Platelet transfusions constitute approximately 19% of transfusions to pediatric patients in children’s hospitals [1]. Outside the neonatal period, most platelets that are transfused to pediatric patients are given to those who are thrombocytopenic secondary to malignancy and associated therapy and/or hematopoietic progenitor cell transplant, or to those with significant bleeding associated with surgery, especially cardiac surgery. Indications for platelet transfusion, doses, and other practices for children largely mimic adult platelet transfusion protocols because there are few pediatric-specific studies in this area. Pediatric platelet transfusion practices would benefit from focused pediatric research. The appropriate indications and doses for platelet transfusions in oncology, hematopoietic progenitor cell transplant, and cardiac surgery patients need to be determined.
individual's platelet count was greater than 20 000/μL [8-10]. More recently, this transfusion trigger has been decreased to less than 10 000/μL. Children, adolescents, and young adults were included in the initial patient groups from which these transfusion guidelines were developed, but most guidelines pertaining to current platelet transfusion practices were informed by adult studies. The justification for using similar guidelines for both children and adults is based on the similarity between children and adults in “normal” platelet count. However, platelet function may not be identical. When surface expression of physiologically important adhesion receptors is analyzed by flow cytometry, children demonstrate decreased expression of glycoprotein Iib/IIa (integrin αIIbβ3) on their platelets as of age 2 years, and less α3 is expressed on platelets in children up to age 15 years [11]. In addition, platelets from children of all ages demonstrate a decreased ability to change the conformation of αIIbβ3 to its “activated” form critical for binding of fibrinogen, and exhibit less efficient internalization of glycoprotein Iib/IX upon activation. [11] However, despite these differences in surface receptor expression in platelets noted in children, functional studies (ie, ability to respond to platelet agonists in a flow/shear environment) reveal no differences between platelets from adults and children beyond the newborn period [12,13]. At least 1 analysis has demonstrated an increased incidence of bleeding in pediatric oncology patients as compared with adult patients across a wide spectrum of platelet counts [14]. Consequently, the authors hypothesized that other non–platelet-related factors were the cause for this observed difference.

This review focuses on platelet transfusions in children. Neonatal platelet transfusions are discussed elsewhere in this edition. Consistent with the literature, this review distinguishes prophylactic platelet transfusions administered to prevent bleeding from therapeutic platelet transfusions given to control and stop bleeding.

Current Practice

Use of Prophylactic Transfusions

As early as the 1960s, studies supported the efficacy of prophylactic platelet transfusions administered to patients receiving cancer chemotherapy [8-10,15]. The patients in these studies included children and adolescents in addition to young adults. A platelet threshold of less than 20 000/μL was arbitrarily set as the transfusion trigger based on an observation that serious bleeding rarely occurred with a platelet count above this value. Subsequent studies in adults found safety in using a lower platelet count of 10 000/μL to trigger a platelet transfusion [16]. In aggregate, these studies demonstrated a reduction in hemorrhagic morbidity. Because the older studies that included children often relied on historic controls and many patients received aspirin as an antipyretic, the quality and applicability of these studies to current pediatric practice is questionable.

More recent studies have found that prophylactic platelet transfusions administered for a platelet count less than 10 × 10^9/L reduced the rate of hemorrhage in adult patients who have undergone HPC transplants or therapy for acute myeloid leukemia compared with no prophylactic transfusions [17,18]. Stanworth et al [17] found World Health Organization (WHO) grade 2 or higher bleeding occurring on 50% of the days for patients who did not receive prophylactic transfusions vs 43% of the days for patients who received prophylactic transfusions. Wandt et al [18] had similar findings, with 42% of patients developing WHO grade 2 or higher bleeding per treatment cycle compared with 19% of patients who received prophylactic transfusions. Although Wandt et al found a lower incidence of bleeding associated with prophylactic transfusions in each patient group including those who received autologous HPC transplants, they argued that autologous HPC patients may not require routine prophylactic platelet transfusions because their overall bleeding rates were lower than those of patients with acute myelogenous leukemia. Although the safety of this recommendation is controversial, the applicability of these data to pediatric autologous HPC transplant patients is even more in question given the potential higher bleeding incidence noted in pediatric HPC patients as compared with adults [14].

Transfusion Threshold

Current pediatric platelet transfusion practice largely mirrors adult practice. If a patient is unable to produce platelets because of either the impact of disease on the bone marrow or the effects of therapy, then a prophylactic platelet transfusion is generally administered when the platelet count is less than 10 000/μL. There is no “target” post-transfusion platelet count for prophylactic platelet transfusions, and consequently, a follow-up platelet count is generally not obtained until the next day. An additional indication for a platelet transfusion is in a patient with a qualitative platelet defect who is to undergo an invasive procedure or who is actively bleeding. However, in contrast to the practice of transfusing platelets in the presence of thrombocytopenia and deficient platelet production, guidelines for the transfusion of platelets to treat bleeding due to a qualitative platelet defect are not universally accepted [2]. In this setting, the baseline platelet count is generally normal and the trigger for a transfusion is unrelated to the platelet count. Case reports suggest that adequate surgical hemostasis can usually be achieved when transfusions increase the platelet by approximately 100 000/μL, although fewer platelets may be adequate when used in combination with factor VIIIa and/or tranexamic acid. However, because of a high incidence of alloantibody induction in disorders characterized by deficiencies of platelet surface glycoproteins (ie, Glanzmann thrombasthenia, Bernard-Soulier syndrome), treatment with recombinant factor VIIIa for severe bleeding is an additional option to be considered [19,20].

In contrast, if a patient is bleeding and is thrombocytopenic, a therapeutic platelet transfusion may be administered to support hemostasis. Under these conditions, transfusion to achieve a specific platelet count is often the goal. Evidence supporting a specific threshold to trigger a therapeutic platelet transfusion is limited and guidelines often rely on “expert opinion” developed from case series. Although there are no studies comparing no platelet transfusion to platelet transfusion for surgery or the performance of invasive procedures [21], several studies in adults have suggested that a platelet count of 20 000/μL is sufficient for placement of a central venous catheter, whereas a platelet count of 50 000/μL is recommended for a lumbar puncture (LP) [22,23]. A single retrospective case series in children concluded that a central venous catheter can safely be placed when the platelet count is at least 50 000/μL [24]. Other retrospective studies have found that LPs can be safely performed in thrombocytopenic patients. Although the incidence of traumatic LPs with greater than 500 erythrocytes per high-power field increases with lower platelet counts [25], Howard et al [26] reported that no serious complications occurred in a retrospective analysis of 5223 LPS performed on children, including 199 patients with platelet counts less than 20 000/μL. Based on their data, Howard et al recommended that platelet transfusions are unnecessary before LPS in children whose platelet count is greater than 10 000/μL. A retrospective report in adults did not demonstrate any reduction in red blood cell transfusions after surgery in patients who received a prophylactic platelet transfusion preoperatively [27].

Platelet Dose

The platelet selection and preparation methods used are generally identical for pediatric and adult patients, with the exception that smaller doses are prepared for pediatric patients. The doses usually are close to the dose per kilogram of body weight administered to adult patients. Some of the early studies that reported on the efficacy of prophylactic transfusions also investigated the dosing administered to patients receiving cancer chemotherapy [8-10,15]. In general, no added benefit (in regard to bleeding episodes) was noted with the transfusion of a
high platelet dose (10 equivalent units) over that for a low platelet dose (4 equivalent units). This finding has been confirmed more recently with the transfusion of platelets collected by apheresis techniques [28–32]. At least 2 meta-analyses of randomized controlled trials addressing the issue of platelet dose have also been published and each has concluded that there was evidence, though of low quality, to support the position that low-dose platelet transfusion was no less effective than transfusion of higher doses [33,34]. However, a recent randomized controlled trial addressing the issue of standard (150–300 × 10^6 platelets) vs high (300–600 × 10^6 platelets) dose prophylactic platelet transfusion to patients with hypoproliferative thrombocytopenia was stopped early for safety concerns because of an increase in WHO grade 2 or higher bleeding in the group that received standard dose platelet products [35]. Taken in total, analysis of the literature suggests equivalent efficacy of low and standard doses equivalent to one apheresis platelet per average size adult patient, and AABB practice guidelines recommends 1 unit of apheresis platelets for adult patients but adds that lower doses are equally effective [22].

**Transfusion in the Setting of Increased Platelet Consumption**

Most clinical practices have been established for patients whose thrombocytopenia results from deficient platelet production and are not applicable to patients with thrombocytopenia secondary to increased immune-mediated platelet destruction, including those patients who have become alloimmunized to platelet antigens as a result of prior transfusions. Although several strategies have been used to enhance post–platelet transfusion platelet counts in these patients, none have been tested in randomized trials. Indeed, current guidelines from the American Society of Hematology recommend platelet transfusions in immune thrombocytopenia be reserved for the treatment of severe, life-threatening hemorrhage or for preparation for selected surgical procedures [36]. At this time, conclusions that could be drawn from the literature are as follows: (1) transfusion of large numbers of platelets is more likely to result in a greater increase in posttransfusion platelet count; (2) survival of transfused platelets will be transient with the duration determined by the intensity of the process causing increased platelet consumption; and (3) transfusion of platelets in the setting of platelet activation (eg, thrombotic thrombocytopenic purpura, heparin induced thrombocytopenia) may increase the risk of the development of arterial thrombi and death [37,38].

**Cold- vs Room Temperature–Stored Platelets**

The standard platelet unit in the United States is stored at room temperature, although Food and Drug Administration regulations allow for either 22°C or 4°C storage. The primary advantage of room temperature storage is that posttransfusion platelet increment and survival in the circulation are greater when compared with platelets stored at 4°C [39]. However, some in vitro studies comparing platelets stored at 22°C vs 4°C demonstrated improved hemostatic function in the 4°C platelets [40–42] and anecdotal reports from military battle field hospitals suggest improved hemostasis after the transfusion of cold-stored platelets. Taken together, these results suggest that 4°C platelets may offer advantages to control acute hemorrhage. However, there have been no studies assessing in vivo efficacy and safety of cold–stored platelets in the civilian population. Significant studies are needed before 4°C stored platelets would be routinely used in the nonmilitary setting, but the results of such could offer significant improvements in transfusion medicine.

**Gaps in Current Knowledge**

**Platelet Transfusion Indications—Hematology/Oncology Patients**

Several studies have demonstrated that prophylactic platelet transfusions should be administered when the platelet count is at or below 10 000 platelets per microliter in adult patients. Similar studies have not been performed for children, and platelet transfusion practice in pediatrics is based on little evidence. As previously discussed, pediatric hematology-oncology patients may be at higher risk for bleeding. Indeed, pediatric hematology-oncology patients of all age ranges appear to have an increased bleeding propensity compared with their adult counterparts; this increased risk of bleeding appears to be most pronounced in patients who had undergone autologous HPC transplants and was not found to be related to platelet count [14]. Hence, the platelet count at which platelets should be transfused in this patient population should be rigorously studied with attention to recovery, survival, and hemostatic efficacy.

Pediatric patients who have undergone HPC transplants are at risk for hepatic veno-occlusive disease, also known as hepatic sinusoidal obstructive syndrome, in which hepatic venous outflow obstruction causes hepatomegaly, right upper quadrant pain, jaundice, and ascites. The disease is thought to begin with injury to the hepatic endothelium expressing ABO antigens on the endothelial cell surface. Hence, that endothelium may be at risk for damage from antibodies to ABO antigens which are often present in transfused platelets. Indeed, one study of pediatric HPC transplant patients found an increased risk for hepatic veno-occlusive disease after transfusion of blood components, usually platelets, containing antibodies against ABO antigens present on the patient’s cells [43]. If further studies confirm this observation, then there would be compelling evidence to strictly avoid transfusing platelets containing minor–incompatible ABO antibodies to pediatric HPC transplant patients.

**Cardiac Surgery Patients**

Children requiring cardiopulmonary bypass (CPB) develop both thrombocytopenia and thrombocytopenias due to the bypass circuit. Cardiopulmonary bypass–induced thrombocytopenia is most pronounced in the smallest children who have the smallest pool of platelets in reserves for release into the circulation [44]. This is due to both dilution and consumption that occurs during the procedure. In addition, these young patients have CPB-induced platelet dysfunction. In patients younger than 3 years, CPB-induced platelet dysfunction can be measured by decreased expression of activated GPIIb/IIIa and P-selectin after stimulation with ADP or thrombin receptor agonist peptide. In addition, prolonged circulation through an extracorporeal circuit may result in platelets becoming “exhausted” due to degradation of alpha and dense granules, rendering them unable to fully respond to agonists produced as a result of bleeding.

Cardiopulmonary bypass–induced thrombocytopenia and platelet dysfunction may be partially offset by platelet activation during cardiopulmonary surgery that may result in enhanced hemostatic function [44,45]. This platelet activation has been measured by increased concentration of plasma β-thromboglobulin and increased expression of P-selectin (CD62) on the platelet surface.

The combined effects of thrombocytopenia, coagulopathy, and acquired qualitative platelet defects may lead to a bleeding diathesis requiring platelet transfusion. Indeed, one study has found that pediatric cardiac surgery patients transfused with “reconstituted” whole blood exhibited more depressed platelet function and experienced increased, rather than decreased, bleeding when compared with those patients who received fresh (~48 hours) whole blood [46]. Further studies are warranted to determine the optimal platelet transfusion strategies for these patients who are susceptible to bleeding, thrombosis, and volume overload [47].

**Photochemically Treated Platelets**

Photochemical-treated platelets using psoralen, amotosalen, or riboflavin have been approved for use in several countries. These treatments reduced pathogen load decreasing the likelihood of transfusion...
transmitted infectious diseases. Transfusion of these photochemically treated platelets results in lower platelet count increments compared with transfusion of untreated platelets. However, when administered prophylactically to hematol-ogy-oncology patients, including children, photochemically treated platelets are equivalent to nontreated platelets in protecting against bleeding.[48–50].

Although photochemically treated platelets appear effective for prophylactic prevention of bleeding in hematol-ogy-oncology patients, it is not clear whether they have the same efficacy in promoting hemostasis in the actively bleeding patient. Some of the patients most dependent on transfused platelets for clot formation are young surgical patients, especially cardiac surgery patients, with limited endogenous platelet reserves. In vitro data suggest that photochemically treated platelets are functionally inferior to untreated platelets. Photochemically treated platelets have reduced thrombus formation kinetics [51], reduced response to some agonists [52], and premature activation as suggested by premature integrin αIIbβ3 activation, spontaneous aggregation, and increased P-selectin surface expression [52–54]. Although these in vitro effects have not been shown to be clinically important in patients studied to date, the impact of these effects on young pediatric surgical patients is unknown and should be studied.

**Conclusions/Recommendations**

Current guidelines on the use of platelet transfusions in the pediatric population are based on data that are largely derived from adults. At the present time, those guidelines support:

1. prophylactic transfusion of platelets to pediatric patients with chemotherapy-induced thrombocytopenia when platelet count is less than 10,000/μL;
2. transfusion dose of platelets equivalent to 4 to 5 units of platelets for older or larger children and 10 to 15 mL/kg body weight for younger children or those with less than 30 kg body weight; and
3. transfusion of platelets to a target of at least 50,000/μL in bleeding patients or in preparation for major surgical procedures.

These recommendations are based on data that are not considered “high quality,” and for many situations, only “expert opinion” is available to guide recommendations. Consequently, there is both a need for high-quality clinical studies in pediatric platelet transfusion and an opportunity to improve clinical practice in this area. Although pilot studies can be performed using patients from a single institution (or a limited number of institutions), to generate high-quality data with broad applicability, large multi-institutional studies will likely be required. Consequently, the feasibility of performing any study in this context must be considered when determining priorities. Examples of high-priority questions for which equipoise exists justifying randomized clinical trials include:

1. platelet transfusion threshold: 10,000/μL vs 20,000/μL; primary end point of major bleeding (eg, WHO grade 2 or greater);
2. a reappraisal of platelet transfusion dose: a randomized study between 2 well-defined platelet doses, with the end points being major bleeding and donor exposure; and
3. cold vs room temperature storage: platelet transfusion in bleeding patients; end points being control of bleeding, need for additional blood product support.

Additional studies that may require observational data to inform the specifics of a randomized trial include:

1. determination of platelet count threshold before various invasive procedures and clinical settings (eg, central line placement, solid organ biopsy [liver, kidney], IP, intracranial hemorrhage, surgery);
2. platelet transfusion parameters in thrombocytopenia characterized by increased platelet consumption (eg, immune thrombocytopenia, microangiopathic processes [thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, etc]);
3. age-dependent bleeding in children with cancer chemotherapy-related thrombocytopenia and effect of (standardized) prophylactic platelet transfusions on bleeding; and
4. effect of routine platelet transfusion in cardiac surgery on postoperative outcome (eg, bleeding, subsequent red blood cell transfusion, morbidity, intensive care length of stay, ventilator days, etc).

Finally, to better inform the need for platelet transfusion in the setting of extracorporeal circulation (eg, extracorporeal membrane oxygenation, CPB), it will be critical to have data obtained from a laboratory study investigating the nature of the acquired coagulopathy, including any acquired platelet function abnormality.

**Conflict of Interest Statement**

None.

**References**


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