



Bloodless Management of the Anemic Patient in the Emergency Department

Kelly Johnson-Arbor, MD*; Richard Verstraete, RN

*Corresponding Author. E-mail: kkja@me.com.

Anemia is a commonly encountered condition in emergency medicine; transfusion of packed red blood cells is commonly performed for anemic patients in the emergency department (ED), but some patients are unable to accept transfusion of blood products due to medical or religious concerns. The unique, acute, and time-sensitive nature of emergency medicine practice requires that physicians maintain an enhanced awareness of bloodless medicine treatment modalities. Identification of bloodless medicine patient preferences in the ED can help guide physicians in the recommendation of acceptable methods of treating anemia in this patient population. A focus on early hemostasis and resuscitation, instead of attempts to convince the patient to accept blood transfusion, can be lifesaving in patients with acute bleeding. Treatment strategies including the use of methods to reduce unnecessary blood loss, enhance red blood cell production, and increase the oxygen-carrying capacity of blood should also be considered early in patient presentation. Timely involvement of the Hospital Liaison Committee can help facilitate successful interpersonal communication and shared decisionmaking between emergency physicians and bloodless medicine patients. By embracing an understanding of bloodless medicine patient needs as well as available treatment strategies, ED physicians can contribute to optimal overall outcomes for anemic bloodless medicine patients. [Ann Emerg Med. 2022;79:48-57.]

Continuing Medical Education exam for this article is available at <http://www.acep.org/ACEPeCME/>.

0196-0644/\$-see front matter

Copyright © 2021 by the American College of Emergency Physicians.

<https://doi.org/10.1016/j.annemergmed.2021.06.015>

INTRODUCTION

Anemia affects approximately one third of the world's population and is a common condition encountered in the emergency department (ED) setting.¹ In a tertiary care ED, as many as 27% of patients may carry the diagnosis of anemia, and many patients may report sequelae of anemia, including chest pain, dyspnea, and fatigue.² Currently, packed red blood cell transfusion remains the accepted standard of care for the treatment of acutely anemic patients and is a commonly performed ED procedure. Blood transfusions are also common in hospitalized patients; in 2013, more than 13 million blood products were transfused to patients in the United States.³

Historically, indications for transfusion of red blood cells were based on hemoglobin concentrations. Prior to the 1980s, the "10/30" rule was a commonly followed transfusion protocol; according to this paradigm, a patient's hemoglobin or hematocrit should exceed 10 g/dL or 30%, respectively, prior to operative procedures.⁴ In recent years, the clinical utility of unrestricted blood transfusions has come under scrutiny, as there is scant evidence that this practice enhances clinical outcomes.⁵ Additionally, restrictive blood transfusion strategies are associated with decreases in health care costs as well as reductions in hospital length of stay, morbidity, and mortality.

Currently, generally accepted recommendations for management of anemic patients include transfusion thresholds that are based on both laboratory values and patient-specific factors.⁶ A commonly utilized threshold for transfusion of packed red blood cells is a hemoglobin concentration of 7 g/dL in patients who exhibit signs or symptoms of anemia. This threshold is based on the disequilibrium of oxygen delivery and extraction as well as the clinical symptoms that occur at higher frequency below this hemoglobin concentration.⁷

While blood transfusion is the most commonly utilized therapeutic intervention in anemic ED patients, some patients may be unable to receive transfusion of blood products due to medical or religious concerns.² Autoimmune hemolysis and ABO incompatibility are medical issues that may preclude patients from receiving blood transfusions in the ED setting; however, the majority of patients who are unable to receive blood transfusions are members of the Jehovah's Witness faith.⁸ There are more than 8 million Jehovah's Witnesses worldwide and more than a million in the United States.⁸ Members of this religion interpret the Bible's command to abstain from blood (Acts 15:20) as avoiding transfusion of blood products, including packed red blood cells, platelets, and fresh frozen plasma.⁹ Jehovah's Witnesses believe that

acceptance of blood transfusions will damage their relationship with God; because of this, their avoidance of blood product transfusions has been described as a religious obligation, not an option.¹⁰ Jehovah's Witnesses may also decline the administration of plasma-derived proteins, such as albumin, coagulation factors, and fibrin sealants such as Gelfoam, as these are derived from blood. Additionally, there are procedures performed in the ED that involve the transfer of blood and thus may be unsuitable for Jehovah's Witnesses; such procedures include hemodialysis, epidural blood patch placement, extracorporeal membrane oxygenation, plasmapheresis, and tagged red blood cell scans.

The time-sensitive and around-the-clock nature of emergency medicine presents unique challenges to the management of bloodless medicine patients. In the trauma population, bleeding-related deaths can be reduced with increased attention to hemodynamic resuscitation, hemorrhage control, and decreases in time to definitive surgical intervention.¹¹ Prompt attention to these same factors may also reduce morbidity and mortality in the bloodless medicine population. Early operative intervention, endoscopy, or interventional radiology procedures may be lifesaving in patients with acute and life-threatening hemorrhage from gastrointestinal, genitourinary, or pulmonary etiologies.¹² Significant nasal or dental bleeding may be controlled with tamponade, suturing, cauterization, or use of topical hemostatic agents.¹² Since large-volume resuscitation may cause hypothermia and coagulopathy, which may lead to increased bleeding, administration of warmed intravenous fluids is warranted for the bloodless medicine population.^{13,14}

While many hospitals have "patient blood management" or bloodless medicine programs that can suggest medical and surgical management strategies for this patient population, these programs may be unavailable for emergency consultations or on nights, weekends, and holidays. To minimize treatment delays and optimize provider awareness as well as patient satisfaction, it is advisable for hospitals and emergency departments to create bloodless medicine consent forms that delineate patients' wishes for receipt of major blood products, minor blood fractions, or procedures involving the use of blood (Figure). This form can be presented to all bloodless medicine patients on ED triage or hospital admission. At the authors' institution, the nurse coordinator for the bloodless medicine and surgery program is on call 24 hours a day for telephone consultations concerning the management of patients who are unable to receive blood transfusion. When

in the hospital, the nurse coordinator assists patients in the completion of the form, which is then scanned into the patient's electronic medical record. In an after-hours emergency, the nurse coordinator can assist patients, their relatives, and physicians in the completion of the form over the phone. Prompt completion of the form can assist in clarification of a patient's wishes and reduce unnecessary time delays in the management of this patient population. While many Jehovah's Witnesses often carry cards or health care directive forms that delineate their preferences about accepting transfusion of blood products, this information is, unfortunately, not always readily available in the ED setting.

Once a bloodless medicine patient is identified in the ED setting, health care professionals can utilize techniques to optimize the medical care of the patient without the use of blood transfusion. These techniques include strategies to reduce unnecessary blood loss, enhance red blood cell production, and increase the oxygen-carrying capacity of blood. In the bloodless medicine patient, the knowledge and implementation of these techniques can result in improved patient outcomes and enhanced satisfaction of patients and medical care providers. A brief discussion of each technique is presented here.

TECHNIQUE 1: STRATEGIES TO REDUCE UNNECESSARY BLOOD LOSS

In the hospital setting, phlebotomy can result in significant blood loss. Typical vacutainers can hold between 2 and 10 milliliters of blood. In the ED setting, phlebotomists often draw a "rainbow" of 7 vacutainers in anticipation of tests being ordered by a physician, and a single blood draw can result in an acute blood loss of 20 milliliters or more. When treating bloodless medicine patients, use of a careful phlebotomy technique, with attention to the number and size of vacutainers used, can result in reduction of unnecessary blood loss. In the ED setting, this can be accomplished by requesting that phlebotomists abstain from drawing blood on bloodless medicine patients until a physician has evaluated the patient and determined the need for laboratory testing. Identification of bloodless medicine patients can be easily accomplished by application of an identifying wristband at triage or application of a "bloodless medicine" sign above the patient's stretcher. Once a bloodless medicine patient has been identified and evaluated, a focused phlebotomy attempt may be performed. In addition, smaller vacutainers can be used to minimize iatrogenic blood loss. Pediatric or


**ATTACHMENT A
HOSPITAL POLICY 107**
**BLOODLESS MEDICINE AND SURGERY PROGRAM (BMSP)
INSTRUCTIONS OF THE PATIENT (CONSENT)**

I direct that **NO BLOOD COMPONENTS** or fresh plasma are to be given to me under ANY circumstances even if physicians deem a transfusion is necessary to preserve my life or health.
The following are my wishes and directions regarding procedures and medical treatments using plasma derived or white cell derived proteins.

	Accept	Refuse	
Major Components			Packed Red Blood Cells Cells that transport oxygen from the lungs to body cells.
			Fresh Plasma Liquid part of blood made of water, ions, sugar, hormones and protein.
			Platelets Cells that prevent blood loss by stopping the bleeding at site of injury.
Plasma Derived Proteins			Albumin Protein extracted from plasma. Used as a blood volume expander. Also used in medications such as Erythropoietin and Neupogen.
			Clotting Factors Various proteins extracted from plasma used to stop active bleeding. <i>Examples: Cryoprecipitate, Prothrombin, Complex Concentrate, Factor VII.</i>
			Immunoglobulins Proteins extracted from plasma. Used in medications to provide immunity, improve immune response to infections and for Rh incompatibility (RhoGam).
			Platelet Gel Autologous Platelet-rich plasma. Centrifuged from patient's blood and applied to surgical sites to reduce bleeding and enhance healing.
			Sealants Proteins from plasma. Used to stop bleeding. <i>Examples: Tisseel, Gel foam, BioGlue, Fibrin Glue and Autologous Platelet Gel.</i>
White Cell Derived Proteins			Interferon Protein extracted from white blood cells. Used for cancer treatments and viral infections. <i>Examples: Roferon-A and Intron-A.</i>
Equipment and Procedures			Cell Salvage Patient's blood is retrieved, filtered and returned in a closed loop process during surgery.
			Dialysis Patient's blood is filtered through a machine to clean the blood when there is insufficient kidney function.
			Epidural Blood Patch Patient's blood is removed from vein and injected into spinal membrane to seal a spinal fluid leak.
			Heart-Lung Machine Patient's blood is directed to a cardiopulmonary bypass pump that oxygenates and returns the blood during cardiovascular surgery.
			Hemodilution Specific amounts of patient's blood is removed at initiation of surgery and replaced with intravenous fluids. Blood is then returned in a closed loop process at the end of surgery.
			Labeling or Tagging Patient's blood is combined with radioactive material to mark (tag) the red cell then mixed for several minutes and returned via vein. Often utilized to locate site of bleeding in GI tract.
			Plasmapheresis Patient's blood is filtered and plasma removed. Plasma may be replaced with albumin. Utilized for autoimmune, neurologic or clotting disorders.
I hereby consent to everything I have accepted on this form.			

Patient's Printed Name: _____

Patient's Signature: _____ Date: _____ Time: _____

Witness' Printed Name: _____

Witness' Signature: _____ Date: _____ Time: _____

GUH 05018600 (4/13/16) (INDD)

Figure. An example of a bloodless medicine patient consent form.

neonatal microtainers, which hold 200 to 600 microliters of blood, can be substituted for typical adult-sized vacutainers in the bloodless medicine population. The use of pediatric phlebotomy tubes is associated with logistical challenges, including the need for adjustments in specimen collection and laboratory processing, which may result in delays in obtaining results.¹⁵ While the use of alternative phlebotomy tubes has not been studied in the ED setting, in a study of ICU patients, the use of pediatric-sized phlebotomy tubes was found to be a feasible alternative to the use of adult tubes.¹⁵ Another study of hospitalized patients demonstrated that the use of pediatric phlebotomy tubes was associated with a reduction in iatrogenic blood loss.¹⁶ Even though phlebotomy frequency and volumes are likely to be lower in ED patients than in hospitalized patients, initiation of judicious phlebotomy in the ED may contribute to an overall reduction in iatrogenic blood loss for bloodless medicine patients. Point-of-care testing, which requires significantly reduced quantities of blood compared with traditional phlebotomy, is another resource for laboratory testing in the ED.

In actively bleeding patients, reversal of coagulopathy should be promptly addressed. Bleeding in patients who take anticoagulant medications is often treated with fresh frozen plasma or coagulation factors such as human prothrombin complex concentrate. As fresh frozen plasma is a major blood component, it is unlikely that a bloodless medicine patient will accept transfusion of this product. Prothrombin complex concentrate contains coagulation factor concentrates; the overall concentration of clotting factors in prothrombin complex concentrate is approximately 25 times higher than in normal plasma.¹⁷ Prothrombin complex concentrate containing factors II, IX, and X is referred to as “3-factor prothrombin complex concentrate”; these factors, along with factor VII, are also included in the “4-factor prothrombin complex concentrate” currently available in the United States and indicated for the reversal of acute major bleeding associated with the use of vitamin K antagonists (eg, warfarin).^{18,19} Advantages of prothrombin complex concentrate over fresh frozen plasma include a lower volume of infusion, lack of blood group specificity, and ease of use (it is stored at room temperature and can be reconstituted quickly).^{18,20} Dosing of prothrombin complex concentrate is based on the patient’s body weight as well as the international normalized ratio. However, as the coagulation factors contained in prothrombin complex concentrate are derived from human plasma, they are considered as minor blood fractions and may not be acceptable to all bloodless medicine patients.

Recombinant factor VII (rFVII) is derived from hamster kidney cells; it does not contain any human proteins and is therefore generally accepted by Jehovah’s Witnesses.²¹ Initially developed as a treatment for hemophilia, purified rFVIIa is currently indicated in the United States for treatment of bleeding associated with hemophilia A and B, congenital factor VII deficiency, Glanzmann’s thrombasthenia, and acquired hemophilia.²² Dosing of rFVIIa is weight-based. When bound to tissue factor, factor VIIa activates factors IX and X and promotes conversion of prothrombin to thrombin.²³ Successful use of rFVIIa, with rapid control of hemostasis, has been reported in bloodless medicine patients.^{21,24} In a review of 3,176 patients with critical bleeding who were treated with rFVIIa, hemostatic outcomes of Jehovah’s Witnesses and non-Jehovah’s Witnesses were compared.²¹ The percent of patients who had a hemostatic response after rFVIIa administration was similar (74% to 75%) in the Jehovah’s Witness and non-Jehovah’s Witness cohorts, indicating that the use of rFVIIa can result in clinically significant hemostasis with or without concomitant transfusion of blood products. The hemostasis induced by rFVIIa administration can result in systemic thromboses; in this study, approximately 10% of subjects in both cohorts experienced thromboembolic complications. Given that rFVIIa is generally accepted in the Jehovah’s Witness community, use of this product should be considered as a primary treatment for bloodless medicine patients with ongoing bleeding and coagulopathy. In settings where rFVIIa is not available or when a more cost-effective option is desired, the use of desmopressin can also be considered. Desmopressin administration induces increases in factor VIII and von Willebrand factor as well as shortened activated partial thromboplastin time and bleeding time, with a resultant hemostatic effect.²⁵

In recent years, tranexamic acid has been explored as a treatment for uncontrolled or coagulopathic bleeding in emergency medicine. Tranexamic acid is a synthetic lysine derivative that is commonly used as an antifibrinolytic agent. Tranexamic acid has a high affinity for, and binds competitively with, the lysine binding site of plasminogen.²⁶ This binding results in inhibition of the conversion of plasminogen to plasmin, leading to decreased plasmin-mediated fibrin clot degradation. Through this mechanism, tranexamic acid stabilizes existing fibrin clots rather than promoting new clot formation.²⁷ Although the antifibrinolytic effects of tranexamic acid have been recognized since the 1960s, its use in the treatment of hemorrhagic conditions has expended within the past decade.²⁷ The therapeutic use of tranexamic acid has been described in cases of dysfunctional uterine bleeding,

postpartum hemorrhage, acute trauma, bleeding as a result of dental extractions, and other hemorrhagic conditions.²⁸ The drug has also been successfully used in a Jehovah's Witness patient with postpartum hemorrhage.²⁹ In the trauma patient population, early tranexamic acid administration was shown to reduce the risk of death from trauma-related bleeding.³⁰ Tranexamic acid is available in oral and intravenous formulations; topical use for the treatment of epistaxis and surgical-related bleeding has also been described.³¹ Its availability as a generic drug makes tranexamic acid a lower-cost therapeutic option for many patients. The dose of tranexamic acid is not standardized and varies by indication.²⁸ Adverse effects, including seizures and acute thromboses, have been reported after drug administration.^{32,33} Antagonism of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) can result in seizure activity; tranexamic acid acts as a GABA inhibitor and may increase seizure risk through this mechanism.³⁴ High doses of tranexamic acid (more than 100 mg/kg) are associated with an increased risk of seizure activity.³⁵ The risk of acute thromboses after tranexamic acid administration is largely theoretical in nature, and large studies in the surgical population have not demonstrated an increased risk of thromboembolic complications after tranexamic acid use.^{36,37} Despite initial enthusiasm for the use of tranexamic acid in patients with bleeding-related emergencies, recent literature has not demonstrated a mortality benefit of tranexamic acid in this patient population. In a multicenter study of 12,009 patients with gastrointestinal bleeding who received either tranexamic acid or placebo, the administration of tranexamic acid was not associated with a lower risk of death.³⁸ In a meta-analysis of the use of tranexamic acid in patients with cerebral hemorrhage, tranexamic acid use was not associated with a change in mortality or need for surgical intervention.³⁹ Given the lack of mortality reduction associated with its use, the utility and effectiveness of tranexamic acid in the ED bloodless medicine population remains unclear.

In addition to the previously described pharmacologic therapies, some bloodless medicine patients may also benefit from nonpharmacologic interventions to reduce blood loss. The use of autologous autotransfusion using cell salvage devices may be an acceptable alternative to transfusion of blood products.⁴⁰ In trauma patients with significant hemothorax, use of chest tube autotransfusion can be considered. However, autologous autotransfusion is not uniformly accepted among bloodless medicine patients; for Jehovah's Witnesses, the decision of whether to accept this treatment modality is often dependent on whether the

autotransfused blood maintains constant continuity with the patient's circulatory system.⁴¹

TECHNIQUE 2: STRATEGIES TO ENHANCE RED BLOOD CELL PRODUCTION

Pharmacologic interventions may also be utilized in the management of the anemic bloodless medicine patient population. In stable bloodless medicine patients, iron and erythropoietin are adjunctive treatments commonly used to enhance red blood cell mass. Iron supplementation is indicated for patients with anemia due to iron deficiency. Iron deficiency anemia is characterized by a low hemoglobin concentration in conjunction with a low mean corpuscular volume, low ferritin concentration, and/or decreased iron saturation.⁴² Oral iron supplementation is frequently used as a first-line therapy for iron deficiency anemia; a recommended starting dose is 325 mg of ferrous gluconate (equivalent to 65 mg of elemental iron).⁴³ Administration of iron supplements on alternate days instead of consecutive days may result in enhanced absorption of iron with fewer reported adverse events.⁴⁴ Intravenous iron formulations are also available; the use of these preparations has historically been associated with serious adverse events, including anaphylaxis. The incidence of these adverse events was likely associated with the use of higher-molecular weight iron dextran products.⁴⁵ The currently available lower-molecular weight iron dextran formulations have a favorable safety profile with a much lower incidence of serious adverse events.⁴⁶ In addition to low-molecular weight iron dextran, there are currently several other intravenous iron formulations that are currently approved by the United States Food and Drug Administration (FDA). Of the currently available and FDA-approved formulations, iron repletion can be achieved through single-dose infusions of ferumoxytol, ferric carboxymaltose, or low-molecular weight iron dextran.⁴² The ability to replenish iron stores with a single-dose intravenous infusion makes these iron formulations ideal for administration in the ED setting. A review of patients treated for iron deficiency anemia with intravenous iron in an ED setting demonstrated that this therapy was associated with reduced need for transfusion, reduced need for hospitalization, and decreased ED length of stay.⁴⁷ While intravenous iron is more expensive than oral iron formulations, the use of intravenous iron is also associated with significant overall cost savings for patients with iron deficiency anemia diagnosed in the ED.^{47,48} Considering these characteristics as well as its favorable safety profile, intravenous iron is a reasonable treatment for iron

deficiency anemia in the ED setting and should be especially considered for the treatment of iron deficiency anemia in patients who are unable to receive transfusion of blood products.

Erythropoietin-stimulating agents represent another important treatment option for bloodless medicine patients. Recombinant human erythropoietin stimulates erythropoiesis in the bone marrow; this results in enhancement of reticulocytosis and eventual improvement in hemoglobin concentration. It is important to recognize that some formulations of recombinant human erythropoietin (eg, epoetin alfa [Procrit, Epogen]) contain albumin, a minor blood fraction, as a preservative. As some bloodless medicine patients may not accept albumin as a treatment option, emergency physicians should become familiar with institutional formulary offerings and be prepared to discuss alternative options that do not contain albumin (epoetin alfa-epbx [Retacrit] and darbepoetin [Aranesp]) with bloodless medicine patients as well as other medical providers. Recombinant human erythropoietin dosing results in increases in hemoglobin concentration within 7 days, with a peak at 14 days.⁴⁹ Given the lengthy duration of time required to enhance erythropoiesis after recombinant human erythropoietin is administered, its use in the ED population is likely of minimal immediate benefit. However, administration of a single dose of recombinant human erythropoietin in the ED may assist with the acceleration of erythropoiesis over subsequent days, especially in patients who require hospitalization for continued evaluation and treatment. In this patient population, the early initiation of erythropoiesis in the ED setting may result in a more rapid anemia recovery and a shorter hospital length of stay.

TECHNIQUE 3: STRATEGIES TO INCREASE THE OXYGEN-CARRYING CAPACITY OF BLOOD

Oxygen transfer agents, hemoglobin-based oxygen carriers, and hyperbaric oxygen therapy may be used to increase the oxygen-carrying capacity of blood. Currently recognized oxygen transfer agents used as blood substitutes include perfluorocarbons and hemoglobin-based oxygen carriers. The toxicities of perfluorocarbons have significantly limited the clinical use of these compounds.⁵⁰ Hemoglobin-based oxygen carriers have been successfully used in the management of anemic bloodless medicine patients, alone and in conjunction with other therapies such as hyperbaric oxygenation.^{51,52} Currently, the use of these remains experimental. These agents are not approved by the FDA for clinical use and, therefore, are not readily available in the hospital or ED setting.⁵³ Hyperbaric

oxygen therapy is a treatment in which patients breathe 100% oxygen while pressurized to a depth more than that of sea level. The use of hyperbaric pressurization as a treatment for medical conditions dates back to the 1600s, prior to the discovery of oxygen.⁵⁴ Currently, hyperbaric oxygen therapy is used as a primary treatment for decompression sickness, air embolism, and carbon monoxide poisoning. It is also used as an adjunctive treatment for additional medical conditions, including compromised grafts and flaps, chronic refractory osteomyelitis, and diabetic foot ulcerations. Severe anemia, with inability to receive blood transfusion due to medical or religious beliefs, is also an accepted indication for the use of hyperbaric oxygen therapy.

In 1960, the Dutch surgeon Boerema⁵⁵ published "Life Without Blood," a manuscript detailing the use of hyperbaric oxygen therapy for the treatment of anemia. Boerema exsanguinated healthy piglets and replaced the blood volume with a plasma-like solution. The piglets' resulting hemoglobin concentration was 0.4 g/dL, a hemoglobin concentration that is incompatible with life. The piglets were then pressurized in a hyperbaric chamber to 3 absolute atmospheres for 45 minutes. The animals survived this exposure, despite having essentially no hemoglobin present, and recovered uneventfully after they were reinfused with normal blood. Boerema noted that under hyperbaric conditions, the amount of oxygen dissolved in the plasma can greatly exceed the amount present while breathing air under normobaric conditions. This phenomenon is due to Henry's Law, which states that the amount of gas dissolved in a solution is directly proportional to the partial pressure of the gas. When partial pressures of a gas increase, such as under hyperbaric pressurization, more of that gas dissolves in solution. Breathing room air (21% oxygen) under normobaric conditions results in a PaO₂ of approximately 100 mm Hg; breathing 100% oxygen under hyperbaric conditions results in a PaO₂ of more than 1600 mm Hg.⁵⁶ Under hyperbaric conditions, oxygen dissolved in the plasma can approximate or meet the body's metabolic demands of oxygen extraction.⁵⁷ This increase in oxygen dissolved in plasma represents the basis for the use of hyperbaric oxygen therapy for patients with severe anemia who are unable to receive transfusion. Since Boerema's initial publication on this subject, there have been multiple reported cases of the use of hyperbaric oxygen therapy for the treatment of acute blood loss anemia in patients who are unable to receive transfusion of blood products.⁵⁶⁻⁵⁸ In these cases, patients received 1 to 3 hyperbaric oxygen therapy treatments daily; treatment frequency was based on the patient's clinical presentation and was titrated based on improvement or

resolution of the signs and symptoms of oxygen debt. At the authors' institution, anemic bloodless medicine patients who present to the ED are referred for hyperbaric oxygen therapy as well as administration of recombinant human erythropoietin and intravenous iron, if indicated. The use of this regimen has resulted in a reduced need for hospital admission, as well as reduced hospital length of stay, for multiple patients.

There are currently more than 1,300 hyperbaric facilities in the United States. While a minority of these facilities are available for emergencies or after-hours care, hyperbaric oxygen therapy is readily available at many hospitals during daytime hours and should therefore be considered as a potential treatment for selected anemic bloodless medicine patients. Hyperbaric oxygen therapy is often administered in a single-person (monoplace) chamber where intravenous infusions, telemetry monitoring, and hands-on critical care are not available. Due to these restrictions, this treatment is likely to be of highest utility to stable bloodless medicine patients and can be administered on either an inpatient or outpatient basis. Some hospitals may have hyperbaric medicine facilities within, or in close proximity to, the ED, with emergency physicians staffing the hyperbaric unit. These institutions may be able to treat anemic bloodless medicine patients as hyperbaric medicine emergencies, with rapid referral from the ED setting. Additionally, as many clinicians are unfamiliar with the use of hyperbaric oxygen therapy in the bloodless medicine population, emergency physicians who are knowledgeable about this particular hyperbaric indication can minimize treatment delays and optimize patient care by referring appropriate patients for this treatment in an expedient manner. A majority of insurance carriers consider hyperbaric oxygen therapy to be a medically necessary treatment for patients with anemia who cannot receive blood transfusion and will provide reimbursement for the procedure.

INTERPERSONAL INTERACTIONS

The concepts mentioned above are important in the management of the hospitalized bloodless medicine patient population; however, the significance of interpersonal interactions with bloodless medicine patients is infrequently discussed but also requires attention. Bloodless medicine patients, and specifically the Jehovah's Witness population, are an educated and knowledgeable group of patients, and they are not opposed to modern medical care.⁵⁹ Jehovah's Witnesses are familiar with the risks of not accepting blood products, including the possibility of worsening anemia and death. While Jehovah's Witnesses do not desire death, they are keenly aware that avoidance of

blood transfusions does not necessarily equate with death, even when an emergency medical condition is present. The minimum hemoglobin level needed to sustain life has not been defined.⁶⁰ In addition, the severity of anemia, including its clinical consequences and patient outcomes, is dependent on both the hemoglobin level and the chronicity of the disease process. Because of this, the discussion of the risks of not accepting blood products must be balanced within the context of each individual patient's situation. For example, the risks associated with lack of blood transfusion after acute and significant blood loss (including end-organ damage, such as myocardial and cerebral ischemia, as well as death) are quite different than the risks associated with lack of blood transfusion in a hemodynamically stable patient with chronic anemia.

When blood transfusion cannot be performed due to medical or religious reasons, physicians may react with frustration or anger; despite the emotional response associated with this scenario, medical providers still have a duty to respect the autonomy and religious freedom of patients. The ability to honor patient autonomy may be challenging for some physicians; in one survey of European intensivists, 63% of those surveyed reported that they would transfuse a Jehovah's Witness patient who was exsanguinating; 26% of the physicians stated that they would never inform the patient about the transfusion.⁶¹ In the time-sensitive ED setting, the focus on the perceived needs for transfusion, as well as the associated emotional response, may distract the medical team from identifying and utilizing interventions that can be used to successfully treat the bloodless medicine population. Some physicians may ask to interview the patient without their family or caregiver present in an attempt to remove any external influencers who may contribute to the patient's desire to avoid blood transfusion. Other providers may tell the patient that they will likely die if they do not receive blood or state that there is "nothing else that can be done" for the patient if a blood transfusion is declined. These techniques represent undue coercion and should be avoided when interacting with bloodless medicine patients.

For bloodless medicine patients who are unconscious or mentally incapacitated, providers should seek guidance from the hospital ethics and/or legal departments if transfusion of blood products is being considered.¹² Pediatric bloodless medicine patients (eg, the children of Jehovah's Witnesses) represent a unique patient subgroup. In the United States, courts generally abide by the doctrine of *parens patriae* ("parent of the nation"), which permits states to intervene on behalf of a child whose welfare is in question; however, some states do recognize a "mature minor" law, which allows some children to make their own

health care choices.⁶² Due to variations in legal standards between states, physicians should consider involvement of the hospital legal and/or ethics teams when caring for pediatric bloodless medicine patients. Ultimately, both physicians and parents desire the best outcome for pediatric patients, and effective communication and utilization of available supporting resources may allow both parties to achieve a mutually acceptable and favorable decision for pediatric patient care.

Communication about the avoidance of blood transfusion and use of alternative medical techniques can be challenging for both the patient and the physician. The Hospital Liaison Committee can be utilized as a method to enhance medical communication with the Jehovah's Witness population. The Hospital Liaison Committee are community-based Jehovah's Witness ministers who volunteer in hospitals worldwide.⁹ A primary role of the Hospital Liaison Committee is to assist hospitalized Jehovah's Witness patients by facilitating nonconfrontational and evidence-based communication between the patients and their physicians; Hospital Liaison Committee members can also suggest clinical strategies for the management of patients without blood transfusion and provide spiritual support to hospitalized Jehovah's Witness patients. The Hospital Liaison Committee network is widespread; even in hospitals that lack dedicated bloodless medicine programs, it is likely that Hospital Liaison Committee members are available. Medical providers can locate local Hospital Liaison Committee representatives by calling Jehovah's Witness Hospital Information Services (HIS) at 1-718-560-4700. The HIS department is available 24 hours a day, 7 days a week and is staffed from 8:00 AM to 5:00 PM Eastern Standard Time; after hours, a live operator will connect callers to an on-call HIS representative. Even though Hospital Liaison Committee members may not be immediately available in the ED setting, early involvement of these representatives in person or by telephone may result in improved clinical interactions and enhanced communication between patients and the medical care providers over subsequent hours to days.

Although the emergency treatment of anemic bloodless medicine patients may be perceived as emotionally stressful and medically formidable, there are many basic strategies that can be implemented in the ED for the care of this patient population. Careful attention to resuscitation and hemorrhage control, along with utilization of techniques to reduce unnecessary blood loss, enhance red blood cell production, and increase

hemoglobin oxygenation, can result in improved outcomes for bloodless medicine patients treated in the ED setting. Emergency physicians who treat anemic bloodless medicine patients may also find it helpful to utilize available resources such as the Hospital Liaison Committee. While some interventions for the care of bloodless medicine patients may be more relevant to inpatient providers, an increased awareness of these techniques by emergency physicians can result in a more rapid implementation of these strategies, both in the ED and inpatient settings. Utilization of these interventions can lead to decreased morbidity and mortality as well as enhanced patient and physician satisfaction in the care of bloodless medicine patients.

Supervising editor: Allan B. Wolfson, MD. Specific detailed information about possible conflict of interest for individual editors is available at <https://www.annemergmed.com/editors>.

Author affiliations: From the Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, Washington, DC (Johnson-Arbor); the MedStar Institute for Quality and Safety, MedStar Health, Columbia, MD (Johnson-Arbor); and the MedStar Georgetown University Hospital, Washington, DC (Verstraete).

Funding and support: By *Annals* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

Publication dates: Received for publication March 29, 2021. Revision received May 26, 2021. Accepted for publication June 14, 2021.

REFERENCES

1. Marchi G, Busti F, Girelli D. Sparing unnecessary transfusions through patient blood management: time for application also in internal and emergency medicine. *Intern Emerg Med*. 2020;15:559-561.
2. Beverina I, Brando B. Prevalence of anemia and therapeutic behavior in the emergency department at a tertiary care hospital: are patient blood management principles applied? *Transfus Apher Sci*. 2019;58:688-692.
3. Chung KW, Basavaraju SV, Mu Y, et al. Declining blood collection and utilization in the United States. *Transfusion*. 2016;56:2184-2192.
4. Klein HG, Spahn DR, Carson JL. Red blood cell transfusion in clinical practice. *Lancet*. 2007;370:415-426.
5. Salpeter SR, Buckley JS, Chatterjee S. Impact of more restrictive blood transfusion strategies on clinical outcomes: a meta-analysis and systematic review. *Am J Med*. 2014;127:124-131.e3.
6. Goodnough LT, Levy JH, Murphy MF. Concepts of blood transfusion in adults. *Lancet*. 2013;381:1845-1854.
7. Weiskopf RB, Kramer JH, Viele M, et al. Acute severe isovolemic anemia impairs cognitive function and memory in humans. *Anesthesiology*. 2000;92:1646-1652.

8. Resar LMS, Frank SM. Bloodless medicine: what to do when you can't transfuse. *Hematology Am Soc Hematol Educ Program*. 2014;2014:553-558.
9. Johnson-Arbor K, Verstraete R. No bad blood—surviving severe anemia without transfusion. *JAMA Intern Med*. 2021;181:7-8.
10. Guarino S, Di Matteo FM, Sorrenti S, et al. Bloodless surgery in geriatric surgery. *Int J Surg*. 2014;12:S82-S85.
11. Meizoso JP, Ray JJ, Karcutskie CAIV, et al. Effect of time to operation on mortality for hypotensive patients with gunshot wounds to the torso: the golden 10 minutes. *J Trauma Acute Care Surg*. 2016;81:685-691.
12. Berend K, Levi M. Management of adult Jehovah's Witness patients with acute bleeding. *Am J Med*. 2009;122:1071-1076.
13. Farkash U, Lynn M, Scope A, et al. Does prehospital fluid administration impact core body temperature and coagulation functions in combat casualties? *Injury*. 2002;33:103-110.
14. Rohrer MJ, Natale AM. Effect of hypothermia on the coagulation cascade. *Crit Care Med*. 1992;20:1402-1405.
15. Barreda Garcia J, Xian JZ, Pedroza C, et al. Pediatric size phlebotomy tubes and transfusions in adult critically ill patients: a pilot randomized controlled trial. *Pilot Feasibility Stud*. 2020;6:112.
16. Sanchez-Giron F, Alvarez-Mora F. Reduction of blood loss from laboratory testing in hospitalized adult patients using small-volume (pediatric) tubes. *Arch Pathol Lab Med*. 2008;132:1916-1919.
17. Franchini M, Lippi G. Prothrombin complex concentrates: an update. *Blood Transfus*. 2010;8:149-154.
18. Siegal DM, Savage WJ. Plasma versus prothrombin complex concentrate for warfarin-associated major bleeding: a systematic review. *Hematology Am Soc Hematol Educ Program*. 2015;2015:448-453.
19. Cole JL, McLeod ND. Administration of four-factor prothrombin complex concentrate for a life-threatening bleed in a Jehovah's Witness patient. *Blood Coagul Fibrinolysis*. 2018;29:120-122.
20. KCentra Prescribing Information. CSL Behring LLC. Kankakee, Illinois. Revised October 2018.
21. Kandane-Rathnayake RK, Isbister JP, Zatta AJ, et al. Use of recombinant activated factor VII in Jehovah's Witness patients with critical bleeding. *ANZ J Surg*. 2013;83:155-160.
22. NovoSeven RT Prescribing Information. Novo Nordisk Inc. Plainboro, New Jersey. Revised July 2020.
23. Franchini M, Lippi G. Recombinant activated factor VII: mechanisms of action and current indications. *Semin Thromb Hemost*. 2010;36:485-492.
24. Hsieh A, Cheong I. Use of recombinant activated factor VII in a Jehovah's Witness patient. *Am J Emerg Med*. 2007;25:1085.e1-2.
25. Franchini M. The use of desmopressin as a hemostatic agent: a concise review. *Am J Hematol*. 2007;82:731-735.
26. Lier H, Maegele M, Shander A. Tranexamic acid for acute hemorrhage: a narrative review of landmark studies and a critical reappraisal of its use over the last decade. *Anesth Analg*. 2019;129:1574-1584.
27. Goobie SM, Frank SM. Tranexamic acid: what is known and unknown, and where do we go from here? *Anesthesiology*. 2017;127:405-407.
28. Cai J, Ribkoff J, Olson S, et al. The many roles of tranexamic acid: an overview of the clinical indications for TXA in medical and surgical patients. *Eur J Haematol*. 2020;104:79-87.
29. Arab TS, Al-Wazzan AB, Maslow K. Postpartum hemorrhage in a Jehovah's Witness patient controlled with Tisseel, tranexamic acid, and recombinant factor VIIa. *J Obstet Gynaecol Can*. 2010;32:984-987.
30. CRASH-2 trial collaborators Shaker H, Roberts I, et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet*. 2010;376:23-32.
31. Montroy J, Hutton B, Moodley P, et al. The efficacy and safety of topical tranexamic acid: a systematic review and meta-analysis. *Transfus Med Rev*. 2018;S0887-7963(17):30151-30157.
32. Murkin JM, Falter F, Granton J, et al. High-dose tranexamic acid is associated with nonischemic clinical seizures in cardiac surgical patients. *Anesth Analg*. 2010;110:350-353.
33. Upadhyay SP, Mallick PN, Jagia M, et al. Acute arterial thrombosis associated with inadvertent high dose of tranexamic acid. *Indian J Crit Care Med*. 2013;17:237-239.
34. Kratzner S, Irl H, Mattusch C, et al. Tranexamic acid impairs γ -aminobutyric acid receptor type A-mediated synaptic transmission in the murine amygdala: a potential mechanism for drug-induced seizures? *Anesthesiology*. 2014;120:639-649.
35. Kalavrouziotis D, Voisine P, Mohammadi S, et al. High-dose tranexamic acid is an independent predictor of early seizure after cardiopulmonary bypass. *Ann Thorac Surg*. 2012;93:148-154.
36. Wei Z, Liu M. The effectiveness and safety of tranexamic acid in total hip or knee arthroplasty: a meta-analysis of 2720 cases. *Transfus Med*. 2015;25:151-162.
37. Badenoch A, Sharma A, Gower S, et al. The effectiveness and safety of tranexamic acid in orthotopic liver transplantation clinical practice: a propensity score matched cohort study. *Transplantation*. 2017;101:1658-1665.
38. HALT-IT Trial Collaborators. Effects of a high-dose 24-h infusion of tranexamic acid on death and thromboembolic events in patients with acute gastrointestinal bleeding (HALT-IT): an international randomised, double-blind, placebo-controlled trial. *Lancet*. 2020;395:1927-1936.
39. Huang B, Xu Q, Ye R, et al. Influence of tranexamic acid on cerebral hemorrhage: a meta-analysis of randomized controlled trials. *Clin Neurol Neurosurg*. 2018;171:174-178.
40. Hughes DB, Ullery BW, Barie PS. The contemporary approach to the care of Jehovah's Witnesses. *J Trauma*. 2008;65:237-247.
41. Lin ES, Kaye AD, Baluch AR. Preanesthetic assessment of the Jehovah's Witness patient. *Ochsner J*. 2012;12:61-69.
42. Boone S, Powers JM, Goodgame B, et al. Identification and management of iron deficiency anemia in the emergency department. *J Emerg Med*. 2019;57:637-645.
43. Lopez A, Cacoub P, Macdougall IC, et al. Iron deficiency anaemia. *Lancet*. 2016;387:907-916.
44. Stoffel NU, Cercamondi CI, Brittenham G, et al. Iron absorption from oral iron supplements given on consecutive versus alternate days and as single morning doses versus twice-daily split dosing in iron-depleted women: two open-label, randomised controlled trials. *Lancet Haematol*. 2017;4:e524-e533.
45. Chertow GM, Mason PD, Vaage-Nilsen O, et al. Update on adverse drug events associated with parenteral iron. *Nephrol Dial Transplant*. 2006;21:378-382.
46. Okam MM, Mandell E, Hevelone N, et al. Comparative rates of adverse events with different formulations of intravenous iron. *Am J Hematol*. 2012;87:E123-E124.
47. Beverina I, Rationale G, Ranzini M, et al. Early intravenous iron administration in the emergency department reduces red blood cell unit transfusion, hospitalisation, re-transfusion, length of stay and costs. *Blood Transfus*. 2020;18:106-116.
48. Quintana-Díaz M, Muñoz-Romo R, Gómez-Ramírez S, et al. A fast-track anaemia clinic in the emergency department: cost-analysis of intravenous iron administration for treating iron-deficiency anaemia. *Blood Transfus*. 2017;15:438-446.
49. Charles A, Purtil M, Napolitano LM. Recombinant human erythropoietin in severe anaemia: issues of dosing and duration. *Anaesth Intensive Care*. 2006;34:793-796.
50. Kim HW, Greenburg AG. Artificial oxygen carriers as red blood cell substitutes: a selected review and current status. *Artif Organs*. 2004;28:813-828.
51. Thenuwara K, Thomas J, Ibsen M, et al. Use of hyperbaric oxygen therapy and PEGylated carboxyhemoglobin bovine in a Jehovah's Witness with life-threatening anemia following

- postpartum hemorrhage. *Int J Obstet Anesth.* 2017;29:73-80.
52. Posluszny JA, Napolitano LM. Hemoglobin-based oxygen carrier for traumatic hemorrhagic shock treatment in a Jehovah's Witness. *Arch Trauma Res.* 2016;5:e30610.
 53. Khan F, Singh K, Friedman MT. Artificial blood: the history and current perspectives of blood substitutes. *Discoveries (Craiova).* 2020;8:e104.
 54. Edwards ML. Hyperbaric oxygen therapy. Part 1: history and principles. *J Vet Emerg Crit Care (San Antonio).* 2010;20:284-288.
 55. Boerema I, Meyne NG, Brummelkamp WH, et al. Life without blood. *Ned Tijdschr Geneesk.* 1960;104:949-954.
 56. Greensmith JE. Hyperbaric oxygen reverses organ dysfunction in severe anemia. *Anesthesiology.* 2000;93:1149-1152.
 57. McLoughlin PL, Cope TM, Harrison JC. Hyperbaric oxygen therapy in the management of severe acute anaemia in a Jehovah's Witness. *Anaesthesia.* 1999;54:891-895.
 58. Graffeo C, Dishong W. Severe blood loss anemia in a Jehovah's Witness treated with adjunctive hyperbaric oxygen therapy. *Am J Emerg Med.* 2013;31:756.e3-4.
 59. Doyle DJ. Blood transfusions and the Jehovah's Witness patient. *Am J Ther.* 2002;9:417-424.
 60. Scharman CD, Burger D, Shatzel JJ, et al. Treatment of individuals who cannot receive blood products for religious or other reasons. *Am J Hematol.* 2017;92:1370-1381.
 61. Vincent JL. Transfusion in the exsanguinating Jehovah's Witness patient—the attitude of intensive-care doctors. *Eur J Anaesthesiol.* 1991;8:297-300.
 62. Woolley S. Children of Jehovah's Witnesses and adolescent Jehovah's Witnesses: what are their rights? *Arch Dis Child.* 2005;90:715-719.

IMAGES IN EMERGENCY MEDICINE

(continued from p. 19)

DIAGNOSIS:

Type A aortic dissection. The patient received emergency aortic arch graft reconstruction resulting in complete recovery, and the culprit was thought to be previously undiagnosed hypertension. Painless dissection occurs in 5% to 15% of cases,^{1,2} and approximately half display exclusively neurological symptoms.³ Dissection very rarely presents solely as seizure, which is attributed to cerebral malperfusion.^{4,5}

Author affiliations: From the Department of Emergency Medicine, Far Eastern Memorial Hospital, New Taipei City, Taiwan (C-J Chang, Sun); the Department of Neurology, Chang Gung Memorial Hospital-Linkou Medical Center, Taoyuan City, Taiwan (B-L Chang); the College of Medicine, Chang Gung University, Taoyuan City, Taiwan (B-L Chang); and the Institute of Emergency and Critical care Medicine, National Yang-Ming University, Taipei, Taiwan (Sun).

Chih-Jung Chang and Bao-Luen Chang contributed equally to this work.

REFERENCES

1. Hagan PG, Nienaber CA, Isselbacher EM, et al. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. *JAMA.* 2000;283:897-903.
2. Imamura H, Sekiguchi Y, Iwashita T, et al. Painless acute aortic dissection. - Diagnostic, prognostic and clinical implications. *Circ J.* 2011;75:59-66.
3. Subhi J, Al'Aref LG, Devereux R, et al. A contemporary review of acute aortic dissection. *Emerg Med (Los Angel).* 2015;5:1-10.
4. Eikelboom R, Katz N. Acute aortic dissection presenting as status epilepticus. *CMAJ.* 2020;192:E283-E285.
5. Finsterer J, Frank M, Keller H, et al. Seizure as initial manifestation of aortic dissection type A. *West J Emerg Med.* 2010;11:510-511.