



SABM[®]
SOCIETY FOR THE ADVANCEMENT
OF PATIENT BLOOD MANAGEMENT

April 2023

NEWSLETTER

Letter from the President



We are squarely into 2023 and what a flurry of activity we have already witnessed within SABM.

2022 closed out with an amazing face-to-face Annual Meeting in Vegas and a busy PBM Awareness Week with a bevy of educational events and campaigns shared among our members. The Annual

Meeting Planning Committee, with Co-Chairs Sarah Walbolt and MaryAnn Sromoski at the helm, are already securing 2023 topics, faculty and exhibitors. They are on fire! Save the date for Nashville, TN., my southern neighbor, October 4th-7th where PBM and Blood Health will Top the Charts. I encourage you to submit your topics, abstracts and research grant applications. There is so much talent and knowledge within our society. We want to showcase it all!

And speaking of Sarah and MaryAnn, if you haven't tuned in to their podcast Let's Talk PBM, you must. The ladies are truly putting PBM out there in an entirely new venue. Listen, learn, enjoy and share.

Our global partners are going gangbusters with PBM webinars and educational materials. Watch the Scoop, social media, and email blasts for links to many of these. The WHO PBM Steering Committee is diligently working to develop tools we can all use to push the Policy Brief, embedding PBM as the standard of care. As these become available, the SABM office will actively work to get them into your hands.

2023 has seen the inaugural World Anemia Awareness Day, February 13th. I hope your program celebrated with awareness campaigns and activities within your institution and your community. This was envisioned by SABM, the

Western Australia PBM Group, NATA and IFPBM with unbelievable educational input from Human Touch Media, the supporters of the soon-to-be-published book, Blood Works: An Owner's Guide (another item not to miss; a true must-read).

SABM governance will see 2023 as a huge year for leadership. Opportunities for service await. Join a committee or task force and bring your ideas and talents to the table. A call for nominations for the Board of Directors will be going out soon. Nominate a colleague or throw your own hat into the ring. As a dear colleague of mine always reminds me: *Leadership is everything and leadership begins with you.* I, personally, wish nothing more than to see new bright minds becoming the leaders for our future.

Of great importance is our Society's recently finalized Strategic Plan. With the support and guidance of the Talley Management team we solidified our goals and established our pillars. I have shared them here with you all as a PowerPoint slide. Note the new vision statement which includes our concept of Blood Health as aligned with PBM. I hope each and every one of you will review these pillars and incorporate them into what you do as SABM members, as well as within your daily practice of PBM.

The broader our message, the bigger the win for our patients. So, I encourage you to go forth and make 2023 *the* year of PBM *expansion*, no...explosion! Let us share in this collective vision, mission and pillars to engage with each other and leverage every resource we have to improve patient outcomes and optimize Blood Health.

It is such an honor to be a part of this organization, and as your President, I shall avail myself to help in any way possible to move together with SABM and its purpose. Thank you for what you do and how you serve. We soldier on!

Best,

Carolyn Burns, MD



**SABM NEWSLETTER
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ISSUE**

Donate to SABM

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.

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Featured Affiliates

Gold Level Corporate Affiliate Member



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Cover photo courtesy of
National Cancer Institute on Unsplash



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 Summer 2023 issue is June 1, 2023.

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 Breaking News

SABM Embraces and Supports Diversity Welcoming Applications for Corresponding Membership

SABM was established in 2001 and has more than 500 members worldwide. It has been the view of many, that SABM membership is limited to a selected sphere. However, SABM has been leading efforts in reaching out and empowering many individuals with PBM. The understanding of the global situation and limitations placed by economic challenges has moved SABM for years, to open up an opportunity for individuals from lower- and middle-income

countries (according to World bank data) to enroll as SABM members at a discounted rate.

SABM continues to invite individuals who qualify for this special rate, to apply to be a Corresponding Member of SABM. Corresponding membership allows access to all SABM membership benefits, however does not include the right to vote, serve on the Board of Directors, or hold office. For more information, please visit

<https://sabm.org/individual-memberships>.

SABM awaits to welcome and work along with you!

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.

Patient Blood Management Literature Updates

We are pleased to include excerpts from NATA's biweekly literature update on PBM, Haemostasis and Thrombosis.

Systematic review and meta-analysis of intravenous iron therapy for adults with non-anaemic iron deficiency: An abridged Cochrane review

PICO SUMMARY

Population

Adults with non-anaemic iron deficiency (21 randomised controlled trials, n= 3,514).

Intervention

Intravenous iron.

Comparison

Placebo.

Outcome

Intravenous iron compared with placebo resulted in significantly increased physical function measured by mean peak oxygen consumption (mean difference [MD] 1.77 mL/kg/min, 95% confidence interval (CI) 0.57 to 2.97). An overall improvement in fatigue was seen (standardized MD 0.30, 95% CI -0.52 to -0.09) but no overall difference in quality of life (MD 0.15, 95% CI -0.01 to 0.31). Biochemically, intravenous iron resulted in improved serum ferritin (MD 245.52 µg/L, 95% CI 152.1 to 338.9) and haemoglobin levels (MD 4.65 g/L, 95% CI 2.53 to 6.78). There was a higher risk of developing mild adverse events in the intravenous iron group compared with the placebo group (risk ratio 1.77, 95% CI 1.10 to 2.83); however, no differences were seen in serious adverse events (risk difference 0, 95% CI -0.01 to 0.01). The quality of evidence was rated 'low' and 'very low' for all outcome variables, except for fatigue, mainly due to most studies being judged as having a high risk of bias.

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Intravenous ferric derisomaltose in patients with heart failure and iron deficiency in the UK (IRONMAN): an investigator-initiated, prospective, randomised, open-label, blinded-endpoint trial.

PICO SUMMARY

Population

Patients with heart failure and iron deficiency enrolled in the IRONMAN trial in 70 UK hospitals (n= 1,137).

Intervention

Intravenous ferric derisomaltose (n= 569).

Comparison

Usual care (n= 568).

Outcome

Median follow-up was 2.7 years (IQR 1.8-3.6). 336 primary endpoints (22.4 per 100 patient-years) occurred in the ferric derisomaltose group and 411 (27.5 per 100 patient-years) occurred in the usual care group (rate ratio [RR] 0.82 [95% CI 0.66 to 1.02]). In the COVID-19 analysis, 210 primary endpoints (22.3 per 100 patient-years) occurred in the ferric derisomaltose group compared with 280 (29.3 per 100 patient-years) in the usual care group (RR 0.76 [95% CI 0.58 to 1.00]). No between-group differences in deaths or hospitalisations due to infections were observed. Fewer patients in the ferric derisomaltose group had cardiac serious adverse events (200 [36%]) than in the usual care group (243 [43%]; difference -7.00% [95% CI -12.69 to -1.32]).

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For more information go to: [Homepage - NATA ONLINE](#)

International PBM – Asia

The Asia-Pacific Society for Patient Blood Management (ASPBM) 2022 Virtual Annual Meeting—Connecting Great Minds and Hearts

ASPBM 2022 was held virtually on December 17, 2022, as there were still challenges with travel and due to a surge in COVID-19 cases. Despite it being virtual, this event in no way dampened the spirit of the faculty members or participants. The one-day event which spanned almost 8 hours, included some 30 faculty members, from 13 countries, and 7 organizations promoting PBM and bloodless medicine. Pre-registration for the event gathered more than 300 participants, while 180 tuned in live. The entire recorded program is now available to access for free, at the ASPBM website, www.aspbm.net.

Session 1, with the theme “Driving PBM Globally,” led the way which included PBM leaders from SABM, Australia and Korea, sharing great insights from different vantage points. The session revealed that the understanding of PBM and its implementation is progressive. It also highlighted the vision, tenacity, and dedication these and other PBM champions have - valuable qualities needed to initiate and sustain successful implementation of PBM/Bloodless Medicine and Surgery programs. Session 2 focused on “Fundamental Clinical Practice - the Foundation of Excellent Patient Care.” Experts and PBM leaders from SABM and ASPBM shared lessons which are building blocks of PBM. They showed that these principles are within reach of all and should be applied by all who are connected to patient care.

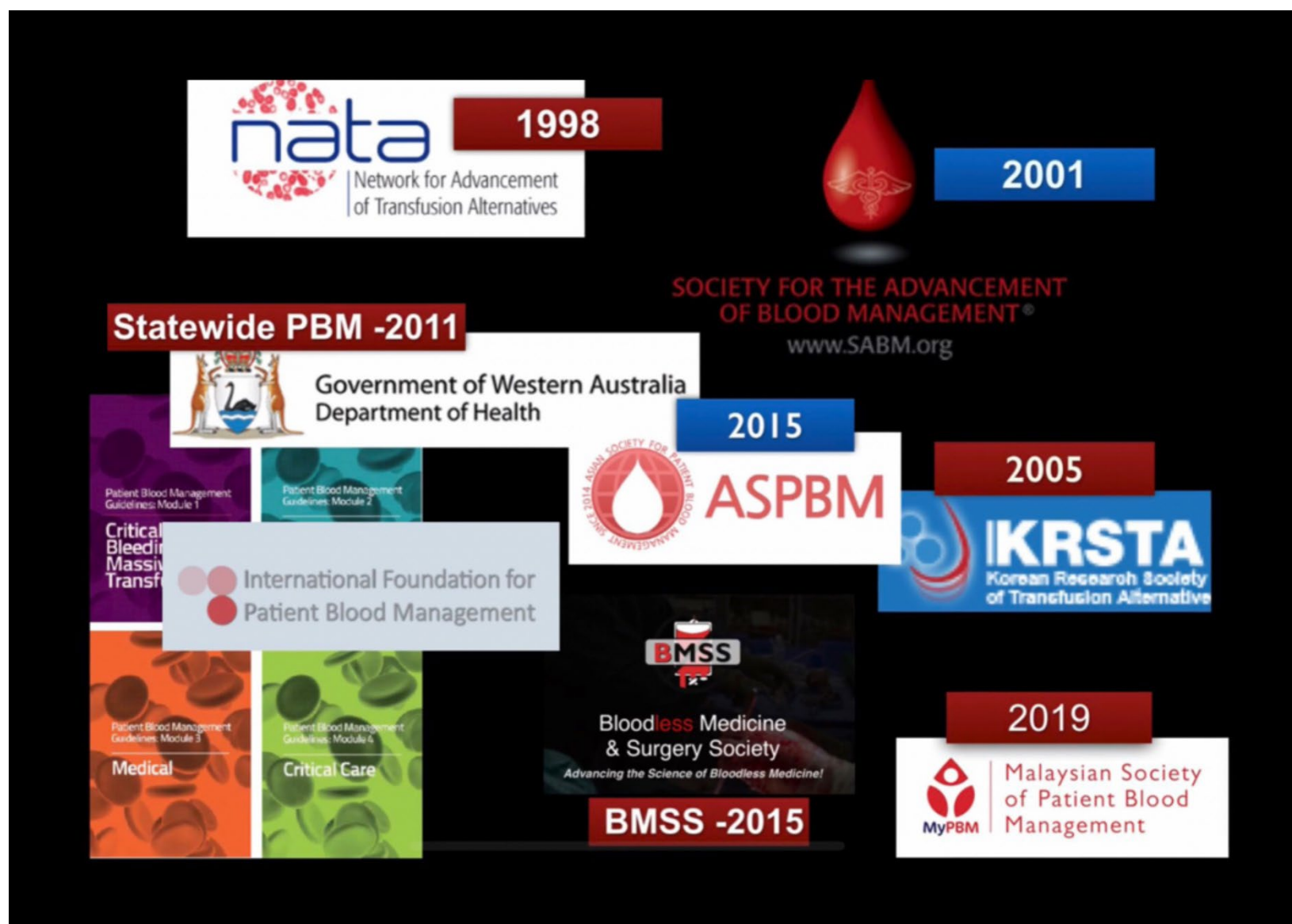
The afternoon session opened with Session 3, highlighting the details of formulas, equipment and teamwork. PBM

experts from Korea and Italy illustrated through evidence and their clinical practice, how this “winning combination” can be employed in the OR and ICU. Any doubts about the efficacy of these were nicely addressed in this session, and their role in the success of PBM practice were clearly shown. Session 4 targeted certain challenging populations or medical conditions, for example cancer surgery, pediatrics and trauma. It is remarkable to learn how these skilled consultants incorporated PBM strategies in such challenging circumstance and produced superior outcomes.

The day’s program closed with a panel discussion for Session 5, discussing the theme: “Fast Forwarding to the future- The Power of Education and Economics.” PBM leaders from more than 5 countries and varied PBM and bloodless medicine organizations presented a stimulating discussion on their unique background, challenges and strategies to move PBM forward. Valuable insights were shared and the need for identifying the stakeholders as well as targeting efforts to push PBM forward was reiterated.

In all, the ASPBM 2022 annual meeting was a whirlwind tour around the world of PBM and bloodless medicine, right from the comfort of one’s own home. It enabled participants to access crucial PBM education, while being convinced that PBM is beneficial, accessible and possible for all to learn and practice. As for faculty members, it was an opportunity to connect virtually, share ideas, mutually encourage and renew one’s motivation for the need to continue the good efforts for the same, superior purpose of promoting good health in all.

Contributor: Ananthi Krishnamoorthy, MD



There is a huge global gap in the awareness & need for PBM:

- Lack of knowledge and education.
- General complacency re: transfusion.
- Lack of willingness to change practice patterns and culture.

Challenge necessitates **change**.

- Lack of infrastructure to manage a complex healthcare initiative.



“Education is the most powerful weapon which you can use to change the world.”

Nelson Mandela



ORIGINAL ARTICLE

Effect of patient blood management system and feedback programme on appropriateness of transfusion: An experience of Asia's first Bloodless Medicine Center on a hospital basis

Hyeon Ju Shin¹ | Jong Hun Kim² | Yujin Park³ | Ki Hoon Ahn⁴ | Jae Seung Jung⁵ | Jong Hoon Park⁶ | Korea University Bloodless Medicine Center Scientific Committee


Transfusion Medicine. 2020;1-8.

Scientific Committee

- Bloodless center data
- National insurance big data
- AI center

Already published many of articles and planed

Year	1	2	3	4	5	6	7	8	9	10	11	12
2018	1532	1282	1332	1222	1316	1278	1180	1173	1106	1318	1296	1265
2019	1462	1115	1136	1091	1289	1391	1218	1331	1306	1343	1281	1148



- * ANH (Acute Normovolemic Hemodilutional autotransfusion)
- * Cell salvage (recovery)
- * Hypotensive anesthesia
- * Reduced tidal volume
- * Head-down positioning
- * Vascular control technique
 - Pringle occlusion
 - IVC half-occlusion
 - Liver hanging
- * Pharmacological agents
 - Tranexamic acid
 - Hemostatic matrix
 - TachoSil tissue sealing sheet
 - Surgical cotton
- * Liver preservation
 - Corticosteroid
 - (Prostaglandin E2)

Ethics of Patient Centered PBM – Questions for Clinicians



- What is the status of the patient's/person's blood?
- If there are specific abnormalities, how should they be managed?
- If allogeneic blood is being considered, is there no reasonable alternative therapy?

There are compelling scientific reasons to implement a ***nontransfusion default position*** when there is clinical uncertainty and questionable evidence of clinical efficacy for allogeneic blood transfusion due to known potential hazards

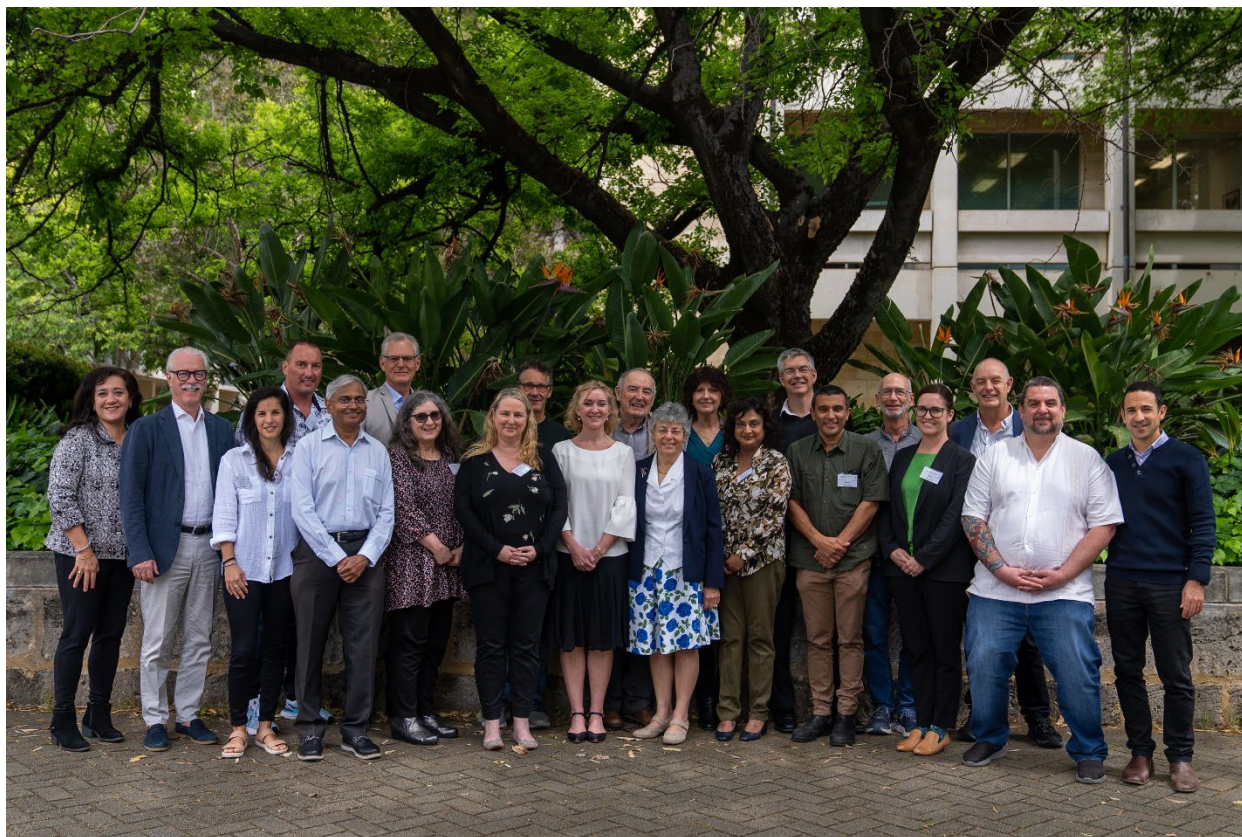


Photo courtesy University of Western Australia

Pictured above (left to right): Sherri Ozawa, MSN; Axel Hofmann, Dr rer medic; Laura Trentino, DCom; Nolan McDonnell, MBChB; Pradeep Jayasuriya, MBBS; Shannon Farmer, DHS; Julie Mcmorrow, BPharm; Claire McNally, MSN; Bernd Froessler, PhD; Bronwyn Pearce, PhD; James Isbister, MD; Wendy Erber, PhD; Kristen Farmer, Sunalene Devadason, PhD; Vernon Louw, PhD; James Savundra, MBBS; Irwin Gross, MD; Kylie Symons, BN; Jeff Hamdorf, PhD; Angel Augusto Pérez Calatayud, Kevin Trentino, PhD.

WHO expert working group meet in Western Australia for the implementation of Patient Blood Management

On the 31st October 2022, an international group of Patient Blood Management (PBM) experts convened in Western Australia for a week-long World Health Organisation (WHO) workshop to develop implementation guidance for PBM.¹

The workshop was organized in response to The WHO's call to action on the "The Urgent Need to Implement Patient Blood Management."² The purpose of the workshop was to commence work on a guide for the implementation of PBM which will serve as a framework for healthcare leaders worldwide.

Speaking about the importance of this implementation guide, Professor Axel Hofmann, chair of the steering committee said, "this work will assist all member states to implement PBM therefore representing another important step towards ensuring that it is adopted as the standard of care worldwide."

The experts invited to the initial workshop in Australia represented the healthcare systems of a wide variety of regions including Oceania, Africa, Latin America, North America, and Europe.

The location of the workshop reflects the important role Western Australia has played in implementing a comprehensive PBM program at a jurisdictional level. Western Australia is home to several Patient Blood Management experts across a wide variety of clinical and non-clinical disciplines. As a result of the PBM program, the Western Australian healthcare system experienced significant improvements in patient outcomes, reductions in blood use, and reductions in costs.³

A WHO Guidance on how to implement PBM can extend the benefits seen in Western Australia to other healthcare systems worldwide. Research indicates the potential to improve the health of millions of lives globally, while saving billions of healthcare dollars is enormous.⁴

Sherri Ozawa, an expert in PBM, who founded and directed the program at Englewood Health in New Jersey for more than 25 years, was part of the expert working group. "We should not forget that PBM represents a considerable population health issue," she said. The burden of anemia and iron deficiency is significant and currently has a profound effect on well-being, economic productivity, and maternal and fetal outcomes."

A key component of the guide will be the modules designed to assist healthcare leaders tailor Patient Blood Management implementation to their healthcare systems. Among other things these modules will cover guidance on who should be taking the lead in implementation, how to develop nation-specific PBM execution strategies, how to use a versatile PBM therapeutic toolbox to build national programs, and how PBM supports the concept of patient empowerment.

The working group will meet again in the first quarter of 2023 and the Implementation Guidance report is expected to be released in the second half of 2023.

Contributor: Kevin Trentino, PhD, MPH

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Anemia in Pregnancy



In pregnancy, the daily requirements of iron increases from 0.8 mg in the first trimester to over 7.5 mg near the end of gestation, despite the average Western diet only ranging from 1-5 mg daily. (Achebe & Gafter-Gvili, 2017) The depleted iron status of a woman is a well-known fact, and there are

several physiological insults before and throughout pregnancy which increases the iron demand including monthly menstruation, increased nutritional needs of a developing fetus, and blood loss related to delivery. Managing the iron status for a woman is an increasingly important thing to do, especially during pregnancy. However, guidelines are conflicting. The lack of standardization stems from the underrepresentation of women's health in research. Despite this, there have been several articles published that have shown a clinical benefit from both intravenous and oral iron supplementation, with little to no adverse outcomes. Implementation of these treatment protocols in practice is ideal.

However, many of the premier medical organizations give conflicting recommendations regarding the definition, screening and management of iron deficiency anemia in pregnancy. The United States Preventative Services Task Forces (USPSTF) notes that there is little to no supportive evidence or clinical research to support the screening or treatment of antepartum anemia ("Iron Deficiency Anemia in Pregnant Women", 2015). The Centers for Disease Control (CDC) "recommends universal iron supplementation to meet the iron requirements of pregnancy" ("Recommendations to Prevent and Control ...", 1998, para. 6) while recognizing the contradiction to the USPSTF recommendations. Similarly, the American College of Obstetricians and Gynecologists (ACOG) recommends that all pregnant women should be screened for anemia with a CBC and encourages further investigation into those with a hemoglobin less than 11 g/dL ("Anemia in Pregnancy", 2021). ACOG further supports low dosed oral iron supplementation in the first trimester and parenteral iron "for those who cannot tolerate or do not respond to oral iron or for those with severe iron deficiency later in pregnancy" and has also highlighted a "critical gap in evidence" in regards to the USPSTF contradictory recommendations ("Anemia in Pregnancy", 2021, p. 60). The lack of standardization of care represents a major limitation in properly treating iron deficiency anemia.

Irrespective of the beneficial evidence of IV iron use in pregnancy, still many clinicians are hesitant to prescribe intravenous iron. Caritis and Venkataramanan discussed the absence of fetal research in the obstetric population due to regulatory constraints in such a vulnerable class, disincentives to study this population, medico-legal risks, and limited financial gain to be of several reasons (2021). However, the safety and efficacy of both oral and intravenous iron treatments have flourished over the years, and treatment of anemia in pregnancy with intravenous iron is now a widely accepted clinical practice today.

Flores et al. describes an Australian Institution that devised a plan to create a multidisciplinary team to develop implementation strategies using the quality improvement methodology plan, study, do, act (PSDA) cycles (2017). Their goal was to optimize an anemic patient's hemoglobin prior to surgery with proper anemia management. By doing this, they were able to map antenatal care processes, identify knowledge gaps, and consult with providers on issues that needed to be addressed (Flores et al., 2017). As a result, they educated on ways to better identify and improve antepartum anemia practices by putting a primary focus on an increase in both ferritin testing and use of intravenous iron. This indicated that patients were both being screened and subsequently treated for iron deficiency anemia, making the connection that earlier identification of anemia typically leads to treatment. They also implemented educational handouts for patients on oral iron supplementation, and as a result noticed a reduction in anemia on admission from 12.2% falling down to a mere 3.6% and an increase in one red blood cell unit transfusions from 35.4% to 50%, also indicating a lesser need for blood products (Flores et al., 2017). This highlights a need for better education on both a patient and a provider level. Patients can benefit from more educational materials to help them in being successful with first line anemia treatments, and providers can also benefit from further education and awareness of the importance of screening for and treatment of iron deficiency anemia.

In conclusion, the topic of iron deficiency anemia disproportionately impacts the obstetric patient population, and lack of treatment can cause significant harms to both the mother and the fetus. With even just a surface overview of the literature, correcting anemia seems to be an obvious choice. Despite hesitancy to treat, the research is clear, and it does show that both intravenous and oral iron treatments are proven to be both safe and effective in this patient population. Application of these treatments can be approached in several different ways in order to improve upon both anemia management in an antepartum patient.

Anemia in Pregnancy

Ultimately institutions that dedicate themselves to redefining how they treat anemia in obstetric care will eventually become premier facilities.

Contributor: Ann Marie Gordon, PA-C, MLS (ASCP), MHA

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HAEMONETICS[®]

Anemia Across the Perioperative Period: a Three-Part Series

Pre-Op Anemia

The presence of preoperative anemia continues to affect a significant number of people worldwide. The total number of surgeries continues to increase as described by the WHO in 2017 that about 1 in 25 people will have a surgical procedure each year. Depending on other co-morbidities, the presence of preoperative anemia ranges from 10-60%. Nevertheless, anemia is still listed as a global health problem according to the WHO.

The concept of preoperative anemia is not new. In a JAMA article from 1927 discussing laboratory aids in abdominal surgeries, it was noted that “Blood counting is one of the oldest, simplest, and most reliable of the modern laboratory method in use today. Definite information can be obtained by complete blood count (CBC) test yet, this information is often ignored by most treating teams.”

In the early 2000s, a growing literature of the risks of poor surgical outcomes associated with the presence of preoperative anemia. Both mortality and morbidity were increased, usually in a dose dependent relationship with severity of preoperative anemia across many surgical subtypes. As evidence of poor outcomes mounted, the role of transfusions also was shown to add to surgical risk. Correction of just the hemoglobin number with blood transfusions was not the ideal management of a surgical patient.

As the concept of Patient Blood Management solidified, its emphasis on identification, treatment and management of anemia began to play a larger role in improving outcomes in surgical patients. As mentioned earlier, the presence of anemia in the surgical population is common and often not optimized. Iron deficiency is extremely prevalent either due to nutritional deficiencies, ongoing blood loss or inability of the patient’s iron metabolism to function appropriately due to other co-morbidities. Essential to preoperative optimization is identification and diagnosis of anemia and its underlying reasons in order to initiate prompt treatment. Often hepcidin, the peptide hormone which plays a crucial role in iron homeostasis, is elevated in the setting of chronic disease leading to poor GI uptake of oral iron and decrease release of iron stores causing a functional iron deficiency for erythropoiesis.

Recent literature by Guinn, et al shows the effectiveness of a bundled perioperative anemia program with improvement in anemia, reduction in transfusions along with trends towards reduce length of stay, ICU admission and 30-day readmission rates (though paper was not powered to detect these secondary outcomes). The use of IV iron in the perioperative setting is both an effective and efficient way to

treat many iron deficient patients who are need of an optimization in the near future (<6 weeks).

Patients with chronic medical conditions that can limit function of erythropoiesis, there is a role for short term use of erythropoietin stimulating agent to optimize the patient’s hemoglobin levels and bone marrow function. Discussion about the use of thrombosis prevention as hemoglobin levels rise should be discussed on a case-by-case situation.

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Postoperative Anemia – A Dark Horse in Anemia Management

Postoperative anemia is remarkably common after major surgery, although it receives far less attention than its preoperative counterpart. Common causes of postoperative anemia include surgical blood loss, exacerbation of pre-existing anemia, inflammation, and iatrogenic blood loss through phlebotomy practices.^{1,2} It's important to recognize that postoperative anemia is often multifactorial and is readily magnified in the presence of iatrogenic hemodilution (i.e., dilutional anemia that arises from intravenous fluid-driven plasma volume expansion, which causes a relative but not absolute reduction in hemoglobin concentrations). Given that many clinicians use the hemoglobin concentration as a primary driver of red blood cell (RBC) transfusion decisions, dilutional anemia may contribute substantially to overall transfusion exposure.³

Recent evidence suggests that postoperative anemia is not a benign bystander of the surgical encounter. In a recent observational study employing 2 large population-based health databases and more than 30,000 unique patients undergoing major surgery, more than 80% of patients had prevalent anemia at the time of hospital discharge, whereas less than 30% had anemia at the time of surgery.⁴ Greater severity of postoperative anemia was associated with a higher rate of unanticipated readmissions in the first 30 days after hospitalization, such that each 1 g/dL decrease in the discharge hemoglobin concentration was associated with a nearly 10% increase in the hazard for readmission. These results were consistent across preoperative anemia severity, surgery types, patient transfusion status, and hospital duration, which highlights the importance of postoperative anemia for all patient groups. The hemoglobin concentration inflection point at which unanticipated readmissions rates began increasing was 11 g/dL, suggesting that this may serve as a potential minimum hemoglobin target or threshold for treatment in future clinical trials of postoperative anemia optimization. In another study using data from surgical patients across 47 centers, approximately 80% of patients experienced postoperative anemia, and this anemia was associated with a higher adjusted risk of death or disability through 90 days after surgery, lower quality of life scores, higher complication rates, and longer hospital durations.⁵

Given the clear associations between postoperative anemia and adverse outcomes, it is essential to employ common sense strategies from the patient blood management (PBM) framework to prevent and/or attenuate the severity of postoperative anemia. Such strategies include, but are not limited to, 1) Timely identification and treatment of preoperative anemia, 2) Employment of strategies to minimize perioperative blood loss (i.e., antifibrinolytic therapy, meticulous surgical techniques, low volume and low frequency phlebotomy practices) and recapture shed blood (i.e., cell salvage), and 3) Prevention of excessive hemodilution. Future studies are essential to assess the safety and efficacy of pharmacologic therapies such as intravenous iron and/or erythropoiesis stimulating agents for the management of postoperative anemia, with an emphasis not only on hemoglobin recovery but also on patient-important outcomes such as readmissions and functional recovery.

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Iron in the ICU – A Must or Seldomly Indicated?



Photo by Kev Bation on Unsplash

Anemia is very common in critically ill patients, affecting about two-thirds of patients on admission.¹ Severity of anemia on admission to the intensive care unit (ICU) is associated with poorer outcomes¹ and may persist with 50% of patients still anemic one-year after discharge.² The pathophysiology of this anemia is complex, involving blood loss, secondary to repeated blood sampling, surgeries, invasive procedures, and inflammation which impacts iron metabolism.³ Inflammation is responsible for iron sequestration and for a repression of dietary iron absorption. Iron deficiency is thus expected to be frequent at ICU admission but also may persist at discharge. This phenomenon is the rationale for giving IV iron to ICU patients.

Indeed, 2 RCTs have evaluated the practice of giving IV iron to ICU patients, soon after admission, with the goal of limiting blood transfusion. This practice did not report a reduction of blood transfusion, however, IV iron was efficient in increasing long term hemoglobin.⁴ One important point is that IV iron appeared to be safe in this population, which is supported by

a second study, showing that IV iron does not induce more oxidative stress in critically ill patients than in healthy volunteers.⁵

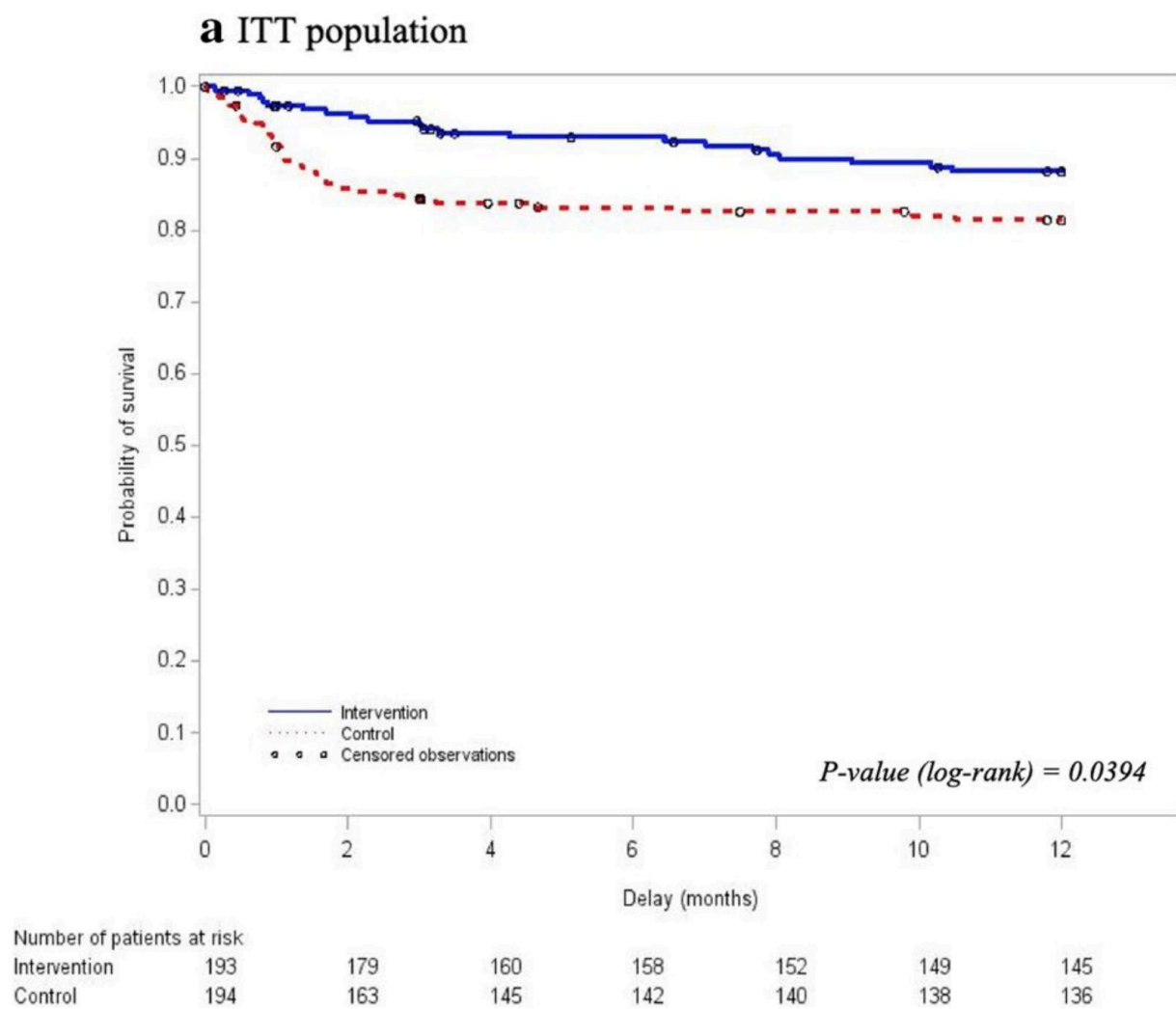
A multicenter prospective observational study showed that ID at discharge and/or at hospital day 28 was associated with increased fatigue. Nevertheless, ID prevalence increased from 10% to 35% at 6 months following ICU discharge.⁶ A feasibility randomized controlled study enrolling 98 ICU patients, evaluated the benefit of giving 1000 mg of carboxymaltose ferric IV at discharge from ICU (compared with no treatment) and observed that IV iron increased D28 and D90 Hb and was also associated with fewer hospital readmission at D90.⁷ Based on this data, administering IV iron in anemic (Hb < 10 g/dL) patients prior to discharge may be beneficial.

Finally, treating the root cause of iron deficiency anemia, rather than with RBC transfusion may be key better outcomes in the ICU. The question is then how to diagnose ID in this context of inflammation? Indeed, usual iron parameters (ferritin and transferrin saturation) are not usable. Hepcidin dosage may be proposed³. Hepcidin is a small peptide, synthesized by the liver and is the master regulator of iron metabolism. Low iron stores repress hepcidin synthesis, while iron overload (and inflammation) induce it. We have shown in a cohort of 1161 ICU patients, that a low hepcidin (indicating ID) was frequent (37%) and associated with lower quality of life and higher mortality up to one year after ICU discharge.⁸ This was the rationale for the Hepcidin RCT, which compared usual care to a strategy of detecting ID according to a low hepcidin levels, (and treating with IV iron ± erythropoietin) in patients about to be discharge after an ICU stay of ≥ 5 days.⁹ We demonstrated that diagnosing and treating ID according to hepcidin levels increased survival rates at 3 months and one year (figure).⁹

In summary, ID is very frequent in critically ill patients notably at discharge, and its treatment may improve outcomes, including survival rates.

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Iron in the ICU – A Must or Seldomly Indicated?



*ITT-Intention to treat

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Approach to Management of Iron Deficiency Anemia in Adults

One third of the world's population is anemic, with iron deficiency being the most common cause of anemia.¹ Once iron deficiency has been identified as the cause of anemia, a major challenge includes selecting the appropriate therapy.

If we proceed with treatment, what are the options?

The two main treatment options include oral iron and intravenous (IV) iron. Selection of either therapy depends on various factors including acuity of anemia, cost and availability of iron replacement products, and ability to tolerate oral iron products.

Oral Iron Most patients are treated with oral iron initially because it is easily administered, readily available and inexpensive.¹ The major drawback is associated gastrointestinal side effects, which are reported by approximately 70% of patients.^{1,2} The side effects include metallic taste, nausea, flatulence, constipation, diarrhea, epigastric distress, and/or vomiting.¹

Numerous oral iron formulations exist with varying iron content. These formulations include ferrous fumarate, ferrous gluconate, ferrous sulfate, polysaccharide-iron complex, and ferric maltol (see Table).³ The formulations come in a liquid or tablet form and are commonly taken daily or every other day. Foods containing phosphates, phytates and tannates may impair iron absorption while acidic foods facilitate absorption.³ Treatment with oral iron may take as long as six to eight weeks to correct anemia and up to six months to replete iron stores, and all formulations have been found to be equally effective.³ Because of the prominent GI side effects, nonadherence and treatment failure often occur.^{1,2}

IV iron For those who have not responded to, tolerated or adhered to oral iron, IV iron is an alternative option. IV iron is also preferred for pregnant women, those with ongoing blood loss and individuals with inflammatory bowel disease, gastric surgery or chronic kidney disease which may limit absorption of oral iron or affect iron homeostasis.^{3,4} IV iron may be avoided in those with active infections as some infectious agents thrive on iron.³ IV iron does require infusion monitoring due to the possibility of infusion reactions including anaphylaxis. IV iron can also cause staining of the skin if extravasation occurs.⁵

Numerous IV iron formulations exist, with low molecular weight iron dextran (LMW ID) being the most popular due to lower cost and single infusion.³ IV iron formulations include ferric carboxymaltose, ferric derisomaltose, ferric gluconate, ferumoxytol, low molecular weight iron dextran and iron sucrose (see Table).³ Commonly, a fixed dose of approximately 1000 mg is given, which is sufficient to treat anemia and replete iron stores.³ Patients are evaluated four to eight weeks after treatment, and iron lab testing is repeated at that time.³

How do we measure the effectiveness of treatment?

Effective treatment of iron deficiency whether via oral or IV iron results in resolution of symptoms, modest reticulocytosis (peaking in 7 to 10 days), and normalization of the hemoglobin level in six to eight weeks.³

Compared to oral iron, IV iron provides more rapid correction of anemia, ability to administer large doses in one setting (one hour versus months),⁵ and improved compliance due to no gastrointestinal side effects.^{1,3}

	• Oral Iron	• IV iron
Drug formulations	<ul style="list-style-type: none"> • Ferrous fumarate • Ferrous gluconate • Ferrous sulfate • Polysaccharide-iron complex (PIC) • Ferric maltol 	<ul style="list-style-type: none"> • Ferric carboxymaltose (FCM) • Ferric derisomaltose (previously called iron isomaltoside) • Ferric gluconate (FG) • Ferumoxytol • Iron dextran, low molecular weight (LMW ID) • Iron sucrose (IS)
Side Effects	<ul style="list-style-type: none"> • Gastrointestinal side effects • Very low risk of serious adverse events 	<ul style="list-style-type: none"> • No gastrointestinal side effects • Risk of serious adverse events (allergic or anaphylactic reactions) (rare)
Advantages	<ul style="list-style-type: none"> • Effective for most patients • Initial costs very low 	<ul style="list-style-type: none"> • Effective for most patients • More rapid correction of anemia and resolution of symptoms • Ability to administer large doses in single infusion • High compliance
Disadvantages	<ul style="list-style-type: none"> • Low compliance • May be inadequate for severe or ongoing blood loss • May require administration for several months • Total costs may be higher 	<ul style="list-style-type: none"> • Requires monitored intravenous infusion, equipment and personnel for possible infusion reactions • Initial costs may be higher

Adapted from UpToDate[®] tables³

Approach to Management of Iron Deficiency Anemia in Adults

How safe is IV iron really?

There remains a reluctance to use IV iron due to historical safety concerns despite improvements in formulations and evidence of their safety.¹ IV iron has the potential to cause allergic reactions, including fatal anaphylactic reactions. However, this concern was based on experience using high-molecular-weight iron dextran (HMNWD) when it was widely available years ago. Now, newer formulations have been developed that demonstrate improved safety, with serious allergic reactions being very rare.⁶

The results of a retrospective analysis of over 30 million doses of IV iron showed a large majority of serious adverse events were attributed to HMW formulations. The absolute rates of life-threatening adverse events were 0.6, 0.9, 3.3 and 11.3 per million for iron sucrose, sodium ferric gluconate complex, lower molecular weight iron dextran and higher molecular weight iron dextran, respectively.⁷ These conclusions are supported by prospective and intra-institutional retrospective studies as well. A meta-analysis comprising 10,391 patients treated with IV iron compared with 4044 who received oral iron, 1329 with no iron, and 3335 with placebo showed that serious adverse events were not increased compared with any other product.⁸

With increasing data showing the safety of IV iron along with increasing use in populations in which oral iron is not feasible, the paradigm of managing iron deficiency anemia is shifting. Of note, some suggest that perceived reactions to IV iron may be caused by infusion premedication and mistakenly attributed to the iron.⁶ Although there are risks with IV iron, they are exceedingly rare with newer formulations, equally effective and last gastrointestinal side effects hindering oral iron compliance. For these reasons, limiting the use of IV iron can have consequences, including increasing use of erythropoietin stimulating agents (ESAs) and transfusions, which both carry their own risk of complications.⁶

What about erythropoiesis stimulating agents (ESAs)?

Two common ESAs, epoetin alfa and darbepoetin alfa, are FDA approved for treatment of anemia due to chronic kidney disease, chemotherapy, and HIV drugs rather than for iron deficiency associated anemia.⁹ Interestingly, ESAs can rapidly deplete iron stores leading to functional iron deficiency and prompting the need for iron replacement.¹⁰ ESAs are associated with venous thromboembolism, thrombophlebitis, hypertension, ischemic heart disease, cardiac failure, arrhythmia, arterial thromboembolism and cardiac arrest.¹¹

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