# Preoperative Anemia Evaluation and Treatment



Ankit J. Kansagra, мр<sup>а,\*</sup>, Mihaela S. Stefan, мр<sup>b</sup>

# **KEYWORDS**

- Preoperative period Transfusion Surgery Optimization
- Patient blood management

# **KEY POINTS**

- Preoperative anemia is the most frequent hematological condition identified before surgery.
- Preoperative anemia is associated with an increased likelihood of red blood cell (RBC) transfusion, which in turn has been associated with increased morbidity, mortality, and length of stay.
- Preoperative optimization of patients undergoing elective surgical procedures associated with significant blood loss, along with strategies to minimize intraoperative blood loss, shows promise for reducing postoperative transfusions and improving outcomes.
- Patients should be evaluated as early as possible in the preoperative pathway to coordinate optimization of patient hemoglobin and iron stores.
- Further research should evaluate if correcting preoperative anemia improves postoperative outcomes.

## INTRODUCTION Definition

Anemia is defined as a condition in which the body has a decreased amount of circulating erythrocytes, or RBCs, (and consequently their oxygen carrying capacity) compared with age-matched controls.<sup>1</sup> The World Health Organization (WHO) defines anemia as hemoglobin less than 13 g/dL in adult men (15 years of age and above) and less than 12 g/dL in adult nonpregnant women (15 years of age and above).<sup>2,3</sup> The WHO acknowledges, however, that these values were chosen somewhat arbitrarily; most laboratories define anemia as the lowest 2.5% of the distribution of hemoglobin values from a normal, healthy population.<sup>2</sup>

<sup>&</sup>lt;sup>a</sup> Department of Hematology/Oncology, Baystate Medical Center, Tufts University, 376 Birnie Avenue, Springfield, MA 01199, USA; <sup>b</sup> Division of Hospital Medicine, Department of General Medicine, Tufts University, 759 Chestnut Street, S2660, Springfield, MA 01199, USA \* Corresponding author.

E-mail address: ankit.kansagramd@baystatehealth.org

#### Epidemiology

#### Prevalence in general population

In the United States, prevalence estimates of anemia are approximately 5% in the general population, with preschool, pregnant, and elderly populations affected most significantly. In those older than 65, the prevalence of anemia climbs to  $11\%^4$  and increases to more than 30% in those older than 85 years.<sup>5</sup>

#### Prevalence in surgical population

The reported prevalence of anemia in surgical patients varies largely due to the criteria for definition of anemia, population studied, and type of surgery. In studies published after 2000, preoperative anemia was found in 34% of all veterans undergoing noncardiac surgeries, in 46% of colorectal surgeries, in 25% to 45% of hip and knee surgeries, in 46% of elderly patients undergoing hip fracture surgery, and in 75% of patients with advanced colon cancer undergoing colectomy.<sup>5,6</sup>

Bleeding and blood loss are expected in major surgical procedures (especially cardiac, orthopedic, gynecologic, and cancer) despite the use of techniques to reduce blood loss; for example, a patient undergoing a major orthopedic surgery can lose as much as 1 litre of blood perioperatively.

Elderly patients and those with comorbidities, such as renal disease, cancer, heart failure, and diabetes mellitus, have an increased risk of being anemic.<sup>5</sup> Female patients are also at an increased risk of being anemic compared with men, likely because female patients have lower circulating blood volume and if the amount of blood loss is the same it may result in a higher probability of postoperative anemia.<sup>7</sup>

In 2011, the availability of allogenic whole blood/RBCs in the United States was approximately 14.5 million units, and 13.7 million units were transfused.<sup>8</sup> It is estimated that yearly 60% to 70% of all RBC units are transfused to surgical patients.<sup>9,10</sup> In the United States, the whole blood/RBC transfusion rate in 2011 was 44.0 allogenic units per 1000 overall population; although this rate is lower than in 2008, it is still substantially higher than the rates reported in Canada and in European countries.<sup>11</sup> It is postulated that the decline in transfusion is an indicator of better blood management practices, including a reduction in transfusion rates in surgical patients.

## PREOPERATIVE OPTIMIZATION OF PATIENTS AND ANEMIA EVALUATION Should Evaluation for Anemia Be Part of the Preoperative Risk Assessment and Optimization?

The preoperative evaluation can be considered to serve 2 broad purposes: (1) to risk stratify patients in order that providers and patients and their families are well informed on the risks in undergoing the surgical procedure and (2) to proactively identify and optimize preoperatively modifiable factors and thus improve a patient's chance for a successful outcome.

Although several studies suggest that anemia is associated with an increase in postoperative transfusions, morbidity, and mortality, patients with anemia frequent proceed with surgery without optimization and often the hemoglobin is measured only a few days before surgery when there is little to be done for work-up and treatment.<sup>12,13</sup> One of the reasons may be the belief that anemia is readily correctable by means of transfusion, giving clinicians a sense that it is not a problem that necessarily needs to be addressed before surgery. Preoperative assessment

provides an opportunity for proactive recognition and management of the anemia and may avoid postoperative anemia and blood transfusions.

# Which Surgeries Require Measurement of Hemoglobin Preoperatively and When Should the Test be Scheduled?

Anemia screening should be individualized based on a patient's symptoms, age, and comorbidities; type of surgery; and anticipated blood loss.

As a general rule a complete blood cell count is indicated in

- Surgery with potential for large (>15% estimated blood volume) blood loss
- Surgery with potential for moderate (>10% estimated blood volume) blood loss and
  - Known or suspected anemia, or
  - An established coagulation abnormality, or
  - Known or suspected RBC antibodies, or
  - Symptomatic anemia

A hemoglobin measurement is not indicated for low-risk surgeries or healthy, young patients undergoing surgeries with anticipated minimal blood loss.

The preoperative office visit represents an opportunity for timely detection and management of perioperative anemia before elective surgery. The decision to complete a work-up for diagnostic evaluation of anemia depends on the severity of anemia and the urgency of the surgery, and each case must be evaluated separately. To be able to appropriately manage a patient found to be anemic, however, the hemoglobin has to be determined at least 3 to 4 weeks prior to the surgery.

#### What Should Be the Target Hemoglobin Preoperatively?

Generally speaking, there is no reason to think that a patient undergoing an elective surgery should have a different target from a normal range; however, the decision to postpone surgery to achieve this target has to be individualized to the patient and type of procedure.

Only a few good-quality studies have evaluated the effect of preoperative hemoglobin on postoperative outcomes. One study, which assessed a cohort of patients who refused blood transfusions for religious reasons, found that there was an increase in mortality in patients with a hemoblogin level less than 7 g/dL preoperatively.<sup>14</sup> When deciding the threshold for hemoglobin, other factors to consider include patient age and presence of comorbidities. In a large retrospective study of 310,311 veterans aged 65 years and older who underwent major noncardiac surgery, Wu and colleagues<sup>15</sup> showed a 1.6% increase in postoperative mortality with every percentage point decrease in hematocrit value (Hct) from normal range.

An approximate estimate of calculating the hemoglobin/Hct after surgery can be obtained by modifying a calculator of allowed blood loss in surgery by replacing the allowed blood loss value with the actual estimated blood loss and lowest acceptable Hct with postoperative Hct. It should also be taken into account that in addition to the blood loss with the surgery, postoperative anemia is worsened by hemodilution, inflammatory cytokine release after surgery, decrease in gastro-intestinal uptake, and decreased erythropoietin production.<sup>16–19</sup>

A calculator for the amount of allowed blood loss is provided at: https://www.openanesthesia.org/maximum\_abl\_calculation/.

Allowed blood loss = Estimated blood volume  $\times$  (Initial Hct – Lowest acceptable Hct)/Initial Hct; average blood volume = 75 mL/kg for adult men and 65 mL/kg for adult women

## When Should the Surgery Be Postponed for Anemia Work-up and Treatment?

Several recent consensus guidelines recommend routine preoperative anemia management for elective surgery.<sup>20,21</sup> Elective surgery offers the potential for preoperative work-up and optimization of hemoglobin before surgery and, when possible, patients with unexpected preoperative anemia should be rescheduled until evaluation and treatment are finalized.

In 2011, the Network for Advancement of Transfusion Alternatives, which included a multidisciplinary panel of physicians from 13 countries, including the United States, published practice guidelines for detection, evaluation, and management of anemia in elective orthopedic surgeries; it may be reasonable to consider these recommendations for any surgery with potential significant blood loss.<sup>20</sup>

The group has the following recommendations:

- 1. Patients should have a hemoglobin level measured 28 days before the scheduled surgery.
- 2. Target hemoglobin before the surgery should be in the normal range.
- 3. If anemia is identified, further testing should be performed to evaluate for nutritional deficiencies, chronic renal insufficiency, and/or chronic inflammatory disease.
- Nutritional deficiencies should be treated and erythropoietin-stimulating agents (ESAs) may be used in patients in whom nutritional deficiencies have been ruled out or corrected.

An example of a pathway for evaluation of anemia prior to an elective procedure is given in **Fig. 1**.

# PREOPERATIVE ANEMIA, PERIOPERATIVE BLOOD TRANSFUSIONS, AND POSTOPERATIVE OUTCOMES

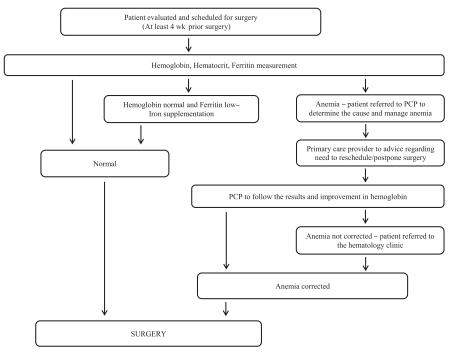
Preoperative anemia contributes to postoperative anemia and increases the chance of RBC transfusion,<sup>22–24</sup> which in itself is associated with adverse outcomes.<sup>25</sup> In a large study of more than 6000 noncardiac surgical patients, the subgroup with preexisting anemia required 5 times more blood than nonanemic patients.<sup>26</sup>

Several retrospective observational studies suggest that transfusions are associated with increased rates of infection, ischemic complications, and death<sup>12,13</sup> and that preoperative anemia is associated with an increase in postoperative complications, length of hospital stay, and mortality.<sup>15,26–29</sup> Preoperative anemia, postoperative anemia, and blood transfusion are interlinked, however, and sick patients are more likely to be transfused and develop complications. Identifying the independent effect of each is challenging and anemia is often a sign of an underlying disease that could have an impact on surgical outcomes.

Randomized controlled trials did not find any difference in mortality of patients assigned to restrictive transfusion (hemoglobin <8 g/dL) compared with those assigned to liberal transfusion strategy (hemoglobin  $\geq$ 10 g/dL),<sup>30,31</sup> but these studies did not address specifically the impact of perioperative anemia on the outcomes.

#### Mortality

Preoperative anemia was found an independent risk factor for in-hospital, 30-day, and 90-day mortality after several types of surgery. A large retrospective study using a



**Fig. 1.** Preoperative anemia pathway for a patient scheduled for an elective surgery. For hospitals with a preoperative clinic for risk assessment and optimization, anemia assessment and management can be performed in the clinic.

National Surgical Quality Improvement Program database found that patients with preexisting anemia has an increased risk for mortality, especially if they also had preexisting cardiovascular disease and an increased risk in a composite outcome of myocardial infarction, stroke, renal insufficiency, or death within 30 days of surgery.<sup>6</sup>

# Postoperative Complications

The vast majority of evidence suggest that preoperative anemia has a deleterious impact on the medical postoperative outcomes and complications in both elective and emergent surgical populations. In patients with hip fracture, anemia on admission had been associated with an increase length of hospital stay and readmission rate and with worse postoperative function.<sup>32–34</sup> In elective cardiac and noncardiac surgeries, preexisting anemia is associated with increased risk of infective complications, respiratory failure, renal failure, delirium in the elderly, and perioperative cardiac events.<sup>28,35–37</sup> The relationship with functional outcomes after elective orthopedic surgeries is not clear, with some more recent studies finding that postoperative anemia is not related to quality-of-life and functional outcome.<sup>38,39</sup>

# **EVALUATION FOR ANEMIA**

Preoperative evaluation for patients at risk of being anemic or who are anemic include the following:

- 1. Detailed medical and surgical history
- 2. Review of prior medical records

- 3. Physical examination
- 4. Review of existing laboratory results
- 5. Ordering laboratory tests if indicated

The 3 main causes of anemia are:

- Blood loss
- Underproduction of RBCs
- Increased destruction of RBCs

#### History

History should inquire about symptoms of bleeding; chronic diseases, which may be associated with anemia; past history of anemia; medications; and symptoms related to anemia.

Various history-taking clues that can aid in the evaluation of anemia are described briefly (**Box 1**).<sup>3,40</sup>

Answering the following questions helps define a framework for further work-up:

- 1. Is the patient bleeding (now or in the past)?
- 2. Is the patient iron deficient? If so, why?
- 3. Is the patient folate or vitamin B<sub>12</sub> deficient? If so, why?
- 4. Is the patient's bone marrow suppressed? If so, why?
- 5. Is there any evidence of increased RBC destruction?

#### Box 1

#### Etiology of anemia

Blood loss (acute or chronic)

- Gastrointestinal tract (ie, hematemesis or hematochezia)
- Genitourinary tract (ie, hematuria)
- Respiratory tract (ie, hemoptysis or nose bleeds)
- Menstrual history
- Recent surgeries (direct loss or secondary bleeding [eg, retroperitoneal hemorrhage after cardiac catheterization])

Chronic medical problems

- Renal disease
- Inflammatory disease (eg, rheumatoid arthritis or inflammatory bowel disease)
- Congestive heart failure
- Prosthetic valves
- Malignancy
- Infections (eg, HIV)
- Liver disease
- Intestinal malabsorption, celiac disease

Past history of anemia and prior treatment

- History of transfusions
- Splenectomy
- Blood donation

#### Medications

- Nonsteroidal anti-inflammatory drugs
- Antibiotics (eg, cephalosporin and sulfa drugs)
- Chemotherapeutic agents
- Dapsone
- Anticonvulsants (eg, phenytoin and carbamazepine)
- Herbal and over-the-counter medications

#### Family history

- Sickle cell anemia
- Thalassemia
- Hereditary spherocytosis

Social history

- Nutritional status especially in older adults (eg, tea and toast diet)
- Alcohol usage

## Signs, Symptoms, and Physical Examination

Symptoms related to anemia can result from 2 factors: decreased oxygen delivery to tissues and, in patients with acute bleeding, the added effect of hypovolemia. Many patients, however, are asymptomatic/minimally symptomatic although they have anemia, and the diagnosis of anemia is found on routine preoperative laboratory work.

Patients can complain of symptoms, such as fatigue, weakness, lightheadedness or dizziness, chest pain, and decreased exercise tolerance. Patients with chronic anemia or congenital forms of anemia (eg, sickle cell disease [SCD] and hereditary spherocytosis) may not report symptoms until hemoglobin decreases to less than 5 g/dL.

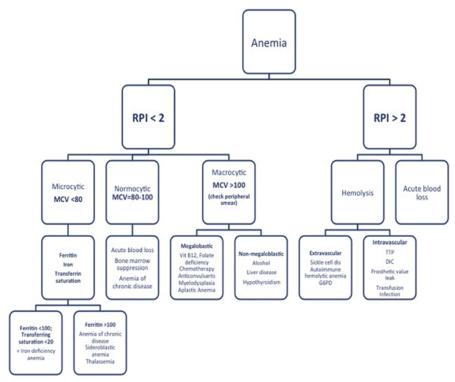
Physical examination findings of pallor, jaundice, or scleral icterus may suggest a hemolytic anemia. Other signs of underlying disease may include cardiac murmurs, hepatosplenomegaly, lymphadenopathy, petechial rash, or blood on digital rectal examination.<sup>3</sup>

#### Laboratory Evaluation

Initial laboratory evaluation of anemia includes complete blood cell count, peripheral blood smear, and a reticulocyte count. Fig. 2 describes a practical approach to the work-up of anemia.

Two important RBC indices that help determine the cause of anemia include mean corpuscular value (MCV) (ie, size of an RBC) and reticulocyte production index (RPI) (measurement of reticulocyte response with correction for the degree of anemia and reticulocyte maturation time). Most laboratory reports calculate RPI; however, if that is not available, it can be calculated as RPI = reticulocytes (percent) × (Hct  $\div$  45) × (1  $\div$  RMT) [Reticulocyte maturation time (RMT) is used to correct for the longer life span of prematurely released reticulocyte maturation time, use the following guide-lines. For the Hct value for the patient use the given maturation time in provided equation,

- HCT 36-45, the maturation time = 1.0
- HCT 26-35, the maturation time = 1.5



**Fig. 2.** Differential diagnosis of anemia flow diagram. This list of causes is not meant to be exhaustive; only the most common are included. DIC, disseminated intravascular coagulation; G6PD, Glucose-6-Phosphate Dehydrogenase deficiency; MCV, mean corpuscular volume; RPI, reticulocyte production induction; TTP, thrombotic thrombocytopenia. Items listed in bold indicate laboratory investigation. (*Adapted from* Vieth JT, Lane DR. Anemia. Emerg Med Clin North Am 2014;32(3):613–28; with permission; and *Data from* Patel MS, Carson JL. Anemia in the preoperative patient. Anesthesiol Clin 2009;27(4):751–60.)

- HCT of 16-25, the maturation time = 2
- HCT 15 and below, the maturation time = 2.5].
- An RPI greater than 2 indicates an appropriate bone marrow response and differential diagnosis includes blood loss or hemolysis.
- Next steps include
  - Assessing for sources of blood loss: careful history, stool guaiac, and endoscopy/colonoscopy if indicated
  - Assessing for hemolysis: lactate dehydrogenase, haptoglobin, and peripheral smear. An elevated direct bilirubin and lactate dehydrogenase and a low haptoglobin level along with a positive direct and indirect Coombs test point toward hemolysis.
  - Peripheral smear should be reviewed for clues to underlying process and hemoglobin electrophoresis may be helpful. Various peripheral smear findings are described in Table 1.
- An RPI less than 2 indicates hypoproliferative anemia or an inappropriate/attenuated bone marrow response to anemia.
- The next step includes checking the MCV and further characterizing the anemia as microcytic, normocytic, or macrocytic and a peripheral blood smear. Fig. 2 also

| Table 1<br>Common peripheral smear findings and their associated disease |   |  |  |  |  |
|--|---|--|--|--|--|
| Abnormal Peripheral<br>Blood Smear Findings                              |   |  |  |  |  |
| Schistocytes   | Microangiopathic hemolytic anemia<br>Hemolysis                                  |  |  |  |  |
| Spherocytes  | Hereditary spherocytosis<br>Autoimmune hemolytic anemia                         |  |  |  |  |
| Sickle cells   | SCD   |  |  |  |  |
| Burr cells   | Chronic renal failure   |  |  |  |  |
| Target cells   | Hemoglobinopathies<br>IDA   |  |  |  |  |
| Teardrop cells   | Leukoerythroblastic syndrome – for example, myelofibrosis and<br>myelodysplasia |  |  |  |  |
| Nucleated RBCs   | Severe hemolysis<br>Myelophthisic condition – for example, myelofibrosis        |  |  |  |  |
| Rouleaux<br>formation  | Multiple myeloma  |  |  |  |  |
| Blasts   | Leukemia<br>Lymphoma<br>Myelodysplasia  |  |  |  |  |
| Smudge cells   | Chronic lymphocytic luekemia  |  |  |  |  |

Adapted from Vieth JT, Lane DR. Anemia. Emerg Med Clin North Am 2014;32(3):613–28; with permission; and *Data from* Bain BJ. Diagnosis from the blood smear. N Engl J Med 2005;353(5):498–507.

describes the most common causes of anemia based on MCV. **Table 2** describes the laboratory parameters that help differentiate between most common causes of anemia (iron deficiency anemia [IDA] and anemia of chronic disease).

A hematology consultation prior to surgery in patients with newly diagnosed anemia is recommended in the following situations:

- 1. Abnormal cells in circulation (eg, nucleated RBCs and blasts)
- Increase/decrease in absolute counts for granulocyte, lymphocyte, monocyte, or platelets, which likely suggests a complex hematological problem (eg, leukemia, aplastic anemia, myelodysplasia, or myeloproliferative neoplasm)
- 3. Lack of improvement of anemia after 3 to 4 weeks of adequate treatment

| Table 2<br>Differential diagnosis of microcytic anemia |                    |            |                                |                          |  |  |
|--|--------------------|------------|--------------------------------|--------------------------|--|--|
| Causes of<br>Hypochromic Anemia                        | Serum<br>Iron (Fe) | Ferritin   | Total Iron<br>Binding Capacity | Percentage<br>Saturation |  |  |
| Iron deficiency  | Decreased          | Low (<100) | Increased                      | Decreased (<16%)         |  |  |
| Anemia of chronic disease                              | Decreased          | Normal     | Decreased                      | Decreased                |  |  |
| Thalassemia  | Normal/increased   | Normal     | Normal                         | Normal/increased         |  |  |

Adapted from Vieth JT, Lane DR, Anemia. Emerg Med Clin North Am 2014;32(3):613–28; with permission; and *Data from* Goodnough LT, Maniatis A, Earnshaw P, et al. Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines. Br J Anaesth 2011;106(1):13–22.

## TREATMENT OF ANEMIA

Management of perioperative anemia is driven by the cause of the anemia and urgency of the surgery.

## Nutritional Deficiency

## Iron deficiency anemia

Once a diagnosis of IDA is made, it is important to identify the underlying cause, such as blood loss, and treat it. Ferrous sulfate is an inexpensive and easy way of correcting iron deficiency. An appropriate daily dose for treating IDA in adults is in the range of 150 to 200 mg/d of elemental iron. Various iron preparations are available, including ferrous sulfate, 325 mg (65 mg elemental iron), or ferrous gluconate, 325 mg (36 mg elemental iron), given 2 or 3 times a day. There is no evidence of one more effective than another. Oral iron is more readily absorbed in an acidic gastric environment and, therefore, often given with ascorbic acid. Clinical response with feeling of well-being is noted within first few days, with laboratory improvement of hemoglobin by approximately 2 g/dL over 3 weeks. Occasionally patients may not respond to oral iron and need intravenous iron and further evaluation of underlying causes. Common clinical conditions include nonadherence, concomitant uses of antacids, *Helicobacter pylori* infection, malabsorption (eg, celiac disease), and ongoing blood losses.<sup>40,41</sup>

## Vitamin B<sub>12</sub> or folate deficiency

Patients with gastric surgeries (subtotal gastrectomy or bariatric surgery), pure vegetarians, and pregnant women on Mediterranean diets are at a risk of vitamin B<sub>12</sub> deficiency. Intramuscular vitamin B<sub>12</sub> is given at a dose of 1000  $\mu$ g every day for 7 days, followed by 1000  $\mu$ g weekly for 4 weeks. Hemoglobin concentration begins to rise within 10 days and normalizes within 8 weeks. Folate deficiency, very uncommon in the United States, is treated with folic acid, 1 mg/d orally, for 1 to 4 months.<sup>42</sup>

# Stimulation of Erythropoiesis

Several randomized controlled trials have evaluated the role of ESAs in correcting preoperative anemia and avoiding or reducing postoperative blood transfusion in various surgical settings (orthopedic, cardiovascular, and oncological). The American Society of Anesthesiologists (ASA) Task Force on Preoperative Blood Management recommends ESAs with or without iron in select patient populations (eg, renal insufficiency, anemia of chronic disease, and refusal of transfusion).<sup>43</sup>

The current recommendation for perioperative use of epoetin alfa (Procrit) as it appears on the package insert is  $^{44}$ 

- 300 Units/kg per day subcutaneously for 15 days total: administered daily for 10 days before surgery, 1 dose on the day of surgery and then for 4 days after surgery, or
- 600 Units/kg subcutaneously in 4 doses administered 21, 14, and 7 days before surgery and on the day of surgery.

The package insert also recommends deep venous thrombosis prophylaxis during epoetin alfa therapy. Suggested precautions and contraindications for the use of ESAs in-patient with preoperative anemia are listed<sup>44,45</sup>:

- Uncontrolled hypertension (systolic blood pressure >160 mm Hg and diastolic blood pressure >90 mm Hg)
- Pure RBC aplasia that begins after treatment with erythropoietin protein drugs

- Previous history of thrombotic vascular events (myocardial infarction/cerebrovascular accident/transient ischemic attack/deep vein thrombosis/pulmonary embolism). Using ESAs to target a hemoglobin level of greater than 11 g/dL increased the risk of serious adverse cardiovascular reactions.
- Previous history of seizures
- Risk factors predisposing to preoperative deep vein thrombosis (eg, immobility and fracture joint)
- Hypercoagulable disease states (eg, positive lupus anticoagulant)
- Cancer diagnosis/treatment (in past 3 years); not an absolute exclusion, consider each patient individually; if proceeding, close monitoring and Hb not to exceed 13.5 g/dL

# **Red Cell Transfusion**

# Allogeneic transfusion

In 2006 the ASA launched a task force to establish new guidelines for perioperative blood management. In an updated report in February 2015, the ASA task force strongly recommends a restrictive strategy for blood transfusion and administration of RBCs with hemoglobin level less than 6 g/dL. To determine who would benefit from blood transfusion when hemoglobin level falls between 6 g/dL and 10 g/dL is based on factors like potential or actual ongoing bleeding (rate and magnitude), intravascular volume status, signs of organ ischemia, and adequacy of cardiopulmonary reserve.<sup>43</sup>

The task force also recommends administration of unit-by-unit transfusion with interval re-evaluation. In the published updates in 2015, the task force endorses use of transfusion algorithms, especially those based on thromboelastographic testing, and blood ordering schedules. The ASA has selected restrictive transfusion strategy in the perioperative period as 1 of the top 5 Choosing Wisely initiatives.

#### Autologous transfusion

Over the past several years, there has been a steady decline in the use of preoperative autologous blood donations (PADs). Compared with 2008, 59.4% fewer units of autologous blood were transfused in 2011. Approximately half of all autologous donations were not used in 2011.<sup>11</sup> This decline can be explained by a combination of several factors, including a decreasing real and perceived risk of disease transmission through allogeneic transfusion, the adoption of better patient blood management (PBM) practices, and the increasing logistical and cost constraints of PAD programs. Various national societies recommend that PADs be considered exclusively for patients refusing necessary allotransfusion (eg, religious belief), those with RBC alloantibodies necessitating rare blood unavailable in volumes likely to be required, and, possibly, selected healthy individuals planning procedures with at least a 50% risk of requiring 3 or more units of transfusion.<sup>46</sup>

# PREOPERATIVE ANEMIA MANAGEMENT IN PATIENTS WITH SICKLE CELL DISEASE

Surgical procedures in patients with SCD are associated with significant risk of perioperative complications. Surgical stress and trauma can increase the rate of anemia and sickle cell formation, and RBC transfusions are often used to preserve oxygen carrying capacity and to dilute the sickle cells. The Transfusion Alternatives Preoperatively in Sickle Cell Disease study is a multicenter randomized control trial that demonstrated a lowered risk of postoperative complications in patients with SCD undergoing medium-risk surgery when preoperative hemoglobin level was increased to 10 g/dL. Based on these results, an expert panel reviewing recommendations in management of SCD recommends RBC transfusion to bring preoperative hemoglobin level to 10 g/dL prior to any surgical procedures involving general anesthesia.<sup>47,48</sup> Hematology consultation should be considered in patients with SCD receiving hydroxyurea therapy, planning to undergo high-risk surgery (eg, neurosurgery, prolonged anesthesia, or cardiac bypass), or those with hemoglobin SC or hemoglobin SB plus thalassemia.

# PATIENT BLOOD MANAGEMENT

PBM, a term has that emerged in the past few years, is a patient-centered evidencebased multidisciplinary approach to improve the care of patients who may need transfusion.<sup>7,49–51</sup>

PBM has 3 main pillars:

- 1. Optimization of blood volume and RBC mass preoperative, which includes anemia screening, assessment, and management
- 2. Minimization of blood loss and blood conservation modalities
- 3. Making patient-centered decisions for transfusions

Many transfusions may be avoided if, for example, patients' iron deficiency is treated and patients have enough time to generate their own RBCs. Still there is a significant challenge to making sure that anemia is diagnosed and treated in a timely manner. Implementation of a PBM program represents a great opportunity to address the perioperative anemia and reduce the need for transfusions. This requires, however, a collaborative strategy to include primary care providers, surgeons, transfusion specialists, anesthesiologists, and the hospitals and, most importantly, a change in the culture of health care providers.

#### SUMMARY

Preoperative anemia is the most frequent hematological condition identified before surgery and the most common cause is iron deficiency. Preoperative anemia is associated with an increased likelihood of RBC transfusion, which in turn has been associated with increased morbidity, mortality, and length of stay. Anemia is often overlooked in the preoperative evaluation based on the misconception that it is easily corrected with blood transfusions. Patients should be evaluated as early as possible in the preoperative pathway to coordinate optimization of the patient hemoglobin and, when possible, patients with unexpected preoperative anemia should be rescheduled until evaluation and treatment are finalized.

#### REFERENCES

- 1. Skjelbakken T, Langbakk B, Dahl IM, et al. Haemoglobin and anaemia in a gender perspective: the Tromso Study. Eur J Haematol 2005;74(5):381–8.
- Bryan LJ, Zakai NA. Why is my patient anemic? Hematol Oncol Clin North Am 2012;26(2):205–30, vii.
- 3. Vieth JT, Lane DR. Anemia. Emerg Med Clin North Am 2014;32(3):613–28.
- 4. Dubois RW, Goodnough LT, Ershler WB, et al. Identification, diagnosis, and management of anemia in adult ambulatory patients treated by primary care physicians: evidence-based and consensus recommendations. Curr Med Res Opin 2006;22(2):385–95.
- Shander A, Knight K, Thurer R, et al. Prevalence and outcomes of anemia in surgery: a systematic review of the literature. Am J Med 2004;116(Suppl 7A): 58S–69S.

- Leichtle SW, Mouawad NJ, Lampman R, et al. Does preoperative anemia adversely affect colon and rectal surgery outcomes? J Am Coll Surg 2011; 212(2):187–94.
- Munoz M, Gómez-Ramírez S, Kozek-Langeneker S, et al. 'Fit to fly': overcoming barriers to preoperative haemoglobin optimization in surgical patientsdagger. Br J Anaesth 2015;115(1):15–24.
- 8. McLean E, Cogswell M, Egli I, et al. Worldwide prevalence of anaemia, WHO Vitamin and Mineral Nutrition Information System, 1993-2005. Public Health Nutr 2009;12(4):444–54.
- Wells AW, Mounter PJ, Chapman CE, et al. Where does blood go? Prospective observational study of red cell transfusion in north England. BMJ 2002; 325(7368):803.
- 10. Patel MS, Carson JL. Anemia in the preoperative patient. Anesthesiol Clin 2009; 27(4):751–60.
- 11. Whitaker BI. The 2011 National Blood collection and utilization survery report. 2011. Available at: http://www.aabb.org/research/hemovigilance/bloodsurvey/ Documents/11-nbcus-report.pdf. Accessed July 27, 2015.
- 12. Shokoohi A, Stanworth S, Mistry D, et al. The risks of red cell transfusion for hip fracture surgery in the elderly. Vox Sang 2012;103(3):223–30.
- **13.** Weber WP, Zwahlen M, Reck S, et al. The association of preoperative anemia and perioperative allogeneic blood transfusion with the risk of surgical site infection. Transfusion 2009;49(9):1964–70.
- Carson JL, Noveck H, Berlin JA, et al. Mortality and morbidity in patients with very low postoperative Hb levels who decline blood transfusion. Transfusion 2002; 42(7):812–8.
- 15. Wu WC, Schifftner TL, Henderson WG, et al. Preoperative hematocrit levels and postoperative outcomes in older patients undergoing noncardiac surgery. JAMA 2007;297(22):2481–8.
- Weiss G, Goodnough LT. Anemia of chronic disease. N Engl J Med 2005;352(10): 1011–23.
- 17. Tilg H, Ulmer H, Kaser A, et al. Role of IL-10 for induction of anemia during inflammation. J Immunol 2002;169(4):2204–9.
- 18. Clemens J, Spivak JL. Serum immunoreactive erythropoietin during the perioperative period. Surgery 1994;115(4):510–5.
- Garcia-Erce JA, Cuenca J, Muñoz M, et al. Perioperative stimulation of erythropoiesis with intravenous iron and erythropoietin reduces transfusion requirements in patients with hip fracture. A prospective observational study. Vox Sang 2005; 88(4):235–43.
- 20. Goodnough LT, Maniatis A, Earnshaw P, et al. Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines. Br J Anaesth 2011;106(1):13–22.
- Leal-Noval SR, Muñoz M, Asuero M, et al. Spanish consensus statement on alternatives to allogeneic blood transfusion: the 2013 update of the "Seville Document". Blood Transfus 2013;11(4):585–610.
- 22. Melis M, McLoughlin JM, Dean EM, et al. Correlations between neoadjuvant treatment, anemia, and perioperative complications in patients undergoing esophagectomy for cancer. J Surg Res 2009;153(1):114–20.
- 23. Gombotz H, Rehak PH, Shander A, et al. Blood use in elective surgery: the Austrian benchmark study. Transfusion 2007;47(8):1468–80.
- 24. Spahn DR. Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. Anesthesiology 2010;113(2):482–95.

- 25. Glance LG, Dick AW, Mukamel DB, et al. Association between intraoperative blood transfusion and mortality and morbidity in patients undergoing noncardiac surgery. Anesthesiology 2011;114(2):283–92.
- 26. Dunne JR, Malone D, Tracy JK, et al. Perioperative anemia: an independent risk factor for infection, mortality, and resource utilization in surgery. J Surg Res 2002; 102(2):237–44.
- 27. Hagino T, Ochiai S, Sato E, et al. The relationship between anemia at admission and outcome in patients older than 60 years with hip fracture. J Orthop Traumatol 2009;10(3):119–22.
- 28. Kulier A, Levin J, Moser R, et al. Impact of preoperative anemia on outcome in patients undergoing coronary artery bypass graft surgery. Circulation 2007; 116(5):471–9.
- 29. Beattie WS, Karkouti K, Wijeysundera DN, et al. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. Anesthesiology 2009;110(3):574–81.
- 30. Carson JL, Terrin ML, Noveck H, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. N Engl J Med 2011;365(26):2453–62.
- Foss NB, Kristensen MT, Jensen PS, et al. The effects of liberal versus restrictive transfusion thresholds on ambulation after hip fracture surgery. Transfusion 2009; 49(2):227–34.
- 32. Gruson KI, Aharonoff GB, Egol KA, et al. The relationship between admission hemoglobin level and outcome after hip fracture. J Orthop Trauma 2002;16(1):39–44.
- **33.** Halm EA, Wang JJ, Boockvar K, et al. The effect of perioperative anemia on clinical and functional outcomes in patients with hip fracture. J Orthop Trauma 2004;18(6):369–74.
- **34.** Lawrence VA, Silverstein JH, Cornell JE, et al. Higher Hb level is associated with better early functional recovery after hip fracture repair. Transfusion 2003;43(12): 1717–22.
- **35.** Carson JL, Duff A, Poses RM, et al. Effect of anaemia and cardiovascular disease on surgical mortality and morbidity. Lancet 1996;348(9034):1055–60.
- **36.** Musallam KM, Tamim HM, Richards T, et al. Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. Lancet 2011;378(9800):1396–407.
- 37. Marcantonio ER, Goldman L, Orav EJ, et al. The association of intraoperative factors with the development of postoperative delirium. Am J Med 1998;105(5):380–4.
- **38.** Vuille-Lessard E, Boudreault D, Girard F, et al. Postoperative anemia does not impede functional outcome and quality of life early after hip and knee arthroplasties. Transfusion 2012;52(2):261–70.
- **39.** So-Osman C, Nelissen R, Brand R, et al. Postoperative anemia after joint replacement surgery is not related to quality of life during the first two weeks postoperatively. Transfusion 2011;51(1):71–81.
- 40. Hershko C, Camaschella C. How I treat unexplained refractory iron deficiency anemia. Blood 2014;123(3):326–33.
- **41.** Tefferi A. Anemia in adults: a contemporary approach to diagnosis. Mayo Clin Proc 2003;78(10):1274–80.
- 42. Stabler SP. Clinical practice. Vitamin B12 deficiency. N Engl J Med 2013;368(2): 149–60.
- 43. American Society of Anesthesiologists Task Force on Perioperative Blood Management. Practice guidelines for perioperative blood management: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management. Anesthesiology 2015;122(2):241–75.

- 44. Procrit [Package Insert]. Available at: http://assets.procrit.com/shared/product/ procrit/procrit-prescribing-information.pdf. Accessed July 27, 2015.
- **45.** Ralley FE. Erythropoietin and intravenous iron in PBM. Transfus Apher Sci 2014; 50(1):16–9.
- Vassallo R, Goldman M, Germain M, et al. Preoperative autologous blood donation: waning indications in an era of improved blood safety. Transfus Med Rev 2015;29(4):268–75.
- Howard J, Malfroy M, Llewelyn C, et al. The Transfusion Alternatives Preoperatively in Sickle Cell Disease (TAPS) study: a randomised, controlled, multicentre clinical trial. Lancet 2013;381(9870):930–8.
- Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. JAMA 2014;312(10):1033–48.
- Building a Better Patient Blood Management Program. 2015. Available at: http:// www.aabb.org/pbm/Documents/AABB-PBM-Whitepaper.pdf. Accessed July 27, 2015.
- 50. Isbister JP. The three-pillar matrix of patient blood management–an overview. Best Pract Res Clin Anaesthesiol 2013;27(1):69–84.
- 51. What is Patient Blood Management. Available at: http://www.blood.gov.au/ patient-blood-management-pbm-whatispbm. Accessed July 27, 2015.