

# May 2022 NEWSLETTER

## SABM NEWSLETTER MAY 2022 ISSUE

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# **ACCUMEN**°



## SABM 2022 Newsletter Publication

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Cover photo courtesy iStock by Getty Images<sup>™</sup> 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.

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# Letter from the President – A Conversation with Carolyn Burns, MD



For this edition, we've prepared an interview with SABM President, Carolyn Burns, MD, nearing the mid-point of her two-year term. Dr. Burns is a board-certified pathologist (Anatomic and Clinical Pathology) with a medical career that extends over 35 years, including some 20 years

as Medical Director and Chief of Pathology for the Jewish Hospital Healthcare System, Department of Pathology in Louisville, KY. Kevin T. Wright, Editor

Wright: Dr. Burns, please tell us about your background?

**Burns:** It sounds silly, but from the time I was in 4<sup>th</sup> or 5<sup>th</sup> grade I wanted to be a physician. Rather odd as no one in my family was ever in medicine.

Wright: Was there a specific event that stirred this desire?

Burns: Not really, I suppose it was because I liked the sciences and also saw it as a way to show care for others. Was I truly that altruistic as a 10-year-old? Perhaps? Maybe I just watched a lot of TV...Marcus Welby and such. (chuckle) I stuck with the dream through high school and did some volunteer work during those years as well as in college. Once I was in medical school, I was certain it had been the right choice. I matched in urology and thus started with a year of general surgery internship. It became pretty clear that year that a surgical specialty was not the "match" for me and so I moved into pathology, both surgical and clinical for an additional 4 years. In clinical pathology, I really enjoyed hematology and coagulation and transfusion medicine.

**Wright:** Then on to Jewish Hospital Healthcare in Louisville, KY?

We performed solid organ transplants, including the 1st 5 hand transplants in the US; Surgical Oncology and Hematology/Oncology were also very busy services. We did not have Obstetrics or Pediatrics and Neonatal services as the hospitals connected to us provided those services.

Wright: With such accomplishments, what attracted you to hematology/coagulation and transfusion medicine?

**Burns:** Pathology, by nature, is mostly indirect patient care, however, there are many pathologists, such as myself who were hands-on. For example, our group performed bone marrow biopsies, coagulation and transfusion medicine. These consultations with other healthcare providers and patients were so important to my development as a physician. It kept me connected with patient care. I never wished to be the pathologist that "hid behind the microscope."

Wright: Those who know you would agree! Many of us remember first-hand the challenges with issues surrounding HIV & HCV from the late 1980's into the 1990's. How did this influence your view of transfusion medicine?

Burns: Being the early 1990's the Transfusion "world" was still being rocked with issues surrounding HIV & HCV. Thus, lookbacks and recalls were the primary focus within our donor centers and for our in-house transfusion services. Everyone was in a blood avoidance/conservation mode if possible. I believe this was a true turning point for many of us, that blood transfusion can be harmful.

Wright: And Jewish Hospital Healthcare had a bloodless medicine program?

**Burns:** Yes, a robust program that preceded me; it was the only "game" in the entire state and patients would come from all around. We had excellent involvement from our physicians and therefore it was not difficult to begin applying those strategies to all patients given this worry of TTD. I learned so much from these patients. Once you see the outcomes in patients where blood is not an option you begin to ask yourself why you are not doing this for all patients, right?

Burns: Yes, after 5 years of residency, I joined the group at Jewish Hospital; that was 1991. (Ouch, I'm dating myself!) I was appointed Medical Director of Transfusion Services along with my general surgical and clinical pathology duties. This is typical for private practice groups to assign areas in the clinical laboratory to each physician. Ultimately this was a service for 6 hospitals in our system. Our Surgical and Clinical Pathology services were extremely busy as well. Our hospital laboratory performed over 95% of testing inhouse. Our Transfusion Service handled not just blood components, but factor concentrates, albumin, etc. supporting a huge CVS program, including VADS, ECMO.

Wright: This would seem to be a logical transition to PBM?

Burns: It was a rather natural transition to PBM, as it became known, and more was published on the adverse events associated with transfusion. I venture to say this is true of the majority of PBM practitioners, physicians, mid-level providers etc. I still remember the TRICC Trial in NEJM! This was such a landmark study and so many others followed. It became



hard to ignore. As mentioned, we were fairly comfortable with transfusion alternatives, but I began really pushing the concept of comprehensive PBM in the mid-2000's.

Wright: You then left private practice and into a role of a PBM physician?

Burns: I remember being so nervous when I jumped ship from the world of private practice. I had 20 years invested, having been the head of the group for 17 of those years. Change is scary. I knew, though, that I needed this change. And, thankfully, along the way there have been countless wonderful mentors, colleagues, and friends who have helped me grow professionally, to broaden my range, and truly contribute to what I firmly believe is the best, safest and highest value care we can provide to patients.

Wright: What were some of the challenges you encountered?

**Burns:** I believe my challenges have been similar to others in this field. PBM is a broad and complex initiative that demands infrastructure, communication with multiple providers and services that can seem overwhelming. It takes dedication and consistency to implement and then sustain a program.

Wright: You're certainly speaking for so many of us in PBM program management.

Burns: I must also mention the knowledge gap, defining what PBM actually is and better yet why we should practice it. Layer that on with the significant complacency surrounding transfusion and general lack of familiarity with the most current state-of-the-science. As we say in SABM: evidence, education, better patient outcomes. We must deliver this message and change the culture from where it currently is. We are seeing more providers and institutions engaging in comprehensive PBM, but we know this must become the standard of care.

PBM consulting. I was able to do this as a part-time employee of a small company at first and then ultimately moved to independent PBM work. I have never looked back.

**Wright:** Who were some of those that helped along the way?

Burns: Heartfelt thanks to Tiffany Hall and Sherri Ozawa for originally bringing me into the fold of SABM. To Dr. Gross, Dr. Tibi, Dr. Shander, Richard and Carmen Melseth, and the many Committee and Board members (you know who you are!) who embraced me and helped me learn and expand my leadership roles over these years. I was so new and inexperienced comparatively and they took me under their wing. Still learning from them all, by the way...it never stops. That's the goodness of it all.

Wright: Please speak to the changes in definition for PBM?

Burns: I love the new global definition of PBM as it empowers us as caregivers and empowers patients. The SABM concept of Blood Health is also taking PBM along a whole new trajectory. Blood Health and PBM are what our patients deserve. I am honored to be the current SABM President during this time of a global "awakening" to PBM.

Wright: What are your goals during your tenure as President?

**Burns:** I hope to continue our global reach and collaboration. It would be amazing to double or triple our Memoranda of Understanding to many other societies and organizations. Increasing our membership and hospital affiliations is also vitally important. I want to encourage all current members to stay engaged, encourage other colleagues from more subspecialties and areas of healthcare to join SABM. The multidisciplinary nature of our society is what differentiates us from any other. We are already expanding our range and use of social media to put out the Blood Health message. Check out the recent Blood Health YouTube video! These personal goals are also a focus of the SABM Board of Directors Strategic Plan that we are working on now. Stay

Wright: How did SABM membership influence your decisions?

Burns: When I joined SABM in 2007, there were so many supportive people and resources that I just felt this "vibe", this feeling from this unique multi-professional group that spurred me on to learn and do more. As time went on, I found I was less enamored with surgical pathology and general pathology practice and decided to leave my group to pursue

tuned for the Plan "reveal" at the Annual Meeting.

Wright: Finally, where do you see SABM in 5 years?

Burns: I see SABM as one of the most influential professional societies in the U.S. and internationally. We will be THE resource for comprehensive Patient Blood Management and Blood Health. If we continue our current trajectory, this will happen!



# **Looking for Newsletter Content**

SABM members want to know:

- Do you have an interesting case study?
- · News about your 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 2022 issue is August 1, 2022.

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# 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 <u>info@sabm.org</u>. Be sure to include your full name and details regarding the award, the recognition you received, or the publication citation.

# **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 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 <u>info@sabm.org</u> with your request for consideration.



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Rugved Shrikant Pattarkine, MD, is a board-certified pathologist in Anatomic and Clinical Pathology. Dr. Pattarkine began his medical education 2012 in at Smolensk State Medical University, Russia, continued as a resident in Anatomic / Clinical Pathology at New

York Medical College, and currently is a transfusion medicine fellow at UCLA Medical Center in Los Angeles, California, USA. Of note, Dr. Pattarkine is a former Chief Resident and Pathology Instructor at New York Medical College, and a member of several professional societies including: College of American Pathologists; American Society of Clinical Pathologists; AABB, and American Society of Hematology. He joined SABM last year and is involved in various PBM initiatives at UCLA. We are delighted to welcome him to the newsletter team and look forward to his contribution.

# **Nurses Notes**

# Prevention of Anemia in Pregnancy Protocol

Patient Blood Management (PBM) improves outcomes through the application of evidence-based concepts that maintain hemoglobin concentration, optimize hemostasis, and minimize blood loss. PBM professionals achieve this through interdisciplinary methods, anemia management, coagulation optimization, and patient-centered decisionmaking. A recent example includes the Geisinger Prevention of Anemia in Pregnancy Protocol. The project is a collaborative effort among Geisinger Patient Blood Management (PBM), Obstetrics (OB), Maternal-Fetal Medicine (MFM), Anemia Pharmacy, Home Infusion Pharmacy, Laboratory, HemeOnc, Pediatric HemeOnc, Acute Care Clinics, and Infusion Centers.

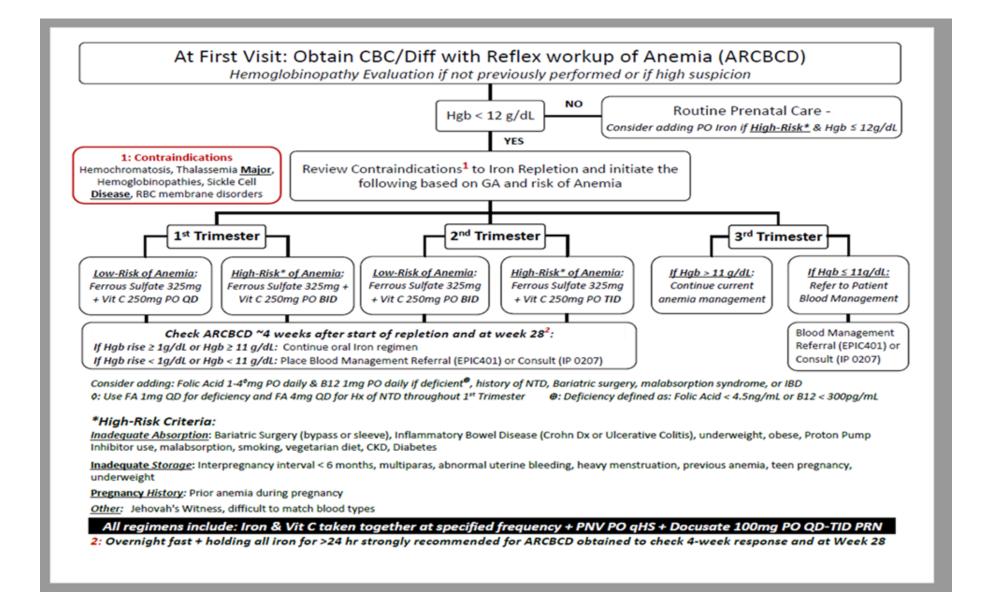
We noticed that OB and MFM patients often are or become anemic, which can negatively influence fetal health and result in unnecessary transfusion of components before and/or during delivery. Not only was there no system-wide approach to managing anemia for this population, but also moms had difficulty procuring necessary pre-natal meds and getting to iron infusion appointments. Additionally, there was not a consistent iron infusions process for pregnant women under 18 years of age. We created the Anemia in Pregnancy Protocol to identify and treat anemia in the OB and MFM population. Embedded within Geisinger's electronic medical record system, the protocol begins at the first pre-natal appointment. Each trimester gives direction for lab testing including reflex anemia testing, and recommendations for iron replacement. The OB/MFM providers use the Geisinger mail order pharmacy to send necessary pre-natal meds to each patient's home after the first visit. If the patient requires intravenous iron, PBM consultative service helps coordinate an at-home infusion. When a patient is under 18 years of age, the protocol directs for a consult with a pediatric HemOnc, who prepares the patient to receive infusions close to her home.

This protocol helps establish a system-wide, nine-hospital, consistent approach to identifying and assertively treating anemia in pregnancy. A dashboard is tracking metrics including order set usage, mail order frequency, intravenous iron infusions ordered, blood component transfusions and pediatric infusions. An update will be provided in a future edition of the newsletter.

Problems	Solutions
<ul> <li>OB and MFM patients are/or tend to</li> </ul>	<ul> <li>A PBM consult offers early intervention to</li> </ul>
become anemic, which can negatively	manage anemia and optimize hemoglobin.

- influence fetal health and result in unnecessary transfusion of components before and/or during delivery
- No current system-wide approach manages anemia in this population
- Moms have difficulty procuring necessary pre-natal meds
- Moms have difficulty getting to iron infusion appointments
- No consistent process to provide infusions for those under 18 years of age
- which improves fetus health and avoids unnecessary transfusions
- System-wide, consistent approach created by anemia, OBGYN and MFM experts
- OB/MFM providers prescribe meds that are delivered to patients' homes via mail order pharmacy
- Moms get intravenous iron infusions at home-bringing care to the patient
- New process in NE and Central Pennsylvania provides care close to home for pregnant women under 18 years of age





da Silva Lopes, K., Yamaji, N., Rahman, M. O., Suto, M., Takemoto, Y., Garcia-Casal, M. N., & Ota, E. (2021). Nutrition-specific interventions for preventing and controlling anaemia throughout the life cycle: an overview of systematic reviews. *The Cochrane database of systematic reviews*, *9*(9), CD013092. World Health Organization, & Centers for Disease Control and Prevention. (2007). Assessing the iron status of populations. *Geneva: World Health Organization*.

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https://doi.org/10.1002/14651858.CD013092.pub2





# Major Surgery in a Jehovah's Witness with Sickle Cell Disease

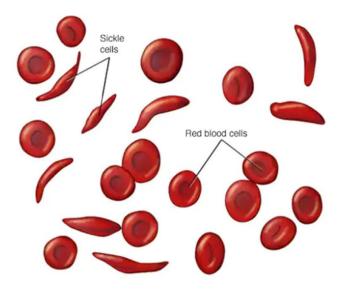


Photo courtesy of Mayo Foundation for Medical Education and Research

#### Introduction

Major surgery is often associated with high intraoperative blood loss and blood transfusion. Blood transfusion has hitherto been the default therapy for sickle cell disease (SCD) patients. Jehovah's Witnesses (JW's) decline blood transfusion for religious reasons.

Major surgery, elective or emergency, can be performed safely in JW's by employing bloodless surgery techniques perioperatively. In JW's with SCD, additional measures and precautions are needed to prevent complications due to sickling.

#### Sickle Cell Disease

SCD is a group of haemoglobinopathies characterized by sickling of red blood cells, chronic hemolytic anemia, painful vaso-occlusive crises, and acute and chronic end-organ damage. First described by James Herrick in 1910, it is the commonest inherited blood disorder, and affects > 30 million people worldwide, mainly persons of sub-Saharan descent, but also persons from South Asia, the Middle East, and the Mediterranean.

Normal haemoglobin is HbAA with 2  $\alpha$  and 2  $\beta$  globin chains. The abnormal haemoglobin in SCD, HbS, on deoxygenation is prone to polymerization, causing sickling, rigidity of RBC, hemolysis, and vaso-occlusion. HbS causes disease only when both  $\beta$  globin chains are abnormal (HbSS, HbS $\beta$ , HbSC, etc). HbAS is thus sickle cell trait, not considered a disease.

#### The Challenge of Surgery in Sickle Cell Disease

SCD patients may require surgery due to complications of SCD, e.g., hip replacement for necrosis of femoral head, cholecystectomy for gall stones, and splenectomy for hypersplenism. On the other hand, surgery may be incidental in SCD patients, e.g., caesarean section, cardiac surgery, and appendectomy.

Surgical procedures in SCD are associated with increased risks of peri-operative mortality and morbidity from vasoocclusive (painful) crisis, acute chest syndrome, acute kidney injury, cerebrovascular accident, congestive heart failure, post-operative infections, and venous thromboembolism. Majority of complications occur postoperatively.

#### Problems of transfusion in SCD

Routine preoperative transfusion in SCD patients is now discouraged due to hazard of alloimmunization, hemolytic and non-hemolytic reactions, hyperhaemolysis, infections, and increased blood viscosity which can result in sickling. Other hazards of blood transfusion such as hyperkalemia, hypothermia, acidosis, and hypoxia due to storage lesions can also induce sickling in SCD patients.

#### **Pillars of Bloodless Surgery**

Bloodless surgery techniques are grouped under 4 'pillars': 1) Optimizing the hematocrit (HCT); 2) Minimizing blood loss; 3) Optimizing tissue oxygenation; and 4) Supporting patient's tolerance of anemia. All the techniques under the 4 pillars may find application throughout the perioperative period for all patients including SCD patients, but they are selected according to what is appropriate for and acceptable to the individual patient.

#### Prevention of complications of surgery in SCD

Prevention of complications of surgery in SCD requires meticulous perioperative care, which involves full preoperative assessment, adequate hydration, thermoregulation, avoidance of hypoxia, adequate pain control, and indeed, avoidance of all factors predisposing to sickling as outlined earlier.

#### **Preoperative Care**

Factors which precipitate sickling in SCD are hypoxia, dehydration, acidosis, hypothermia, hypotension, pain, hyperkalemia, increased blood viscosity, vascular stasis, vasoconstriction, infections (bacterial, viral, or protozoal), extremes of weather, and stress. **Preoperative Assessment.** History and physical examination of SCD patient will include ascertaining the frequency of crisis and the date of the patient's last crisis, known triggers for crisis, baseline level of activity, baseline opioid use, steady-state hemoglobin and hematocrit, assessing for co-morbidities, and cardiac and pulmonary complications.

Investigations will include complete blood count, iron studies, genotype confirmation, baseline oxygen saturation (SpO<sub>2</sub> by pulse oximetry), urinalysis, serum urea, electrolytes, and creatinine, chest x-ray, and other investigations as indicated,



e.g., ABG, Pulmonary Function Tests, ECG, LFT, and neurological imaging).

A multidisciplinary review of the patient is necessary, and would involve at least the surgeon, anesthesiologist, hematologist, pain management team, nutritionist, and chest physician.

**Optimizing the Hematocrit Preoperatively.** Target HCT in SCD preoperatively should  $\ge 30\%$  (Hb  $\ge 10$  g/dL). The hemoglobin may be successfully raised with folic acid 5mg/day, Vitamin B12 150 µg/day, Vitamin C 500 mg/day, nutritional support (green vegetables, fruits, proteins, and water), erythropoietin 100-150 U/kg s.c. on alternate days, and cautious iron therapy.

Iron overload in SCD is related to multiple transfusions. Iron deficiency anemia has been found to be a significant problem in young non-transfused SCD patients, and it responds to iron therapy. Pregnant sicklers who have *not* been transfused are also predisposed to iron deficiency anemia due to urinary losses from intravascular hemolysis and increased dietary requirement in pregnancy, so they can benefit from iron supplementation. Serum ferritin < 25 ng/mL and low MCV are useful screening tools.

**Other Preoperative Measures and Intervention.** The patient would need to be admitted ahead of surgery, and a cold environment should be avoided. Phlebotomies should be restricted, to avoid anemia.

Adequate hydration should be ensured, and hypotonic fluids are preferred (4.3% dextrose in 1/5 saline). Much normal saline can result in acidosis and sickling, and excessive intravenous fluids can result in pulmonary edema, which predisposes to acute chest syndrome. Prolonged preoperative fast should be avoided.

Anticoagulants, NSAIDs, and herbal supplements can lead to increased hemorrhage, and should be stopped days ahead of surgery. Hydroxyureas, L-Glutamine, and other newer drugs can help prevent or mitigate crisis.

The patient's choices of bloodless surgery techniques should be ascertained, written informed consent obtained, and any objections documented. The Hospital Liaison Committee of Jehovah's Witnesses can be helpful in the holistic care of the of blood which can result in sickling. Adrenaline should be avoided, and dopamine may be used if inotropic agent is needed.

Tissue oxygenation should be optimized through preoxygenation and maintenance of  $SpO_2$  above 96% or basal level, whichever is higher, using 30-50% inspired oxygen (Henderson 1994).

Meticulous volume replacement is important, but caution should be exercised with normal saline, and fluid overload should be avoided for the reasons stated earlier. Colloids should be used for blood loss  $\geq$  1000 mL or 1/4 of the patient's blood volume. The patient's blood pressure should be maintained just above the lower end of normal to minimize blood loss.

**Monitoring.** Continuous oxygen monitoring (pulse oximetry) is an important component of the standard monitoring during anesthesia in SCD patients. Arterial blood gases are sometimes necessary to confirm hypoxia. Urine output should be monitored by urethral catheterization.

**Bloodless surgery techniques.** The patient should be positioned with the op site above the right atrium and avoiding pressure on large vessels (e.g. pregnant women are turned slightly to the left) to reduce blood loss. Pharmacological agents to minimize blood loss should also be used pre-emptively whenever possible, e.g., tranexamic acid, vitamin K, Epsilon aminocaproic acid, Desmopressin, and recombinant Factor VIIa.

Meticulous hemostasis is important, and a dry field should be maintained by pre-emptive and prompt ligation of vessels. Judicious use of topical hemostats, electrosurgery, harmonic scalpel, CUSA knife, laser, plasma jet, and other devices, can help minimize blood loss. Laparoscopic and robotic surgery are also associated with less blood loss.

Blood salvage/cell salvage can be used safely in SCD, as can tourniquet. Use of acute normovolemic hemodilution has been reported in sicklers but seems to be rarely needed nowadays.

#### **Postoperative Care**

Postoperatively, oxygen therapy should be continued to

JW patient.

#### **Intraoperative Care**

**Normothermia** is important not only to avoid sickling but to minimize blood loss. Operating room temperature should be maintained at  $\geq 27^{\circ}$  C. Thermal suits or blankets may be used as appropriate, and intravenous infusions should be warmed if necessary.

**Anesthesia.** Spinal or epidural anesthesia is preferred for less blood loss and better pain control postop with epidural. However, there is need to beware of hypotension and pooling

maintain SpO<sub>2</sub> above 96% or basal level, whichever is higher, for 24 hours to support the patient's tolerance of anemia. Continuous oxygen monitoring should be maintained until SpO<sub>2</sub> is sustained at baseline with room air.

Adequate analgesia should be administered to avoid hypoxia which can result in sickling. Normal haemodynamic status and fluid balance should be maintained to avoid hypotension, dehydration, and fluid overload. Fluid administration should not exceed 1½ times patient's maintenance fluid requirement to avoid pulmonary oedema which can result in acute chest syndrome as stated earlier. Incentive spirometry helps to prevent atelectasis and acute chest syndrome.



Prompt treatment of febrile illness, infection, or sepsis should be done to avoid sickling. Anaemia should be treated according to severity with iron therapy, erythropoietin and adjuncts outlined earlier.

### **Outcomes of Bloodless Surgery in SCD patients**

A systematic review and meta-analysis of randomized and observational studies by Alotaibi and co-workers (2014) comparing transfusion vs non-transfusion strategy in SCD found no difference in perioperative mortality, and vascular and non-vascular complications. Steven Frank, MD, (Medical Director: Bloodless Medicine and Surgery Program, Johns Hopkins Hospital, Baltimore, USA) based on his own studies in a wide spectrum of patients stated: "the use of appropriate blood conservation measures for patients who do not accept transfusions results in similar or better outcomes."

#### Conclusion

Major surgery in SCD patients is associated with higher morbidity and mortality than in the general population. Blood transfusion in SCD is associated with alloimmunization, haemolytic & non-haemolytic reactions, hyperhaemolysis, infections, and increased viscosity predisposing to sickling.

Major surgery can be performed safely in JW's with SCD by judiciously employing bloodless surgery techniques with good outcomes. Experience gained in bloodless surgery with JW's can benefit non-JW SCD patients too!

Contributor: Nathaniel Usoro, MD, FWACS, FICS

#### **Further Reading**

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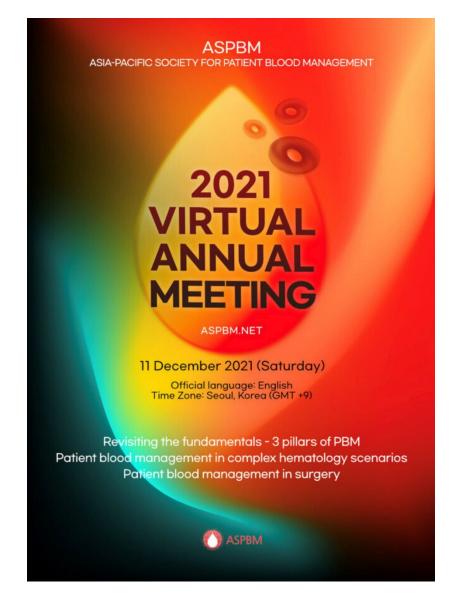


# MANAGEMENT AWARENESS WEEK® November 7-11, 2022 #PBMAW2022 #SABMPBMAWARENESSWEEK





# The ASPBM 2021 Virtual Annual Meeting – A Symphony in PBM



The Covid 19 pandemic has brought along immense challenges and changes, ones that we would not have ever imagined. On the reverse side of the coin, the pandemic has opened up new opportunities, including that of learning from or meeting with those from four corners of the earth despite restrictions in travel. Along with other virtual conferences held by leaders in PBM, the Asia Pacific Society for Patient Blood Management (ASPBM) also had their 2021 annual meeting virtually, on 11th December 2021. The meeting brought together experts and advocates of PBM and bloodless medicine, from around the world, all with the same purpose of advancing this superior medical field for the benefit of all.

The meeting spanned some 9 hours, with 7 exciting, fast moving sessions. This ASPBM meeting was the first time that several PBM and other bloodless organizations had their Zooming in on two particular topics alone, we can learn valuable lessons that reiterate the fact that, what may seem impossible, is actually possible and can be done with tenacious and creative efforts. Radheshyam Naik, MD, a consultant medical oncologist and bone marrow transplant (BMT) physician from Samprada Cancer Center & HCG Cancer Center, India, presented the topic: Role of PBM in Bone Marrow Transplant in Patients for Whom Blood is Not an Option. It is understood that high dose chemotherapy (HDC) is required to enable a possible cure or a prolonged life free from a blood cancer, but it is also known to severely affect the marrow. Hence the role of BMT is important. Until recently, "bloodless" BMT was thought to be impossible. However, some crucial conceptual changes have made this possible, which include:

- No prophylactic platelet transfusions are necessary in patients until the platelet count is less than 5000
- Conditions which consume platelets have to be aggressively managed
- Anemia: IV Iron and Erythropoietin (up to 40,000 units twice a week)
- Fever: Paracetamol
- · Infection: Nip in the bud, with prompt antimicrobial
- Reduce repeated blood tests: only when necessary or even use finger prick tests
- Drugs that reduce platelet activity (e.g.: Aspirin or NSAIDS) are withdrawn

Of interest too is that a patient needs to be well optimized, with IV iron and erythropoietin to reach a hemoglobin level of almost 14 g/dL, as it was expected to drop extremely low even below 3 g/dL after the HDC, while awaiting the BMT to become active on the marrow. These patients are supported with growth factors, and infection risks are minimized, with the "Transplant room" only being accessed by well-trained transplant team members, with strict hygiene, well monitored and changed catheters and only home cooked food (double cooked). During the time of extremely low platelet counts (up to zero in count and when the patient had bleeding), was controlled with the Factor VII concentrate, NovoSeven. Dr Naik noted that he had used these principles in successfully treating 8 patients, for bloodless BMT, with only one patient succumbing due to infection, and not due to bleeding or anaemia.

Jae Suk Yoo, MD, a cardiothoracic surgeon from Korea,

own or combined sessions. SABM, which the ASPBM is affiliated to, had a power-packed session with advances in cardiac surgery and antifibrinolytics being discussed; SABM also introduced the concept of "Blood Health." The Bloodless Medicine and Surgery Society (BMSS) and Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis (NATA), affiliate organizations of SABM, delivered topics with unique approaches on bloodless medicine and PBM. Of note too, were topics on emergencies, complex surgeries and unique hematological diseases, such as Sickle cell disease, presented by a variety of expert speakers. presented the topic PBM in Cardiac Surgery. He has perfomed over 45 cardiac surgeries utilizing PBM options in patients for whom blood is not an option. Of interest is that almost half is accomplished using Minimally Invasive Cardiac Surgery (MICS) techniques. This approach serves to open a whole new realm in the field of bloodless cardiothoracic surgery, in addition to the already proven multiple strategies during the preoperative, intraoperative and postoperative period. To attempt approaching a beating heart and precisely manipulating the sections of this organ requires skills, resourcefulness and adaptability as the team needs to quickly convert to full sternotomy if the need arises.



Among the remarkably complex patients who have benefited includes a 55-year-old Jehovah's Witness woman, undergoing Quadredo - mitral valve replacement. She had a past history of aortic valve replacement in 1984, mitral valve replacement in 1994, and triple-redo surgery in 2012. She had paravalvular leakage, resulting in hemolytic anemia and heart failure, with pulmonary oedema. She was rushed to surgery with a hemoglobin of 8.5 g/dL as she was already in failure, NYHA 3. Nevertheless, she was optimised with IV iron and erythropoietin 10,000 units pre- and post-operative, on alternate days, and was discharged with hemoglobin 11 g/dL. Another incredible example is of a 53-year-old man, with chronic severe aortic regurgitation (AR), annuloaortic ectasia and ascending aortic aneurysm, with heart failure, NYHA 3. The surgery was complicated, and thus the team employed Cabrol patch and quickly converted to full sternotomy, including a revision of Cabrol patch. Post operative care was complex, and the patient also benefited from an excellent team who kept him on VA ECMO. Both of these patients are firsts in the world, in their own respects. One for Quad-redo cardiac surgery performed bloodless, and another for being maintained on VA ECMO for 19 days, without a transfusion. Both patients are living examples of the success of the PBM and bloodless medicine programs, with exceptional teamwork.

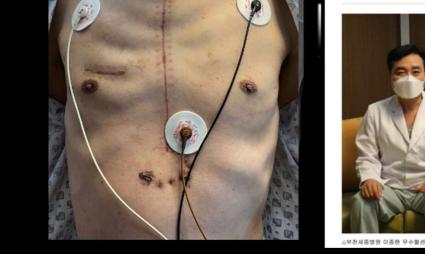
To gain greater insights into these topics and other excellent examples, please visit and register to watch replays, at the ASPBM website: <u>www.aspbm.net</u>

As a whole, this educational event was a symphony, bringing together incredible individuals to share their beautiful pieces of work, that benefit many. It is hoped that the delightful "music" created not only warms the heart but also propels many others to join in the efforts to practice the superior field of PBM and bloodless medicine.

Contributor: Ananthi Krishnamoorthy, MD









△부천세종병원 이종현 무수혈센터장(왼쪽)과 흥부외과 유재석 과장(오른쪽)이 환자와 기념촬영을 하고 있다

Patient at post op day 70+



# The Highest-Level Evidence Comparing Non-Transfusable and Transfusable Patients

My colleagues and I had the privilege of collaborating with researchers from the Helios Klinikum, Gotha, Germany on a recent systematic review and meta-analysis published in the journal Transfusion. "What makes this review important is that it searched for the best available evidence to answer the question, do patients treated without the possibility of receiving allogeneic blood have worse outcomes when compared to patients able to receive allogeneic blood transfusions" says Kai-Uwe Döbel, chief physician of the anaesthesia, palliative, intensive care and pain therapy department at the Helios Klinikum.



Photo courtesy of Peoplecreations

It is surprisingly difficult to assess the efficacy of red cell transfusion from available research. Some point to randomized trials that compare transfusion strategies for the answer. These trials often report no difference in outcomes between liberal and restrictive strategies, and in some cases better outcomes with restrictive strategies. However, as these studies do not compare red cell transfusion to placebo or another intervention, they are not designed to assess transfusion efficacy.

Others point to the results of observational studies comparing patients transfused red cells to those not transfused. These studies consistently suggest a link between red cell transfusion and increased death and hospital complications. However, this research is frequently criticised as overestimating the effect of transfusion on outcome.

This recent publication adds another dimension. The authors compared outcomes in patients considered non-transfusable to patients who were transfusable, irrespective of whether they did or did not receive a transfusion. Some may initially question how this differs from observational studies comparing transfused and non-transfused patients. This difference, though subtle is very important.

Non-transfusable patients refers to patients declining

had their own blood optimized through the principles of Patient Blood Management (clinical strategies to manage anemia, bleeding, and coagulopathy). In general, the results from the included studies revealed no difference in death or complication rates between patient groups, with patients considered non-transfusable treated at similar or reduced hospital costs.

Of interest, those considered non-transfusable were more likely to have a shorter stay in the intensive care unit and, while there were no significant differences in complication rates from a statistical perspective, the non-transfusable patients tended to have fewer infections, acute myocardial infarctions, and reoperations than transfusable patients.

"The results are certainly consistent with what we have seen in our clinical practice," says Petra Seeber, lead author and anaesthesiologist at The Institute for Blood Management, Gotha, Germany. "We've found that non-transfusable patients who receive appropriate care do really well."

The results are also consistent with other research: "The trend toward fewer infections in non-transfusable patients is consistent with the results of randomized controlled trials and observational studies," says Matthias Lucas, senior author and general surgeon at The Institute for Blood Management, Gotha, Germany.

transfusions (regardless of reason), patients treated under conditions where transfusions were not available (pandemics, natural disasters, combat settings, resource limitations), or patients with rare blood types or complex antibody patterns. Transfusable patients refers to patients able to receive transfusions regardless of whether or not they were administered one. With this in mind, the intervention of interest examined in this study is not transfusion, rather it is the different bundles of care received.

The authors screened 2848 research outputs and assessed the results of 41 studies including over 150,000 patients across North America, Europe, Africa, Australia, and Asia. As expected, non-transfusable patients were more likely to have The research, available as open access, reassures clinicians that current evidence indicates patients unable to receive allogeneic blood transfusions have similar outcomes and, in some cases, may even have better outcomes than patients able to receive transfusions. These results may be a catalyst to provide further clinical and economic incentives to deliver more aspects of Patient Blood Management to transfusable patients.

Contributor: Kevin Trentino, MPH

Full text available at: https://onlinelibrary.wiley.com/doi/epdf/10.1111/trf.16788



# Severe Hyperthermic Coagulopathy and Small Vessel Thrombosis Secondary to Cocaine Overdose

### Introduction:

Coagulopathy is a frequent complication of hyperthermia syndromes such as malignant hypertension and heat stroke, but are also associated with illicit and pharmaceutical overdoses. Here we present a case of cocaine-induced hyperthermia with profound acute coagulopathy, resulting in disseminated intravascular coagulation (DIC), multiorgan failure, and multifocal intracranial infarction.

#### History:

A 30-year-old male presented to the emergency department after a witnessed fall and erratic behavior. His past medical history is significant for bipolar disorder type 1, paranoid schizophrenia, and polysubstance abuse (cocaine, marijuana, and tobacco). An unidentified white powder was discovered on the patient by emergency medical personnel during transport to the Emergency department. Upon arrival to the critical care bay the patient was hypotensive (80/50), hyperpyretic (41.1 C), tachycardic (> 160 bpm), diaphoretic, and tachypneic. He was intubated and sedated secondary to worsening acute hypoxemic respiratory failure. Mild mucocutaneous bleeding was present but no life-threatening bleeding was evident.

#### Hospital Course:

Initial labs demonstrated mild transaminitis, acute kidney injury, metabolic acidosis, elevated creatine kinase (Table 1), as well as an increased prothrombin time (PT), activated partial thromboplastin time (aPTT), and D-dimer. Thromboelastography (TEG) demonstrated a severely increased R-time (20.8 sec), decreased alpha angle (6.4 degrees), and decreased maximum amplitude (8.4 mm). He also presented with acute kidney injury, progressing to acute renal failure (requiring continuous renal replacement therapy; CRRT) secondary to rhabdomyolysis, a clinical feature commonly seen in cases of prolonged hyperthermia<sup>1</sup>. An initial urine toxicology screen was positive for cocaine and benzodiazepine. He was treated with internal and external cooling therapy for hyperpyresis and given fresh frozen plasma (6 units) with platelets (2 units) for his clinical coagulopathy (Table 2). Additionally, he was transfused with 1 unit of red blood cells for persistent mild anemia with mild mucocutaneous bleeding.

of writing the patient is still hospitalized (196 days) receiving physical, speech, and neurocognitive therapy. Despite longterm inpatient physical and occupational therapy, the patient continues to have significant difficulty ambulating and performing routine daily activities.

#### **Discussion:**

Illicit stimulant usage is a rare but known cause of acute hyperthermic coagulopathy and is similar in symptomology to anticholinergic and salicylates overdose. Common manifestations include altered mental status, coma, increased muscle activity, hyperthermia, seizure, rhabdomyolysis, hypotension, coagulopathy, and acidosis.<sup>1</sup> In this case the patient's polysubstance abuse was part of his documented past medical history and the suspected agent was recovered on the patient. While the substance was not available for definitive identification, the patient did test positive for cocaine metabolites on initial urine toxicology. Hyperthermic coagulopathy most often presents in cases of heat-stroke<sup>2</sup> but case reports of hyperthermic coagulopathy associated with cocaine overdose have been reported in literature.1,3-6

Cocaine raises core body temperature by increasing inducing agitation and locomotion<sup>5,7</sup> while impairing sweating, cutaneous vasodilation, and subjective heat perception.<sup>8</sup> In warm ambient temperatures, such as the summer heat the patient was exposed to, extreme hyperthermia develops rapidly. The effect of extreme hyperthermia on coagulation is well documented.<sup>9-11</sup> The optimal temperature for enzymatic interactions within the body is approximately 37.5°C, with sustained hyperthermia above 42°C resulting in improper folding of proteins and resultant loss of catalytic activity. The effect on the coagulation cascade is somewhat counterintuitive, as ex vivo studies demonstrated a decrease in R-time in heated specimens, leading to a transient global hypercoagulable state.<sup>10</sup> As protein components of the coagulation cascade become consumed, clinical coagulopathy becomes apparent and manifests as substantially elevated PT, aPTT, and an increased R-time on TEG. An acute rise in D-dimer levels and reciprocal thrombocytopenia are also commonly seen, which progresses to life-threatening DIC in approximately half of cases.<sup>12,13</sup> In the absence of trauma, mucocutaneous bleeding may be the only initial manifestation of the occult coagulopathy; however, as underlying DIC develops, thrombotic complications and consumptive coagulopathy become increasingly prevalent. DIC is an independent prognostic factor of hospital mortality in patients with heat stroke.14

The patient's underlying coagulopathy gradually improved over the first week of inpatient treatment, however noncontrast head CT scan done on day 7 revealed a growing hypodensity in the right cerebellum with loss of gray-white matter differentiation, consistent with evolving acute infarction. Two days later, cranial MRI demonstrated multiple bilateral infarcts in the frontal and parietal lobes, bilateral caudate nuclei, and middle cerebellar peduncles. At the time

Animal models have partially elucidated the cellular mechanisms of hyperthemia-induced coagulopathy and DIC. Extreme elevations in body temperature directly and indirectly lead to hepatocyte injury<sup>15,16</sup> and neutrophil activation<sup>13</sup>, leading to the release of tumor necrosis factor- $\alpha$ , interleukin (IL)–1 $\beta$ , and IL-6.<sup>17,18</sup> Damage to endothelial cells releases tissue factor, which activates the coagulation cascade.<sup>13,19</sup> Prompt cooling inhibits fibrinolysis but not the



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activation of the coagulation cascade, leading to a sepsis-like pattern of consumptive coagulopathy and microthrombi formation.<sup>20,21</sup> Tissue factor appears to play a key role in the development of this coagulopathy; animal models of heatstroke coagulopathy is partially attenuated by administration of tissue factor inhibitors.22

## Conclusions:

Sustained hyperthermia acutely causes hypocoagulation through abnormal protein function and liver damage; subacutely through the development of DIC and consumptive coagulopathy.

- DIC is an independent prognostic factor for hospital ٠ mortality in cases of hyperthermic coagulopathy.DIC is an independent prognostic factor for hospital
- Hyperthemic coagulopathy and DIC are mediated by ٠ tissue factor released from damaged endothelial cells.
- Microvascular complications can cause multi-organ damage and intracranial infarction.

## Tables:

	Normal Results	Initial presentation	Day 1	Day 2	Day 3	Day 5	Day 8
WBC	4.2 - 9.1 thou/uL	6.2	2	2.2	7.9	3.7	7.4
RBC	4.6 - 6.1 mil/uL	4.7	3.6	3.4	2.2	2.3	2.6
Hemoglobin	13.7 - 17.5 g/dL	14.1	10.9	10.3	6.7	7.2	8.1
Platelets	150 - 330 thou/uL	192	42	67	67	28	82
PT	10.0 - 12.9 sec	>100	>100	45.1	29.9	24.3	15.4
INR	0.9 - 1.1 units	>8.4	>8.4	3.9	2.6	2.1	1.3
aPTT	25.8 - 27.9 sec	>200	>200	61.9	45.2	37	33.1
Fibrinogen	172 - 409 mg/dL	52	65	39	69	155	238
D-Dimer	0.0 - 0.5 ug/dL	>128	>128	>128	>128	44.06	16.4
R Time	4 - 10 min	20.8	20.8	11	10.6	8.2	5
K Time	1 - 3 min			9.9	5	2.8	1.2
A Angle	53 - 73 degrees	6.4	6.4	25.2	40.4	56.7	73
MA	50 - 72 mm	8.4	8.4	30.9	42.9	47.2	67.2
LY30	0 - 8%	0	0	0	0	0	0
Creatinine	0.67 - 1.17 mg/dL	3.7	4.9	6.22	4.3	3.4	5.4
GFR	-	24	17	13	20	27	15
AST	0 - 50 U/L	54	489	784	2990	1804	729
ALT	0 - 50 U/L	146	868	1080	2833	1251	685
Alk Phos	40 - 130 U/L	51	57	57	71	80	143
Bilirubin, direct	0.0 - 0.3 mg/dL	0.2	0.8	1.2	3.1	3.9	7.2
Bilirubin, indirect	0.1 - 1.0 mg/dL	0.2	0.3	0.4	1.1	1.5	1.5
Bilirubin, total	0.0 - 1.2 mg/dL	0.4	1.1	1.6	4.2	5.4	8.7
Haptoglobin	30 - 200 mg/dL	-	<20	-	-	-	-

## Table 1: Relevant Coagulation and Chemistry labs

Lactate 0.5 - 2.2 mmc	/L 4.5	3.1	-	-	-	-	
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#### Table 2: Initial Transfusion Therapy

	Day 1	Day 2	Day 3
FFP	6 U	4 U	2 U
PLT	2 U	1 U	-
RBC	1 U	1 U	1 U

Fresh Frozen Plasma (FFP), Platelet (PLT), Red Blood Cell (RBC)



## QUESTIONS

1. Which of the following organs systems are affected early by sustained hyperthermia?

- a. Hepatobiliary system
- b. Renal system
- c. Central nervous system
- d. Musculoskeletal system
- e. All of the above
- 2. Direct complications of sustained hyperthermia include:
  - a. Life threatening bleeding
  - b. Cerebral vascular accident
  - c. Meningitis
  - d. Diffuse rash
  - e. Answers A & B
  - f. Answers D & E

3. DIC is an independent prognostic factor for hospital mortality in cases of hyperthermic coagulopathy.

- A. True
- B. False

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While patient blood management (PBM) initiatives are increasingly adopted across the globe as part of standard of care, there is need for a clear and widely accepted definition of PBM. Endorsed by the World Health Organization (WHO), experts representing 16 PBM organizations\* convened to develop this definition:

## "Patient blood management is a patient-centered, systematic, evidence-based approach to improve patient outcomes by managing and preserving a patient's own blood, while promoting patient safety and empowerment."

A common definition for PBM will assist all those involved (PBM organizations, hospital administrators, individual clinicians including primary care physicians, etc.) to focus on the appropriate issues when discussing, teaching, and implementing PBM, thereby contributing to improved patient care and outcomes.

Before transfusion became a routine option, clinicians often utilized effective strategies to manage and preserve a patient's own blood by treating anemia and meticulously preventing/stopping bleeding. The emergence of transfusion medicine seemed to make those strategies obsolete. Illustrating how terminology can influence practice: Allogeneic blood transfusions were described as "life-saving" and became one of the most common and overused invasive hospital procedures.

In the early 1960s, renowned cardiovascular surgeon Dr. Denton Cooley pioneered what later became known as "bloodless surgery," treatment without allogeneic transfusion. His team adopted a 3-step approach that evolved into the "three pillars of PBM." By the mid-1990s, there were over 100 hospital-based bloodless medicine and surgery (BMS) programs that utilized multidisciplinary teams to combine and coordinate different strategies. In time, all forms of complex surgery and medical conditions were treated without resorting to blood transfusion. The outcomes were equivalent or better than those of patients with transfusion, so the principles were extended to their total patient populations.

The term "blood conservation" communicated a broader application: that a patient's own blood is a highly valuable and limited resource that must be "conserved and managed appropriately." However, the expanding list of available modalities go beyond simple "conservation," thus making the case for the more inclusive term "blood management." To underscore the "patient-centered" versus "product-centered" approach, the modern term "*patient* blood management" is the new standard of care for all patients. It focuses attention on good clinical management of the patient's own blood, just like any other organ or organ system, and is not about a specific intervention. patient engagement, shared decision-making, informed consent, and clinical follow-up. This overall approach is most likely to improve patient satisfaction and clinical outcome.

In contrast, a focus on appropriate transfusion and transfusion strategies can result in a practice that forgets that PBM is much more than a single therapeutic option. In fact, even appropriate transfusions can often be avoided with PBM. Within the context of acute surgical blood loss, blood transfusions are only a supportive therapy with limited effectiveness and safety concerns, especially if the source of bleeding is not controlled. PBM, however, is an integrated and comprehensive strategy that addresses the etiology of those anomalies, when possible, rather than promoting a short-term therapy (transfusion) without addressing the underlying cause. The approach includes some 100 measures that grouped under the problem-based "ABC Toolbox of PBM": anemia, blood loss, and coagulation.

The proposed definition also extends beyond patients about to undergo invasive procedures with high risk for transfusion. For example, across the globe, an estimated 2.4 billion people (predominantly women) are anemic, and half of them have iron deficiency anemia (IDA). Those suffering from iron deficiency without anemia could be at least double those with IDA. Many of these patients are probably not "in need of a transfusion" but they are definitely in need of PBM. Clearly, there is an unmet need that PBM can address.

Just as the application of PBM is a dynamic process, its definition will evolve with time as science, medical practice, and patient preoccupations, priorities, and preferences change. The endeavor is a work in progress. Accordingly, those involved in the preparation of this definition call upon all stakeholders including other PBM organizations to join them and reconvene to review and revise the definition over the coming years.

## Contributor: Leilani Rangel

\* The Global Definition of PBM is endorsed by International Foundation for Patient Blood Management (IFPBM); the Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis (NATA); the Society for the Advancement of Patient Blood Management (SABM); the Western Australia Patient Blood Management (WAPBM) Group; the American Society of Anesthesiologists' (ASA) Committee on PBM; the Asia-Pacific Society for Patient Blood Management (ASPBM); the Chinese Society for Patient Blood Management (CSPBM); the Korean Society for Patient Blood Management (KPBM); the Korean Society of Anesthesiologists (KSA); the Malaysian Society of Haematology (MSH); the Canadian Ontario Nurse Transfusion Coordinator (ONTraC) Program; the South African National Blood Service (SANBS); National Association of Patient Blood Management Specialists Russia Federation (NAS PBM); the American Society of Extracorporeal Technology (AmSECT); the Anemia Working Group Spain (AWGE); and the Society of Cardiovascular Anesthesiologists (SCA).

Accordingly, PBM starts with diagnosis, followed by the consideration of appropriate patient-specific therapeutic options for management of that patient's diagnosis, with

Full text article available here: <u>https://journals.lww.com/anesthesia-</u> analgesia/Abstract/9900/A\_Global\_Definition\_of\_Patient\_Blood\_Manage ment.312.aspx



Advancements in modern medicine have presented a range of options for patients who refuse blood transfusions. Questions arise regarding various procedures, and recently a Jehovah's Witness patient with a high triglyceride level was informed that he needed "plasmapheresis" to significantly lower the 4,400 mg/dL of triglycerides in his system prior to a coronary artery bypass procedure. He wondered, as a patient refusing blood transfusions, if this procedure could be utilized?

**RECENT HISTORY:** In the late 1950s, apheresis was used routinely to treat a type of lymphoma and in the 1970s further successful treatment of a wide range of autoimmune diseases. The American Society of Apheresis (AFSA) was developed in the late 1970's for the purpose of presenting scientific research on donor and therapeutic apheresis (TA) modalities. Currently, ASFA's most recent guidelines include 84 fact sheets for relevant treatment of disease with 157 indications for the use of therapeutic apheresis.<sup>1</sup>

WHY DEVELOPED: Apheresis covers a broad category that encompasses therapeutic apheresis to separate and remove components and/or other substances in a patient's blood; secondly, the donation of blood components and thirdly, the increasing use of apheresis to collect products for cellular therapy manufacturing. Therapeutic apheresis is commonly used in solid organ transplant in the area of histocompatibility and human leukocyte antigen (HLA) crossmatching which helps to predict which donated organs are most compatible with certain prescreened recipients.<sup>2</sup>

Therapeutic plasma exchange is a procedure remove antibodies from a patient's blood to treat autoimmune diseases. Along with TA, there are emerging alternative therapies involving monoclonal antibody therapies. Research and clinical trials are receiving increased funding to explore even broader applications.<sup>3</sup>

**WHAT THERAPIES:** Therapeutic apheresis is basically the process of separating a patient's blood into the major components and then removing or sometimes manipulating the selected component to treat the disease effecting the patient. While there are about six (6) common procedures termed therapeutic apheresis, we will discuss these four below:<sup>4</sup>

<u>Therapeutic plasma exchange (TPE)</u> is essentially removing the patient's plasma by utilizing either centrifugation or

LDL (or low-density lipoprotein) apheresis is usually necessary for disorders that are genetic mutations that may cause high levels of LDL cholesterol.

<u>Extracorporeal photopheresis (ECP)</u> is a treatment of mononuclear blood cells that have a round nucleus, then a photoactivating agent is introduced and these cells are exposed to ultraviolet A light. It is used to treat erythrodermic manifestations of cutaneous T-cell lymphoma, primary graftversus-host disease usually following allogeneic stem cell or bone marrow transplant, solid organ transplant rejection, systemic sclerosis and inflammatory bowel disease. If a patient is refusing blood transfusions for religious reasons, the acceptability of this procedure would depend on their view of blood treated outside the body and reinfused.

**HOW IS IT ACCOMPLISHED:** Apheresis includes three steps: first, drawing whole blood/adding anticoagulant and then separating the blood components. Second: the targeted component(s) is removed. Third: the remaining components are returned to the patient with or without replacement fluids. Basically, these steps require a piece of equipment that uses filtration, centrifugation or a combination of both.<sup>5</sup> Modern apheresis equipment has made such advancements in technologies that, along with expanding the practice of therapeutic apheresis and the potential to benefit a vast patient population, it can also be utilized by patients who may refuse blood product transfusions.

The patient mentioned at the beginning opted for the TA procedure to remove the triglycerides in the amount of 5 liters from his system. Four days later, he had a successful cardiovascular pulmonary bypass procedure without a blood transfusion.

## Contributor: Jessica Varisco

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filtration techniques, with the goal to remove pathological substances associated with disease. These substances may include antibodies, immune complexes, cryoglobulins, toxins or lipids. Replacement of fluids for a patient refusing blood could be albumin, if acceptable to the patient, but not plasma.

<u>Red blood cell exchange (RBCX</u>) uses the therapeutic apheresis technique to rapidly remove abnormal red blood cells that may be contributing to a disease process. They are replaced with allogeneic or donated red blood cells, so the procedure would not be acceptable to patients who refuse blood transfusions. exchange with 5% albumin to modify cerebrospinal fluid and plasma amyloid-concentrations and cognition outcomes in Alzheimer's disease patients: a multicenter, randomized controlled clinical trial. *J Alzheimer's Dis.* 2017;56-129-143.

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