SABM®

SOCIETY FOR THE ADVANCEMENT
OF PATIENT BLOOD MANAGEMENT

August 2023

NEWSLETTER

Letter from the President

Welcome to the SABM Summer Newsletter!

Let me share a quick story and then some comments: Recently, I was at a get-together on Mother's Day where four of us ladies, two of us older (bet you can guess who *one* was!) and two were in their late teens to 20s. The host and hostess were kindly taking drink requests and the one young lady asked for a cup of ice. The host asked if she would like a soft drink, iced tea, or something with this. She stated she would not as she prefers to chew the ice. So, I imagine you know that my antennae went straight up and I asked her about this. She commented that she chews on ice throughout the day and has for many months. I mentioned to her that this might be an indicator of iron deficiency. She, along with the rest of the ladies were somewhat dumbfounded, having never heard this. I recommended that she make an appointment with her primary caregiver to check her hemoglobin and iron studies. She texted the following week to say she, indeed, was iron deficient and mildly anemic. They had started her on oral iron. Oh, how I like a success story!

I share this, for had this been someone I met 10-11 years ago before my complete immersion into the world of PBM, I would not have recognized this as a sign of iron deficiency. The first time I heard pagophagia was indicative of this was at a my first SABM meeting! I would have never thought to ask more questions or recommend to her that she be seen. This encounter shows the truth in the statistic that 1 of 4 people is anemic. She was the one of the four of us ladies together that day. How we live and learn…

With that story in mind, I want each of you to think about SABM and how this society brings so much to us all. We have a common passion for PBM as the standard of care. We learn together and share our common experiences as we push ourselves to remain THE tour de force for PBM education, resources and advocacy. I can assure you 2023 has seen no shortage of activity over these past 5-6 months. Let me recap just some of these. As always, SABM stands out!

We celebrated our first World Anemia Awareness Day, February 13th and the visits to the associated website have attracted a flurry of contacts and conversation. The friends we have at Human Touch Media Foundation kindly support SABM and put their heart and soul into working with us for the excellent content and resources. The Foundation has offered special pricing to our membership for the magnificent book Blood Works: An Owner's Guide. If you do not have your copy, it is a MUST! (www.bloodworks.com) This book provides healthcare providers, and most importantly, patients with the information they need to maintain and sustain their blood health.

Many SABM members have been busy with research and article submissions. We anxiously await the publications of the International Consensus Conference on Anemia Management in Surgical Patients (ICCAMS), the Return of Investment of Preoperative Anemia Management Programs in Cardiac Surgery, the manuscript Defining and Framing the Concept of Blood Health, and Patient Blood Management as an Emerging Concept in Quality: The Role of Nurses. Such scholarly activity is vital to our mission.

The SABM Resource Development Work Group is engaged with the American Nurses Association (ANA) to develop a PBM certification. This has been a longstanding goal for the RDWG and will align with the global definition and the SABM Standards. The timing couldn't be better, the need more so.

The votes are in and we have the 2024 Board of Directors members and officers who will begin their terms after the Annual Meeting. Welcome to them and I thank them for their willingness to serve. They bring so much talent to the table. The names of at-large members are Tiffany, Peter, Jacob, Susan, Sarah, Christine. Matt is Secretary, Gagan Treasurer.

The Certificate Course team will be "live" at the Annual Meeting featuring refreshed timely topics. This will become the basis of the updated on-line course beginning in 2024. Encourage new members to attend and if you wish for a refresher, this is a golden opportunity to be a part of this.

The Industry Council is garnering new members, engaging its original members, planning projects with us and securing support for the Annual Meeting and beyond. This Council has been a mainstay for us over the years.

Pursuant to the 2023 Annual Meeting, please join us in lovely Nashville, TN., October 4-7. The theme is PBM and Blood Health: They Top the Charts. A perfect theme for Music City and for all of us steeped in PBM. Here is the link to register, view the program and check out the exhibitors: Society for the Advancement of Blood Management (memberclicks.net). Let's enjoy this in-person meeting where we can put our heads and hearts together on our journey to expand PBM around the globe. Bring a friend, bring a co-worker! The experience they will have will be like no other, I can guarantee.

As for me, in this role as your SABM President, it is an honor and a true joy to serve. My thanks go out to each and every one of you for your personal service and support. I shall persist in my efforts to represent you and society to the level which is expected and much deserved. Looking back over my years with PBM, my focus, practice and tenure with SABM, I am reminded of the immense value of this society. I have learned so much from you, my SABM colleagues. This organization continues to enrich me. I hope it does for you as well.

Enjoy the summer newsletter. It is packed with a wealth of information. We move forward, never back. We soldier on. I look forward to seeing you in the Fall.

My best,

Carolyn Burns, MD

SABM NEWSLETTER
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Please consider making a donation to SABM. Your donations will help us to improve the lives of people throughout the world through Patient Blood Management.

SABM 2023 Newsletter Publication

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ANESTHESIA & ANALGESIA®

Consider submitting your future manuscripts in PBM for peer review and publication in this new section. The success of this endeavor will depend on the provision of material to make it lively and attractive to our colleagues and other professionals in the field.

Members Invited to Submit Papers CLICK HERE

Looking for Newsletter Content

SABM members want to know:

- Do you have an interesting case study?
- News about your patient blood management program?
- News about a new program at your institution?
- Have an article about some of the latest technology?
- Submitted an article to a journal for publication?

Deadline for the 2023 Annual Meeting Edition issue is November 1.

Don't wait! Send your articles today to the Newsletter Editorial team at info@sabm.org

Call for Interesting Case Studies

Authors: Can be submitted by any discipline (MD's, RN's, technologists, perfusionists, students)

Description/Format/components:

- Patient history and diagnosis
- Problem statement
- Relevant laboratory results or tests
- Medical management
- Follow up
- Brief discussion of the disease/problem/condition with up-to-date literature
- Provide 3-4 multiple choice questions
- Answers to questions to be provided on SABM website 2-3 weeks after publication
- Tables/Figures/images are welcome
- 5-10 annotated references

Call for Member Accomplishments

If you have been given an award, received recognition, or have been recently published, we would like to publish it in the next issue of the SABM newsletter.

Please send an e-mail with the details to info@sabm.org. Be sure to include your full name and details regarding the award, the recognition you received, or the publication citation.

Call for Book Reviewers!

The newsletter editorial team is looking for members to review books. You can choose to review a book that you already have, or volunteer to review a book of SABM's choice. If you have a book that you would like to submit a review for, or to be considered as a book reviewer, you can send an email to info@sabm.org with your request for consideration.

SABM 2023 Annual Meeting
Gaylord Opryland
Nashville, TN
October 4 – 7, 2023

Conference Theme: Patient Blood Management and Blood Health: They Top the Charts!

We are excited to invite you to join our SABM Annual Meeting this coming October 2023 in Nashville, Tennessee, USA. The program will be rich with content that reinforces the clinical importance of Patient Blood Management (PBM), in line with the new Global Definition of PBM which emphasizes optimizing the care of our patients' own blood as a renewable and vital resource, with the goal of improving safety and outcomes. Presentations and content from global PBM experts will expand our comprehension of how PBM, an urgent international public health initiative, can be promoted and implemented, with critical social, economic, and clinical implications. By doing so, we can improve the lives of millions of people worldwide. Our target audience includes a range of multidisciplinary healthcare professionals, including but not limited to physicians, nurses, perfusionists, laboratorians, administrators, clinical quality and safety specialists, and patient advocates. There will be outstanding opportunities for collaboration, networking, and mentorship connections. Our meeting attendance reflects our diverse membership, and we warmly welcome you to join us.

Meeting The Challenge of Managing Severe Acute Anemia In A Low-Resource Setting

Introduction

Acute anemia is usually due to hemorrhage, but may also be hemolytic, and is classified as severe when the hemoglobin (Hb) is < 8 g/dL (or < 7 g/dL in pregnancy).[1] Typical causes of severe acute anemia in a low-resource setting are obstetric hemorrhage, trauma, and upper and lower gastrointestinal hemorrhage.[2] This discussion will focus on severe acute anemia due to hemorrhage.

Managing severe hemorrhage in a low-resource setting poses some challenges, especially for transfusion-based therapies. Allogeneic blood is typically scarce and expensive, and 95% of donor blood is said to be unsafe in my setting.[3] The extensive monitoring and labs required for massive transfusion protocols is typically unavailable. Transfusion alternatives or bloodless medicine and surgery (BMS) techniques have been advocated as the solution in this situation.[4,5]

Resuscitation

In acute severe hemorrhage the immediate threat to the patient's life is hemodynamic instability rather than anemia. It is critical to replace lost volume promptly, and normal saline is usually readily available in a low-resource setting for that purpose. A recent study of patients in hemorrhagic shock concluded that there was no superiority of blood transfusion over normal saline in resuscitation.[6]

There is danger of fluid overload, hypernatremia, and acidosis in using large volumes of normal saline for resuscitation.[7] In cases of severe hemorrhage > 1000 mL or with associated hemodynamic instability, we usually switch to colloids after 1.5-2 L of normal saline. 4% polyvinylpyrrolidone (Isoplasma® 4% w/v; Bioflex, Ilorin, Nigeria) is readily available in my setting, relatively cheap, and effective. We maintain the patient's blood pressure at the lower end of normal to minimize further blood loss.

Pulse oximetry is required in severe acute anemia and is usually available. Oxygen therapy 3-5 L/minute may be required to optimize tissue oxygenation. Maintaining SpO2 at > 95% through transfusion alternatives is more practical and scientific than blood transfusion which has been found to cause hypoxia due to storage lesions and increase in viscosity.[8]

Hemostasis

Efforts at hemostasis should go alongside resuscitation, otherwise we would be 'pouring water into a sieve.' Tranexamic acid (TXA) is usually readily available, and we administer 500 mg IV slow bolus, and another 500 mg in the IV infusion, which may be repeated after 1 hour to a maximum of 3 g in 24 hours. IM Vitamin K3 25 mg (or K1 10 mg in adults only) in addition to TXA is effective in hemostasis, and may be repeated daily for 2-3 days.[9]

Practical physical maneuvers are applied as appropriate (e.g. direct pressure, packing, pressure bandaging), as well as topical hemostats. Surgery or endoscopy may be required for definitive hemostasis and should be carried out as soon as the patient is adequately resuscitated. Principles of bloodless surgery are observed to minimize blood loss.[10]

Raising the hematocrit

Efforts at raising the hematocrit should be started as soon as possible when the patient is hemodynamically stable. Intravenous iron dextran is readily available and cheap. Iron sucrose is also available but much more expensive and less common.

Ganzoni formula may be employed to determine the dosage (total iron dose in mg = [body weight in kg × (target Hb-actual Hb)] × 2.4 + iron stores). A modified version may also be used in adults, total iron dose in mg = [target Hb-actual Hb] × 200 + 500. We use HemoCue® for point-of-care determination of Hb.

We administer 250 mg of iron dextran in 300 mL of normal saline daily until the total dose is completed. We run the infusion at 20 drops/minute for 10 minutes as test dose, and if there is no reaction, we increase it to 30-40 drops per minute. If there is a reaction we stop the infusion, administer normal saline, IV promethazine 25 mg, IV hydrocortisone 100 mg, and oxygen therapy if necessary. We may successfully resume IV iron the following day by premedicating the patient who reacted with IV hydrocortisone 100 mg 10-15 minutes before IV iron infusion.

We administer intravenous vitamin C 500 mg, and vitamin B Complex 2 ml with each dose of IV iron. We also administer folic acid 5 mg daily, multivitamins with vitamin B12 and high protein diet when the patient can take food by mouth, or IV amino acids (e.g. Astymin®), and at least 3 L of fluids daily for an adult.

Erythropoietin is available but somewhat expensive in our setting. We administer 100-150 IU/kg SC on alternate days for 1-2 weeks in severe acute anemia, especially when Hb is < 7 g/dL.

Tolerance of anemia

To support the patient's tolerance of anemia, we limit the patient's movement for the first few days (balancing any risk of VTE), give adequate analgesia, eradicate any infections and febrile illnesses, and institute/continue other measures needed to optimize tissue oxygenation. We monitor the patient's serum electolytes, avoid hypernatremia, and counter acidosis with sodium bicarbonate if necessary.[7] We also limit phlebotomies so as not to aggravate the anemia.

Conclusion

Stabilizing the patient's hemodynamic status in severe acute anemia due to hemorrhage is paramount initially, alongside stopping the hemorrhage. Crystalloids and colloids are simple, safer, cheaper, and as effective as blood transfusion[11] – if not more effective. The efficacy of TXA has been validated in multiple studies in various scenarios (except upper GI hemorrhage).[12] Intravenous iron is the rational and scientific method of raising the hematocrit in any setting.[13]

The pillars of BMS containing these techniques are (1) Optimizing the hematocrit, (2) Minimizing blood loss, (3) Optimizing tissue oxygenation, and (4) Supporting patient's tolerance of anemia. BMS techniques are associated with lower morbidity and mortality, and they successfully meet the challenge of managing severe acute anemia due to hemorrhage in a low-resource setting.[7,10,14] A multidisciplinary approach to BMS and following a protocol has yielded good results in my center, even in patients with extreme life-threatening acute anemia.

Contributor: Nathaniel Usoro, MD

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NATA scientific newsletter articles:

Bunn HF. **Oxygen delivery in the treatment of anemia.** *N Engl J Med* 2022;387:2362-2365.
PubMed: https://www.ncbi.nlm.nih.gov/pubmed/36546628
Summary
When hemoglobin is exposed to increasing oxygen pressure, the presence of 2,3-BPG lowers the fractional oxygen saturation, and the oxygen-binding curve is shifted to the right. A patient with anemia and a hemoglobin level of 7.5 g per deciliter has an oxygen-binding capacity that is half the normal value (i.e., 10 ml of oxygen per deciliter). If this patient had red cells with normal oxygen affinity, 20% of the oxygen, or approximately 2 ml, would be unloaded per deciliter of blood. However, because the patient's red cells have an elevated level of 2,3-BPG, and thus a lower affinity for oxygen, about 3 ml is released, allowing partial compensation for the deficit in the red-cell mass.

Hawkins T, *et al.* Centre for Perioperative Care anaemia guideline: implications for anaesthesia. *Br J Anaesth* 2022; Dec 19 [Online ahead of print].
PubMed: https://www.ncbi.nlm.nih.gov/pubmed/36593165
Summary
The Centre for Perioperative Care (CPOC) has published in September 2022 guidance addressing perioperative anaemia. This editorial addresses the definition of anaemia for women and management of borderline anaemia in women. Wealso address implications of the CPOC guidance for anaesthetists and the future direction of anaemia research and management. Novel oral iron-Sucrosomialsup® iron (Alesco S.r.l., Pisa, Italy) is an exciting development that could change the landscape of anaemia treatment. It is a new-generation oral iron that avoids the normal ferroportin absorption pathway.[26] It can be tolerated at high doses, and its absorption is unaffected by hepcidin, a hormone up-regulated by inflammatory processes that normally reduces iron absorption.

Call to Action…

Iron deficiency anemia can cause heath complications, debilitating fatigue, weakness, and reduced quality of life. IV iron therapy offers a swift and effective solution, rapidly

replenishing iron stores. This can enhance patient outcomes, accelerating their recovery and reducing the need for blood transfusions. SABM has published a statement as a call to action for healthcare professionals to utilize this superior treatment and to address the need for reimbursement of IV iron therapy to third party payers. Click the link below for more information.

SABM COMMENTARY RE: IV Iron preparations and reimbursement

Managing Blood Shortages with Patient Blood Management

As transfusion medicine professionals, we are all faced with blood shortages that occur seasonally as well as those that occur during times of disasters. Seasonal shortages are relatively predictable, but disasters can strike at any time and are unpredictable. While the U.S. blood supply has been robust for many decades, the sustainability of the current system is at risk because of changes in blood use and in health care delivery.[1,2] In addition, donor collections are declining with a narrowing gap between distributed and transfused red blood cells (RBC's) and because they have become more reliant on older donors (≥ 65 years).[3] This makes patient blood management (PBM) increasingly important and relevant.

Disasters come in many varieties and may be global (e.g., the COVID-19 pandemic), regional (e.g., hurricanes), local to a specific area (e.g., a train derailment) or limited to a health care facility (e.g., building fire or flood). Disasters may also have advanced warning (e.g., a storm) or hit without any warning (e.g., a mass shooting or terrorist action). Regardless of the nature of the disaster, preparation is key to crisis management and getting through the resulting blood shortages that may occur. Blood shortages may be classified as mild (i.e., when the blood supplier's inventory is 25% lower than expected), moderate (i.e., supply 50% lower than expected), or severe (i.e., supply ≥75% lower than expected).[4] Although no two disasters are exactly alike, there are some common basic preparations for the transfusion service that one can use immediately. These include actions such as reviewing and updating one's disaster plan, ensuring that all personnel and contacts are correct including those of the blood supplier, engaging the hospital's emergency management team, which typically conducts disaster drills involving all key departments, reviewing and updating the hospital transfusion guidelines, hiring a transfusion safety officer, and ensuring that the hospital computer-physician order entry with clinical decision support system is in place to guide transfusion practices. Developing a green, yellow, and red stepped approach to managing blood shortages is yet another strategy whereby progressive actions are taken based on degree of the blood shortage from none/mild to moderate and severe, respectively (Table).

During blood shortages, it may become important to address specific patient populations and/or clinical services in regard to blood utilization, particularly those patients who may require many or large volume transfusions for supportive care. Massive transfusion protocols (MTPs) for trauma support can be one source of large volume blood use with potential for product wastage when the MTP is not deactivated in a timely manner such that prepared blood products (i.e., thawed plasma and cryoprecipitate) expire on the shelf or at the site of the MTP, or when the MTP is over utilized/inappropriately utilized for non-trauma bleeding (i.e., minor gastrointestinal bleeding or hemorrhage related to disseminated intravascular coagulation [DIC]). In addition, because there are not validated scoring systems for predictors of MTP need, MTP termination decisions may be controversial.[5] One study, however, found higher mortality associated with older age (≥65 years), nadir pH <7.0, and peak lactate ≥10 mmol/L, suggesting futility in prolonging the MTP in those circumstances and offering one possible route to standardize decisions on when to discontinue a MTP.[6]

Orthotopic liver transplantation (OLT) can be another source of high perioperative blood product use due to anemia and hemostatic derangements that occur. Yet blood transfusions are associated with higher OLT complications, including hepatic artery thrombosis, early surgery re-intervention, and higher graft loss. One study found that intraoperative OLT transfusion was the largest driver of post-operative transfusions. Higher OLT transfusion rate was also associated with female gender and virus-associated cirrhosis while hepatocellular carcinoma was associated with fewer transfusions in OLT.[7]

Hematology-oncology patients also frequently require support with blood products, and they tend to use platelets

more often. During shortages, it may become necessary to split platelet apheresis units, a practice which has gained support, considering that the U.S. apheresis platelet dose minimum is greater than in Europe (3.0 vs. 2.0-2.5 x 10^{11} platelets/unit).[8,9] For some hematology-oncology patients, maintaining platelet counts above 50, 20, or even 10,000 /µL may be challenging given that they have become refractory to platelet transfusions through development of antibodies to HLA and/or human platelet antigens. Discussion with hematologists on appropriate platelet count levels, which may be at a level lower than targeted for a given patient, is warranted in these situations in light of an ongoing blood product shortage.

Table

Blood Inventory Alert Status	Response Action
Green	Normal to mild shortage of blood component inventory levels are able to meet the needs of routine clinical operations of hospital services without routine rationing. No action is indicated.
Yellow	Moderate shortage of any major blood component type are or may become inadequate to meet the needs of routine clinical operations of hospital services. Evaluate demand and supply; be prepared to escalate if the situation worsens.
	Communicate blood component inventory at least daily; inventory levels may be shared with executive leadership at the discretion of the transfusion medicine (TM) service medical director.
	Directors of high utilization services (i.e., surgery, trauma, transplant, hematology/oncology, outpatient transfusion, etc.) may be contacted at the discretion of the TM service medical director.
	Review the operating room schedule each day for case type and patient's ABO type. Review outpatient transfusion orders for excessive demand; avoid topping off patients.
	The TM service medical director may institute triaging of blood product requests to reduce excessive utilization.
	Encourage employees to donate blood; consider hosting an onsite blood drive.
	The TM service medical director must continue to evaluate the inventory status relative to ongoing need and move to condition red alert as indicated.
Red	Inventories of major blood components are inadequate to meet the needs of routine clinical operations of hospital services. Activate blood emergency procedures, including communication plan.
	Communicate blood component inventory levels and notify directors of high utilization services and executive leadership.
	Triage all orders for blood product requests.
	Do not issue blood to stock refrigerators external to the blood bank (e.g., trauma blood refrigerator).
	Release any crossmatched blood not transfused within 24 hours back to inventory unless authorized by the blood bank supervisor or TM service medical director to leave in crossmatch status.
	Advise cancellation of elective surgical procedures if the blood shortage is expected to be prolonged.

Adapted from reference 4 and author's (MTF) institutional blood inventory shortage plan.

Managing Blood Shortages with Patient Blood Management

Finally, some patients undergoing plasmapheresis may require large amounts of plasma each day for replacement. For example, a patient with thrombotic thrombocytopenic purpura (TTP) undergoing daily therapeutic plasma exchanges (TPE's) may require 3,000 mL (i.e., 10-12 units) or more per day of plasma, which may not be sustainable during a severe blood shortage, particularly if the patient is blood type AB. In these situations, strategies include using alternative plasma products, such as solvent-detergent plasma, replacing a portion of the of the plasma volume with 5% albumin solution, and using caplacizumab which has been reported to enhance recovery and reduce the number of TPE's needed for treatment of TTP.[10,11,12]

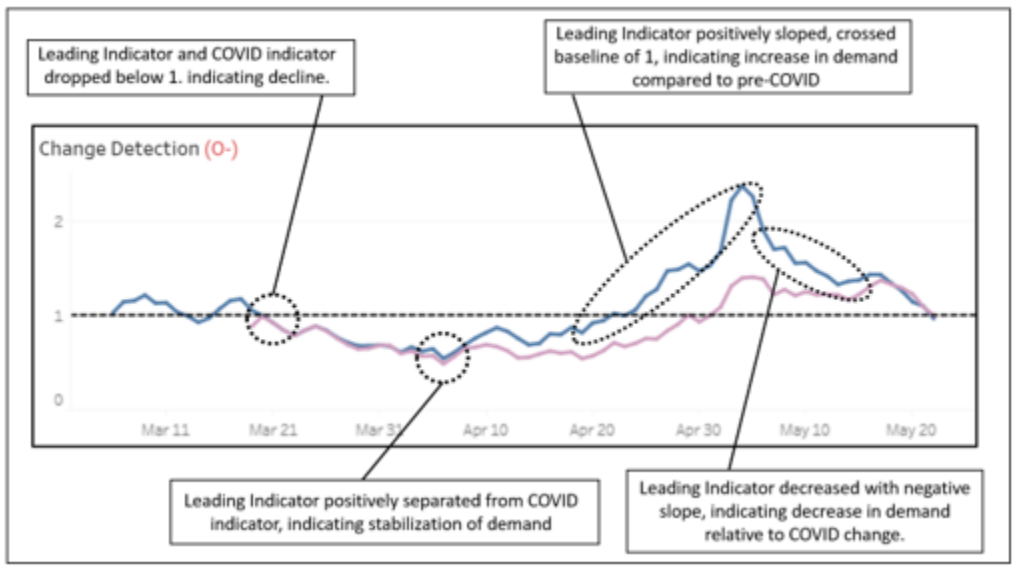
From the blood center's (BCs) perspective, maintaining an adequate inventory of O negative and rare RBCs, and platelets to meet the hospitals' needs becomes an even greater challenge particularly during the holidays and summer months when blood donors may not be engaged or available. In recent years, with the ability to mine large amounts of data, predictive modelling has helped to refine BC inventory management. A good example occurred at the beginning of the COVID-19 pandemic that resulted in a rapidly decreased blood demand when elective surgeries were cancelled. The BC had the challenge of having adequate collections and inventory to meet hospital's orders during changing demands. It used its data science methodologies to develop a demand model that consisted of a time series-forecasting algorithm to predict future values on previously observed data. A change comparison of demand to pre-COVID demand was calculated by comparing the same day demand to the previous four same day pre-COVID averages (purple line). A leading demand indictor was calculated by comparing the current demand to four previous same day demand averages (blue line). (Figure 1) The combination of two the metrics was beneficial and allowed for a sensitive understanding of the shifts in demand relative to decrease usage caused by COVID.

After an initial increase in inventory, data management (DM) allowed collections to be adjusted to bring inventory levels into equilibrium with predicted demand. This reduced inventory by 11,244 units in 21 days. (Figure 2) The BC nimbly adapted to rapidly changing donor conditions and transfusions though use of DM to ensure collections met orders while minimizing wastage. This also helped ensure an adequate blood supply when elective surgeries resumed.[13]

In conclusion, while it is known that disasters will strike, the nature, timing, and length of a disaster are unknown. Therefore, taking important preparatory measures to protect the blood supply today as well as being able to nimbly adapt during rapid changes in supply and demand are important first steps toward becoming prepared when that disaster hits.

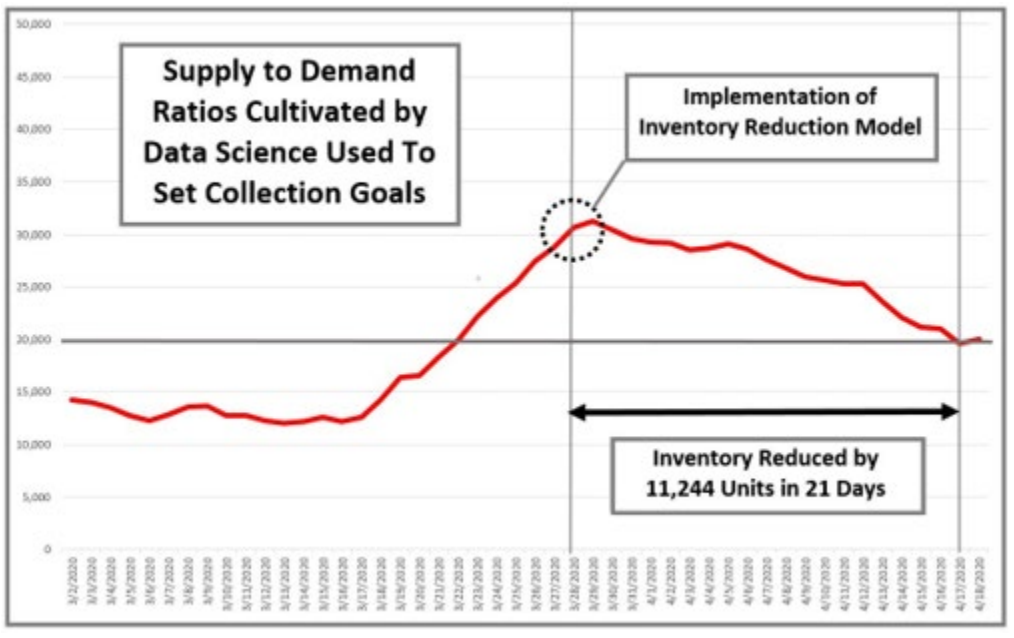
Contributors: Mark T. Friedman, DO; Richard R. Gammon, MD

Figure 1



Managing Blood Shortages with Patient Blood Management

Figure 2



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Artificial Oxygen Carriers

Anemia resulting from hemorrhage advancing to shock causes 1.9 million deaths each year worldwide.[1] Anemia is also responsible for poor outcomes after surgery and must be addressed pre/intra/and postoperatively.[2] In fact, hypoxia, hypotension, and anemia are the leading causes of postoperative mortality, which is the third leading cause of death in the US.[3] It is clear that while allogeneic blood transfusions carry significant risks, poorly treated anemia has similar or greater risk.[4]

Artificial oxygen carriers (AOC) have been studied for almost 100 years and the most successful hemoglobin-based oxygen carriers (HBOC) to date have been approved for humans in South Africa. In the US some HBOC are approved for compassionate use only. In the EU they are approved for perfusate in kidney transplant donor organs.[4]

HBOCs are purified hemoglobin of bovine or sea worm hemoglobin, repolymerized and provided in room

temperature stable bags for infusion not requiring crossmatching and universally compatible. All red cell coat antigens and pathogens are removed, including prions. They have undergone extensive testing in humans and two products (Hemopure and Hemarina) are clinically available with multiple products are in progress.[5]

Challenges to second generation HBOCs (Hemopure) are nitric oxide scavenging, and elevated systemic and pulmonary blood pressures; however, these effects are relatively short lived and treatable with standard therapy and no platelet dysfunction or coagulopathies have been documented.[6,7] Concerns of increased mortality and cardiac issues have been scientifically addressed.[8,9] Advanced generation HBOCs, like Hemarina, are benefiting from naturally occurring hemoglobins and due to the biomimicry, are likely to have improved benefits.[10]

Regulatory approval hurdles have plagued HBOCs from the first generation (HemAssist and Hemolink) and beyond, due to a misguided metanalysis combining first and second generation HBOCs into one broad brush stroke, rather than looking at each independently. HBOCs are formulated differently (Hb/P50/Oncotic pressure/Viscosity, etc.) and have been evaluated with clinical trials for varying medical indications.[8]

Oxyvita is a very large polymer HBOC with no nitric oxide scavenging, and Erythromer has been developed to reformulate a red blood cell with all its functions; both are in preclinical testing.[11,12]

The future of HBOCs will depend on collaboration with regulatory agencies to identify areas of medical unmet need, defining areas where HBOCs may fill gaps as AOCs, and combine with procoagulants to form multifunctional resuscitation fluids (MRF).[13,14]

Ultimately, it is possible that with regulatory agency support, large, multicenter studies will be initiated to evaluate the purported improved outcomes over standard of care, improving acute anemia with HBOCs, when blood is unavailable or not an option.[15] The salutary hemotinic effect of HBOCs provide usable iron and protein from breakdown of hemoglobin as HBOC's circulatory half-lives are around 24h. This benefit, when exogenous protein and iron are rarely administered in a hemorrhagic trauma or an acute severely anemic state, may be lifesaving.[6]

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An Analysis of Hospital Acquired Anemia: Is There a Better Approach to Diagnostic Medicine?

What is hospital acquired anemia and why is it important?

Hospital acquired anemia (HAA), defined as anemia that develops during the hospitalization of patients admitted with normal hemoglobin levels, has been recognized and discussed over the past half-century and remains a concern.[1] Diagnostic phlebotomy can result in significant wastage of blood, in fact, some studies have shown when blood is drawn for diagnostic purposes, and only 10% is used for laboratory tests. Additionally, when large volumes of phlebotomy are performed, iron-deficiency anemia may develop resulting in increased risk of poor outcomes. This is highlighted in audits of lab sampling in critically ill patients finding that 13 mL/patient/day was drawn for diagnostic purposes.[2] Another study reports that hemoglobin dropped by 0.7 g/dL per 100 mL of blood drawn which leads to increased likelihood of transfusion.[1]

What causes hospital acquired anemia?

Both anemia of chronic inflammation, iron deficiency anemia, and blood loss may play a role in HAA. The causes of are complex and multifactorial and include:

- Nutritional deficiencies, such as in iron or vitamin B12
- Changes in iron metabolism, including increased levels of hepcidin
- Impaired bone marrow RBC synthesis
- Impaired kidney function
- Impaired coagulation due to reduced synthetic ability of the liver or administration of anticoagulants
- Surgical bleeding /phlebotomy
- Fluid administration leading to hemodilution

Why is it important to recognize hospital acquired anemia?

HAA can have a significant impact on patient outcomes, thus it is important to understand causation and implement strategies to prevent it from developing or mitigate its effects. The WHO highlighted the significance of HAA in its recent Policy Brief “The Urgent Need to Implement Patient Blood Management,” noting the high prevalence of HAA, between 35% and 75% of hospitalized patients and up to 100% patients admitted to the ICU for more than 7 days.[3] The WHO also notes the lasting effects of HAA, with roughly half of patients discharged with anemia remaining so up to one-year post-discharge.[3] Patients with HAA may require more transfusions, and studies have shown negative findings associated with increased transfusion needs, including increased length of hospital stay, increased time spent in the ICU and increased mortality.[1] HAA is also associated with all-cause mortality, regardless of transfusion requirements.[1] Cost of medical care can also increase in the presence of HAA.[4] While it’s important to recognize the correlation between HAA and worse patient outcomes, it is unclear if HAA actually causes such outcomes, or if it merely correlates with them. It is possible that patients with more severe disease require more frequent blood draws.

What can be done to prevent hospital acquired anemia?

It is important to recognize which patients may be most at risk of developing HAA, including those with multiple organ failure, sepsis and extended ICU admissions. While many studies examining HAA have focused on patients in the ICU, a study which examined internal medicine patients found that 20.9% of patients developed HAA, with a median reduction in hemoglobin of 0.63 g/dl and a maximum reduction of 2.3 g/dL.[4] Thus all services should be aware of and involved in mitigating HAA.

One strategy to address HAA is to limit the volume of blood drawn for diagnostic purposes. Implementing smaller tubes, including pediatric tubes, for blood draws may be considered. Using pediatric tubes could reduce the amount of blood drawn by 50%. One study found that switching to smaller tubes in the ICU led to a reduction in transfusion of red blood cells and an increase in hemoglobin level at discharge.[5] Another study even found a significant decrease in mortality when small-volume tubes were used in place of adult sized tubes ($p= 0.04$).[6]

Reducing the frequency of blood draws without compromising care is the main objective. In order to accomplish this each lab draw should be necessary, provide useful clinical information, ensuring that redundant tests are not performed, and utilizing shared samples among different laboratories. Decision support imbedded in the electronic medical record is an important tool and should make placing standing blood draw orders more difficult rather than a default. Providing clinicians with education and feedback on their blood draw practices holds providers accountable and raises awareness of HAA. Involving all stakeholders such as clinicians, hematology, the transfusion medicine service and the laboratory service leads to best practice and buy in of patient blood management initiatives.

Overall Message:

HAA is a complex phenomenon with multiple contributing factors and thus addressing it may require various strategies and a multidisciplinary approach.

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Anemia Optimization Initiatives at the University of Rochester Medical Center

Anemia is a common diagnosis impacting over 30% of preoperative patients that are planning to undergo elective procedures and is often undiagnosed.[1] Untreated perioperative anemia is associated with increased morbidity, mortality, length of stay, and admission to intensive care units following elective high blood loss surgery.[2] Perioperative management and treatment of anemia in the weeks preceding an elective high blood loss surgery can reduce poor patient outcomes.

It is well established in the literature that perioperative anemia is associated with increased complications in cardiac surgical patients. To investigate the potential for optimization of preexisting anemia in perioperative cardiac surgical patients, the Center for Perioperative Medicine (CPM) – a part of the Department of Anesthesiology and Perioperative Medicine through the University of Rochester Medical Center (URMC) paired with a multidisciplinary team that included the Patent Blood Management team, cardiac surgery, and hematology on a pilot preoperative anemia optimization initiative in 2016. Patients were screened for anemia during a patient's preoperative cardiovascular visit and a baseline point of care hemoglobin level was obtained. If their hemoglobin level was <13g/dL for males and <12g/dL for females, they were referred to CPM for optimization and additional anemia blood work was obtained to assess the etiology of the anemia. If a patient was found to be iron deficient, they were treated with either intravenous (IV) iron +/- folate or oral iron. The study showed a higher day-of-surgery hemoglobin level, lower utilization of red blood cell (RBC) transfusions, fewer days in the intensive care unit (ICU), lower overall complication rates, and a significant cost savings. This anemia initiative success resulted in expansion of this project to all surgeries with a high blood loss potential.

The current process involves an anemia optimization consultation with the CPM clinic, focused questions are asked, a point of care hemoglobin level is obtained, an anemia laboratory panel is obtained if their hemoglobin level is <12g/dl, and when the laboratory data is resulted, it is reviewed by an Advanced Practice Provider (APP). Using an algorithm created during the preoperative cardiovascular anemia study, a treatment or referral plan is established. If the patient has iron deficiency anemia, IV iron is ordered for two doses to be administered about a week apart prior to surgery. In cases where IV iron is not possible or there is insufficient time for two doses the patient may receive only one infusion or oral iron instead. The anemia and plan for treatment is communicated to the PCP and surgeon. Communicating with surgeons is key as some surgeries may be delayed to complete therapy if the risk of unoptimized anemia is greater than the risk of a surgical delay. Nutritional deficiency, chronic kidney disease, or unknown cause of the patients' anemia is referred back to the patients Primary Care Provider (PCP) to investigate the underlying etiology of the anemia and for further management and treatment.

In an effort to expand the benefit of the anemia optimization initiative, in early 2022 through the CPM clinic, I completed an evidence-based practice change project for a Doctoral candidate for nursing practice degree that was aimed to educate registered nurses in a perioperative clinic about anemia and improve earlier recognition of patients likely to benefit from anemia optimization. The goal was to educate them about anemia's diagnosis and treatments, identifying high blood loss surgeries, the use of the maximum surgical blood order schedule (MSBOS), the use of the electronic medical record (EMR) eRecord spreadsheets, and the EMR InBasket messaging program to notify a surgeon pre-operatively that their patient is anemic.

Pre- and post-educational surveys were conducted based on a PowerPoint presentation about these topics. Outcomes showed an increase in a nurse's knowledge for all the participants based on scores of these surveys. The nurses then spent an hour each week for the following six weeks reviewing a scheduled surgeries spreadsheet to identify anemic patients based on their last hemoglobin level for all surgeries with more than minimal blood loss surgery based on the MSBOS. A communication letter through an InBasket

message was then generated notifying the surgeon(s) that their patient was anemic and would benefit from an anemia optimization consultation through the CPM clinic. The surgeon(s) was responsible for ordering the consult. There was a total of 52 patients identified as being anemic and 25 of those patients were referred by their surgeon for an anemia optimization consult. This greatly improved the number of patients that were able to be optimized prior to surgery.

Our most recent expansion of the CPM anemia optimization initiative is to optimize patients unwilling or unable to receive a blood transfusion. For those patients that request a blood-less surgery, the Patient Blood Management (PBM) program nurse coordinator or director is notified to educate and assist patients to fill out the Supplemental Consent Form for Blood fractions used During Bloodless Surgery and the Health Care Proxy for No Blood. Patients in the Jehovah's Witness community will be given the contact information for a local minister with the Hospital Liaison Committee to educate patients and assist completing these forms. This initiative allows patients an opportunity to clearly express their desires related to blood management, have a detailed risk benefit conversation with a perioperative provider and blood management specialist, and have all the necessary information to make informed decisions related to their care.

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Anemia Management in Patients who Require Bloodless Care

Some patients cannot receive blood due to a religious or personal declination, an unusual blood type, or alloimmunization for whom components are unavailable or in circumstances of inadequate supply. We recognized that providers were contacting our Anemia Consultative service or our Blood Bank Triage for guidance on managing patients with profound anemia who cannot receive transfusions. As part of our commitment to providing care to patients who cannot receive blood, our Patient Blood Management (PBM) team, including Pathology and Nursing, collaborated with Pharmacy and Hematology Oncology to create a guideline for anemia management in patients who require bloodless care. The aim is to provide direction to staff who may need to become more familiar with the management of profound anemia in this patient population.

General Considerations

- Consult Patient Blood Management (PBM) and Hematology (as clinically appropriate) in Epic when it is recognized that a patient will require bloodless care
    - This includes those who chose to decline for religious or personal reasons and those who cannot receive due to medical restrictions
- Complete consent to decline transfusion form. If a patient declines transfusion, add it to the problem list
- Ask the patient if their care can be discussed with a specific local elder if appropriate.
- Seek assistance from PBM staff or Pathologist on call if patient is critically ill
- Goal of treatment is hemoglobin > 7 g/dL, continue treatment until goal hemoglobin is achieved
- DVT Prophylaxis
    - If not otherwise contraindicated, patients receiving epoetin alfa should receive DVT prophylaxis
    - Consider risk vs benefit of pharmacologic vs non-pharmacologic DVT prophylaxis
    - Avoid use of pharmacologic DVT prophylaxis for active bleeding
- In patients with Hgb <10g/dL and active bleeding
    - Consider pharmacologic and supportive care measures below
        - Recommend against erythropoiesis stimulating agent (ESA) in lieu of appropriate additional indication due to thromboembolic risks

Anemia Management in Patients who Require Bloodless Care

Table 1: Bloodless Medicine Protocol for Management of Severe Anemia
Adapted from Shander, 2018 and modified by Geisinger Patient Blood Management Committee

Baseline Hgb	Pharmacologic Management
>7 g/dL	Epoetin alfa (Retacrit)* • 40,000 units SUBQ once per week Iron sucrose (Venofer)** • 200 mg IV daily for 5 days Folic acid (folate) • 1 mg IVPB once daily for duration of admission Vitamin B12 (cyanocobalamin) • 1,000 mcg IM once GI stress ulcer prophylaxis+
5-7 g/dL	Epoetin alfa (Retacrit)* • 20,000 units SUBQ once daily x 5 days • If weekly corrected reticulocyte count <6% then re-dose epoetin alfa 40,000 units SUBQ once daily x 4 days Iron sucrose (Venofer)** • 200 mg IV daily for 5 days Folic acid (folate) • 1 mg IVPB once daily for duration of admission Vitamin B12 (cyanocobalamin) • 1,000 mcg IM once GI stress ulcer prophylaxis+
<5 g/dL	Epoetin alfa (Retacrit)* • 20,000 units SUBQ Q12h x 5 days week • If weekly corrected reticulocyte count <6% then re-dose epoetin alfa 40,000units IV Q12h x 5 days Iron sucrose (Venofer)** • 200 mg IV daily for 5 days Folic acid (folate) • 1 mg IVPB once daily for duration of admission Vitamin B12 (cyanocobalamin) • 1,000 mcg IM once GI stress ulcer prophylaxis+

SUBQ, subcutaneous; IV, Intravenous; IVPB, intravenous piggyback; DVT, deep-vein thrombosis

*Epoetin alfa: use IV only if SUBQ unsuitable (e.g., edema)

**Iron sucrose (Venofer): (no test dose required); or other appropriate iron preparations (e.g., low molecular weight iron dextran)

+ Proton pump inhibitor or H-2 blocker (IV or PO)

Supportive Care
- Supplemental O2
- Optimize nutritional support
- Proper infection management
- Minimize laboratory testing
- Optimize hemodynamics
- DVT prophylaxis (in absence of contraindication)

Additional considerations

Monitor for tissue dysoxia
- Daily EKG
- Baseline evaluation of mental status and frequent re-evaluation
- Periodic lactate determination

Minimize oxygen utilization
- Strict bed rest
- Supplemental O2

Reduce intrapulmonary shunt
- Head of bed greater than 30 degrees
- ”Standing order” bronchodilator therapy
- Chest PT and incentive spirometry (if not ventilated and patient able to perform)

If signs of end organ dysoxia
- Supplemental oxygen to ensure 100% oxygen saturation
- Analgesics or sedatives to reduce oxygen consumption

Anemia Management in Patients who Require Bloodless Care

Keep euthermic, active cooling if elevated temperature (fever increases consumption and reduces SaO2) utilize order-set EM Therapeutic Hypothermia / ARCTIC Alert [10196]

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Other resources

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