Perioperative Blood Transfusion Therapy in Pediatric Patients

Heather A. Hume1* and Pierre Limoges2

In general, transfusion guidelines for non-neonatal pediatric patients are similar to those for adults. However, some differences do exist and certain precautions may be necessary particularly in the setting of massive transfusions. We review these differences as they apply to general pediatric surgery outside of the neonatal period, with respect to the transfusion of red blood cells (RBCs), platelets, fresh-frozen plasma (FFP), and cryoprecipitate. We include a discussion of the indications for transfusion and practical considerations such as dosing and administration. Finally, we briefly review the use of directed donations and specialized (irradiated, CMV seronegative) blood components.

Keywords: perioperative blood transfusion, pediatric blood transfusion.

INTRODUCTION

In general, transfusion guidelines for nonneonatal pediatric patients are similar to those for adults. Some differences do exist, however, and certain precautions may be necessary, particularly in the setting of massive transfusions. We review these differences as they apply to general pediatric surgery outside the neonatal period with respect to the transfusion of red blood cells (RBCs), platelets, fresh-frozen plasma (FFP), and cryoprecipitate. For guidelines concerning transfusion therapy in the neonatal period or transfusions in particular surgical settings (eg, pediatric cardiovascular surgery), the reader is referred to several recent reviews on these topics.1–4 Perioperative autologous blood donation and transfusion in children have also been reviewed in depth recently5 and are not addressed in this review.

RED BLOOD CELL TRANSFUSIONS

Preoperative evaluation

The decision to perform a preoperative hemoglobin (Hb)/hematocrit (Hct) evaluation depends on the presence of risk factors for hematologic disease and/or the risk of perioperative blood loss.

Iron deficiency anemia is the most common hematologic disease of infancy and childhood, primarily as a result of preterm birth or inadequate iron intake. Adolescents, particularly girls, are also susceptible to iron deficiency anemia because of high requirements due to the growth spurt, dietary deficiencies, and menstrual blood loss. In the United States, approximately 9% of 1- to 2-year-olds and 9% of adolescent girls are iron-deficient; iron deficiency anemia is present in 3% of toddlers and 2% of adolescent girls.6

With the increasing ethnic diversity of the North American population, it is also important to consider the possibility of the presence of a congenital hematologic disorder, particularly thalassemia or a sickling hemoglobinopathy. Thalassemia minor results in a mild microcytic anemia with no clinical consequences; however, Hb levels in thalassemia intermedia, which is particularly prevalent in children of Southeast Asian origin, may be 80 g/L or lower.

Children (and adults) with sickling hemoglobinopathies or sickle cell disease (SCD) are at increased risk for perioperative complications and therefore require
specialized perioperative care, frequently including preoperative transfusion therapy.17–19 SCD patients must be identified before any surgical intervention and, except in extreme emergencies, should undergo surgical interventions only in centers experienced in the care of such patients. Sickling hemoglobinopathies include sickle cell anemia (homozygosity for Hemoglobin S [HbS]) and the compound heterozygous disorders Hemoglobin SC (HbSC) disease and HbS/β thalassemia. Persons with sickle cell trait (ie, heterozygotes for Hemoglobin A and HbS) are not at increased risk for perioperative complications. SCD is found predominantly (but not exclusively) in black persons (persons of African origin). In addition to this group, SCD also occurs in persons of Mediterranean, Indian, Middle Eastern, and South and Central American origins.

A complete blood cell count (CBC) alone is not an appropriate test to screen for the presence of SCD, because the Hb concentration may be normal in HbSC disease. In patients over 6 months of age, a CBC and screening test for SCD (eg, a sickling test or a solubility test) may be used for preoperative evaluation; in infants 6 months of age or less, a screening test may not detect the presence of Hbs (because of the relatively high levels of Hemoglobin F and low levels of Hbs), and a more definitive test such as hemoglobin electrophoresis should be performed.

At our institution, preoperative CBCs are performed routinely in infants less than 12 months of age, and tests to detect SCD are performed in populations at risk as described previously. Otherwise, CBCs are performed only if the clinical evaluation is suggestive of the presence of anemia or as a baseline for interventions for which large blood losses are anticipated.

In interpreting the CBC in a child, one must remember that the normal values for Hb and mean corpuscular volume are different from those in adults and that there are age-related changes (Table 1).11 The slightly lower Hb values in children versus adults is thought to be a result of the increased intraerythrocytic concentration of 2,3-diphosphoglycerate, which, in turn, results in increased offloading of oxygen to tissues at any given blood oxygen tension.12

### Indications for red blood cell transfusion

There are only two valid reasons for transfusing RBCs to children: the most common is to correct an (or avoid an imminent) inadequate oxygen-carrying capacity that is caused by an inadequate RBC mass; the second and rarer indication is to suppress endogenous Hb/RBC production in selected thalassemia or SCD patients.

Indices of oxygen delivery and tissue oxygenation may accurately indicate the need to transfuse RBCs; however, invasive monitoring is required to generate these indices. Decisions about RBC transfusions are usually made on the basis of easily available but less precise clinical data. Although Hb concentration is certainly one important factor to consider in the decision to administer an RBC transfusion, most experts agree that it is not the only factor; in certain situations such as acute hemorrhage without volume replacement, it may even be misleading. As discussed in detail in several reviews, healthy adults and children have an impressive capacity to increase oxygen delivery to tissues.13–16 A recent study (albeit in a small number of patients/volunteers) demonstrated that healthy adults subjected to acute normovolemic hemodilution were able to tolerate an Hb concentration of 50 g/L with no adverse effects.17 It seems reasonable to assume that this would also be the case for otherwise healthy adolescents and older children.

In 1997, the Canadian Medical Association (CMA) published guidelines for RBC and plasma transfusion for adults and children.18 As background for the development of those guidelines, systematic reviews to identify evidence-based reports on allogeneic RBC and plasma transfusions in adults as well as children were performed.15,19,20

Unfortunately, there are few studies in either pediatric or adult settings in which the validity of clinical criteria has been examined. Thus, the efficacy of RBC transfusion in most scenarios has not been established by evidence-based data. At the time that the CMA guidelines were developed, only seven studies (3 randomized controlled trials and 4 nonrandomized studies) addressing the indications for RBC transfusions in children (excluding neonates or infants less than 4 months of age or patients with thalassemia or sickle cell disease) were identified.21–27 Since that time, to these authors’ knowledge, no additional studies addressing the efficacy of RBC transfusions in pediatric patients have been reported.

### Table 1. Normal values for hemoglobin concentration and MCV in infancy and childhood. Adapted from Nathan and Orkin.11

<table>
<thead>
<tr>
<th>Age</th>
<th>Hemoglobin (g/L) Mean</th>
<th>Hemoglobin (g/L) −2 SD</th>
<th>Hematocrit Mean</th>
<th>Hematocrit −2 D</th>
<th>MCV (fl) Mean</th>
<th>MCV (fl) −2 D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–3 days</td>
<td>185 145</td>
<td>0.56 0.45</td>
<td>108 95</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3–6 months</td>
<td>115 95</td>
<td>0.35 0.29</td>
<td>91 74</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5–2 years</td>
<td>120 105</td>
<td>0.36 0.33</td>
<td>78 70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2–6 years</td>
<td>125 115</td>
<td>0.37 0.34</td>
<td>81 75</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6–12 years</td>
<td>135 115</td>
<td>0.40 0.35</td>
<td>86 77</td>
<td></td>
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MCV, mean corpuscular volume.
Of the seven studies referred to, two were performed in children undergoing treatment of acute leukemia in the 1970s and are of historical interest only, two addressed the treatment of anemia caused by malaria in African children, two addressed the utility of RBC transfusions to improve tissue oxygenation in children with sepsis (each arrived at a different and opposing conclusion), and the remaining study examined the relation between oxygen delivery and consumption and RBC transfusion after cardiac bypass surgery.21–27 The results of the studies performed in Africa are not generalizable to the North American setting, but they do speak to the tolerance of children for severe anemia. In one of the studies, there was no difference in mortality between the transfused and nontransfused groups in spite of mean admission Hcts of 0.140 and 0.144, respectively.23 In the second study, the authors’ conclusion was that in their setting, RBC transfusions should be administered to children with congestive heart failure or respiratory distress if the Hb concentration is less than 50 g/L but in the absence of cardiorespiratory symptoms or signs only if the Hb concentration is less than 30 g/L.24

Since the publication of these guidelines, a randomized controlled trial of a restrictive versus liberal RBC transfusion study in critically ill adult patients has been reported.25 End points measured in this study were death and the severity of organ dysfunction. Overall, the 30-day mortality rates were similar in the two groups; however, the rates were significantly lower with the restrictive transfusion strategy among patients who were less acutely ill. The authors concluded that a restrictive RBC transfusion strategy is at least as effective as a liberal transfusion strategy, with the possible exception of patients with acute myocardial infarction and unstable angina. Although no such data are available for children, a similar multicenter, prospective, randomized study is currently underway in children admitted to critical care units (J. Lacroix, personal communication, 2001). This study, when completed, will represent the only large, prospective, randomized, controlled trial of RBC transfusion therapy in children outside the neonatal period (with the exception of studies performed in children with SCD or thalassemia).

In the absence of studies that could be used to allow the practice of evidence-based RBC transfusion therapy, guidelines for RBC transfusions in children (as well as adults) have been based on expert opinion. The recommendations of a National Institutes of Health-sponsored consensus conference on perioperative RBC transfusion29 published in 1988 stated the following:

- Available evidence does not support the use of a single criterion for transfusion such as Hb concentration of less than 100 g/L. No single measure can replace good clinical judgment as the basis for decision-making regarding perioperative transfusion.
- There is no evidence that mild-to-moderate anemia contributes to perioperative mortality.

The CMA guidelines published in 1997 similarly stated that “there is no single value of Hb concentration that justifies or requires transfusion; an evaluation of the patient’s clinical situation should also be a factor in the decision.”18

In 1996, the American Society of Anesthesiologists (ASA) Task Force on Blood Component Therapy published transfusion practice guidelines.30 Although a number of years have passed since these guidelines were developed, in the authors’ opinion, these guidelines remain valid (ie, there are no subsequently published studies that would invalidate the guidelines). The members of the task force specifically state that the guidelines were not intended to apply to children. Nevertheless, it is our belief that these guidelines can be used for pediatric patients, with the possible exception of infants and toddlers. In summary, the recommendations of the task force with respect to RBC transfusions are as follows:

- Transfusion is rarely indicated when the Hb concentration is greater than 100 g/L and is almost always indicated when it is less than 60 g/L, especially when the anemia is acute.
- The determination of whether intermediate Hb concentrations (60–100 g/L) justify or require RBC transfusion should be based on the patient’s risk for complications of inadequate oxygenation.
- The use of a single Hb “trigger” for all patients and other approaches that fail to consider all important physiologic and surgical factors affecting oxygenation are not recommended.
- When appropriate, preoperative autologous blood donation, intraoperative and postoperative blood recovery, acute normovolemic hemodilution, and measures to decrease blood loss (deliberate hypotension and pharmacologic agents) may be beneficial.
- The indications for transfusion of autologous RBCs may be more liberal than for allogeneic RBCs because of the lower (but still significant) risks associated with the former.

The last recommendation of the ASA task force cited here is in fact rather controversial. Although this group of experts is not alone in recommending more liberal indications for autologous RBC transfusions.
than for allogeneic RBC transfusions, not all experts agree. In particular, the 1997 CMA guidelines state explicitly that “indications for the transfusion of autologous blood should be the same as those for allogeneic blood.”

To apply these ASA guidelines to the intraoperative setting, it is useful, before or during surgery, to estimate the maximal allowable blood loss (MABL). The MABL can be calculated as follows:

$$\text{MABL} = \frac{\text{EBV} (H_0 - H_L)}{H_0}$$

where EBV is the estimated total blood volume, $H_0$ is the initial Hct, and $H_L$ is the lowest acceptable Hct (where Hct is expressed as a percentage). RBC replacement should start earlier if hemodynamic instability occurs despite adequate volume replacement and/or if timely laboratory monitoring is lacking.

With respect to the correction of postoperative anemia, the need for iron replacement is often overlooked. Any child who has had blood loss of more than 5% of his/her total blood volume should receive iron replacement after surgery. Unless the losses have been large, elemental iron at a rate of 3 mg/kg per day for a period of 2 to 3 months should be sufficient.

**Practical considerations**

The principles for the choice of blood group of RBC units for transfusion are the same in children as in adults, with the exception that in the case of massive emergency transfusion in a child, one should avoid the transfusion of Rhesus D antigen (RhD)-positive blood to an RhD-negative patient. This is especially important for girls, in whom the development of an RhD antibody could, in subsequent pregnancies, lead to hemolytic disease of the newborn.

The quantity of RBCs to be transfused depends on the Hct of the RBC unit, and that, in turn, depends on the storage medium. RBCs stored in citrate-phosphate-dextrose-adrenaline-1 have an Hct of 0.70 to 0.75; in the absence of ongoing blood losses, a transfusion of 10 mL/kg can be expected to raise the Hb concentration by approximately 25 g/L. Currently, most RBCs are stored in additive solutions (eg, AS-1 or AS-3) and have an Hct of 0.50 to 0.60. To obtain an increase of 25 g/L, 14 mL/kg must be administered.

When blood centers began using additive solutions in the late 1980s, concerns were raised about their safety for use in neonatal and pediatric patients. Calculations of the quantities of the constituents of additive solutions that would be transfused to neonates suggested that small volumes (<20 mL/kg) could be infused without problems but that massive transfusions could potentially be harmful. At our institution, we remove the supernatant fluid from RBC units stored in additive solution for massive (but not small-volume) transfusion in infants less than 4 months of age. For infants more than 4 months of age, we do not routinely remove the supernatant fluid even for massive transfusion.

Concern has also been raised in the literature about the risk of hyperkalemia in massive transfusion in pediatric patients. The RBC membrane storage lesion results in gradual leakage of potassium from the RBCs to the plasma/preservative medium. At the end of the permitted storage period (35 days for RBCs stored in CPDA-1 and 42 days for additive solutions), the supernatant potassium concentrations are approximately 75 to 100 mmol/L (75–100 mEq/L) and 50 mmol/L (50 mEq/L), respectively. Considering the volumes of supernatant in each unit, these concentrations correspond to an absolute quantity of potassium at outdate of 5 to 7 mmol (approximately the same in the two types of units). The concentration of potassium in the supernatant fluid increases considerably more rapidly in units irradiated before storage (see below).

In adults, transfusion rates not exceeding 100 to 150 mL/min are rarely associated with significant potassium abnormalities. In pediatric patients, however, rapid massive transfusion of stored blood has been reported to lead to hyperkalemia and, in at least one report, to the death of a neonate. Situations in which significant hyperkalemia may occur seem to include a combination of risk factors, namely, rapid large-volume transfusion of RBCs near the end of the permitted storage period, particularly if infused to a central venous catheter and/or in the presence of low cardiac output or renal failure. In such high-risk situations, electrocardiographic monitoring and monitoring of potassium levels should be performed, and, if possible, especially in young children, RBCs stored for less than 2 to 3 weeks should be used. In infants less than 4 months of age, we do not use blood stored for more than 10 to 14 days for large-volume transfusions unless the supernatant fluid is removed.

**PLATELET TRANSFUSIONS**

**Indications**

The indications for platelet transfusions in patients with malignancies, particularly acute leukemia, have been reasonably well studied, and at least some of the studies have included pediatric patients. Clinical practice guidelines for platelet transfusion in patients with cancer have recently been published by the American Journal of Therapeutics (2002) 9(5)
Society of Clinical Oncology and are essentially the same for children as for adults. With respect to surgery or invasive procedures, these guidelines state the following:

- In the absence of associated coagulation abnormalities, a platelet count of 40 to $50 \times 10^9/L$ is sufficient to perform major invasive procedures with safety.
- If platelet transfusions are administered before a procedure, it is critical that a posttransfusion platelet count be obtained to prove that the desired platelet count has been reached.
- Platelet transfusions should also be available on short notice in case intraoperative or postoperative bleeding occurs.

The indications for platelet transfusions in children (or even in adults) with thrombocytopenia caused by factors other than decreased platelet production have not been well studied. Thus, as for RBC transfusion, indications are based mainly on expert opinion. Surgical interventions or invasive procedures in children with idiopathic thrombocytopenia purpura or congenital platelet disorders should be undertaken only in consultation with a hematologist familiar with these disorders. Prophylactic platelet transfusion is usually ineffective in patients with idiopathic thrombocytopenia purpura.

Thrombocytopenia may be associated with massive transfusion. Depending on the underlying pathologic changes, the thrombocytopenia may be simply dilutional (ie, caused by platelet loss through hemorrhage and transfusion therapy with platelet-poor products), or there may be additional factors (eg, disseminated intravascular coagulopathy, hypoxia, and/or sepsis) leading to accelerated platelet consumption.

In the absence of specific studies addressing the indications for platelet transfusion in pediatric patients in the setting of massive transfusion, it is reasonable to apply the 1996 ASA guidelines. In this setting, these guidelines state the following:

- Surgical and obstetric patients with microvascular bleeding usually require platelet transfusions if the platelet count is less than $50 \times 10^9/L$; with intermediate platelet counts ($50 \sim 100 \times 10^9/L$), the determination (of whether the patient requires platelet transfusion therapy) should be based on the patient’s risk for more significant bleeding.
- Under normal circumstances, platelet counts should be obtained to determine the need for platelet transfusions; in unusual situations, massively transfused patients with microvascular bleeding suspected to be secondary to platelet deficiency may benefit from empiric platelet transfusion.

**Dosage and administration**

Platelets possess both intrinsic and extrinsically absorbed A and/or B antigens. Nevertheless, ABO-incompatible platelets (ie, platelets with A and/or B antigens given to a recipient with a corresponding natural A or B antibody) are usually clinically effective. Conversely, there are reports of acute intravascular hemolysis after the transfusion of platelet concentrates containing donor A and/or B antibodies incompatible with the recipient’s RBCs. It would thus seem prudent, particularly in small children, where the volume of plasma may be relatively large with respect to the patient’s total blood volume, to use ABO-matched platelets. If these are not available, plasma compatible with the recipient’s RBCs should be chosen. If this is also not possible, for infants and young children, the plasma should be removed, or units with low titer of anti-A or anti-B should be selected.

Platelets do not carry RhD antigens; however, the quantity of RBCs in platelet concentrates is sufficient to induce RhD sensitization even in immunosuppressed cancer patients. RhD sensitization caused by platelet transfusions in RhD-negative patients can be prevented by the administration of RhD immunoprophylaxis. Thus, if platelets from an RhD-positive donor or platelets from a donor of unknown RhD phenotype are given to an RhD-negative recipient, administration of RhD immunoprophylaxis should be considered, especially for female patients.

A suitable starting platelet dose that can be expected to raise the platelet level by $50 \times 10^9/L$ is one platelet concentrate per 10 kg of body weight. Platelet concentrates may be pooled before administration or infused individually. An equivalent dose for apheresis platelets is approximately 5 mL/kg. Patients with increased platelet consumption (eg, with sepsis or disseminated intravascular coagulopathy) or splenomegaly may require larger amounts of platelets.

Platelets may be volume reduced before infusion. This extra manipulation leads to platelet loss, and if not carefully performed, it may potentially adversely affect platelet function and/or be a cause of bacterial contamination. Volume reduction should therefore be limited to patients who require severe volume restriction or to situations where ABO-incompatible platelets are the only available units for a neonate or child.

**FRESH-FROZEN PLASMA**

The indications and contraindications for the transfusion of FFP are essentially the same for children as for...
adults. Hence, the guidelines recommended by the ASA and the CMA are applicable.

Plasma should be ABO compatible with the recipient’s RBCs (ie, it should not contain antibodies that could react with recipient A and/or B antigens). Usually, the RhD group need not be considered. When large volumes of FFP are given to the RhD-negative pediatric patients (or women of childbearing age), however, prevention of RhD immunization by the use of RhD immune globulin should be considered.

The dose of FFP in children is 10 to 20 mL/kg. This dose usually raises the level of coagulation factors by 20% immediately after infusion. Posttransfusion monitoring of the patient’s coagulation status is important for optimal treatment.

In summary the ASA and CMA guidelines recommend that FFP be administered in the following settings:

1. For the emergency reversal of warfarin (ie, when warfarin withdrawal and treatment with vitamin K are inadequate)
2. For correction of microvascular bleeding in the presence of significantly elevated prothrombin time/partial thromboplastin time
3. For correction of microvascular bleeding in the setting of massive transfusion when coagulation tests cannot be obtained in a timely manner

With respect to the second indication, the plasma concentration of each coagulation factor required for hemostasis is around 0.20 to 0.25 U/mL, although for Factor VII, the value is below 0.15 U/mL. These coagulation factor concentrations correspond to partial thromboplastin time and prothrombin time values of approximately 1.5 times normal. In both cases, the values are dependent on the reagents used. It is therefore essential that the anesthesiologist be familiar with the interpretation of coagulation tests as they are performed at his/her institution.

Reference values for coagulation tests are essentially identical for children older than 6 months and adults. Nevertheless, the activated partial thromboplastin time is often prolonged in the first 6 months of life because of the lower concentrations of coagulation factors IX, X, and XI in newborns and young infants.

With respect to the contraindications for FFP, all common congenital bleeding disorders can now be treated with specific therapies and should not be treated with either FFP or cryoprecipitate.

As discussed in many reviews and guideline documents over the past 10 to 15 years, FFP should not be used solely for volume replacement. Albumin may be used for replacement of large-volume losses, although it is preferable to use a nonblood product whenever possible. This has raised a question about the safety of

the use of starches (hetastarch [Hespan] and pentastarch [Pentaspan]) for volume replacement in pediatric patients. There are a few publications on the use of hetastarch as a volume expander in pediatric patients.[42–48] Except for allergic reactions, doses up to 20 mL/kg were well tolerated and do not seem to be associated with coagulation abnormalities. Two additional studies describe the use of lower molecular-weight hydroxyethyl starch solutions in a total of 38 infants and children undergoing surgery.[49,50] Again, the starch solutions (exact volumes used were not stated) seemed to be as efficacious as albumin, and no adverse effects were observed. The total number of pediatric patients reported on in these studies is small, however, and the package inserts for both Pentaspan and Hespan state that the safety and efficacy of these products have not been established in children.

Given concerns about the effects of starches on the coagulation system and also possibly on renal function, pentastarch is not used for neonates or children less than 2 years of age at our hospital.[51,52] For older children and adolescents, pentastarch is used in preference to albumin for volume expansion. The dosage used is 28 mL/kg every 24 hours to a maximum of 2 L every 24 hours.

CRYOPRECIPITATE

The indications for the transfusion of cryoprecipitate are also the same in children as in adults. Thus, the ASA guidelines may be used in children, with the exception of the recommendation to use cryoprecipitate to treat bleeding in patients with severe von Willebrand disease unresponsive to deamino-D-arginine vasopressin. These patients (both children and adults) are now treated with virally inactivated Factor VIII concentrates rich in von Willebrand factor rather than cryoprecipitate.

In children, the use of ABO-compatible units is preferable. RhD group need not be considered. The number of units required is usually based on the amount necessary to obtain a hemostatic level of fibrinogen (ie, a fibrinogen level greater than 0.8–1.0 g/L). If the units are carefully pooled, this can usually be accomplished by the transfusion of 1 U per 5 to 10 kg of recipient weight.

DIRECTED DONATIONS AND LIMITED-EXPOSURE BLOOD DONOR PROGRAMS

A directed blood donation is one in which an individual, at the request of a patient, or in the case of a
child, a parent, donates blood that is reserved specifically for the subsequent transfusion of the requesting patient. When parents wish to be directed donors for their children or request other family members or friends to do so, it is presumably because they believe that blood from such donors is less likely to be a source of transfusion-transmitted diseases than blood from an anonymous volunteer blood donor pool. Whether this is true has been a source of controversy in the literature. Advocates of directed donations argue that such donors would not consider donating for a loved one if they have known risk factors for transfusion-transmitted diseases.53,54 Alternatively, others argue that the absence of confidentiality that this situation entails and/or a strong desire to donate for the given patient may discourage the directed donor from being entirely truthful about his/her eligibility for blood donation.

Studies addressing these questions would involve the follow-up of large numbers of recipients of directed blood donations over a long time and, consequently, are unlikely to be performed. Instead of direct studies, attempts have been made to estimate indirectly the comparative safety of directed and standard donor blood by measuring the frequency of positive infectious disease markers in the two donor groups. This approach is, of course, based on the assumption that the risk of an undetected infectious unit is directly related to the frequency of positive infectious markers in the donor population under study. In three of four studies, there were no statistically significant differences in the results of infectious disease markers in directed donors versus anonymous volunteer donors, whereas in one study, there was an increased frequency of positive markers among directed donors, which could probably be attributed to the relatively larger number of first-time donors.55–58 From the point of view of transfusion-transmitted viral diseases, directed donors are therefore generally considered neither safer nor less safe than regular volunteer donors.

A potential risk of parental blood transfusion is chimeraism and graft-versus-host disease (GVHD). For patients of all ages (including adults), all cellular blood components obtained from biologic relatives must be irradiated before transfusion (see below). In addition, as for autologous donations, it is possible that the added complexity of providing directed donations could lead to an increased frequency of errors.59

One situation in which directed blood donors may actually provide an increased level of safety is a limited-donor blood program. For example, a single donor can often provide all the RBC and/or plasma needs of a small pediatric patient ineligible for autologous donation who must undergo elective surgery for which multiple blood units are normally required.60

**TRANSFUSION-ASSOCIATED GRAFT-VERSUS-HOST DISEASE**

Transfusion-associated (TA) GVHD results from the engraftment of immunocompetent donor T lymphocytes in a recipient whose immune system is unable to reject them. Although it is possible that mild cases of TA-GVHD may occur, TA-GVHD seems to be fatal in at least 90% of cases. TA-GVHD can be prevented by appropriate gamma-irradiation of cellular blood products (ie, whole blood, RBCs, platelets, granulocytes). Frozen products (ie, FFP, cryoprecipitate) do not cause TA-GVHD.

Patients with congenital or acquired immunodeficiency disorders (with the somewhat surprising exception of acquired immunodeficiency syndrome patients) are at risk for TA-GVHD. Cellular blood components should be irradiated for all patients undergoing hematopoietic stem cell transplantation. There is debate about the necessity of irradiating blood components for all adult cancer patients receiving chemo- and/or radiotherapy. However, most pediatric centers do irradiate blood components for these patients.

One situation in which transfusion may be required before the presence of a congenital immunodeficiency syndrome is suspected is in infants with the DiGeorge anomaly. DiGeorge anomaly refers to the combination of thymic hypoplasia, parathyroid hypoplasia, and cardiac defects, particularly conotruncal defects. Unless a diagnosis of DiGeorge anomaly can be definitely ruled out, neonates and infants with these cardiac defects should receive only irradiated cellular blood components.

TA-GVHD may also occur in an immunocompetent recipient if the recipient does not recognize the transfused lymphocytes as foreign, as may occur when there exists donor homozygosity for a human leukocyte antigen haplotype for which the recipient is haploidentical. The potential for the occurrence of this latter situation is the basis of the requirement to irradiate directed donations from biologic relatives.

Generally accepted indications for gamma-irradiation of cellular blood products in pediatric patients are given in Table 2. TA-GVHD in pediatric patients is reviewed in detail by Hume and Preiksaitis.61

Storage of RBCs after gamma-irradiation results in an increase of supernatant potassium to a level of approximately twice that found in unirradiated units of the same postcollection age. When initially reported,
Table 2. Indications for use of gamma-irradiated blood or blood components in pediatric patients over 4 months of age.

<table>
<thead>
<tr>
<th>Condition</th>
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<tr>
<td>Known or suspected congenital cellular immunodeficiency</td>
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<tr>
<td>Malignancy (hematologic or solid tumor) undergoing chemotherapy or radiotherapy</td>
</tr>
<tr>
<td>Recipient of solid organ or hematopoietic stem cell transplantation</td>
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<td>Recipient of familial blood or HLA-matched cellular products</td>
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this led to a debate concerning the need to routinely wash irradiated RBC units intended for neonatal patients. These reports were meticulously reviewed by Strauss, who concluded that such a practice is not routinely necessary. In the situations discussed previously, where pediatric patients may be at risk for hyperkalemia after transfusion, the use of RBCs irradiated before storage could potentially increase this risk. Most pediatric transfusion services therefore try to irradiate RBCs immediately before transfusion. If one cannot avoid using RBC units irradiated before storage, washing the RBCs to remove the supernatant fluid should be considered in those situations with other risk factors for hyperkalemia.

CYTOMEGALOVIRUS LOW-RISK COMPONENTS

Cytomegalovirus (CMV) can be transmitted by cellular blood components. Blood components that have been leukoreduced or are derived from CMV-seronegative donors are at low risk of transmitting CMV. In general, CMV low-risk components are indicated for CMV-seronegative immunosuppressed patients or CMV-seronegative patients receiving a hematopoietic stem cell or solid organ transplant from a CMV-seropositive donor. General surgical patients, either adult or pediatric, do not require CMV low-risk components. Interested readers are referred to recent reviews on transfusion-transmitted CMV and its prevention.

SUMMARY/CONCLUSION

In general, the approach to perioperative transfusion therapy in children and adolescents is similar to that used for young adults. There are a few differences, however, especially for younger children, of which anesthesiologists should be aware and which we have highlighted in this review.

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