

When to transfuse red cell concentrate perioperatively

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The anesthesiologist assumes an important role when administering a blood transfusion. The indication for transfusing packed red blood cells in the perioperative phase has been the subject of many published articles. However, it may be time to re-examine this topic. In light of the literature published over a number of years, a threshold for starting a transfusion based on a double "trigger" (a double indication) is the most reasonable approach. The "therapeutic" threshold (anemia + an anemia-related physiopathological condition) is not directly linked to a minimum hemoglobin (Hb) level, but rather is a dynamic balance between the physiological state of a patient and his/her tolerance. The "preventive" transfusion threshold (anemia + estimated risk) is aimed at preventing an increase in morbidity and mortality that may result from perioperative anemia. This transfusion trigger calls for an Hb concentration of < 70 g/L according to prospective and randomized clinical trials. Based on retrospective studies, the appropriate "trigger" level is somewhere between 50 g/L and 70 g/L. We do not have sufficient information to establish guidelines for patient subgroups or even to identify patients at higher risk of perioperative complications.

Giving a transfusion only on the basis of a low hemoglobin level is no longer justified if one evaluates the risk/benefit and availability/benefit ratios of allogeneic blood products and such a practice is probably detrimental for many patient subgroups.

Allogeneic blood products (ABP) are a natural therapeutic resource that must be constantly renewed. Some 60% to 70% of packed red blood cells are administered during hospitalization for surgery. The anesthesiologist plays a leading role in the area of perioperative transfusional medicine because his expertise enables him to evaluate the risks of, and tolerance to, anemia and the alternatives to giving a transfusion. He often takes on the role of transfusing physician. Different considerations will influence transfusion practice. First, there is always the fear that a shortage of ABPs will limit access to surgery. In addition, with the advent of many transfusion alternatives in the clinical setting, we must redefine our transfusion practice. Finally, despite all preventive measures, ABPs are always a source for potentially pathogenic agents.

Red blood cell transfusion must be considered as the transplantation of foreign tissue. The probability of receiving a perioperative red blood cell transfusion depends on three factors:

- The prescribing physician
- The preoperative hemoglobin mass
- The amount of blood loss.

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The treating physician's attitude toward transfusion remains the most important factor when a transfusion is being considered. This fact, which may be surprising at first glance, is highlighted in the Sanguis study. This examination of 43 European teaching facilities (7,195 patients) demonstrated that, after adjustment for several variables (eg, age, sex, preoperative Hb concentration and blood loss), the most important factor in determining whether a patient would be transfused or not was the treating physician (and his or her institution) and not the patient's physiological condition.¹ The preoperative Hb value takes into account the patient's blood volume (weight and sex) and Hb concentration. This indicator of erythrocyte reserve will strongly influence whether a transfusion is likely. Finally, blood loss is a factor well known to the anesthesiologist. The operations most likely to lead to transfusion are orthopedic surgery and major cardiac, vascular, and abdominal surgery.²

Ideally, the decision to transfuse must be based on 3 ratios: risk/benefit, cost/benefit, and availability/benefit. The common denominator of these 3 ratios is, of course, the demonstration that a red cell transfusion will decrease morbidity and mortality, as well as shorten the postoperative hospital stay. However, one question remains for the clinician: What is the Hb concentration threshold that indicates the need for an allogeneic red cell transfusion?

Three thresholds may be defined:

Therapeutic threshold: When anemia is accompanied by a symptom or anomaly, a red blood cell transfusion can correct the physiological disorder. In this case, the trigger for the decision to transfuse = *anemia + physiopathological condition*.

Prophylactic threshold: Given the desire to prevent complications, a group of patients (eg, the elderly or coronary patients), may be identified who, when exposed to particular conditions, would have an increased risk of morbidity, mortality, or extended hospital stay. The prophylactic transfusion threshold seeks to identify an Hb level indicating transfusion, in the absence of symptoms of severe anemia. Here, the trigger = *anemia + feared risk*.

Comfort zone: This transfusion trigger is influenced by 4 factors:

- The degree of medical consensus on the indication for transfusion
- The hospital's organizational context
- The level of knowledge of the prescribing physician
- The style of practice of the transfusing physician.

The "comfort zone" is a transfusion threshold that is mainly influenced by the last 3 factors above.

This trigger may be based on clinical experience, adherence to a particular mode of practice, or on compensation for a lack of scientific validation for the transfusion. However, this approach may quickly lead to arbitrary transfusion practices. In addition, psychological factors (fear of not acting, lawsuits, or poor prognosis) may influence what should be the optimal approach. In this case, the trigger responsible for the decision to proceed with a transfusion is an *isolated decrease in Hb concentration*.

By definition, anemia is a condition that is characterized by a decrease in the amount of circulating hemoglobin. If the patient has a normal blood volume, anemia may be estimated by measuring the Hb concentration ([Hb]). The World Health Organization defines anemia as an [Hb] that is <130 g/L in men and <120 g/L in women. The challenge for the clinician is estimating the anemic condition when there are great variations in the circulating volume. For example, a lowered [Hb] when large quantities of crystalloids or colloids are administered (hypervolemic hemodilution) does not constitute anemia. Conversely, major blood loss without volume repletion causes anemia with a slight variation in the [Hb].

A THERAPEUTIC APPROACH TO RED BLOOD CELL TRANSFUSION

All professional consensus statements and recommendations on transfusion published over the last 20 years, with a single exception, conclude that there is no universal [Hb] threshold indication for a red blood cell transfusion. These recommendations, therefore, do not justify seeking a "comfort zone." The consensus statements favour a therapeutic or preventive use whereby a transfusion is only indicated in the presence of both anemia and the negative effects resulting from this condition (a threshold with a double trigger).

In this context, the American Society of Anesthesiology has established guidelines regarding the likelihood of receiving packed red blood cells.³ Transfusions will be frequent when the [Hb] is <60 g/L and rather exceptional when the level is >100 g/L. In situations between these two levels, the consensus suggests an evaluation of the patient's physiological condition and risks. It is important to note that these guidelines are not the result of scientific validation based on the incidence of complications related to anemia or the benefit of a preventive correction, but rather, are based on a consensus in clinical practice.

Adding a second element to the indication for a transfusion pushes the limits of anemia necessary for a transfusion. For example, in one study that examined spinal surgery in the adolescent (n = 8), the dual

trigger of [Hb] + venous saturation $\leq 60\%$ delayed red blood cell transfusion until the mean concentration reached a nadir of 30 ± 8 g/L.⁴ This severely anemic state has not been associated with the onset of clinical complications. The goal of a red blood cell transfusion is not only to increase the circulating mass of red blood cells, but also to support oxygen delivery and its compensatory mechanisms thus sustaining oxygen consumption in the tissues. It is still to be determined which elements should comprise the double trigger to make transfusion clinically optimal (Table 1).

The effectiveness of a therapeutic red blood cell transfusion remains to be evaluated and likely depends on various factors. The premise that a red cell transfusion produces immediate and complete correction of morbidity and mortality is not supported in the literature. For example, in a cohort of 4,470 patients admitted to the intensive care unit (ICU), mortality was inversely proportional to the pre-transfusion [Hb], despite the fact that all patients had been transfused.⁵

TWO WAYS TO ASSESS THE EFFECTIVENESS OF A TRANSFUSION

Improvement in the VO₂/DO₂ after a red blood cell transfusion in the ICU

The benefits of a red blood cell transfusion in the ICU context are difficult to define. Many studies have evaluated the effect of red cell transfusions on oxygen delivery (DO₂), its uptake (VO₂), and lactatemia. The great majority show no evidence of improvement in VO₂ or in lactatemia. However, when individual results are reported, it becomes evident that the transfusion response varies. For example, in the study by Gilbert *et al*, the VO₂ improved in three patients, the condition of 2 others deteriorated, and in another 2 patients, the transfusion had no effect whatsoever.⁶ One major limitation in the older studies is the systematic withdrawal of patients whose post-transfusion DO₂ did not improve, which distorts the evaluation of the real effectiveness of this therapy.

More recently, Casutt *et al* evaluated the impact on VO₂/DO₂ of 170 transfusions after cardiovascular surgery.⁷ A transfusion was indicated when the hematocrit was $< 20\%$ - 25% in the presence of a left ventricle ejection fraction $< 40\%$, or when there was a need for catecholamines. About 50% of the transfusions were accompanied by a drop in cardiac output and in almost 30% of cases, this drop was not compensated by the increase in [Hb], to the extent that in these situations, the DO₂ decreased after transfu-

TABLE 1: Elements used to identify the pathophysiological stage of anemia

SYMPTOMATIC THRESHOLDS OF "PERMISSIVE ANEMIA"	USE OF COMPENSATION MECHANISMS
Hemorrhage	PvO ₂
Tissue ischemia	SvO ₂
Fatigue	Hemodynamic parameters
Attention deficit	Acid-base balance
	Lactatemia
	VO ₂ /DO ₂ matching

sion. It is interesting to note that the preoperative ejection fraction of the left ventricle, the age of the patients, and the pre-transfusion [Hb] (50 g/L to 120 g/L) could not predict a benefit from the transfusion. The only indicator of a successful transfusion was a low pre-transfusion VO₂ ($r^2 0.259$, $p < 0.001$). From the available data in this publication, a VO₂ below 100 ml/min/m² elicited an extremely high level of response. When the pre-transfusion VO₂ was higher, a favourable response was observed in less than 50% of cases.

Treatment of fatigue in oncology

Fatigue associated with anemia is frequent in cancer patients. Few studies have been published on the subject despite the very frequent transfusions these patients receive. One study prospectively evaluated the effectiveness of red blood cell transfusion in a subgroup of 31 patients with terminal-phase neoplasms.⁸ These patients (average age 69.5 ± 12 years) all presented with an [Hb] of ≤ 80 g/L, with fatigue and severe dyspnea. Before the transfusion and 24 hours after, the patients were assessed for physical performance, cognitive status, and levels of dyspnea and fatigue at rest and on exertion. A subjective improvement in symptomatology was reported in 51.4% of cases. The severity of the dyspnea, fatigue, or anemia before the transfusion was not predictive of the patients' responses to the transfusion.

Another study (prospective, placebo-controlled) assessed the impact of a transfusion to correct anemia versus the addition of recombinant human erythropoietin in 375 patients with hematologic neoplasms.⁹ Five subjective quality-of-life indicators were used in these patients over 12-24 weeks. While the perception of well-being improved in the erythropoietin group, the patients who had received only packed red cells showed a decline in the 5 quality-of-life indicators ($p < 0.01$).

PREVENTIVE APPROACH WITH RED BLOOD CELL TRANSFUSION

Observation of transfusion practice in the clinical setting points out, however, that a transfusion is often motivated by the fear of the risk of complications linked to the patient's anemic condition. This is of great concern to the clinician who wants to prevent an unfavourable outcome associated with a low [Hb]. In order to identify this threshold, the risks of anemia in the perioperative period must be considered, along with the risks and benefits of transfusion.

Risks associated with anemia

Assessment of the risks associated with perioperative anemia relies on retrospective studies of patients who refuse transfusion for religious reasons or who cannot be transfused because transfusion is not available or who are taking part in comparative studies on different transfusion practices.

Preoperative anemia

Viele and Weiskopf reviewed 54 case studies, including 134 Jehovah Witnesses treated for various medical and surgical conditions, to evaluate the relationship between mortality and anemia ([Hb] \leq 80 g/L).¹⁰ The overall mortality in this nontransfused group of patients was 37%. Anemia was identified as the presumed cause of death in 17% of the 134 patients. Except for 3 patients who underwent cardiac surgery, all the deaths attributed to anemia occurred at [Hb] levels of \leq 50 g/L (from 12 g/L to 45 g/L). A second study established no correlation between postoperative mortality and preoperative anemia ([Hb] 60-120 g/L) in patients without cardiac pathology.¹¹ The proportion of deaths attributed to anemia was 27.9%.

Spence *et al* observed no deaths in 107 Jehovah Witnesses who underwent major surgery and whose preoperative [Hb] was $>$ 60 g/L.¹² The authors underline that a loss of $>$ 500 ml of blood has a much greater impact on mortality than the presence of preoperative anemia. The important role of hemorrhage was also confirmed in a study by Carson, who observed that a perioperative loss of 20 to 39 g/L reduced survival to the same extent as the presence of heart disease in an anemic patient.¹¹

The prevention of excessive bleeding must be a constant concern and should be based on an interdisciplinary approach. More recently, in a retrospective study of 2,059 cases of surgical myocardial revascularization, a preoperative [Hb] \leq 100 g/L was identified as an independent risk factor of hospital mortality (OR) 3.17; CI 95%, 1.243-8.083).¹³ This correlation was observed despite corrective intra-

operative transfusions in all anemic patients ($<$ 100 g/L). Furthermore, patients presenting an [Hb] of $<$ 90 g/L were transfused preoperatively. This underlines the probable importance of comorbidities. Perioperative transfusion seems insufficient to compensate for these prognostic indicators.

The causes of mortality must also be taken into consideration since a proportion of the deaths are certainly attributable in large part to the underlying condition that led to the drop in [Hb] rather than the anemia itself. For these patients, red blood cell transfusion would be ineffective in correcting the primary condition.

Postoperative anemia

A recent retrospective study conducted on 300 Jehovah Witnesses evaluated the effects of a postoperative nadir of [Hb] \leq 80 g/L on 30-day postoperative hospital mortality and morbidity.¹⁴ The majority of surgical procedures were aortic, intrathoracic, or intraperitoneal (65.3% of the population studied). No deaths were noted in the group with an [Hb] of 71 g/L to 80 g/L. The mortality rate of the cohort was 16%, compared to 79% in the Viele and Weiskopf study.¹⁰ The mortality was significantly correlated with a decrease in the nadir of the [Hb] starting at 70 g/L and showed a sudden elevation below 50 g/L. Every decrease of 10 g/L in the [Hb] was accompanied by an adjusted relative risk of mortality of 2.5 (CI 95%, 1.9-3.2) and of morbidity or mortality of 2.1 (CI 95%, 1.7-2.6). The main complications were post-transfusion failure, arrhythmia (7.4%) pneumonia (6.6%), myocardial infarction (1.6%) and deep cutaneous infection (1.2%). Contrary to their previous study, Carson *et al* did not identify the interaction between postoperative [Hb], cardiovascular pathologies, and mortality.

HOW EFFECTIVE IS PREVENTIVE TRANSFUSION? SHOULD WE TRANSFUSE OR NOT?

Two large cohorts enrolled in Kenya evaluated the risk of anemia and benefits of transfusion. The availability of ABPs determined the number of transfusions. The first study evaluated the effects of red blood cell transfusion on hospital mortality in 684 anemic pediatric patients whose [Hb] was $<$ 50 g/L. Only one red cell transfusion could be administered to 201 patients because of the lack of product availability. Early transfusion (in the hours immediately following admission) only reduced mortality when the [Hb] on admission was $<$ 39 g/L (0-24 hours, [OR] 0.30; 95% CI, 0.14-0.61, 24-48 hours, [OR] 0.37; 95% CI 0.14-1.00). If respiratory distress was present, survival was improved by transfusion in children

TABLE 2: The 10 studies considered in the Cochrane Database of Systematic Reviews

	Patients included in the restrictive group	Transfusion threshold Restrictive group	Transfusion threshold Control group
Topley (1956)*	12	Red blood cell volume 70-80% of normal	Red blood cell volume >100% of normal
Blair (1986) ¹⁹	26	< 80 g/L	2 empirical units
Fortune (1987) ²⁰	12	Hct maintained at 30%	Hct maintained at 40%
Johnson (1992) ²¹	20	Hct <25%	Hct maintained at 32%
Hébert (1995) ²²	33	< 70-75 g/L	< 100-105 g/L
Bush (1997) ²³	50	< 90 g/L	<100 g/L
Carson (1998) ²⁴	42	< 80 g/L	≤ 100 g/L
Lotke (1999) ²⁵	62	< 90 g/L	Systematic transfusion
Bracey (1999) ²⁶	216	< 80 g/L	< 90 g/L
Hébert (1999) ²⁷	418	< 70 g/L	< 100 g/L

* Topley ET, Fisher MR. The illness of trauma. *The British Journal of Clinical Practice*. 1956:770-776.

whose [Hb] was <47 g/L ([OR] 0.19; 95% CI, 0.09-0.41).¹⁵

The second study in the same group examined the relationship between [Hb], transfusion exposure or non-exposure, and hospital mortality in 2,986 anemic women. The average [Hb] of the cohort was 104±26 g/L. This cohort included a group of 179 patients with an [Hb] of ≤60 g/L. While a better survival rate was associated with a higher [Hb] ([OR] 0.43; 95% CI, 0.19-0.98), transfusion exposure brought no significant benefit ([OR] 1.56; 95% CI, 0.22-11.03).¹⁶ The causes of death may explain the lack of benefit from the transfusion since, in 75% of the patients, the cause of death was attributed to an HIV complication, while anemia was implicated in 31% of cases.

A large retrospective study evaluated the impact of red blood cell administration, or the absence thereof, on 30-day mortality after surgical repair of hip fracture.¹⁷ The average age of the 8,787 patients was 80.3 years (60 to 106 years). The authors were not able to demonstrate any significant benefits associated with red cell transfusion when the minimum postoperative [Hb] level was > 80 g/L. The small number of patients not transfused because of [Hb] levels that were lower did not allow the authors to draw any conclusions on the benefits of transfusion in these circumstances.

HOW EFFECTIVE IS PREVENTIVE RED BLOOD CELL TRANSFUSION? SHOULD WE TRANSFUSE LESS OFTEN?

The recent Cochrane Database of Systematic Review conclusions on red cell transfusion thresh-

olds allows a further assessment on the basis of 10 randomized studies.¹⁸ These clinical trials included 1,780 patients in a perioperative and ICU environment. Meta-analysis of these data demonstrates that lowering the transfusion threshold reduces the probability of receiving a transfusion by 42% without a negative effect on 30-day mortality or an increase in cardiac events or length of hospital stay. These studies evaluated prophylactic transfusion triggers varying from 70 g/L to 100 g/L (Table 2).

The lack of benefit associated with maintaining the [Hb] within the guidelines evaluated by these studies suggests that the anemia poses no risk whatsoever for groups of patients subjected to various physiological disturbances, or that the correction of anemia was partial or late, or ineffective in terms of improving the prognosis in these patients. It is also possible that transfusion can improve anemic conditions, but at the price of risks that have yet to be assessed (immunomodulation, infection, etc.). In the case of the last hypothesis, the benefits of red cell transfusion therefore would only be observed in conditions of extreme anemia.

Given our present knowledge, preventive transfusion is not indicated when the [Hb] is >70 g/L. This conservative attitude is particularly advisable in patients <55 years old and in those whose APACHE score is ≤20.¹⁹ We have yet to identify an [Hb] threshold at which preventive correction via a red cell transfusion would be beneficial for a group of patients (elderly or suffering from cardiovascular pathologies). We can estimate that the prophylactic threshold is between 50 and 70 g/L.

TABLE 3: Perioperative morbidity and mortality associated with red blood cell transfusion and anemia: recent studies

Authors	Variable	Risk (OR)	Confidence interval (95 %)	P
Non-cardiac surgery				
Arozullah (2001) ²⁸ N = 316,071	Postoperative pneumonia Transfusion > 4 units	1.35	1.07-1.72	
Dunne (2002) ²⁹ N = 6301	Mortality Absence of preoperative anemia Absence of postoperative anemia Peroperative transfusion Transfusion > 4 units Infection Peroperative transfusion Transfusion > 4 units	0.98 0.91 1.08 2.84 1.06 9.28	0.96-0.99 0.89-0.93 1.04-1.13 2.07-3.89 1.01-1.11 5.74-15.0	<0.01 <0.001 <0.001 <0.001 <0.01 <0.001
Cardiac surgery				
Engoren (2002) ³⁰ N = 1915	Mortality at 5 years Transfusion N = 992	1.35	1.18-1.54	<0.001
Zindrou (2002) ¹³ N = 2059	Mortality Preoperative [Hb] ≤ 100 g/L	3.17	1.24-8.08	0.016
Olsen (2002) ³¹ N = 1980	Deep infection Postoperative transfusion > 4 units	2.39	1.13-5.06	0.022
Leal-Noval (2001) ³² N = 738	Pneumonia morbidity Transfusion ≥ 4 units	2.6	1.1-5.8	0.016
Carotid surgery				
Waggoner (2001) ³³ N = 1114	CVA Perioperative transfusion versus no transfusion Infarct Perioperative transfusion versus no transfusion		7.3% versus 2,3% 2.4% versus 1,5%	0.003 NS
Traumatology				
Tornetta (1999) ³⁴ N = 326	Mortality Transfusion	1.11		0.01
Malone (2000)* N = 9539	Mortality Transfusion Morbidity (SIRS) Transfusion	10.33 5.74	4.84-18.80 3.9-8.4	<0.001 <0.001
Intrathoracic surgery				
Harpole (1999) ³⁵ N = 3516	Mortality Preoperative transfusion (> 4 units) Blood loss Morbidity Preoperative transfusion (> 4 units) Preoperative transfusion	7.19 1.001 5.28 1.26		0.0005 0.0001 0.0019 0.0001
Bernard (2001) ³⁶ N = 639	Mortality Lowered [Hb] Cardiovascular morbidity Transfusion	0.78	0.66-0.92	0.003 NS
Langley (2002) ³⁷ N = 234	5-year survival Transfusion ≥ 3 units Transfusion < 3 units Multivariate analysis		17.5% ± 3.3% 10.0% ± 6.1%	0.04
Milot (2001) ³⁸ N = 3278	ARDS Transfusion	1.6		0.03
Colorectal surgery				
Chang (2000) ³⁹ N = 1349	Bacterial infection Transfusion	1.18	1.05-1.33	0.007
Orthopedic surgery				
Carson (1998) ¹⁷ N = 9355	30-day mortality Impact of transfusion in perioperative anemia ([Hb] 70-119 g/L)			NS
Carson (1999) ⁴⁰ N = 9598	Severe bacterial Infection Transfusion Anemia Pneumonia Transfusion	1.35 1.52	1.10-1.66 1.21-1.91	NS

* Malone DL, Kuhls D, Napolitano LM et al. Blood transfusion in the first 24 hours after trauma is associated with higher risk for systemic inflammatory response syndrome (SIRS), ICU admission, and death. *Crit Care Med* 2000;28 (Suppl.):A138

WHY TRANSFUSE?

The indication for transfusion has evolved considerably since the first experiments in the 18th century. When given under extreme hemorrhagic conditions, a transfusion of complete blood corrected both the circulating volume and the hemoglobin mass. After crystalloid and colloid solutions became available, packed red blood cells made it possible to rectify the circulating Hb mass only. However, compensatory mechanisms for oxygen delivery enable patients to tolerate anemic states. The intended goal of transfusion has therefore evolved from increasing [Hb] to supporting the availability of oxygen to the tissues. From replacement of blood to the correction of anemia, it must be demonstrated that red cell transfusions can reduce, if not overturn, the morbidity and mortality associated with anemia.

RISKS OF ALLOGENEIC RED BLOOD CELL TRANSFUSION

Since a perioperative red blood cell transfusion frequently occurs in the setting of blood loss, it is difficult to separate the risks related to anemia from its treatment. Nonetheless, recent large-scale retrospective studies indicate that transfusion exposure is a risk factor for perioperative complications independent of bleeding and anemia (Table 3). Therefore, the risks associated with a transfusion must be considered, particularly when using a preventive transfusion threshold. While the risks of transmission of a virus are well-controlled, certain elements in the transfusion literature are cause for concern. The association between postoperative infection, cerebrovascular accident, and mortality warrants more extensive investigation. It should be emphasized that these associations do not demonstrate a causal link, but until we know more about the real risks, an attitude toward restricting transfusions to certain pathophysiological situations seems prudent.

CONCLUSIONS

A transfusion threshold based on obtaining a “comfort zone” is no longer acceptable. Red blood cell transfusion must correct much more than the [Hb]. A transfusion threshold based on a preventive approach must be defined with prudence. Prudence not only means the contemplation of transfusion because of the fear that the patient will develop complications from his/her anemia. It should also take into account the retrospective studies with multivariate analyses that have established a correlation (but not a causal relation) between transfusion and increased postoperative morbidity and mortality.

The challenge for the clinician is to weigh the potential risks associated with anemia against the risks associated with a red cell transfusion. The preventive transfusion threshold is approximately 50 g/L and 70 g/L, and it becomes crucial only for certain specific subgroups of patients.

A therapeutic transfusion threshold places the primary emphasis on the detection of inadequate oxygenation of tissues and its treatment with packed red cell transfusion if it is accompanied by anemia. It must be emphasized that the response to transfusion varies. While the condition of certain patients improves after packed red cell administration, for many, these products will have no discernible effect, and in others, transfusion will induce adverse effects, even complications. We also need to better understand and measure the effects of leukocyte reduction, age of stored ABPs, and induced immunomodulation on the perioperative prognosis. In order to optimize the risk/benefit and availability/benefit ratios of packed red blood cell transfusion, the decision to transfuse must be made unit by unit, and followed with verification of the “dual-trigger” correction.

*UTI NON ABUTI
(Use but don't abuse)*

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