

# Critically ill children: To transfuse or not to transfuse packed red blood cells, that is the question

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**Objectives:** This article summarizes the current data on packed red blood cell transfusion in the pediatric intensive care unit setting to help providers make evidence-based decisions regarding packed red blood cell transfusions.

**Data Sources:** Review of the literature, including PubMed, citations from relevant articles, and some articles that have been particularly relevant in adult critical care practice regarding packed red blood cell transfusion.

**Conclusions:** The use of packed red blood cell transfusions is common in the pediatric intensive care unit setting. However, until recently there have been little data to guide providers in this practice. Studies in adult intensive care units have shown less

favorable outcomes in patients who received packed red blood cell transfusions. This has led to renewed questioning of the practice of packed red blood cell transfusion in critically ill pediatric patients. New data indicate that using a hemoglobin transfusion threshold of  $>7$  g/dL does not yield improved outcomes. Furthermore, smaller studies have suggested that pediatric intensive care unit patients may be at an increased risk for morbidity and mortality when undergoing transfusion. (*Pediatr Crit Care Med* 2012; 13:204–209)

**KEY WORDS:** critical care; erythrocyte transfusion; morbidity; mortality; pediatrics; red blood cell transfusions

Critically ill pediatric patients have a high incidence of anemia at the time of admission and throughout their pediatric intensive care unit (PICU) stay. The use of packed red blood cell (PRBC) transfusions is common, with approximately 17% of all PICU patients receiving transfusions and close to 50% of long-stay ( $>48$  hrs) PICU patients receiving blood products (1–3).

PRBC transfusions are medically necessary and can be lifesaving in certain situations, including severe anemia, bone marrow failure, and active blood loss. Transfusion is also thought to be a useful intervention in numerous other conditions, including severe sepsis, acute respiratory distress syndrome, malignancy, and sickle cell crisis, to name a few. Additionally, PRBC transfusions are often provided in the perioperative and postoperative settings, either because of anticipated blood loss or in attempt to hasten recovery. Within these settings, there are

many factors that guide an individual intensivist to make the decision to transfuse with PRBC. The decision may be based on a desire to avoid severe levels of anemia that can be dangerous to the patient. Furthermore, because PRBC transfusion will increase oxygen-carrying capacity and oxygen delivery, the intensivist may decide to transfuse in an effort to improve recovery by limiting oxygen debt to the tissues.

However, there are many risks associated with PRBC transfusions, including infections, immunosuppression, transfusion reactions, fluid overload, and medical errors. Given that there are risks associated both with severe anemia and with blood transfusions, critical care providers have been increasingly interested in establishing evidence-based guidelines for PRBC transfusion in critically ill patients.

In the adult critical care world, much work has been performed that increasingly supports a restrictive transfusion strategy and heightened awareness of the dangers of transfusions in many patient subsets. Until recently, there was little evidence to guide pediatric critical care physicians regarding transfusions. However, the emerging data from the adult critical care world in the late 1990s and early 2000s began a transformation of transfusion practice in critical care medicine that ultimately has led to similar

studies to be performed in the PICU setting. These studies have yielded data that can guide physicians in the assessment of the need for PRBC transfusion.

The aim of this review is to summarize recent studies that shed light on the practice of PRBC transfusions in the PICU setting and to provide current evidence-based guidance for those caring for critically ill children to aid in their decisions to transfuse or not transfuse. This is not a systematic review of all PubMed articles, but rather a focused review of what we believe to be the most pertinent articles. This review does not apply to neonatal patients or patients with active bleeding or severe hemodynamic instability.

## Anemia and Transfusion Burden

There are many causes of anemia in critically ill pediatric patients. First, blood loss is common in the PICU, both from hemorrhage and from iatrogenic blood loss caused by phlebotomy. Many patients receive large amounts of intravenous fluids, which lead to further hemodilution. Nutritional deficiency is common in critically ill patients, as is abnormal iron metabolism. Further, erythropoietin levels are decreased and the bone marrow is often suppressed in critical illness (4). Because of these factors, many critically ill patients will have anemia develop at some point in their intensive care unit course.

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A prospective observational study of 1,136 adult intensive care unit patients found that nearly 30% of admissions had hemoglobin (HGB) levels <10 g/dL, the average daily iatrogenic blood loss was 41.1 mL, and the transfusion rate was 37% (5). A retrospective cohort study of 295 pediatric patients admitted to the PICU at a single institution found that anemia (HGB <9.6 g/dL) was present in 13.8% of patients and severe anemia (HGB <7 g/dL) was present in 2.7% (6). The number of patients undergoing transfusion was 22.7%. This study examined only admission and HGB values before transfusion.

In 2008, Bateman et al (3) published the results of a large, prospective, multi-center, observational study investigating the incidence of anemia, the practice of PRBC transfusion, and development of transfusion complications in 977 critically ill pediatric patients. They found that 74% of long-stay (>48 hrs) patients were anemic at some point during their PICU stay (33% were anemic on admission, 41% had anemia develop during the PICU stay). For this study, anemia was defined by HGB cutoff of 14.5 g/dL for neonates, 9 g/dL at 2 months, 10.5 g/dL at 6 months, 11.5 g/dL at 2 yrs, and 12 and 13 g/dL for girls and boys at adolescence. Forty-nine percent of patients received PRBC transfusions during their PICU stay, with a mean pretransfusion HGB level of 9.7 g/d: ( $\pm 2.7$  g/dL). Mean daily blood loss among these patients was 8.25 mL (median, 0.32 mL/kg/day as illustrated in Fig. 1). This study also found that blood loss from phlebotomy was independently associated with later transfusion. This is particularly important in pediatric patients because of the small total circulating volume of blood in children. These data clearly show the large burden of anemia, blood loss, and transfusions in the pediatric critical care population.

### Risks of Anemia

The specific level of anemia that leads to poor outcome attributable to hypoxia is uncertain. In healthy adult volunteers, an iatrogenic isovolemic anemia to HGB level of 5 g/dL continued to supply adequate oxygen to the tissues, as indicated by nonelevated serum lactate levels (7). In two out of 32 volunteers, however, the researchers found ST changes on electrocardiogram indicating possible transient myocardial ischemia that resolved with-

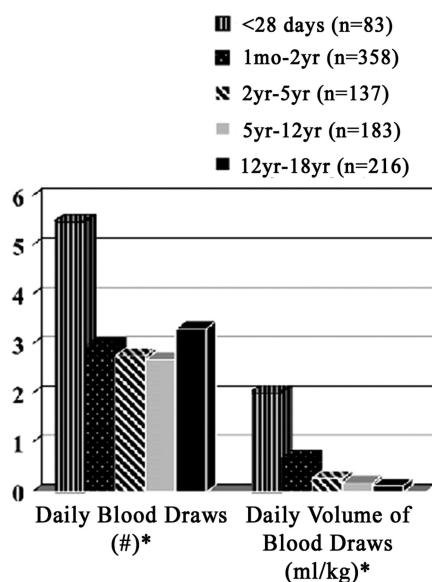


Figure 1. Average number of blood draws per day per patient and average volume of blood collected per day per patient by age of patients. \*Groups were statistically different by age ( $p < .02$ ). Reproduced with permission from Bateman et al (8).

out sequelae. Whereas this level of anemia may be safe in the healthy population, it is unlikely to be well-tolerated in seriously ill pediatric patients. Three studies from Kenya involving large numbers of hospitalized children showed that severe anemia can be dangerous in the hospitalized pediatric population. These studies showed that mortality was significantly higher in patients with HGB levels <5 g/dL and that their risk of mortality decreased if they were treated with PRBC transfusion (8–10).

It is clear that there is some level of anemia that is dangerous. However, the exact level is uncertain and is not likely to be the same for all patients. Because of the inherent risks of randomized studies that would be needed to define the lower limit of anemia that is safe, it is unlikely we will ever know the answer to this question.

### Transfusion Triggers

Data from studies of critically ill adult patients suggest that a restrictive transfusion strategy is associated with improved outcomes. The Transfusion Requirements in Critical Care trial is a large, multi-institutional, randomized, controlled trial that evaluated the use of a restrictive transfusion threshold (HGB <7 g/dL) compared to a liberal transfusion threshold (HGB <10 g/dL) in 838

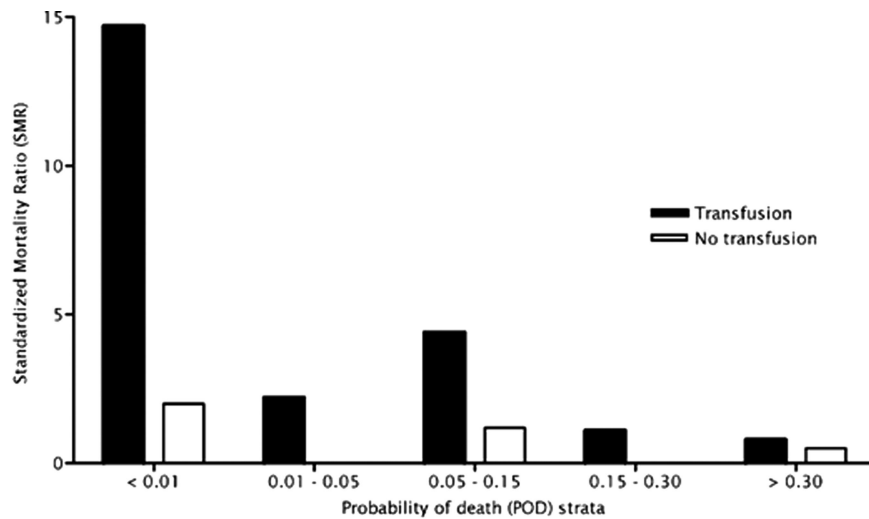
adult patients admitted to the intensive care unit. The study found that patients assigned to the restrictive transfusion threshold had significantly lower in-hospital mortality (22.2 vs. 28.1%;  $p = .05$ ) (11). Despite the publication of the Transfusion Requirements in Critical Care trial in 1999, the question of when to use transfusion in pediatric critically ill patients still remained unanswered through the early part of this decade. In 2002, an article entitled “Guidelines for assessing appropriateness of pediatric transfusion” was published in *Transfusion* and included general guidelines for transfusion for critically ill children. The transfusion threshold hematocrit included a wide range from 24 to 40, depending on the clinical situation (12). Perhaps because of the paucity of data driving such guidelines, there continued to be a great deal of variability in the practice of PRBC transfusion in critically ill children (1, 2). A survey of pediatric intensivists in Canada and Europe found a wide range of PRBC transfusion threshold HGB levels, from 7 to 13 g/dL (13). In 2007, Lacroix et al (14) published the Transfusion Requirements in Pediatric Intensive Care Units study, a multi-institutional, randomized, controlled trial evaluating PRBC transfusion in PICU patients. The study was a noninferiority trial involving 637 hemodynamically stable (mean arterial pressure was not <2 SD below the normal mean for age and cardiovascular treatments had not been increased for at least 2 hrs before enrollment) patients from 19 PICUs in four countries. All patients had HGB levels <9.6 g/dL at the time of enrollment. They were randomized to either receive PRBC transfusions at a threshold HGB level of <9.5 g/dL (liberal criteria) or <7 g/dL (restrictive criteria). This study was conducted with leukocyte reduced PRBC, which was not the case in earlier adult studies and has been a source of criticism of those studies (14). The study protocol allowed clinicians to temporarily suspend the protocol for a number of reasons (i.e., acute respiratory distress syndrome, shock, acute blood loss, or surgery). Patients were followed-up through their stay in the PICU. Primary outcomes included 28-day mortality, the development of multiple organ dysfunction syndrome, and progression of multiple organ dysfunction syndrome. As expected from the protocol design, the two groups had a marked difference in percent of patients receiving PRBC transfusions: 98% in the

Table 1. Primary and secondary outcomes of the patients in the Transfusion Requirements in Pediatric Intensive Care Units study<sup>a</sup>

Variable	Restrictive Strategy Group	Liberal Strategy Group	Absolute Risk Reduction, Odds Ratio, or Difference in Means (95% Confidence Interval)	<i>p</i>
<b>Primary outcome</b>				
New or progressive multiple organ dysfunction syndrome, n/total n (%) <sup>b</sup>	38/320 (12)	39/317 (12)	0.4 (−4.6 to 5.5)	Noninferiority <sup>c</sup>
<b>Age<sup>b</sup></b>				
28 days or younger	1/11 (9)	0	−9.1 (−26.1 to 7.9)	1.00
29–364 days	14/143 (10)	20/142 (14)	4.3 (−3.2 to 11.8)	.28
Older than 364 days	23/166 (14)	19/167 (11)	−2.5 (−9.6 to 4.7)	.51
<b>Country<sup>d</sup></b>				
Belgium	3/66 (5)	4/66 (6)	0.74 (0.16–3.43)	.70
Canada	32/205 (16)	28/203 (14)	1.16 (0.67–2.00)	.60
United Kingdom	2/26 (8)	5/23 (22)	0.30 (0.05–1.73)	.17
United States	1/23 (4)	2/25 (8)	0.52 (0.04–6.18)	.61
<b>Severity of Illness (Pediatric Risk of Mortality score)<sup>b,e</sup></b>				
0 (lowest quartile)	3/64 (5)	4/64 (6)	1.5 (−6.3 to 9.4)	1.00
1–4 (second quartile)	13/128 (10)	11/111 (10)	−0.3 (−7.9 to 7.4)	.94
5–7 (third quartile)	6/54 (11)	6/67 (9)	−2.2 (−13.0 to 8.7)	.69
≥8 (highest quartile)	16/74 (22)	18/75 (24)	2.4 (−11.1 to 15.9)	.73
Suspended protocol, n/total n (%)	18/39 (46)	13/20 (65)	18.9 (−7.3 to 45.0)	.17
<b>Secondary outcomes</b>				
<b>Measures of severity of organ dysfunction<sup>f</sup></b>				
N of dysfunctional organs Pediatric Logistic Organ Dysfunction score <sup>g</sup>	1.6 ± 1.4	1.5 ± 1.2	−0.1 (−0.26 to 0.13)	.87
<b>After randomization</b>				
On day 1	6.3 ± 6.8	5.2 ± 6.2	−1.1 (−2.1 to −0.1)	.09
Highest daily score after day 1	10.2 ± 13.3	8.9 ± 11.9	−1.2 (−3.2 to 0.8)	.34
Change in score	3.8 ± 10.9	3.8 ± 9.9	−0.1 (−1.7 to 1.5)	.97
Average daily score	5.0 ± 6.1	4.2 ± 5.1	−0.8 (−1.7 to 0.1)	.13
<b>Clinical outcomes, n/total n (%)<sup>b</sup></b>				
<b>Death</b>				
In intensive care unit	11/320 (3)	8/317 (3)	−0.9 (−3.6 to 1.7)	.50
From any cause during 28-day study	14/320 (4)	14/317 (4)	0 (−3.2 to 3.2)	.98
Nosocomial infections	65/320 (20)	79/317 (25)	4.6 (−1.9 to 11.1)	.16
At least 1 adverse event	97/320 (30)	90/317 (28)	−1.92 (−9.0 to 5.2)	.59
Reactions to red cell transfusion	3/320 (1)	6/317 (2)	1.0 (−0.9 to 2.8)	.34
<b>Duration of care (d)<sup>f</sup></b>				
Mechanical ventilation	6.2 ± 5.9	6.0 ± 5.4	−0.14 (−1.1 to 0.8)	.76
Intensive care unit stay after randomization	9.5 ± 7.9	9.9 ± 7.4	0.46 (−0.7 to 1.7)	.39

<sup>a</sup>Plus-minus values are means ± SD. <sup>b</sup>the comparison between the restrictive strategy group and the liberal strategy group is given as an absolute reduction in risk. <sup>c</sup>noninferiority was checked only for the primary outcome (the number of patients who had new or progressive multiple organ dysfunction syndrome, including death, after randomization). The absolute risk reduction for new or progressive multiple organ dysfunction syndrome in the restrictive strategy group vs. the liberal strategy group was 0.4% (two-sided 95% confidence interval, −4.6 to 5.5) by intention-to-treat analysis; we also calculated a two-sided 97.5% confidence interval of −5.4 to 6.2. Some experts also consider that a per-protocol analysis should be performed in a noninferiority trial. In the per-protocol analysis, we excluded 11 patients who did not meet the 80% adherence criterion; the number of patients with the primary outcome was 37 of 319 (11.6%) in the restrictive strategy group and 38 of 307 (12.4%) in the liberal strategy group (absolute risk reduction, 0.8%; two-sided 95% confidence interval, −4.3 to 5.9). In all analyses, the upper limit of the confidence interval was lower than the safety margin of error of 10% approved by consensus before the study was undertaken, which means that noninferiority was statistically significant. <sup>d</sup>the comparison between the restrictive strategy group and the liberal strategy group is given as an odds ratio. <sup>e</sup>scores on the Pediatric Risk of Mortality assessment range from 0 to 76, with higher scores indicating a higher risk of death. <sup>f</sup>the comparison between the restrictive strategy group and the liberal strategy group is given as a difference between the means. <sup>g</sup>scores on the Pediatric Logistic Organ Dysfunction assessment range from 0 to 71, with higher scores indicating more severe organ dysfunction. The Pediatric Logistic Organ Dysfunction score can be estimated over the entire stay in the intensive care unit or over 1 day (daily Pediatric Logistic Organ Dysfunction). The change in the Pediatric Logistic Organ Dysfunction score is the difference between the daily Pediatric Logistic Organ Dysfunction score at study entry and the worst daily Pediatric Logistic Organ Dysfunction score thereafter. Patients whose Pediatric Logistic Organ Dysfunction score did not change or decreased after randomization were considered to have a change of 0.

Reprinted with permission from Lacroix et al (14). From the Transfusion Requirements in Pediatric Intensive Care Units study.



Deaths transfused / Total number	N = 4 / 17	N = 2 / 33	N = 3 / 9	N = 1 / 5	N = 1 / 3
Deaths not transfused / Total number	N = 4 / 127	N = 0 / 82	N = 1 / 11	N = 0 / 3	N = 1 / 5
PICE expected deaths	.5%	2.3%	8.1%	20.4%	57.1%
Expected deaths	.72	2.6	1.6	1.6	4.6
SMR transfused patients	$4 / (.005 * 17) = 47.1$	$2 / (.023 * 33) = 2.2$	$3 / (.081 * 9) = 4.4$	$1 / (.204 * 5) = 1.1$	$1 / (.571 * 3) = .8$
SMR non-transfused patients	2.0	N/A	1.1	N/A	.4

Figure 2. Standardized mortality rate (SMR) of patients with and with out transfusions according to five Pediatric Index of Mortality (PIM) probability of death strata. The SMR is calculated by dividing the number of observed deaths by the number of expected deaths. The number of expected deaths was obtained from the Dutch Working Group on Pediatric Intensive Care Evaluation (PICE). N/A, not applicable. Reproduced with permission from Kneyber et al (6).

liberal group and only 46% in the conservative group. As shown in Table 1, Lacroix et al (14) found that the number of deaths, new or progressive multiple organ dysfunction syndrome, adverse events, ventilator days, and nosocomial infections were not significantly different in the two groups.

Further studies have subsequently been performed to investigate whether certain patient subgroups may benefit from a more liberal transfusion strategy or whether the restrictive transfusion strategy can be applied universally in the pediatric critical care population. Two such studies detailing subgroup analysis of the Transfusion Requirements in Pediatric Intensive Care Units data have shown that pediatric cardiac surgery patients (125 patients) and pediatric general surgery patients (124 patients) showed no increase in multiple organ dysfunction syndrome when the restrictive PRBC transfusion strategy was followed (15, 16). Although the number of patients in these articles are small, these findings suggest that treatment with PRBC transfusion for a threshold HGB level >7 g/dL is not useful when caring for stable crit-

ically ill children outside the neonatal period.

### Risks of Transfusion

Although severe anemia can lead to worse outcomes, transfusions have their own risks. Several studies have evaluated the association between transfusions of PRBC and subsequent morbidity and mortality. The Transfusion Requirements in Critical Care trial described certainly suggested that PRBC transfusions may be harmful, because patients who received transfusions more liberally had higher mortality.

In a study of 295 PICU patients published by Kneyber et al (6) in 2007, PRBC transfusion was found to be independently associated with risk of death in critically ill children. This was a retrospective study of PICU patients with anemia (HGB <9.6 g/dL). The researchers found that the patients who received PRBC transfusions had higher mortality, longer ventilator time, greater time requiring vasopressor support, and longer PICU stays. PRBC transfusions were independently associated with increased mortality and morbidity, whereas pre-

transfusion HGB level was not related to mortality. As shown in Figure 2, at every probability of death strata, those who received transfusions had a higher standardized mortality rate.

The risks of transfusion are further explored in a retrospective cohort study of 1,639 pediatric trauma patients performed by Stone et al (17). They found that pediatric trauma patients who received PRBC transfusions within 24 hrs of admission had higher intensive care unit length of stay, hospital length of stay, and mortality rate. When they controlled for injury severity, however, statistical limitations made it impossible to make reliable conclusions about PRBC transfusions being an independent risk factor for mortality. Neither the Kneyber nor the Stone articles compared equally sick patients who had received transfusions with those who had not undergone transfusions. As a result, it is possible that the sicker patients received transfusions and also had worse outcomes but that this finding was not related to the transfusion but rather to the overall level of illness.

The publication by Bateman et al (3) in 2007 was the first large prospective study to provide evidence that transfusions can be harmful in critically ill pediatric patients. After controlling for other factors such as age and severity of illness at admission, PRBC transfusion was found to be significantly associated with increased risk of death (odds ratio, 11.6; 95% confidence interval, 1.43–90.9;  $p = .02$ ), cardiac arrest, nosocomial infections, and longer PICU stay and longer time requiring mechanical ventilation (3). This study clearly demonstrates that there is some increased risk associated with transfusion in pediatric patients.

The mechanisms underlying the harmful effects of transfusions are not fully understood. This may be related to immunosuppressive effects of transfusion or microinjury to organs that are clinically unapparent in healthier patient groups but become apparent in critically ill patients (18). Jeschke et al (19) investigated the link between transfusions and immunosuppression in a retrospective cohort study of 277 pediatric burn patients. They found that higher numbers of transfusions were linked to risk of development of sepsis, particularly in the most severely injured patients (those with total body surface area burn >60% as well as inhalation injury). In this group, patients who received >20 PRBC transfusions and >5 fresh frozen plasma transfusions had a 58% risk of development of sepsis, whereas those receiving <20 PRBC and <5 fresh frozen plasma transfusions had an 8% risk of sepsis ( $p < .05$ ). Mortality was also higher among patients receiving >20 PRBC transfusions (18 out of 60 patients) vs. those who received <20 PRBC transfusions (12 out of 202 patients;  $p < .001$ ; odds ratio, 6.79). The study authors postulate that the etiology of increased sepsis, organ failure, and death in transfused patients is connected to the release of proinflammatory mediators such as interleukin-6, interleukin-8, and acute phase proteins, triggers that enhance protein wasting and organ dysfunction and ultimately lead to death.

Further evidence of the harmful effects of transfusion comes from a study investigating transfusion-related acute lung injury. Transfusion-related acute lung injury is a rare complication of transfusions; however, it is possible that minor lung and organ injury associated with transfusion is much more common than previously believed. In a retrospec-

tive review of critically ill adult patients, Cornet et al (18) found that PRBC transfusion led to a transient decrease in oxygenation, suggesting that transfusion may cause some level of lung injury in critically ill patients. Perhaps minor organ injury is common in all patients receiving transfusions, but only the most seriously ill patients show the effects of this injury because they are so compromised already.

Another issue that may contribute to the harmful effects of PRBC transfusion is the length of storage of PRBC. In a retrospective analysis of 6,002 adult patients undergoing coronary artery bypass grafting who received PRBC transfusions, Koch et al (20) found that patients who received newer PRBC (stored <15 days) had better outcomes (decreased in-hospital mortality, shorter need for ventilatory support, decreased renal failure and sepsis) than those who received older PRBC (stored >14 days). Results from several other studies in adults are mixed; some have shown worse clinical outcomes in patients receiving older blood (20–23) and other studies have shown no difference in patients receiving old vs. new blood (24–27). The pediatric literature on this issue is less robust. One small retrospective study of PICU patients found no evidence of adverse effects associated with length of PRBC storage (28). Another study using an analytical cohort analysis of 455 patients in the Transfusion Requirements in Pediatric Intensive Care Units found that PRBC stored >14 days was independently associated with increased multiple organ dysfunction syndrome (adjusted odds ratio, 2.23; 95% confidence interval, 1.20–4.15) and a storage time >21 days was associated with increased pediatric logistic organ dysfunction scores (adjusted mean difference, 4.26; 95% confidence interval, 1.99–6.53) and higher mortality (9.2% vs. 3.8%) (29). Also, a comprehensive prospective, observational study of 977 patients admitted to 30 different North American PICUs found that transfusion of PRBCs stored >13 days was associated with increased PICU length of stay and increased incidence of multiple organ dysfunction syndrome (30).

## CONCLUSIONS

A review of the current literature indicates that transfusion of PRBCs is a common practice in the PICU setting. Data from adult studies show that a restrictive

rather than a liberal transfusion strategy results in improved patient outcomes. Similarly, a recent study of critically ill children demonstrated that using a liberal transfusion threshold does not confer any clinical benefit over a restrictive threshold (14). PRBC transfusions appear to be independently linked to increased risk of morbidity and mortality in critically ill pediatric patients (3,6,19). Furthermore, clinical outcomes in patients who receive PRBC stored >14 days appear to be worse compared to those of patients who receive newer PRBC (20, 30).

The exploration into the etiology of the risks associated with transfusions is ongoing. In the case of nonleukocyte-reduced PRBC transfusions, transfused leukocytes can lead to an inflammatory cascade that decreases the body's immune response. Many institutions now universally filter PRBC to decrease the number of leukocytes. However, this process does not remove inflammatory cytokines that have already been released by lysed leukocytes. Hence, it is still possible that the free-floating cytokines may elicit an inflammatory process that renders the patient who has received a transfusion somewhat immunosuppressed. There is ongoing debate regarding the usefulness of leukocyte reduction; however, the growing trend of leukocyte reduction for PRBC transfusions will likely expand in pediatrics, even without clear mortality effects related to its practice.

Published guidelines for PRBC transfusions in hemodynamically stable, critically ill adult patients recommend using a restrictive transfusion threshold of HGB levels <7 g/dL except in those with myocardial ischemia or infarction (31). However, to date there are no widely accepted guidelines for PRBC transfusion for critically ill children and, as a result, clinical practice varies widely regarding indications for transfusion and the HGB threshold at which to transfuse (32). It is not likely that there is a "one size fits all" transfusion threshold that addresses the needs of all patients. Further studies are needed to establish appropriate transfusion threshold HGB levels in individual pediatric subgroups such as patients with sepsis, acute respiratory distress syndrome, brain injury, and others. Until such studies are conducted, it is advisable to evaluate each patient individually in the context of the illness, bearing in mind that for hemodynamically stable patients the evidence does not support transfusing until the HGB level decreases to <7 g/dL.

The intensivist must also consider the clear dangers of PRBC transfusions such as infection, transfusion reactions, fluid overload, and medical errors, as well as the more subtle harmful effects such as lung and other organ injury, immunosuppression, and the dangers associated with transfusing old PRBCs. Preventing or at least reducing the development of anemia is another important strategy to reduce exposing patients to the risks associated with transfusion. Iatrogenic blood loss can be substantial in PICU patients and likely contributes to development of anemia to a much greater extent in pediatric patients than in adult patients. Efforts must be made to limit the frequency and quantity of blood draws to reduce the need for PRBC transfusions.

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