. Unlike red blood cells, platelets are traditionally stored at room temperature because refrigeration can alter platelet membrane characteristics and reduce their post-transfusion circulation time [66, 67]. However, room-temperature storage creates conditions that can support bacterial growth, making bacterial risk control a central component of platelet safety [28, 30, 66]. During storage, platelets undergo a series of biochemical, structural, and functional changes collectively known as the platelet storage lesion [66–68]. These changes may include metabolic depletion, accumulation of lactate, reduced pH, membrane alterations, platelet activation, and changes in responsiveness to agonists [67, 68]. The extent of these changes is influenced by storage temperature, storage medium, gas exchange, agitation, collection method, and duration of storage [66–68]. Consequently, validated storage conditions and careful component handling are essential for maintaining platelet quality [28, 66–68]. The allowable shelf life of platelet concentrates depends on the collection system, storage container, bacterial risk-control strategy, and applicable regulatory standards [28, 30, 66]. Historically, many platelet components have been stored for up to five days, while some validated systems permit storage for longer periods [28, 30, 66]. The permitted expiry period should always follow the blood service's validated procedures and national regulations rather than be assumed to be identical across all products [28, 30, 66]. ABO-identical or ABO-compatible platelet components are preferred when feasible because ABO compatibility can influence platelet count increments and may reduce certain plasma-mediated risks [24, 28, 69]. RhD considerations are also relevant because platelet components may contain residual red blood cells, potentially exposing RhD-negative recipients to RhD-positive red-cell antigens [28, 69]. Leucoreduction can reduce donor leukocyte exposure and lower the risk of certain transfusion complications, including HLA alloimmunization and febrile non-haemolytic reactions [28, 63, 69]. Irradiation is indicated for selected patients and clinical circumstances to prevent transfusion-associated graft-versus-host disease; it is not required universally for every platelet transfusion [28, 69]. Bacterial screening, pathogen-reduction technologies where available, appropriate storage practices, and haemovigilance provide additional safeguards against transfusion-associated complications [28–30, 63]. The choice of component should reflect the patient's clinical needs and the safety systems available within the blood service [24, 28, 69].

5. Preparation and Preservation Challenges

The preparation and preservation of platelet concentrates require reliable donor recruitment, blood collection, component processing, laboratory testing, storage, and distribution systems [28, 31, 32, 70]. In resource-limited settings, these requirements may be difficult to sustain because of inadequate infrastructure, limited access to apheresis equipment, unreliable electricity, insufficient temperature-controlled storage, and shortages of trained personnel [32, 70]. These constraints can restrict platelet production and availability, particularly in facilities with limited component-separation capacity [32, 70]. The relatively short shelf life of platelet concentrates increases the risk of product wastage when demand forecasting, inventory management, and distribution systems are inadequate [28, 30, 66]. Conversely, shortages can delay transfusion for patients with severe thrombocytopenia, active bleeding, or urgent procedural requirements [32, 70]. These competing challenges make effective inventory management, regional coordination, and communication between clinical units and blood banks important [28, 32, 70]. Room-temperature storage creates a particular bacterial safety challenge because contaminated components may support bacterial proliferation before transfusion [28–30, 66]. Contamination may originate from donor skin flora, the collection process, or other points in component preparation and handling [28–30]. Appropriate donor assessment, skin disinfection, aseptic collection, validated processing, bacterial risk-control procedures, and careful storage management are therefore essential [28–30, 66]. Pathogen-reduction technologies may provide an additional safeguard where available, although their implementation requires appropriate infrastructure, training, and financial investment [28–30]. Financial constraints may limit the procurement and maintenance of platelet agitators, temperature-monitoring devices, component-processing equipment, and pathogen-reduction systems [32, 70]. Weak supply chains, inadequate quality management, fragmented blood services, and insufficient investment in donor recruitment may further compromise availability and safety [32, 70]. The World Health Organization emphasizes the importance of coordinated national blood systems, quality-assured screening, appropriate component processing, and rational clinical use of blood products [32, 70]. Improving platelet availability requires sustainable funding, voluntary non-remunerated donor recruitment, appropriate component-processing capacity, and robust quality assurance [32, 70]. Regional collaboration and improved inventory management can help match supply to clinical demand and reduce avoidable wastage [28, 32, 70]. Where feasible, validated bacterial risk-reduction measures and pathogen-reduction technologies may provide additional safeguards [28–30]. Continued training of laboratory and transfusion personnel, implementation of clear clinical guidelines, and monitoring of transfusion outcomes are also essential for improving platelet use and patient safety [28, 32, 63, 70].

6. Conclusion

Platelets are indispensable to haemostasis and also contribute to immune regulation, inflammation, vascular integrity, and tissue repair [1–17]. Their production depends on regulated megakaryocyte development, while their structural organization supports adhesion, activation, secretion, aggregation, and coagulation [3–12, 33–52]. Platelet transfusion remains an important intervention for selected patients with thrombocytopenia or platelet dysfunction, but its use should be guided by clinical context, bleeding risk, and current evidence-based recommendations [24–27, 59–64]. Effective component preparation, storage, and quality assurance are necessary to preserve platelet function and minimize transfusion-associated risks [28–31, 63, 66–69]. Strengthening blood-service infrastructure, donor recruitment, staff training, and quality management is particularly important in resource-limited settings to improve the safety, availability, and appropriate use of platelet concentrates [32, 70].

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