Received: 6 November 2022 | Revised: 31 March 2023 | Accepted: 27 April 2023

DOI: 10.1111/vox.13442

REVIEW

Vox Sanguinis ISBT International Society of Blood Transfusion

Patient blood management: Myths and facts about red blood cell transfusions

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Funding information
The authors received no specific funding for this work.

Abstract

Transfusion medicine resembles all of medicine in that expert opinion predominates because hard data on clinical outcomes from randomized controlled trials and high quality observational data are simply unavailable. Indeed, some of the first trials evaluating important outcomes are barely two decades old. Patient blood management (PBM) depends on high quality data for assisting clinicians in making clinical decisions. In this review, we focus on several red blood cell (RBC) transfusion practices that new data suggest need reconsideration. The practices that may need revision include transfusion for iron deficiency anaemia, except in life threatening situations, toleration of anaemia as a largely benign condition and use of haemoglobin/haematocrit as primary indications for RBC transfusion, as opposed to adjuncts to clinical judgement. In addition, the long-standing notion that the minimum transfusion should be two units needs to be abandoned due to the danger to patients and a lack of clinical evidence of benefit. Finally, the difference in indications for leucoreduction versus irradiation needs to be understood by all practitioners. PBM is one of the strategies for managing anaemia and bleeding that holds great promise for patients, and transfusion is only one facet of the bundle of practices.

Keywords

blood safety, patient blood management, RBC components, transfusion strategy

Highlights

- A number of myths about red blood cells encountered by the authors are discussed here. This discussion is followed by evidence-based facts and expert opinion that disprove the myths and support evidence-based practice.
- This manuscript will serve to educate medical students, advanced practice providers, physicians in training and those in practice.
- Adequate patient blood management knowledge has also been linked to higher quality patient care and its implementation can improve important clinical outcomes such as decreased length of stay, a reduction in nosocomial infection and fewer intensive care unit admissions.

INTRODUCTION

Why is it important to address common misconceptions or 'myths'? Blood transfusion is one of the most common procedures performed in the inpatient setting [1,2]. Although ordering a transfusion is a part of routine practice for most physicians, the available literature has shown that non-transfusion medicine physicians have poor to intermediate transfusion medicine knowledge (TMK) [3–5].

Adequate physician TMK has also been linked to higher quality patient care [3,6]. As the composition of hospital medicine providers continues to evolve rapidly, attention is needed not only for physicians but also for advance practice providers (APPs) [3,7]. The growing involvement of APPs in the care of hospitalized patients raises the importance of adequate TMK among APPs. In one survey, 90% of APPs working in haematology and bone marrow transplant reported discomfort in their ability to practice in their specialty and wanted more training in transfusion medicine [3,8].

Unfortunately, medical education at both graduate and postgraduate levels includes minimal transfusion medicine instruction, the majority of which is in the form of passive lectures [3,9]. Therefore, hospital medicine providers are likely to have developed transfusion practices based on the limited knowledge taught in their training [3]. Transfusion decisions for acutely ill patients presenting with multiple co-morbidities may become complex and require a more in-depth understanding in order to minimize risks of transfusion and to identify, treat and report reactions for the health and safety at both the individual and population levels [3].

A study was conducted of 183 hospital medicine providers in the United States (US) (including 155 attending hospitalists and 28 APPs) who completed a 12-question online survey and 20 question exam [3]. The overall mean score was 52% (range 20%–85%) [3]. Forty-one percent of participants reported less than 1 h of training in transfusion medicine [3]. Five of the seven questions with the worst performance (<25% correct) focused on transfusion reactions [3]. Almost all respondents reported consenting a patient for blood transfusion and 60% believed that TMK was very or extremely important in order to provide appropriate care for patients [3]. More than 80% believed that having additional transfusion medicine education would be at least moderately helpful [3]. Although routinely consenting patients for transfusion, hospital medicine providers may have insufficient TMK [3].

A recent letter to the editor [10] made the following recommendations:

1. The best method to educate the physicians about patient blood management (PBM) is to oblige them to participate during their medical studies in courses focused on blood transfusion.
2. If this cannot be achieved, physicians should be educated. This would start with the attending physicians, as residents and fellows 'copy' their mentor's attitude, including their approach towards blood transfusion.
3. Blood myths exist and influence diverse populations. Increasing the level of general knowledge and education can reduce the influence of myths.
4. Finally, the various aspects and causes of blood transfusion overuse lead one to the conclusion that education is the key to success.

The purpose of this manuscript is twofold. First, it will show a number of myths in PBM that have been encountered by the authors and then provide the evidence-based facts that disprove these myths and support the correct practice for optimal patient care. Second, we hope that this manuscript will serve to educate medical students, APPs, physicians in training and those practicing. As stated above, adequate TMK (and PBM knowledge) has also been linked to higher quality patient care [3,6].

METHODS

A group of experienced and active practitioners of transfusion medicine and PBM convened a working group to develop a list of common clinician opinions encountered in daily practice that have dubious scientific evidence, henceforth, defined as 'myths', and which also have potentially adverse clinical consequences when actions are based on these notions. A focused literature review was performed to address the background of each 'myth' and provide evidence against it.

Iron deficiency should be treated with transfusion

Iron deficiency anaemia (IDA) is the most common nutritional disorder worldwide. The diagnosis of IDA is confirmed by the presence of low body iron stores and a haempglobin (Hb) level two standard deviations below normal [11]. The primary treatment for IDA is oral or intravenous iron, but in an emergency setting for patients who are actively bleeding or unstable, red blood cell (RBC) transfusion may be necessary. Choosing Wisely Canada guidelines state, 'Don't transfuse RBCs for iron deficiency without haemodynamic instability' [12]. The consensus is that transfusions should not be considered first line therapy in stable patients with an Hb ≥ 7.0 mg/dL. The question is whether these patients can be managed more efficiently and effectively than with RBC transfusion.

Current practice (myth)

Siddiqi et al. conducted an observational cohort study for a 6-year period following release of Choosing Wisely Canada guidelines [13]. A transfusion was considered outside of clinical guidelines if the patient's Hb was >7.0 mg/dL and if the patient had a heart rate <100 beats per minute and systolic blood pressure ≥100 mmHg [12]. The primary outcome was that the proportion of patients with IDA receiving transfusion outside of clinical guidelines. The rate of total transfusions in patients with IDA was 11.2%, and the rate of potentially avoidable transfusions was 18.7% [13].

Appropriateness of RBC transfusions ordered in the Emergency Department (ED) for management of patients with IDA was studied by Spradbrow et al. [14]. IDA was documented by an emergency physician in 61% of ED patients. Of these, 63% received RBC transfusions: 53% were deemed appropriate, 16% were appropriate for the indication, but received more than the required number of transfusions and 32% were deemed inappropriate [14].

Grey et al. conducted an audit to monitor transfusion practices of patients with confirmed severe iron deficiency. They found that RBC transfusions were commonly administered to elderly patients with severe IDA with Hb < 8.0 mg/dL and uncommon when the Hb was >9.0 mg/dL; and 75% of the patients in the audit were transfused to an Hb ≥ 10.0 mg/dL and 44% to an Hb ≥ 11.0 mg/dL, suggesting excessive transfusion [15]. RBC transfusion is taken as a 'quick fix' of haemoglobin, since it is relatively easy. There are non-evidence-based concerns regarding intravenous iron supplementation in surgical patients, such as increased risk of infection, iron overload or oxidative stress, which has been refuted time and time again [16].

Conclusion (fact)

In IDA, the role of RBC transfusion is controversial. The Association for the Advancement of Blood and Biotherapies (AABB) and other organizations do recognize that RBC transfusion may be indicated if the patient has haemodynamic instability due to anaemia as this helps to alleviate severe morbidity associated with microvascular hypoxemia until the time iron therapy becomes clinically effective [17]. The treatment of pre-operative IDA will improve haemoglobin before surgery, but good evidence exists that correcting anaemia by transfusing blood is detrimental to the outcomes of surgery, by increased risk for post-operative complications [18].

Historically, there has been a reluctance to use intravenous iron formulations due to concerns of hypersensitivity reactions, such as anaphylaxis. Newer preparations are far less likely to be associated with such reactions [19]. It is preferable to use preparations that can deliver a higher dose per infusion over the shortest time period possible.

General unfamiliarity with these newer preparations, the historical concerns regarding anaphylactoid reactions and time delays are likely barriers to the widespread use of these agents in the treatment of IDA [20]. RBC transfusions carry the risk of haemolysis, transfusion-associated circulatory overload (TACO), haemolysis and alloimmunization, and transfusion-related acute lung injury (TRALI) should be considered a less safe alternative to oral and intravenous iron [17].

Guidelines for management of IDA are necessary to reduce the knowledge-to-practice gap for IDA management and avoid inappropriate use of RBC transfusions. Anaemia in the geriatric population may be multifactorial, with nutritional deficiencies, senescence and chronic disease being the most common reason. Mild anaemia is rarely symptomatic and should not be transfused [21]. Symptomatic anaemia and severe anaemia where RBC transfusions may play a role, the emphasis should be on restrictive transfusion strategies and adequate dosing as compensatory mechanisms are overwhelmed [21]. Transfusion of single red cell units followed by clinical assessment including documented Hb increments should be done before ordering subsequent units to ensure that this valuable resource is appropriately and ethically used [22].

Mild anaemia is not clinically significant

Current practice (myth)

Anaemia is one of the most common clinical conditions worldwide and perhaps the single most common source of disability and poor quality of life. Indeed, the most common cause of anaemia is iron deficiency with anaemia being a part of late stage iron deficiency. There is abundant evidence that iron deficiency and IDA are associated with poor cognitive function in children as well as a cause of increased morbidity and mortality [23]. Blood loss anaemia is also quite common and associated with significantly increased risks of morbidity, mortality and hospital/ICU length of stay. Traditionally significant anaemia has been treated with blood transfusions, which are entirely inappropriate except in rare life threatening acute emergencies.

Conclusions (fact)

It is now clear that PBM needs to include pre-operative anaemia management programs and anaemia/iron deficiency screening programs for at-risk patients, such as women with abnormal menses and children with nutritional problems. Such approaches have been associated with improvements in quality of life, lessening of symptoms and a reduction in morbidity and mortality in various settings [24–26].

If the patient does not need two units you should not be transfusing

Current practice (myth)

Due to a lack of expertise and knowledge of transfusion practices in the majority of patients, RBC transfusion practices are driven by only laboratory-based Hb triggers. Some literature continues to suggest RBC transfusion thresholds for critically ill, clinically stable patients—Hb concentration <7 g/dL, for patients undergoing cardiac surgery Hb < 7.5 g/dL, for patients with hip fractures and cardiovascular disease or risk factors Hb < 8 g/dL and for haemodynamically stable patients with acute gastrointestinal bleeding Hb 7–8 g/dL [27]. It is a common myth among the treating physicians that we need to keep the Hb at a level of 9 gm/dL. So, estimating that for a target Hb level, they prefer to order two units of packed RBC transfusion.

Conclusion (fact)

Currently, transfusion practices have been moved to a more scientific and evidence-based approach that is known as PBM. PBM has emerged as an integral part of patient care. World Health Organization (WHO) defined PBM as 'PBM addresses the problems of anaemia, blood loss and coagulopathy. It is a patient centred, systematic, evidence-based approach to improve patient outcomes by managing a patient's own blood through diagnosis and aetiology specific treatment of anaemia and preserving the patient's own blood by minimizing blood loss and bleeding, while promoting patient safety and empowerment. It reduces the utilization of health care resources as well as expenditures, transfusion dependency, and the risks and complications of transfusion' [23]. The primary role of RBC transfusion is to provide adequate perfusion to the cells. The need for RBC transfusion is based on individualized clinical factors not merely on laboratory parameters such as Hb or haematocrit levels.

Keeping a focus on adverse incidents related to transfusion, it is better to avoid unnecessary transfusion. Overenthusiastic transfusions have been associated with increased ventilator days and prolonged ICU stays, and it has also been identified as an independent risk factor for mortality in critically ill patients [28,29].

The rise of Hb level following transfusion is not just a mere mathematical calculation anymore, that is, one unit raises the Hb level by 1.0 g/dL [30,31], whereas the rise in Hb level following transfusion is more dependent on characteristics of the patient such as height, weight, and body mass index as well as the underlying clinical condition [32]. So, transfusion of RBC should be judicious and evidence-based, and transfusion of one unit RBC may be sufficient. Retrospective observational studies done by Berger et al. and Bowman et al. mentions that transfusing malignant haematology and bone marrow transplant patients with single RBC units is safe and efficacious [33,34]. A recent clinical trial conducted on women with haemodynamically stable postpartum anaemia concluded that a single-unit transfusion protocol avoided a second unit of packed RBC in >80% of women without significant impact on morbidity [35]. The real evidence behind the one-unit orders is the fact that all the randomized clinical trials (RCTs) testing transfusion triggers employed a one-unit transfusion strategy and they showed no benefit to giving extra blood—more than is needed [36]. In reality it is necessary to reassess the patient, after one-unit red cell transfusion regarding the clinical condition of the patient. If there remains clinical need in terms of perfusion status and clinical condition, the patient should be scheduled for transfusion of another unit. So, in most cases of chronic anaemias and haemodynamically stable patients, transfusion of 1-unit red cell may be sufficient enough to meet this need and two units of RBC transfusion can be avoided calculating the risks associated [36]. While not widely used outside of paediatric patients, a recent study showed that patient's body weight differentially impacts the change in Hb after RBC transfusion. The authors suggested incorporating body weight into the clinical decision-making process when transfusing blood in adult surgical patients [37].

Transfusions of RBC should Be based on an Hb concentration of 7 g/dL

Current practice (myth)

A plasma Hb concentration of 7 g/dL has become a common 'trigger' for a blood transfusion, and the pervasiveness of this practice in diverse clinical scenarios can only be explained by it attaining mythical status. Figure 1 shows a histogram of the pre-transfusion Hb value for all transfusions of RBCs in one large multiple hospital medical system. The sharp peak centred at an Hb of 7 g/dL clearly illustrates that this laboratory assay value is the main driver of the clinical decision to transfuse in this system. If transfusions were based on individualized clinical factors, there would not be such a sharp peak at a laboratory value. A recent multi-national survey of ICU practice [38] provides additional evidence of the existence of the 'myth of 7 g/dL' in that it is widely used for actively bleeding patients in ICU, despite the complexity and variability of patient conditions there.

Getting to the origin of the myth is difficult. For many years, the practice was to use an Hb of 10 g/dL as a trigger, and this has been attributed [39] to a 1942 paper by Adams and Lundy. The text of that paper actually states 'When concentration of Hb is less than 8 to 10 grams per 100 cubic centimetres of whole blood, it is wise to give a blood transfusion before operation' [40]. The favouring of 10 as the value instead of 8 was likely re-enforced by the physiology studies of Case et al. [41] that demonstrated interference with cardiac function at haematocrit levels less than 30%. The fourth edition of Mollison's transfusion medicine textbook, the pre-eminent transfusion therapy textbook of its day advised 'Therefore, before surgery is undertaken the Hb should be raised above this level, even if only trivial haemorrhage is expected' [42].

The shift of the myth of 10–7 g/dL is easier to understand, as the numbers of clinical trials comparing the use of these two triggers are numerous and more contemporary. They all show either the non-inferiority or possibly superiority of the restrictive transfusion strategy of 7 g/dL as a trigger. We even have an overview of systematic reviews of meta-analysis of these trials, which fully explains the situation [43].

Conclusion (fact)

A trigger of 10 g/dL was never supported by expert practitioners of transfusion even when numerous physicians with less expertise were working under this myth assumption. A review article of the indications for transfusion appearing in JAMA in 1956 advised 'Anemia should be treated with red blood cell transfusion only after diagnostic procedures have excluded specific therapy or when anemia is so severe as to necessitate emergency treatment' as well as 'The frequency of transfusion of red blood cells in patients with marrow failure should be determined by the

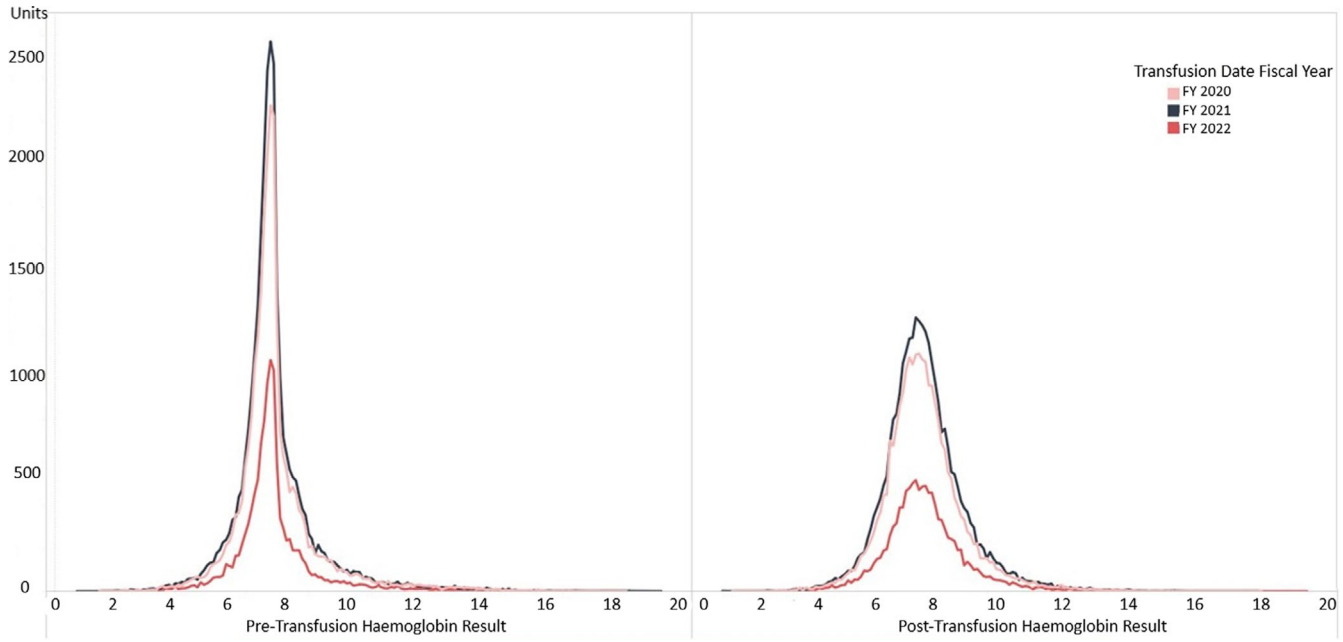

FIGURE 1 Histogram of the pre-transfusion Haemoglobin (Hb) value for all transfusions of red blood cells in one large multiple hospital medical system. The sharp peak centred at Hb of 7.0 g/dL clearly illustrates that this laboratory assay value is the main driver of the clinical decision to transfuse in this system, as opposed to clinical assessment based on other factors.

symptoms of the patient. The desired Hb level may vary from 6 to 11 gm per 100 cc in different persons' [44]. Other sections of the 1967 edition of Mollison included advice that patients with recent haemorrhage 'whose haemoglobin is as low as 7–8 g/100 ml should be transfused' as well as 'In patients with very severe anaemia transfusion may easily overload the circulation and precipitate cardiac failure. Thus, whenever it is probable that anaemia will respond to some other form of treatment transfusion should be avoided'. Also, 'To tide a patient over a short period of very severe anaemia inhalation of 100 percent oxygen can make an important contribution' is advised along with an explanation that plasma content of oxygen can be increased to make an Hb of 3 g/dL effectively 4.5 g/dL [42].

If the myth of 10 g/dL was never true, proving that 7 g/dL is 'non-inferior' does not make this notion true. As the JAMA authors point out by noting 'different persons', the transfusion decision is being made about one patient at a time. Randomized trials can be off-target to the circumstances of a particular patient. The Jehovah Witness population provides an example that most patients can tolerate haemoglobin levels significantly lower than 7.0 g/dL [45] and be supported by temporary oxygen supplementation, iron infusion and/or erythropoietin instead of transfusion. Clinical decision support may be perpetuating the myth by emphasizing a particular transfusion threshold rather than providing diagnostic algorithms to determine causes of anaemia and suggesting appropriate treatments based on diagnosis and symptoms. Monitors of a PBM program should not simply track pre-transfusion Hb levels and see Figure 1 as evidence of success, but perhaps should focus on the anaemia diagnosis and the use of iron when appropriate.

The only goal of transfusion of RBCs is to improve the delivery of oxygen to tissues

Current practice (myth)

Regarding off-target interpretation of results of randomized controlled trials, a straightforward example is the use of the Villanueva et al.'s [46] paper to support using a threshold of 7 g/dL for the broad category of bleeding ICU patients. This trial explicitly states the paradigm underlying the study as 'The goal of red-cell transfusions is to improve the delivery of oxygen to tissues'. As a result, the trial was designed to evaluate patients with an anatomic cause of bleeding and the ability of patients to tolerate an acutely progressive anaemia until a procedure could treat the site of bleeding. Greater than 97% of patients were not thrombocytopenic and required no platelet transfusions. Yet, this study is cited to support a restrictive threshold for bleeding ICU patients even if thrombocytopenic and without a readily correctable cause of bleeding. A common clinical plan seen in patient charts is 'transfuse for Hb < 7, platelets < 50', rather than have their bleeding potentially stopped earlier with only a few RBCs and many fewer platelets.

Conclusion (fact)

Multiple studies have definitively demonstrated that RBCs interact with platelets and play a role in haemostasis. A comprehensive review has been published [47]. Major mechanistic hypotheses include RBCs physically pushing platelets closer to the endothelium under flow

conditions, interaction of nitric oxide metabolism pathways and adenosine diphosphate augmentation of platelet function. The bleeding time has an inverse linear relationship to the haematocrit [48]. It is also becoming clear that RBCs participate in immunity by interacting with immune receptors in the spleen [49]. Better RCTs of RBC transfusions and patient outcomes need to also take into account platelet function and immunity.

Leucoreduction versus irradiation are the same

Current practice (myth)

Leucoreduction (LR) is the reduction of white blood cell (WBC) concentration in blood components, namely, RBC and platelets derived from the component preparation of whole blood or apheresis. There are many methods of LR, but, currently, this process may be performed using selective LR filters, which enable less than 1×10^6 or 5×10^6 residual WBC to be obtained in a RBC or 5×10^5 WBC in a whole blood derived platelet unit [50,51].

Over the past 30 years, it has been demonstrated that LR can reduce some adverse reactions due to blood component transfusion such as febrile non-haemolytic transfusion reactions, immunization against human leucocyte antigens and human platelet antigens, which may cause refractoriness to platelet transfusion and transmission of cytomegalovirus [53,54]. Furthermore, it is also claimed that LR also improves the clinical outcome of reducing post-operative surgical site infections or mortality in patients undergoing cardiac surgery and infection-related complications in trauma patients [52–54].

On the other hand, irradiated blood components are cellular blood components that have been exposed to irradiation to inactivate lymphocytes to stop their proliferation [55]. Irradiating blood components prevents the donor WBCs replicating and mounting an immune response against a vulnerable patient and recipient with the potential to cause transfusion-associated-graft-versus-host disease (TA-GvHD). Usually immunocompromised patients, foetus and premature neonates and patients who received haematopoietic stem cell transplant (HSCT) are prone to develop TA-GvHD. Evidence of TA-GvHD may include rash, fever, elevated liver enzymes, pancytopenia, diarrhoea, bone marrow aplasia or hypocellularity and hepatomegaly. It usually presents within 1–6 weeks after transfusion, with the median time from transfusion to first symptom being 11 days. Overall survival rate is reported to be 8.4% [56]. Patients receiving transfusions from a first-degree relative (e.g., parent, child or sibling) or second-degree relative (e.g., grandparent, grandchild, uncle, aunt, nephew, niece or half sibling), foetus and premature neonates or HSCT recipients and granulocyte transfusions should always be irradiated. The AABB *Standards for Blood Banks and Transfusion Services*, 33rd edition, recommends a dose of 25 Gy to the central area of the component with no portion receiving <15 Gy but sets no upper limit [51,56].

Conclusion (fact)

LR cannot prevent TA-GvHD as it contains a significant amount of residual lymphocytes. TA-GvHD continues to be reported with 66 out of the 348 (18.9%) cases who received nonirradiated LR components between 2000 and 2013 [56]. The British Society for Haematology recommendations note that the evidence is insufficient to recommend LR alone to prevent TA-GvHD in susceptible patients. So, irradiation and LR can never be used interchangeably.

Conclusions—The perpetuation of misconceptions and the ongoing need to address them

PBM has been recently recognized by WHO as an area for urgent intervention in current patient care practices [23]. The rationale is that prevention and appropriate treatment of anaemia and bleeding can lead to better outcomes. Transfusion plays a role in the care of anaemic and bleeding patients, but in general, expert opinion has traditionally been on the side of what we would now consider undue reliance of aggressive transfusion of RBCs and other components. Research in the last two decades has documented that it is unnecessary to transfuse most haemodynamically stable patients with anaemia, particularly those with IDA, for which safer and more precise treatments are available. Anaemia causes significant morbidity and mortality and avoiding transfusions is only part of the approach. Preserving the patient's own red cells is an important strategy. Early data suggest that the use of PBM may improve clinical outcomes such as length of stay, quality of life and even mortality [23]. And because RBC transfusions have serious complications including TRALI, infection, congestive heart failure and thrombosis, the minimum dose needed to achieve the desired clinical goals is more appropriate than arbitrary numbers of RBCs such as 'a minimum of two'.

Randomized trials of transfusion thresholds have been widely misinterpreted as suggesting that the Hb or haematocrit alone (usually 7/21) is a necessary transfusion threshold. Indeed, transfusion remains a clinical decision and laboratory values should be an adjunct. Haemodynamically stable, largely asymptomatic non-bleeding patients may not always need red cell transfusions unless they are unable to respond to normal erythropoietic stimuli, either endogenous or therapeutic. While RBC transfusions may have benefits beyond oxygen transport, high quality trials are needed to assess the risks and benefits of RBC transfusions in improving haemostasis. Finally, while LR and irradiation are important safety modalities and have some overlap in benefit, they have distinctly different indications and mechanisms of action.

ACKNOWLEDGEMENTS

The areas of contribution are as follows: R.R.G., Introduction; N.B., Abstract, Mild Anaemia, Conclusions; C.G., Methods, Red Blood Cells and Hb of 7 g/dL, Red Blood Cells Improve Oxygenation; S.M., Two units, Leukoreduction and Irradiation; A.R.N., Iron Deficiency; C.B., Manuscript Reviewer.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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REFERENCES

1. Jones JM, Sapiano MRP, Savinkina AA, Haass KA, Baker ML, Henry RA, et al. Slowing decline in blood collection and transfusion in the United States—2017. Transfusion. 2020;60:S1–9.
2. Tobian AAR, Heddle NM, Wiegmann TL, Carson JL. Red blood cell transfusion: 2016 clinical practice guidelines from AABB. Transfusion. 2016;56:2627–30.
3. Halford B, Pinheiro A, Haspel RL. Hospital medicine providers' transfusion knowledge: a survey study. Transfus Med Rev. 2021;35:140–5.
4. Lin Y, Tinmouth A, Mallick R, Haspel RL. BEST-TEST2: assessment of hematology trainee knowledge of transfusion medicine. Transfusion. 2016;56:304–10.
5. Haspel RL, Lin Y, Mallick R, Tinmouth A, Cid J, Eichler H, et al. Internal medicine resident knowledge of transfusion medicine: results from the BEST-TEST international education needs assessment. Transfusion. 2015;55:1355–61.
6. Salem-Schatz SR, Avorn J, Soumerai SB. Influence of knowledge and attitudes on the quality of physicians' transfusion practice. Med Care. 1993;31:868–78.
7. Auerbach DI, Staiger DO, Buerhaus PI. Growing ranks of advanced practice clinicians—implications for the physician workforce. N Engl J Med. 2018;378:2358–60.
8. Hwa YL, Marshall AL, Shelly JL, Colborn LK, Nowakowski GS, Lacy MQ. Assessment of the need for a hematology-specific fellowship curriculum for advanced practice providers using a needs-based survey. J Oncol Pract. 2019;15:e593–9.
9. Karp JK, Weston CM, King KE. Transfusion medicine in American undergraduate medical education. Transfusion. 2011;51:2470–9.
10. Braester A, Akria L, Suriu C, Zarfati M, Barhoum M. Educating the educator about patient blood management. Transfus Apheres Sci. 2022;61:103397.
11. World Health Organization. Archived: iron deficiency anaemia: assessment, prevention and control. Geneva: World Health Organization; 2001.
12. Four tests and treatment to questions in perinatal transfusion medicine. Toronto: Choosing Wisely Canada; 2020.
13. Siddiqi AZ, Grigat D, Vatanpour S, McRae A, Lang ES. Transfusions in patients with iron deficiency anemia following release of Choosing Wisely Guidelines. CJEM. 2021;23:475–9.
14. Spradbrow J, Lin Y, Shelton D, Callum J. Iron deficiency anemia in the emergency department: over-utilization of red blood cell transfusion and infrequent use of iron supplementation. CJEM. 2017;19:167–74.
15. Grey DE, Finlayson J. Red cell transfusion for iron-deficiency anaemia: a retrospective audit at a tertiary hospital. Vox Sang. 2007;94:138–42.
16. Gómez-Ramírez S, Bisbe E, Shander A, Spahn DR, Muñoz M. Management of perioperative iron deficiency anemia. Acta Haematol. 2019;142:21–9.
17. Nixon CP, Sweeney JD. Severe iron deficiency anemia: red blood cell transfusion or intravenous iron? Transfusion. 2018;58:1824–6.
18. Muñoz M, Acheson AG, Auerbach M, Besser M, Habler O, Kehlet H, et al. International consensus statement on the peri-operative management of anaemia and iron deficiency. Anaesthesia. 2017;72:233–47.
19. Avni T, Bieber A, Grossman A, Green H, Leibovici L, Gafter-Gvili A. The safety of intravenous iron preparations. Mayo Clin Proc. 2015;90:12–23.
20. Khadadah F, Callum J, Shelton D, Lin Y. Improving quality of care for patients with iron deficiency anemia presenting to the emergency department. Transfusion. 2018;58:1902–8.
21. Beyer I, Compté N, Busuioc A, Cappelle S, Lanoy C, Cytryn E. Anemia and transfusions in geriatric patients: a time for evaluation. Hematology. 2010;15:116–21.
22. Le Calvé S, Somme D, Prud'homm J, Corvol A. Blood transfusion in elderly patients with chronic anemia: a qualitative analysis of the general practitioners' attitudes. BMC Fam Pract. 2017;18:76.
23. World Health Organization. The urgent need to implement patient blood management: policy brief. Geneva: WHO; 2021.
24. Moskowitz DM, McCullough JN, Shander A, Klein JJ, Bodian CA, Goldweit RS, et al. The impact of blood conservation on outcomes in cardiac surgery: is it safe and effective? Ann Thorac Surg. 2010;90:451–8.
25. Leahy MF, Hofmann A, Towler S, Trentino KM, Burrows SA, Swain SG, et al. Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals. Transfusion. 2017;57:1347–58.
26. Gupta PB, DeMario VM, Amin RM, Gehrie EA, Goel R, Lee KHK, et al. Patient blood management program improves blood use and clinical outcomes in orthopedic surgery. Anesthesiology. 2018;129:1082–91.
27. Mueller MM, Van Remoortel H, Meybohm P, Aranko K, Aubron C, Burger R, et al. Patient blood management. JAMA. 2019;321:983.
28. Fayed NA, Abdallah AR, Khalil MK, Marwan IK. Therapeutic rather than prophylactic platelet transfusion policy for severe thrombocytopenia during liver transplantation. Platelets. 2014;25:576–86.
29. Vande Vusse LK, Madtes DK, Guthrie KA, Gernsheimer TB, Curtis JR, Watkins TR. The association between red blood cell and platelet transfusion and subsequently developing idiopathic pneumonia syndrome after hematopoietic stem cell transplantation. Transfusion. 2014;54:1071–80.
30. Ness PM, Kruskall MS. Principles of red blood cell transfusion. In Hoffman K, ed. Hematology: Basic Principles and Practice. 4th ed. Orlando, FL: Churchill Livingstone; 2005.
31. Wiesen AR, Hospenthal DR, Byrd JC, Glass KL, Howard RS, Diehl LF. Equilibration of hemoglobin conentration after transfusion in medical inpatients not actively bleeding. Ann Intern Med. 1994;121:278–30.
32. Noverati N, Federici E, Riley TR. Post-transfusion hemoglobin response in patients with cirrhosis: can we expect a 1 g/dL rise per unit transfused? Transfusion. 2021;61:708–12.
33. Berger MD, Gerber B, Arn K, Senn O, Schanz U, Stussi G. Significant reduction of red blood cell transfusion requirements by changing from a double-unit to a single-unit transfusion policy in patients receiving intensive chemotherapy or stem cell transplantation. Haematologica. 2012;97:116–22.
34. Bowman Z, Fei N, Ahn J, Wen S, Cumpston A, Shah N, et al. Single versus double-unit transfusion: safety and efficacy for patients with hematologic malignancies. Eur J Haematol. 2019;102:383–8.
35. Hamm RF, Perelman S, Wang EY, Levine LD, Srinivas SK. Single-unit vs multiple-unit transfusion in hemodynamically stable postpartum anemia: a pragmatic randomized controlled trial. Am J Obstet Gynecol. 2021;224:84.e1–7.
36. Callum JL, Waters JH, Shaz BH, Sloan SR, Murphy MF. The AABB recommendations for the Choosing Wisely campaign of the American Board of Internal Medicine. Transfusion. 2014;54:2344–52.
37. Lo BD, Cho BC, Hensley NB, Cruz NC, Gehrie EA, Frank SM. Impact of body weight on hemoglobin increments in adult red blood cell transfusion. Transfusion. 2021;61:1412–23.

38. de Bruin S, Eggermont D, van Bruggen R, de Korte D, Scheeren TWL, Bakker J, et al. Transfusion practice in the bleeding critically ill: An international online survey-The TRACE-2 survey. Transfusion. 2022; 62:324–35.
39. Seeber P, Shander A. Basics of blood management. Oxford, UK: Blackwell; 2007.
40. Adams RC, Lundy JS. Anesthesia in cases of poor surgical risk. Anesthesiology. 1942;3:603–7.
41. Case RB, Berglund E, Sarnoff SJ. Ventricular function. Am J Med. 1955;18:397–405.
42. Mollison P. Blood transfusion in clinical medicine. 6th ed. Oxford, UK: Blackwell; 2007.
43. Trentino KM, Farmer SL, Leahy MF, Sanfilippo FM, Isbister JP, Mayberry R, et al. Systematic reviews and meta-analyses comparing mortality in restrictive and liberal haemoglobin thresholds for red cell transfusion: an overview of systematic reviews. BMC Med. 2020; 18:154.
44. Donohue DM. Preservation and transfusion of blood. JAMA. 1956; 161:784.
45. Viele M, Weiskopf R. What can we learn about the need for transfusion from patients who refuse blood? The Experience with Jehovah's Witnesses. Transfusion. 1994;34:396–401.
46. Villanueva C, Colomo A, Bosch A, Concepción M, Hernandez-Gea V, Aracil C, et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med. 2013;368:11–21.
47. Valeri CR, Khuri S, Ragno G. Nonsurgical bleeding diathesis in anemic thrombocytopenic patients: role of temperature, red blood cells, platelets, and plasma-clotting proteins. Transfusion. 2007;47: 206S–48S.
48. Hellem AJ, Borchgrevink CHF, Ames SB. The role of red cells in haemostasis: the relation between haematocrit, bleeding time and platelet adhesiveness. Br J Haematol. 1961;7:42–50.
49. Anderson HL, Brodsky IE, Mangalmurti NS. The evolving erythrocyte: red blood cells as modulators of innate immunity. J Immun. 2018; 201:1343–51.
50. Harris SB, Hillyer CD. Blood manufacturing: component preparation, storage, and transportation. Blood Banking and Transfusion Medicine. Philadelphia, PA: Elsevier; 2007. p. 183, 204.
51. Gammon R, editor. Standards for blood banks and transfusion services. 33rd ed. Bethesda, MD: AABB Press; 2022.
52. Fergusson D, Khanna MP, Tinmouth A, Hébert PC. Transfusion of leukoreduced red blood cells may decrease postoperative infections: two meta-analyses of randomized controlled trials. Can J Anaesth. 2004;51:417–24.
53. Blumberg N, Zhao H, Wang H, Messing S, Heal JM, Lyman GH. The intention-to-treat principle in clinical trials and meta-analyses of leukoreduced blood transfusions in surgical patients. Transfusion. 2007; 47:573–81.
54. Friese RS, Sperry JL, Phelan HA, Gentilello LM. The use of leukoreduced red blood cell products is associated with fewer infectious complications in trauma patients. Am J Surg. 2008;196:56–61.
55. Francis RO. Irradiation of blood products. Transfusion medicine and hemostasis. Cambridge, MA: Elsevier; 2019. p. 261–5.
56. Kopolovic I, Ostro J, Tsubota H, Lin Y, Cserti-Gazdewich CM, Messner HA, et al. A systematic review of transfusion-associated graft-versus-host disease. Blood. 2015;126:406–14.

How to cite this article: Gammon RR, Blumberg N, Gilstad C, Mandal S, Nair AR, Bocquet C. Patient blood management: Myths and facts about red blood cell transfusions. Vox Sang. 2023.