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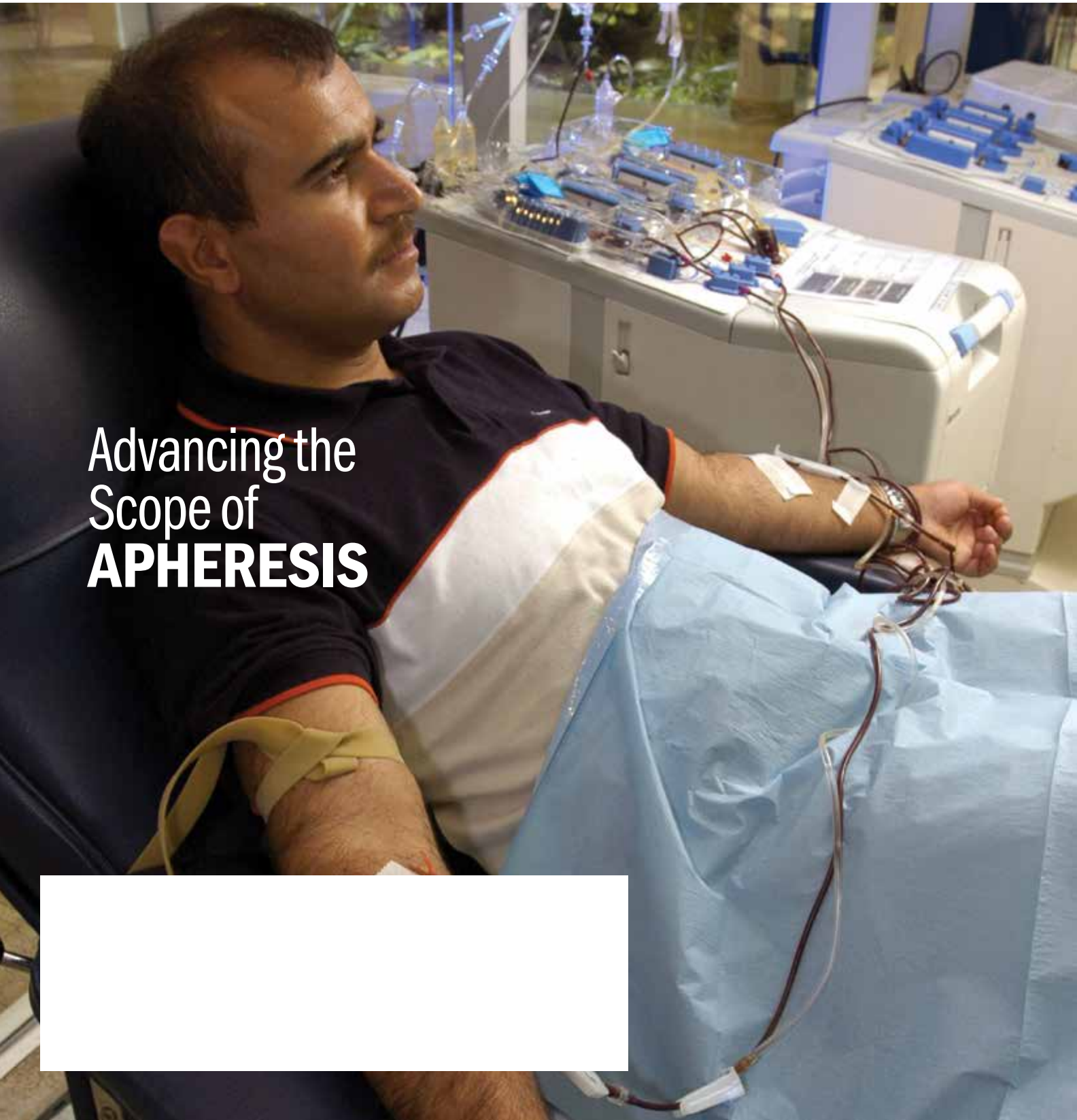
AABB News



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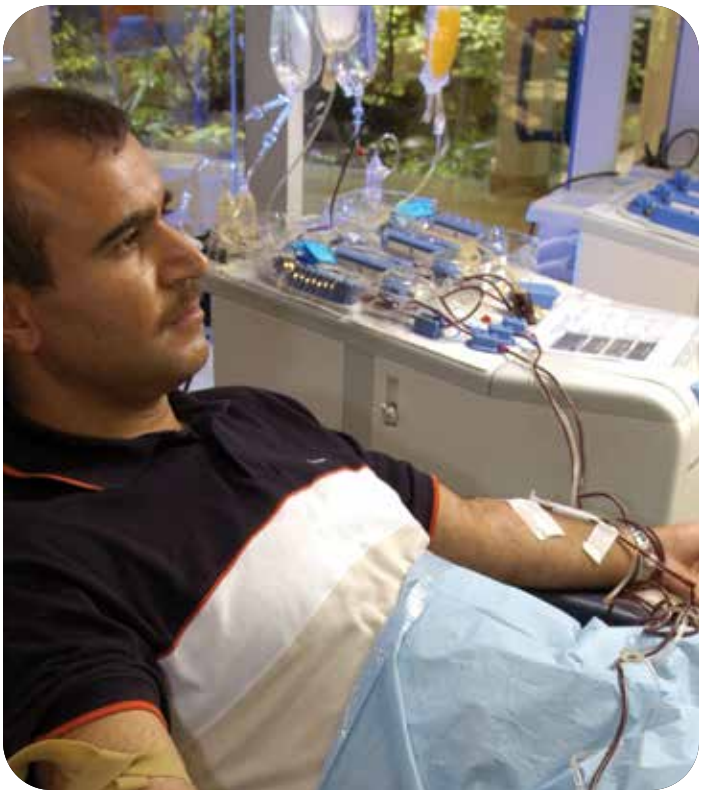

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Alternative or adjunctive therapies may be desirable for some of the diseases treated with therapeutic plasma exchange.

Apheresis Takes Center Stage

When the topic of apheresis comes up, it has become necessary to specify which particular aspect of apheresis. The procedure known as apheresis has become a broad category that encompasses therapeutic apheresis to remove something unwanted from a patient's blood, the donation of blood components like platelets through apheresis and, increasingly, the use of the procedure to collect products for cellular therapy manufacturing. The April issue of *AABB News* focuses on various aspects of apheresis.

Conducting research in therapeutic apheresis is made more complicated by the multitude of rare conditions it is used to treat and the difficulty of finding sufficient patients to complete a study. The first feature article, which begins on page 10, discusses the research supporting therapeutic apheresis and notes the areas in which further research is needed.

One area in which therapeutic apheresis is commonly used is to prevent solid organ transplant recipients from rejecting the transplanted organ. The second feature, starting on page 16, covers the complex area of histocompatibility and HLA crossmatching, and describes procedures that can be used to predict which donor organs are best transplanted into which patients to decrease the need for apheresis in organ donation recipients.

Therapeutic plasma exchange is an important procedure that treats — but does not cure — most of the conditions for which it is used. A third feature article, beginning on page 20, discusses

David Green, MSA

emerging alternatives to therapeutic apheresis and lists several adjunctive therapies, such as the monoclonal antibodies rituximab and eculizumab.

Fourth Edition of *Apheresis: Principles and Practice*

The fourth edition of *Apheresis: Principles and Practice*, the foremost textbook on apheresis is coming out in an expanded three-volume format, which will provide sufficient space to explore each area thoroughly. The first volume, which was published by AABB in December, covers therapeutic apheresis. The second, which should be out shortly, focuses on the collection of blood products through apheresis and donors. The third volume, which will be published this fall, will explore the emerging field of cellular therapy applications of apheresis. In addition to providing eexpanded information and more guidance than in the previous volume, the new three-volume format allows readers to purchase only the volumes that are relevant to their work.

David Green, MSA
AABB President

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Subsections: Additional AABB Membership Benefits

By Christopher Bocquet
Director of Standards

AABB members benefit by having access to a multitude of opportunities to volunteer their time and share their expertise. The various opportunities include committees, work groups, task forces and participation in various educational endeavors. Another key opportunity is the Transfusion Medicine Section and Subsections. "The Transfusion Medicine Section Coordinating Committee [TMSCC] is a great opportunity to learn from others and share your experiences, knowledge and expertise," said Jeff Winters, MD, TMSCC chair. "I have learned so much being involved, which has helped me provide better patient care, all while making friends and contacts."

The AABB Transfusion Medicine Section and its associated subsections are open to all AABB members. Membership usually entails meeting monthly and working on projects, and the group offers the chance for members to expand their networks. But unlike other volunteer opportunities provided by AABB, these positions give members the chance to select precisely how much time they wish to commit to the related activities. Some members choose to lead webinars and direct publication reviews, while others simply participate via listening into monthly or bimonthly conference calls.

The Transfusion Medicine Section comprises 10 subsections based on focused topic areas. The 10 subsections are:

- Clinical Hemotherapy
- Donor and Blood Component Management
- Global Transfusion Forum
- Leadership and Administrative
- Pediatric Transfusion Medicine
- Quality and Regulatory
- Technical Practices and Serology
- Therapeutic Apheresis and Transfusion Practices
- Transfusion Fellowship Directors
- Transfusion Safety and Patient Blood Management


Jeff Winters, MD


Patrick Ooley, MS, MT(ASCP), CQA(ASQ)CMQ/OE


Tracie Nichols, MS, MLS(ASCP)SBB

Each subsection has a leader who is elected by subsection members and who can serve for up to two 3-year terms. Subsection members also determine the group's projects. For instance, the Leadership and Administrative subsection conducted four webinars devoted to specific aspects of leadership, including leading through change, succession planning, virtual leadership and the characteristics of a leader. "Our subsection provides an open forum for likeminded individuals to freely discuss current issues, trends or needs related to leadership," said Patrick Ooley, MS, MT(ASCP), CQA(ASQ)CMQ/OE, chair of the subsection. "Our members transcend all AABB disciplines, and we provide a great venue to share, learn and improve practices, bringing value to all who participate. Our goal is to provide a cost-free environment to develop and grow our leadership skillset," he said.

The Transfusion Safety and Patient Blood Management Subsection meets every other month and devotes a portion of each meeting to the Journal Club, in which members review and discuss relevant studies and articles.

Tracie Nichols, MS, MLS(ASCP)SBB, is the chair of the Quality and Regulatory

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Subsection. She said, "The TMSCC has helped me to grow in my career and push myself to new levels. I have been able to learn and also teach others while being a part of several committees. It is nice to have a large network of colleagues to be able to poll whenever a new and challenging subject arises in order to receive many differing perspectives on the topic and come to a consensus on how to handle the issue."

In 2020, most subsections were involved in revising titles from AABB's Guideline series (now called "Guides") from the 2000s, to bring them up to date with changes in practice and technology since they were first written. In the coming year, the Quality and Regulatory Subsection plans to focus its efforts on creating a webinar series and quality toolkits focused on root cause analysis, the use of different tools to affect change.

The Global Transfusion Forum brings together AABB members from around the world to discuss issues that affect countries in lower- and middle-income countries, as determined by the World Health Organization. The Forum works on projects focused on public policy, research and education that have been published in *Transfusion*, mainly through surveys of interested and known parties.

AABB provides a place for everyone to participate. To sign up for one or more of the subsections, AABB members can click on the "Get Involved" button on the AABB website and select "Committees and Sections" and then "Enroll in a Subsection." This will update your profile to indicate the subsections in which you have expressed an interested. For more information concerning participation in a (or all) subsections, please contact AABB's Standards Department at standards@aabb.org. ■

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Chair of the Leadership and Administrative Subsection of the TMSCC

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Improving Pediatric PBM Using Automated Processes

By Jerilyn Schweitzer, MA
Managing Editor

Evan Orenstein, MD, is an assistant professor of pediatrics and clinical informatics at Emory University in Atlanta. Orenstein received a National Blood Foundation early-career Scientific Research Grant in 2020 for his research project, titled "Improving Patient Blood Management [PBM] in Pediatrics through Automated Medical Error Detection and Clinical Decision Support Design." In this project, Orenstein's team plans to create and validate automated "trigger tools" to detect medical errors related to pediatric blood transfusion. They will then develop and evaluate clinical decision support systems to target the most burdensome errors detected. The researchers believe that these efforts will support future clinical research to determine the best design for electronic health records (EHRs) to promote pediatric PBM. *AABB News* spoke with Orenstein about his research, the NBF and how technological advances are transforming the field.


Evan Orenstein, MD

"My hope is that this research will lead to both automated dashboards that can be used by pediatric health systems to monitor the safety of their pediatric blood management program and a set of clinical decision support interventions targeting identified safety issues to promote safe transfusion practices in children," Orenstein said. He added that he hopes to have early results by next summer that validate a number of trigger tools, with candidate decision support designs by the end of 2021. "We will likely expand work on trigger tools into 2022 and perform more advanced usability studies in 2022 as well," he said.

Technology and Data

When asked how he sees technology transforming the field of transfusion medicine, Orenstein explained that transfusion is very complex from a technological perspective — with many interacting information systems — a medical perspective — in which the "right" thing to do is not always easy to define — and a social perspective based on interactions among physicians, nurses, the blood bank, the lab and so many other factors. "In a complex system, it's very easy to try to develop simple solutions that cannot handle important nuances," he added. "EHRs and clinical decision support have the potential to make a big dent in patient harms from inappropriate patient blood management, but the interventions must be carefully crafted to consider all the sociotechnical features of this system. I think the next phase will be for technology to provide 'just-in-time' education to the many users involved in transfusion to help them make evidence-based decisions at the bedside," he said.

Orenstein told *AABB News* that his interest in data-driven policies began when he was an undergraduate working in infectious disease modeling. When he was in medical school, Orenstein expanded on those interests when he worked on a clinical trial of maternal influenza vaccine in Bamako, Mali. "My role at the time was to serve as a study coordinator for the trial and also lead a sub-study focused on the cost-effectiveness of maternal influenza vaccine in low-resource settings," he said. While in Mali, Orenstein helped build a simple information system to track outcomes for more than 5,000 pregnant women, mothers and infants in an area with one of the highest maternal and infant mortality rates in the world. "Because of that active surveillance," he said, "we identified problems that had little to do with the vaccine trial itself but nonetheless presented opportunities to improve the health of these women — for example gaps in maternal tetanus vaccination, use of antenatal steroids and other evidence-based

interventions." Orenstein added that he had the opportunity to work with local stakeholders and develop interventions addressing some of those gaps, and he fell in love with the idea of information systems driving quality improvement initiatives that could have a real impact on health.

Focus on Pediatrics

In medical school, Orenstein was drawn to pediatrics and internal medicine because he liked the problem-solving aspects of both fields. He chose pediatrics because "working with kids was a little more fun for me, most kids do get better and when you make a difference in a child's health, they have their whole life ahead of them still."

Orenstein added that when he was an intern at Children's Hospital of Philadelphia, he was both impressed and frustrated with another automated process: the facility's EHRs. On one hand, he found that EHRs led to improved care when they were based on well-designed order sets that helped him select appropriate treatments. On the other hand, "the EHR felt very inefficient and cumbersome in other areas where I felt like I was double-documenting, dealing with too many pop-up alerts or where the decision support did not match my workflow," he said. Orenstein added that after taking an elective in clinical informatics, he found a whole field of people interested in using information systems to improve health. "It was a major eye opener for me," he said, "and I haven't looked back since."

A few years after Orenstein completed his residency in pediatrics and a fellowship in clinical informatics, he began working at Emory University and Children's Healthcare of Atlanta. "When I landed here," he said, "the system had prioritized safety issues focused on pediatric transfusion. At the time I did not know very much about the field, but I was blessed with enthusiastic, engaged mentors, and we were able to combine their expertise in transfusion medicine with what I had learned about driving change through information systems." Subsequently, the group developed a series of interventions and demonstrated improved adherence to many evidence-based practices in pediatric transfusion. "Nonetheless, our new surveillance also uncovered additional problems — the complexity of pediatric transfusion combined with its importance for health and quality of life have drawn me in further, and I look forward to working more in this field," he said.

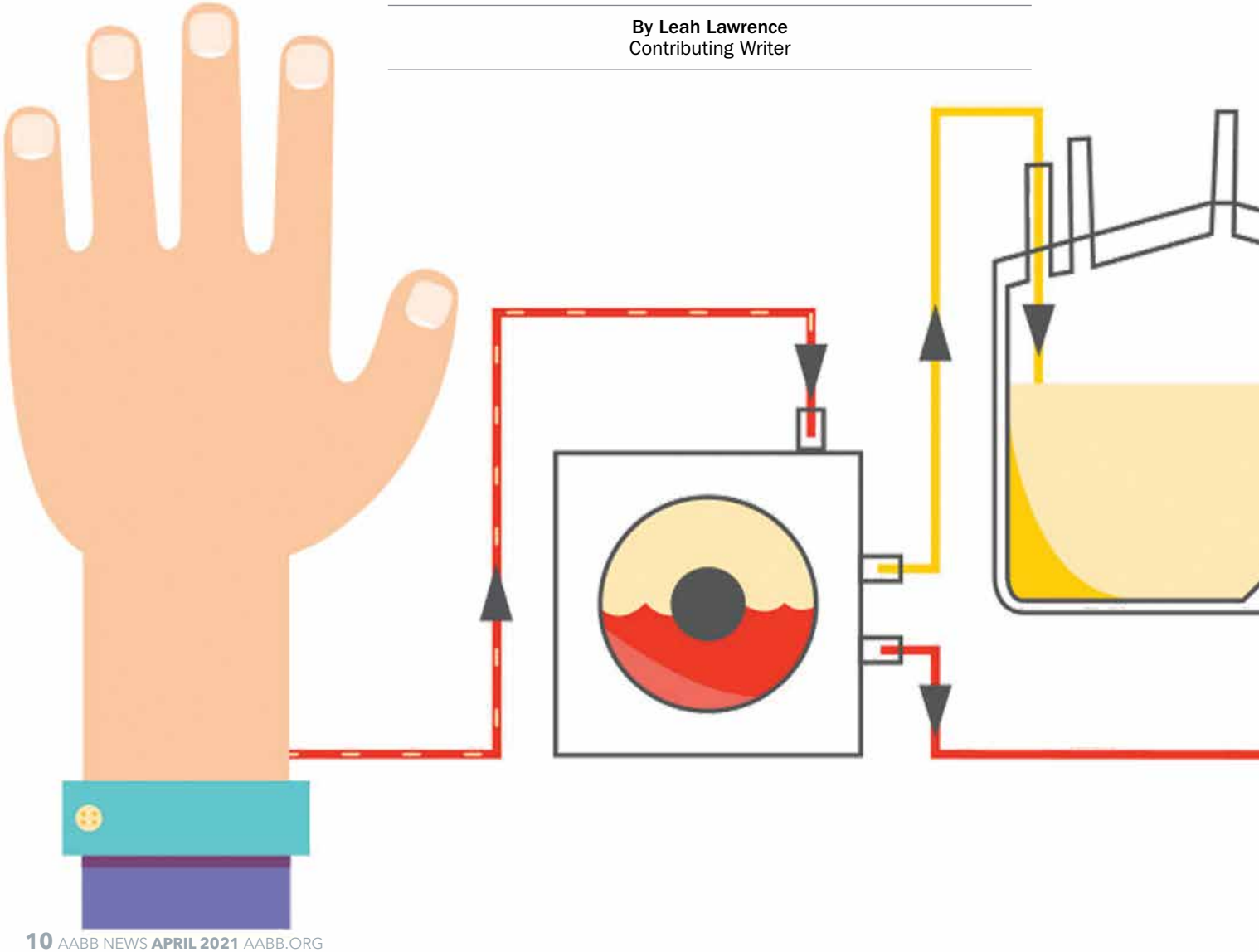
When asked where he was when he learned he had received the NBF early-career Scientific Research Grant, Orenstein said, "I was in my office perusing my email between meetings. It was hard to hide the smile on my face for the rest of the day!" He added that the NBF award has opened a lot of doors for him within the institution by demonstrating how clinical informatics can be used to promote patient safety. "In addition to providing me with extra time to pursue this project," he said, "it has helped garner investment from within the organization to grow our clinical informatics program and integrate it into transfusion safety efforts."

Since its inception in 1983, the National Blood Foundation (NBF) has awarded more than $11 million to early-career investigators and boosted the careers of more than 200 leaders of the blood and biotherapies community. Your donation can help a deserving early-career scientist like Orenstein.

Apheresis: What the Evidence Supports and Where More Research is Needed

Specialists encourage continued use of clinical trials to advance knowledge about the benefit of apheresis.

By Leah Lawrence
Contributing Writer



Clinicians that choose to study and practice apheresis are exposed to a multitude of medical conditions, diverse medical specialties and patients of all ages. This diversity is often what makes the field both exciting and challenging to practice, but it also makes progress in the field more difficult.

"I treat newborns and geriatric patients with a variety of disorders from metabolic disorders to malignant disorders to autoimmune disorders and more," said Jeffrey L. Winters, MD, director of the Therapeutic Apheresis Unit at Mayo Clinic College of Medicine. "The problem, though, is that because so many of the disorders we treat are rare, it is often quite difficult to accrue patients to clinical trials."

Modern apheresis has existed since the 1970s. Despite this long history, there are still conditions for which it is used as a treatment without a good, evidence-based understanding of why or how it works, or even if it provides benefits.

The American Society for Apheresis (ASFA) publishes regular updates to its guidelines on the use of therapeutic apheresis in clinical practice. Its most recent issue included 84 fact sheets for relevant diseases with 157 indications for therapeutic apheresis modalities.[1] Many of these indications were categorized as "optimum role of apheresis therapy is not established."

"These are resource and labor intensive treatments done in specialized institutions," Winters said. "Not only is it important to do trials to show that apheresis provides a benefit, but also to show cases where it may not."

Barriers to Trials

One of the barriers to performing clinical trials in therapeutic apheresis is a lack of funding, according to Yanyun Wu, MD, director of transfusion medicine at University of Miami Health System and Jackson Health System.

"The apheresis approach is often considered not as scientifically driven," Wu said. "It can be considered more like a black box expedition versus specific targeted treatment."

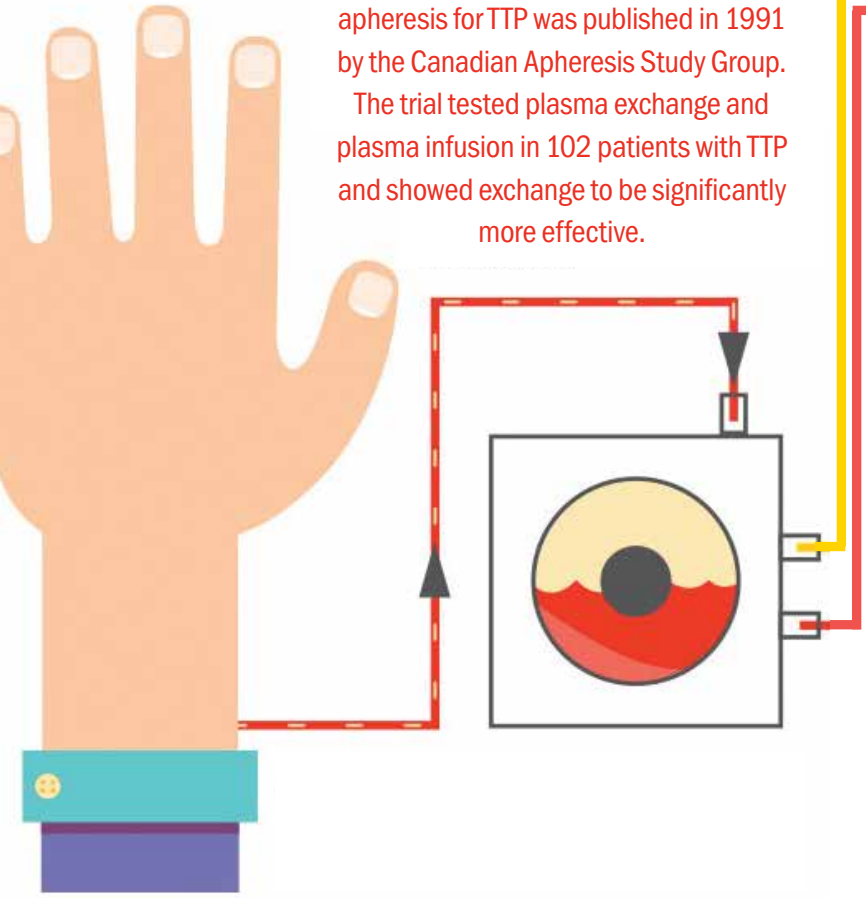
Additionally, there is a lack of industry-funded trials because the conduct of clinical trials may not be much of a value-add for these stakeholders and can be very costly, she said.

Apheresis researchers also struggle to obtain sufficient funding from the National Institutes of Health (NIH), Winters said.

"Apheresis ends up falling into a category where it is competing with trials in the hematology space," Winters said. "The competition is fierce to get that funding, and we struggle because of the rarity of the diseases we deal with."

Many grant applications for other clinical trials are supported by previously conducted basic science. Apheresis does not have a lot of relevant animal models upon which to research various treatments, Winters said. "That works against us as well," he said.

Another barrier is patient accrual, Winters added. Even if one institution decides to lead a trial on apheresis, it is hard to find enough patients with these rare disorders. Often the trial has to be expanded to other centers, making it difficult to find other co-principal investigators



One of the first trials to establish apheresis for TTP was published in 1991 by the Canadian Apheresis Study Group. The trial tested plasma exchange and plasma infusion in 102 patients with TTP and showed exchange to be significantly more effective.

to support the trial, Winters said. Apheresis is also frequently used in acute settings, which are very difficult to study in trials.

Trials are Vital

Based on the available evidence, the ASFA has categorized conditions treated with apheresis into four groups:

Category I – disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.

Category II – disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.

Category III – optimum role of apheresis therapy is not established. Decision making should be individualized.

Category IV – disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB approval is desirable if apheresis treatment is undertaken in these circumstances.

The most commonly known example of a Category I application of apheresis is the treatment of thrombotic microangiopathy (TTP), which also has grade IA evidence, Wu said.

TTP is a potentially fatal thrombotic disease. If untreated, mortality is estimated to be about 90%.[1] The condition is associated with a severe deficiency of plasma ADAMTS13 enzyme activity, which maintains normal distribution of von Willebrand factor multimers.

One of the first trials to establish apheresis for TTP was published in 1991 by the Canadian Apheresis Study Group.[2] The trial tested plasma exchange and plasma infusion in 102 patients with TTP and showed exchange to be significantly more effective.

"They essentially flipped the mortality on its head," Winters said. "Instead of 90% dying, now only 10% were dying."

Another well-established treatment area is in Guillain-Barre syndrome (GBS), a paralyzing disorder caused by inflammation of the peripheral nerves. Here studies have compared intravenous immunoglobulin, plasma exchange, supportive care and combination treatments.

In contrast, a recent trial showed that plasma exchange was not beneficial for severe antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis. In 2020, results of the PEXIVAS study showed that among patients with severe ANCA-associated vasculitis, plasma exchange did not reduce the incidence of death or end-stage kidney disease.[3]

"At my institution, we are not doing plasma exchange for that indication anymore," Winters said. "My colleagues in critical care and pulmonology don't even ask anymore."

New Therapeutic Areas

Another large area of exploration is the role of plasma exchange in the context of diseases related to aging, according to Zbigniew "Ziggy" M. Szczepiorkowski, MD, PhD, FCAP, professor of pathology and laboratory medicine at Dartmouth-Hitchcock Medical Center, Lebanon, N.H. The treatment is especially of interest in treating Alzheimer's disease.

"The cause of Alzheimer's disease still is not well understood, which limits therapeutic options, though many have been tried and failed," Szczepiorkowski said. "However, a group in Barcelona decided to explore the two out of several things we did know about the disease: the accumulation of a protein in

the brain that causes the brain to malfunction and abnormally behaving albumin."

An early study looking at plasma exchange in Alzheimer's showed that plasma exchange with albumin modified cerebrospinal fluid and plasma amyloid-βpeptide levels in patients with mild-to-moderate Alzheimer's disease.[4]

More recently, results of the phase 2b/3 AMBAR randomized controlled study tested three plasma exchange treatment arms of albumin and intravenous immunoglobulin replacement compared with a sham procedure in patients with mild-to-moderate Alzheimer's disease.[5] Patients treated with plasma exchange performed significantly better on an Alzheimer's Disease Cooperative Study–Activities of Daily Living score and had a trend toward better Alzheimer's Disease Assessment Scale-Cognitive Scale.

"This was a big study looking at more than 300 patients for 14 months," Szczepiorkowski said. "It showed an effect of slowing Alzheimer's disease in those patients that received active treatment."

Unfortunately, Wu noted, the results of this study do not seem to be widely accepted by neurologists or other relevant treating groups.

"Despite showing good evidence, it does not seem to have changed the perspective of providers," Wu said. "We have to explore why that is and whether people perhaps think the outcome is not worth the treatment."

Remaining Knowledge Gaps

Continued efforts to conduct clinical trials will help to further narrow down conditions for which treatment with apheresis is clinically and scientifically sound. Foremost among those knowledge gaps is gaining a better understanding of the mechanism of action of these treatments.

A great example of this need is in the area of photopheresis, Wu said. Photopheresis is a cell-based immunomodulatory therapy where leukocytes are collected from the peripheral blood and exposed to a photosensitizing agent then treated with ultraviolet radiation before they are re-infused.

"This was a type of 'black box' treatment where people did not really know what is happening," she said.

Winters agreed, calling it a bit of an "oddball" procedure.

"This procedure can enhance the immune system response," Winters said. "For example, in patients with a certain type of lymphoma, it can teach the immune system to recognize lymphoma cells. On the flip side, it can induce immune suppressive response to prevent things like graft-versus-host disease."

Now there are major advancements in the understanding of the mechanism of photopheresis, the treatment can be polarized into both directions and clinical applications of these advancements need to be explored further, Wu added.

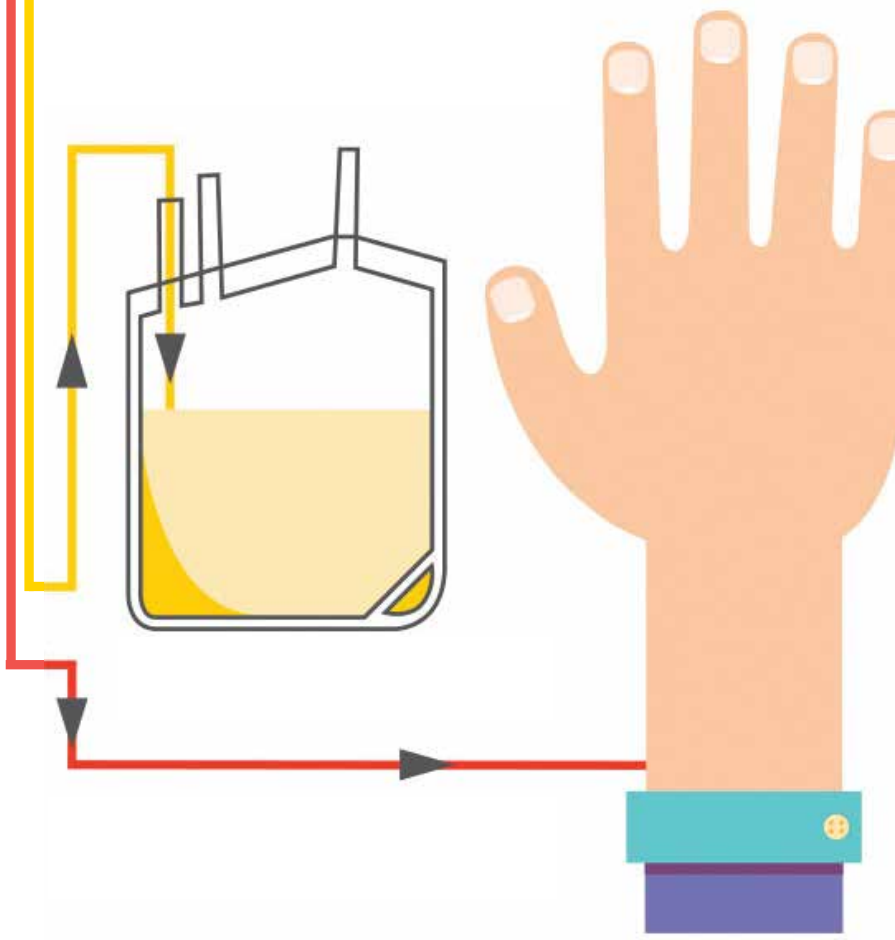
"Continued research can help us to understand how the treatment induces its effect and to adjust parameters of the procedure to try to maximize that effect," Winters said.

Even in areas with more evidence, like in Alzheimer's disease, more data needs to be generated to explain the mechanisms that produced the results seen in the AMBAR study, Winters said.

Future Directions

Finally, Winters said that he hopes the field of apheresis will continue to optimize available treatments.

"If we move outside of the United States and look to



Europe and Japan, we see a lot of apheresis treatment that involves selective removal of substances from the blood," Winters said. "In other words, they separate plasma out and pump that plasma though a column that contains something to clean the plasma before it is returned to the patient."

These plasma fractionators and immunoadsorption columns are only just gaining traction in the U.S., Winters said, and only in certain therapeutic areas. There remains a great lack of access.

A recent example of a use of these columns is the Depuro D2000 Adsorption column used for the treatment of COVID-19, which received emergency authorization from the FDA in 2020.[6] Patients admitted to the intensive care unit with confirmed or imminent respiratory failure can receive treatment with this system, which reduces the number of cytokines and other inflammatory mediators in the blood. [7]

Instead of using these types of columns, clinicians in the U.S. are forced to do bulk extractions.

"One of the big focuses we have is trying to get people to generate antibodies," Winters said. "When I do that plasma exchange, I am removing any antibody the patient has generated."

To continue to make progress, Wu said, apheresis clinicians and researchers have to continue to embrace a pioneering spirit.

"Often apheresis treatments go through a cycle," she said. Meaning apheresis is often initially tried when nothing else is working.

"If it works, we then have to figure out why it worked," Wu said.

Resulting research demonstrating how apheresis was effective often leads to a better understanding of disease mechanisms, and that may lead to a change in treatment or the development of drugs.

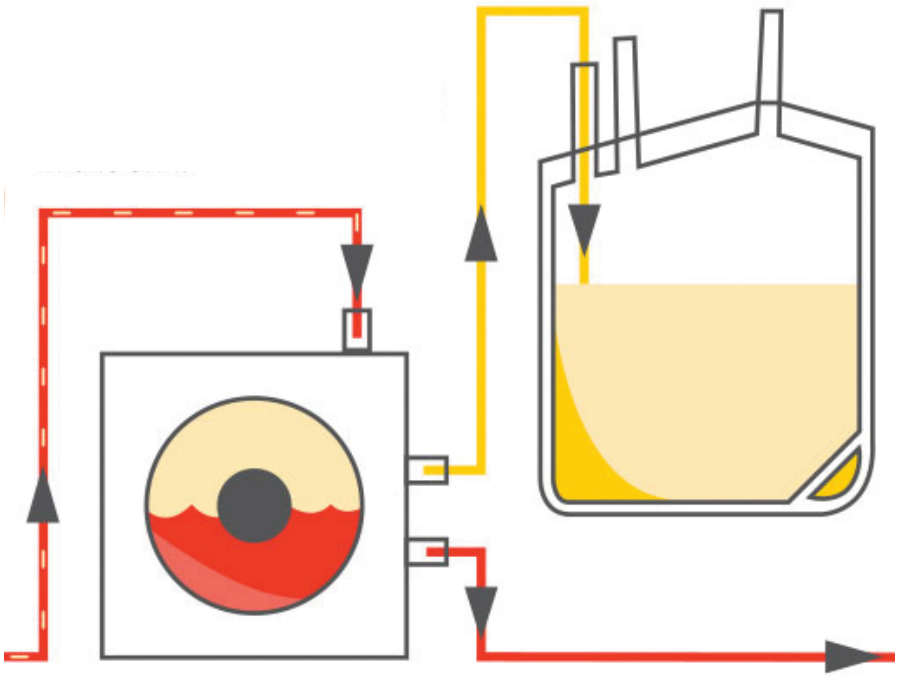
"As a result, apheresis may be removed as a treatment," Wu said.

Szczepiorkowski said this is known in the field as being "one drug away" from extinction.

"Once we know the pathology, we may realize that what we are doing with apheresis could be replaced by a medication," Szczepiorkowski said. "And there is nothing wrong with that."

Specializing in the field of apheresis will likely always be associated with exploring a bit of the unknown, Wu said.

"We must continue to be innovative, adaptive and inquisitive," Wu concluded. "If our discoveries alter treatment for one disease, we must just move on to helping with the next." ■



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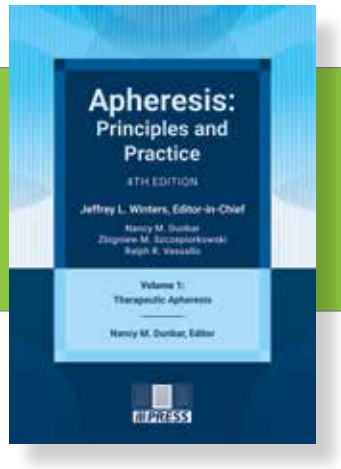
AABB Expands Apheresis Resource Into 3 Volumes



AABB has expanded the fourth edition of *Apheresis: Principles and Practice* into three volumes. The book, considered by many to be the preeminent textbook for apheresis, provides the latest information on the different aspects of apheresis in an expanded, three-volume format that offers expanded information, greater detail and more guidance than was available in the previous editions. In addition to providing expanded space for key topics in apheresis, the three-volume format allows for more timely updates to rapidly changing subjects, such as cellular therapy applications, and for readers to purchase only those volumes that meet their professional needs. The roster of authors for all three volumes represents the top experts in the field of apheresis.

Jeffrey Winters, MD, editor-in-chief of the 4th edition and a member of the AABB Board of Directors, said this new resource is essential for medical professionals. "*Apheresis Principles and Practice* is being updated and expanded to provide coverage of the advances in the field and changes in practice since the publication of the 3rd edition of this AABB classic," he said.

A Focused Approach

The first volume, which was released in December 2020, focuses on therapeutic apheresis and is consistent with the most recent guidelines from the American Society for Apheresis (ASFA) that were published in the *Journal of Clinical Apheresis 8th Special Edition*. In fact, many chapter authors served on the Special Issue Writing Committee that came up with the guidelines. "Volume 1, *Therapeutic Apheresis*, provides comprehensive coverage of the clinical use of apheresis in patient care," said Winters. "It provides detailed and practical information that will be of benefit to both the novice and veteran practitioner of apheresis medicine."

Volume 1 covers the history of apheresis, basic principles, patient management and disease-specific applications, with an updated and expanded list of health conditions not included in the previous edition. Each chapter has been updated with the results of clinical studies that were published after the third edition came out, and suggested readings have been updated to include recently published literature. This volume also includes the perspectives of nurses and technologists who work with apheresis instruments and understand how to care for apheresis patients.

The second volume of *Apheresis Principles and Practice*, fourth edition, which is scheduled to be released in April, deals with the collection of blood products by apheresis. "This volume covers all aspects, including devices available for collections, selection and care of the apheresis donor, as well as the quality and regulatory aspects of the collection and manufacture of apheresis blood products," said Winters. "The book is an essential reference for those working in a stand-alone or hospital-based blood collection center that performs apheresis collections. The volume includes new content since the previous edition, including information concerning pathogen reduction of platelets and this technology's influence on platelet collection by apheresis."

AABB plans to release the third volume in the fall of 2021. This text will explore the emerging field of cellular therapy applications of apheresis, which, according to Winters, will include the collection of cells for hematopoietic stem cell transplantation and chimeric antigen receptor (CAR) T-cell manufacturing, as well as the collection of peripheral blood-derived cells for other regenerative medicine uses. "In addition to describing the apheresis devices used for these collections," explained Winters, "the text also includes those apheresis devices utilized in the cell manufacturing and processing lab for further processing of the cells." As in the second volume — which deals with blood donors — Volume 3 covers the selection and care of donors for cells used for cellular therapy products. It also discusses regulatory and accreditation requirements. Finally, Volume 3 includes information on extracorporeal photopheresis as this therapy represents a cellular therapy used to alter the immune system similar to the other therapies discussed in this volume. "Volume 3 provides an up-to-date review of this rapidly changing area with chapters written by experts," concluded Winters. ■

Demystifying HLA and the importance of consulting with the experts

The Hard Reality of Histocompatibility

By Laura Fusco
Contribuiting Writer

The offer of a donor organ arrives for a 25-year-old man on peritoneal dialysis due to polycystic kidney disease. An offer like this may come at any time of the day or night after coordinators determine a potential match through the web-based application known as the Organ Procurement and Transplantation Network (OPTN) from the United Network for Organ Sharing (UNOS). Based on blood type, a coordinator will contact the human leukocyte antigen (HLA) laboratory and inquire whether the patients on the match run are suitable recipients for the deceased donor's organ based on HLA typing and recipient HLA antibody profile.

"If we have recipient antibody testing results from the last 30 days, we can do a 'virtual crossmatch' (VXM) and if it's negative, we can recommend the patient be transplanted," said Cliff Sullivan, MD, assistant professor of pathology at Emory University in Atlanta. "We don't always have to do a prospective physical crossmatch if the VXM is negative and we have no other immunologic concerns."

This patient was matched with a kidney and doctors were initially optimistic. "There were no concerning antibodies and the physical crossmatch done retrospectively within 24 hours of surgery was cleanly negative," Sullivan told *AABB News*. "But on post-op day 40, we noticed his creatinine levels increasing, and pretty rapidly, his kidney stopped producing urine."

A biopsy showed antibody-mediated rejection. Another antibody profile was ordered and then the HLA laboratory could see donor-specific antibody (DSA) to the donor, evident with Class II antibodies. What had happened? For a better view into this case, it is important to grasp the fundamentals of HLA.

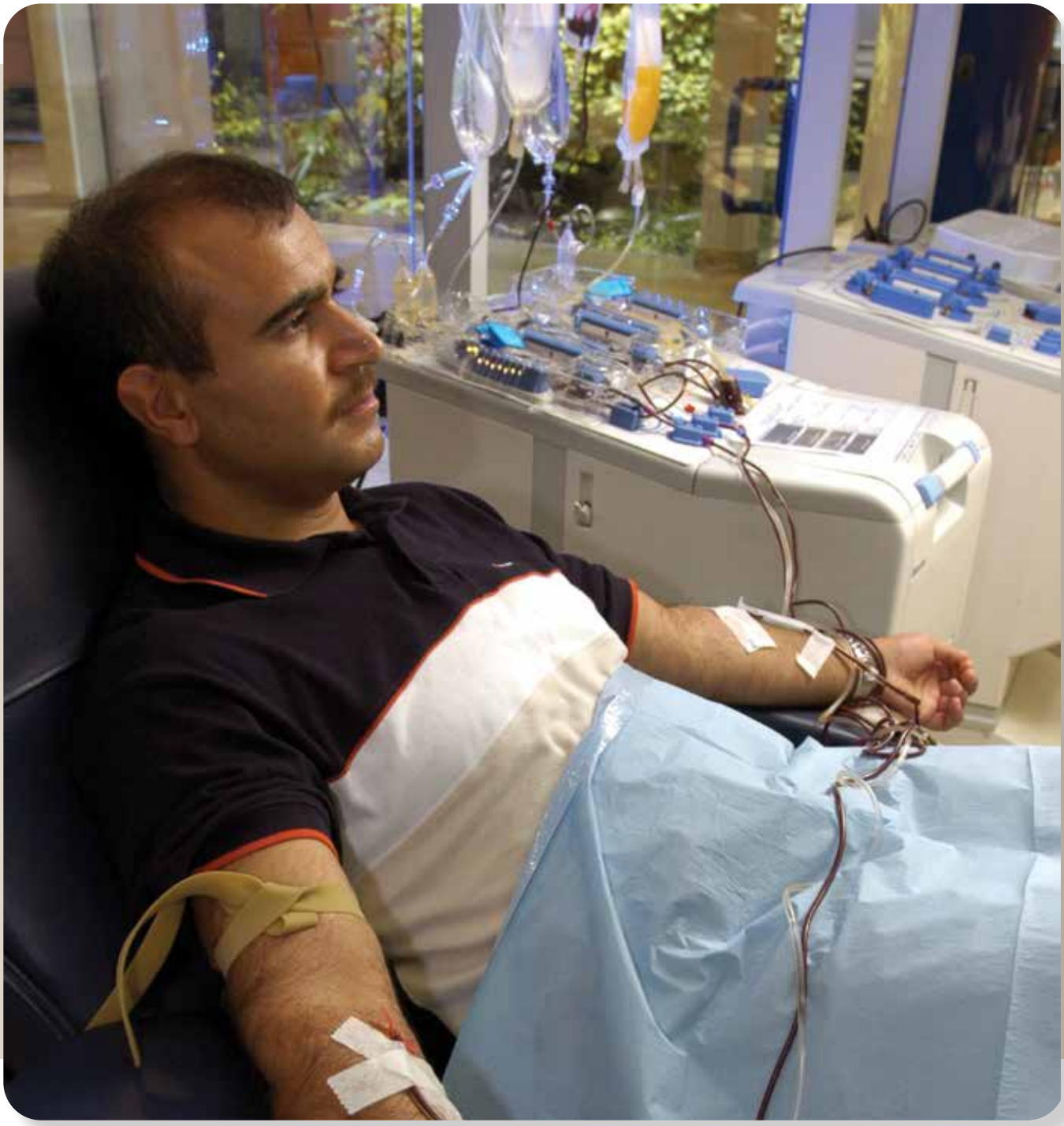
Understanding HLA

"HLA typing is the same thing we do in blood banking with ABO, Rh and antigen typing. Antibody testing is equivalent to the antibody screen and identification. And a crossmatch is a crossmatch, so really, HLA testing is just white blood cell banking. It's the same thing. It's just different enough, though, that senior blood bankers may still perceive it as cumbersome, or that it doesn't result in highly reliable antibody testing," said Patricia Kopko, MD, professor of pathology at University of California at San Diego. "Yet now we have so much more. The testing has changed and we can easily identify HLA antibodies — but it does come with some complexity.

Kopko, along with Sullivan and Deanna Fang, MD, shared the basics of HLA during a virtual session at the 2020 AABB Annual Meeting.

Kopko explained that HLA genes are inherited as a group, and each person gets one haplotype from each parent. Antigens are expressed co-dominantly — meaning that if a person gets an A1 from one parent and an A2 from the other, he or she will typically express A1 and A2.

"It is similar to A, B blood types except HLA genes are exceedingly diverse; there are more than 10,000 known protein coding variants. It is the most polymorphic gene in the genome. A and B are the most polymorphic, especially B. As of 2018, there were 3,000+ protein coding HLA variants of HLA B.

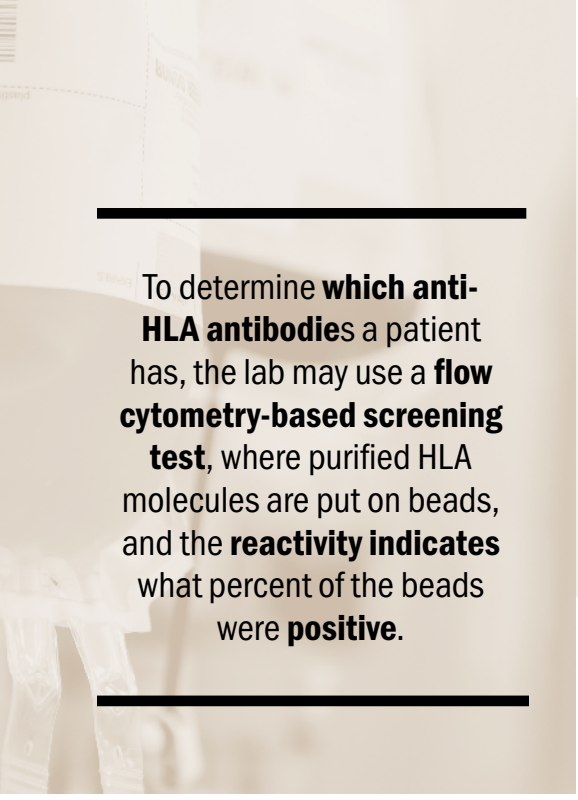


However, even when they're polymorphic, it's limited to a small number of actual serological specificities. Even though there are more than 3,000 B alleles, there are only a few more 60 B-defined serologic specificities or antibodies."

To sort through the nuances that can impact the success of a transfusion or transplantation, many HLA laboratories have three types of molecular HLA typing available: primer-specific PCR, oligonucleotide probes and DNA sequence analysis.

"If you want a high-resolution type and fewer ambiguities, more labs are switching to DNA sequencing," Kopko said. "Since we started, the number of cases requiring follow up with other testing is greatly decreased. We use next-generation sequencing for everything except the first pass typing of deceased donors."

When it comes to evaluating alloimmunization and making clinical decisions for a given patient, the majority of labs are using flow cytometry and Luminex-based testing for HLA antibody testing. While clinicians used to rely on a "percent reactive antibody" (PRA) number, that figure is no longer considered reliable because PRAs were not



To determine **which anti-HLA antibodies** a patient has, the lab may use a **flow cytometry-based screening test**, where purified HLA molecules are put on beads, and the **reactivity indicates** what percent of the beads were **positive**.

standardized from lab to lab or city to city largely due to how the wells were created and the demographics of the people in a given area.

"Now we have the calculated PRA, or the cPRA, in which you obtain an antibody analysis by a flow cytometry-based method and then use a calculator — UNOS has a good one — and you enter the antibodies, click 'calculate' and it will do it for you," Kopko said. "That means a cPRA in our lab is the same cPRA in any other lab, provided we all enter the same antibodies."

The cPRA represents the percent of the deceased donor population to whom the patient has an antibody. That is, if the cPRA equals 20%, the patient will have antibody to one in five donor kidneys.

To determine which anti-HLA antibodies a patient has, the lab may use a flow cytometry-based screening test, where purified HLA molecules are put on beads, and the reactivity indicates what percent of the beads were positive.

"It evaluates for overall HLA sensitization, but it only identifies HLA antibodies," Kopko said. "If there are other antibodies, we're not going to see them because of the purified HLA antigens used in this test."

Another option is to use multiplex immunoassay-enabled identification of anti-HLA antibody specificities, where each bead has a different HLA antigen on it, the beads are incubated with the recipient sera and identified with an antibody fluorescence, distinguishing a patient's antibodies and providing data needed to calculate a cPRA number.

A Crossmatch Made in HLAven

Matching donor and patient continues with the possibility of VXM and two types of physical crossmatch. Whereas a blood bank crossmatch uses recipient plasma and agglutination, an HLA physical crossmatch uses recipient serum and donor white cells from the peripheral blood, spleen or lymph nodes with the complement-dependent cytotoxicity (CDC) assay and/or flow cytometry.

"In both types of labs, we can assess compatibility without a physical crossmatch. In blood banking we use the electronic crossmatch and in HLA we use virtual crossmatch," explained Sullivan. "Our tests allow us to determine the patient's HLA antibody specificities and the molecular tests determine HLA phenotype. Using both of these pieces of information we can do a VXM."

The VXM uses an HLA typing of the proposed donor and an antibody specificity profile of the recipient, preferably performed on a recent serum sample. "The VXM is gaining acceptance as an alternative approach to assess donor/recipient compatibility prior to transplantation," according to an abstract published in *HLA Journal*. In contrast to a physical crossmatch, the VXM does not require viable donor cells… thus the VXM can be performed in minutes, which allows for faster transplant decisions…"

Interpreting Results

While the VXM might give the impression of plug-and-play perfection, interpreting the results of all testing in the HLA lab requires a skilled analyst, with clinical insight as well as close attention to detail.

"When providers look at the data, they don't always know how to interpret them," Kopko said. "For instance, with therapeutic apheresis, which can be used to treat rejection after transplantation, there are limitations to the testing. If you 'listen' to the beads, so to speak, and the beads get saturated, it will affect what information you get. If you have an antibody to HLA A1, and the bead has 1,000 binding sites, it doesn't matter if the clinician asks you to put 5,000 antibody molecules in there, you are going to get the same results as if you put 1,000 molecules, because there aren't 5,000 binding sites."

Kopko explained that if bead saturation is suspected, the team will often run the single antibody test again with serum diluted one to 10 parts saline to see if there is a change in the mean fluorescence intensity (MFI). "If you get the same results with a one to 10 dilution as you do with the original serum, then you don't know how much antibody you have, because you are still binding all the binding sites with one-tenth of the serum. This isn't a linear test; you can't just look at two numbers."

According to Sullivan, there are many misconceptions about the MFI value, including that it indicates the strength or titer of an antibody.

"This is not a quantitative test, at best it is a semi-quantitative test," he said. "You either have antibody or you don't — you can't take an MFI and think that it means something specific."

MFI results cannot be compared between samples, lots, laboratories or manufacturers because the tests have different cut offs, different validations, and variations on protocols — even "standardized" with a lab, variability exists.

Case in point, Sullivan described a patient he recently encountered at Emory. "We had a female who was in end-stage renal disease. When I reviewed her antibody profile against the prospective donor HLA phenotype, there was low-level DSA to C10. C locus antigens have lower expression on the white cell surface compared to other A, B and DR antigens; as such, our threshold for calling C locus antibodies is generally higher. In this case, the MFI was 3,000 and I wouldn't expect this antibody to correlate with a positive physical crossmatch."

However, Sullivan knew the C antigen was part of a "family" of related antigens. "It explains all of the positive beads that were reacting — it was due to one shared epitope, or a string of polymorphic sites that serve as target regions for antibody binding," he said. "There were 12 beads reacting, due to one antibody targeting an epitope shared on all of the beads."

This situation has been explained as the "peanut butter effect."

"Imagine you put a scoop of peanut butter on a piece of bread — chewing that big, sticky glob," Sullivan explained. "Now, picture that peanut butter spread across the whole loaf of bread. When you eat it, there's a little flavor on each piece. There's not less peanut butter, or less antibody, it's just spread out. I don't know if it will cause a positive physical crossmatch, it could be a negative, but I predict it will be at least weakly positive."

In this situation, there were other more suitable recipients. Because the patient had a cPRA of 50%, she had a good likelihood for future donor kidneys that would be better matches.

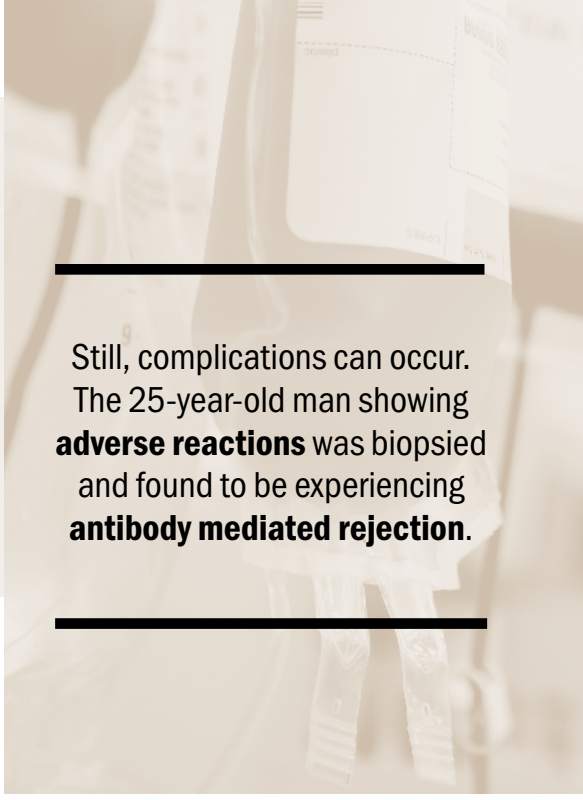
"This is a risk, highlighting the complexity of HLA," Sullivan said. "This is why epitope analysis and matching for solid organ transplant have been at the forefront of HLA literature in recent years."

Out of the Silos, Into Sync

In the old model of medicine, labs would provide test results and "lob them over the wall" to the physicians, where they were expected to know what to do with the information.

Now, the gold standard is a diagnostic management team (DMT) that oversees the diagnostic journey. With so many things a physician is expected to know and a growing number of subspecialties, particularly in pathology, the risk is more delays, mis-ordered tests, and results that lead to less optimal clinical decisions. Ideally, a DMT helps physicians decide how best to use the tests and interpret results, according to a *Transfusion* article published in 2020.

"Clinicians are trained to look at numbers. In some lab tests, results are calibrated against a standard, but not with antigens and antibodies," Sullivan said. "We take the onus off the clinicians, giving them a written report and partnering with them to discuss the data."



Still, complications can occur. The 25-year-old man showing **adverse reactions** was biopsied and found to be experiencing **antibody mediated rejection**.

Still, complications can occur. The 25-year-old man showing adverse reactions was biopsied and found to be experiencing antibody mediated rejection. A subsequent antibody profile, similar to the one prior to transplant, clearly demonstrated HLA Class II DSA to the donor.

"Now it was evident that there were DQ6 beads lining up, representing the donor antigen," Sullivan recalled. "Looking at the pre-transplant results, there was low level reactivity among the DQ6 beads with MFI values ranging from 0-200 MFI, well below the positive threshold; these DQ6 beads were very 'spread out' amongst other beads in the assay panel, but they were the first beads in the row of all the DQ antigen beads. Retrospectively you see it, prospectively it's hard to see."

Was this a case in which there was a memory response? Had this patient previously been exposed to this antigen and generated an antibody that waned below the positive threshold but ramped back up after re-exposure from the new kidney? Fortunately, the clinicians effectively treated the patient, the DSA was no longer detectable on HLA antibody testing and he recovered.

"The lesson is to always look at the antibody order of the beads. Yet, if you pay too close attention, you may end up precluding truly compatible transplants because you're playing it too conservatively. It is a balancing act," Sullivan said. "These tests aren't perfect. There are many shortcomings. Not all reactivity represents genuine HLA antibody, but that is a whole other story for another day." ■

Newer Therapies Could Boost, Supplement Theraputic Plasma Exchange

By Leah Lawrence
Contribuiting Writer

Therapeutic plasma exchange is a temporary measure for most conditions it is used to treat, according to Jeanne Hendrickson, MD, professor of laboratory medicine at Yale University and medical director of Yale New Haven Hospital's apheresis service.

That is because plasma exchange removes antibodies from the blood but does nothing to the antibody production process. The antibodies will build back up.

"It is like bailing out a boat," Hendrickson said. "It is very difficult to ever stay ahead when you are constantly bailing."

Additionally, plasma exchange is a relatively invasive procedure that requires a lot of the patient's time, especially in cases where repeat treatments are required, said Robert Kruse, MD, PhD, a resident physician at Johns Hopkins.

"An intravenous drug treatment infusion or a drug given subcutaneously would not be as invasive or require so many hours on the machine," Kruse said. "That would be preferable."

For these reasons, alternative or adjunctive therapies may be desirable for some of the diseases treated with therapeutic plasma exchange, Hendrickson and Kruse said.

Emerging Alternatives

One alternative approach gaining traction in clinical research is neonatal Fc receptor (FcRn) antagonists. FcRn is a receptor that helps prevent the breakdown of immunoglobin G (IgG).

"These drugs functionally work by binding this receptor that would otherwise recycle an antibody," Kruse said. "With apheresis you are pulling out the antibody; with FcRn you are speeding up the

destruction of the antibody. In both situations, antibodies will become low, but with the inhibitor, potentially, it is simpler because it is given intravenously or subcutaneously."

In January 2021, the manufacturer of one FcRn antagonist, Argenx, filed for Food and Drug Administration approval for efgartigimod to treat generalized myasthenia gravis.[1] In May 2020, the company announced positive topline data from a phase 3 ADAPT trial testing efgartigimod in patients with acetylcholine receptor-antibody positive generalized myasthenia gravis. The primary endpoint — defined as at least a two-point improvement on the Myasthenia Gravis Activities of Daily Living (MGA-DL) score — was achieved in 67.7% of patients treated with the drug, compared with 29.7% treated with placebo ($P<.0001$).[2] Acute treatment for myasthenia gravis is a Category I indication in the American Society for Apheresis guidelines, while chronic treatment with therapeutic plasma exchange is Category II.[3]

Another emerging class of therapies are immunoglobulin G-degrading enzyme of streptococcus pyogenes (IdeS), an endopeptidase that specifically cleaves IgG. Given the specificity of IdeS, it is hypothesized that it may be used to destroy pathogenic IgG.

"The enzyme clips the antibodies into two parts around what is called the hinge region," Kruse said. "Mechanistically, the part that binds to the target is removed from the functional part that triggers the signaling to destroy the cell or recruit complement to destroy the cell."

In 2017, results of phase 1-2 trials assessing the efficacy of IdeS with regard to antibody desensitization prior to kidney transplantation from an HLA-incompatible donor showed that in 24 of 25 patients the treatment reduced or eliminated donor-specific antibodies.[4] The European Union has now granted conditional approval to Idefirix's imlifidase in highly sensitized kidney transplant patients.[5]

There are also currently ongoing studies of IdeS in patients with severe anti-GBM disease in combination with standard care (NCT03157037) and in patients with Guillian-Barre Syndrome in combination with standard of care IVIg (NCT 03943589).

> "An **intravenous drug** treatment infusion or a drug **given subcutaneously** would not be as **invasive** or require so many hours on the machine. That **would be preferable**."
> *Robert Kruse, MD, PhD*

However, Kruse noted, IdeS is likely a one-time treatment for patients because after one treatment, the immune system will likely produce antibodies against the bacterial protein.

"I think it is likely that we will see more of these available alternative treatments for antibody reduction in the next couple of years," Kruse said. "Physicians and patients will have more options in the near future."

Useful Adjunctive Therapies

Beyond agents that could reduce antibody levels in patients, there are currently several biologic therapies being used as alternatives or adjunctive to therapeutic plasma exchange.

One adjunctive therapy already used is rituximab, according to Hendrickson. Rituximab is a B-cell depleting monoclonal antibody. Studies have reported favorable outcomes in patients with refractory myasthenia gravis, if other immunosuppressive agents do not mediate disease control.

"There are some patients where plasma exchange helps, but it is difficult to keep all their symptoms under control," Hendrickson said. "These patients may benefit from adjunctive therapy, and rituximab is a common one."

Another example is eculizumab, a monoclonal antibody targeting complement C5. There is evidence showing that blockade of C5 protected against severe disease in models of myasthenia gravis.[6] More recently, the phase-3 REGAIN trial compared intravenous eculizumab and placebo in 125 patients with MD-ADL score of 6 or more and chronic intravenous immunoglobin or plasma exchange for 12 months without symptom control. Outcomes suggested "a potential benefit of eculizumab treatment in patients with anti-acetylcholine receptor antibody-positive refractory generalized myasthenia gravis."[7]

Hendrickson said she has a number of patients with myasthenia gravis who used to come for plasma

exchange multiple times a week to maintain quality of life and who have been able to transfer to treatment with rituximab or eculizumab.

"At least some patients have had quite a significant response to one of these drugs and are receiving the drug in conjunction with apheresis, and others have been able to come off therapeutic plasma exchange all together," Hendrickson said.

Finally, one other recent topic of interest is the use of caplacizumab in thrombocytopenic purpura (TTP). Caplacizumab is a nanobody directed towards a domain of von Willebrand's factor, Hendrickson explained.

"There are a number of studies using it for TTP and a few that were recently published that suggest it may be used as an upfront therapy," she said.

In 2019, the randomized HERCULES study was published testing caplacizumab or placebo given during plasma exchange in 145 patients with TTP.[8] Treatment with the drug was associated with a faster normalization of the platelet count, as well as lower incidence of a composite TTP-related death, recurrence of TTP or a thromboembolic event during the treatment period.

"There is some speculation that you could use just caplacizumab alone without plasma exchange, but that hasn't been tested in clinical trials," Kruse said

While these alternative agents to apheresis are promising, the cost of caplacizumab and other biologic drugs in development may be a barrier to replacement of plasma exchange, he said.

"Sometimes apheresis practitioners look at newer therapies and wonder, 'is my practice going to go away?'" Kruse said. "Even if these drugs are successful, they might work for some things and not for others. Our practice isn't going away, and it is always good to be aware of what else is out there." ■

While these **alternative agents** to apheresis are **promising**, the cost of caplacizumab and other biologic drugs in development **may be a barrier** to replacement of plasma exchange

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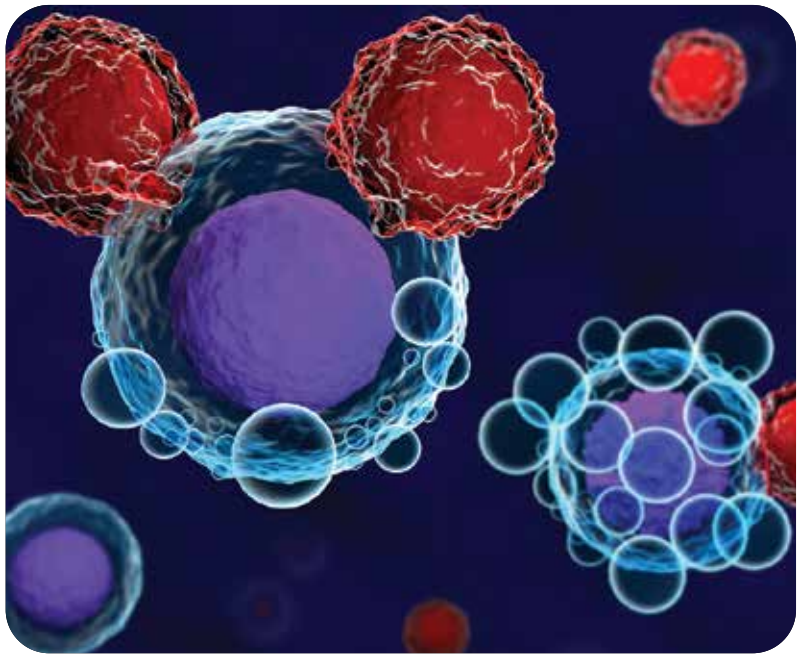
Investigational CAR-T Cell Therapy May Treat Relapsed Multiple Myeloma

By Drew Case
Senior Communications Manager



Treatment with an investigational B-cell maturation antigen (BCMA)-directed chimeric antigen receptor (CAR) T cell immunotherapy led to frequent and deep responses in patients with relapsed and refractory multiple myeloma, according to findings published recently in the *New England Journal of Medicine.*

Patients in the trial received the investigational therapy — Idecabtagene vicleucel (ide-cel, bluebird bio and Bristol Myers Squibb) — after treatment with at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody. The primary endpoint was an overall response (partial response or better).

The trial enrolled 140 patients, of whom 128 received ide-cel doses of 150×10^6 to 450×10^6 CAR-positive (CAR+) T cells. At a median follow-up of 13.3 months, 94 of 128 patients (73%) had a response, and 42 of 128 (33%) had a complete response or better. Investigators confirmed minimal residual disease (MRD)-negative status ($<10^{-5}$ nucleated cells) in 33 patients, representing 26% of all treated patients and 79% of the 42 patients who had a complete response or better.

The median progression-free survival was 8.8 months, and overall survival was 19.4 months among treated patients. The median response duration and progression-free survival were numerically longer at the 450×10^6 dose. Almost all patients had grade 3 or 4 toxic effects.

Ide-cel showed durable persistence in blood, with 36% of patients who could be evaluated having detectable CAR+ T cells at 12 months. However, the investigators noted that the presence of these cells did not guard against disease recurrence, and it is unclear whether the patient became resistant to the CAR T cells or the T cells became functionally compromised. They concluded that the determination of long-term disease-free survival with ide-cel requires additional follow-up.

OneBlood Officials Describe Development of CCP Program in New Research Article

Officials from OneBlood described how their blood center implemented a COVID-19 convalescent plasma (CCP) collection program within 6 weeks in an article published recently in the *Journal of Clinical Apheresis.*

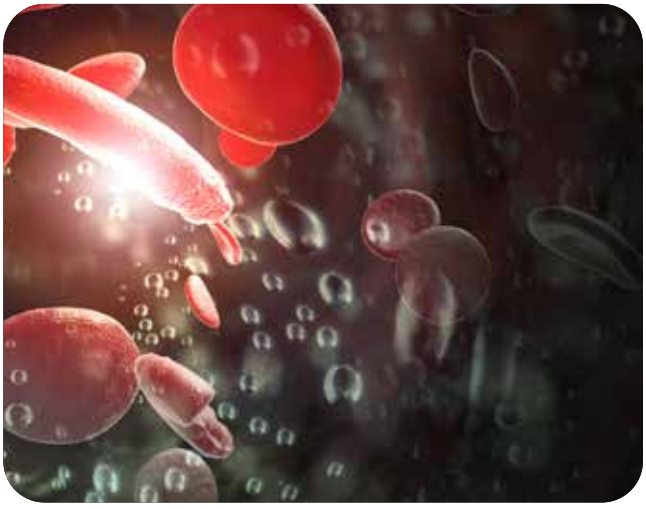
In the publication, the authors described how the center launched a CCP implementation project to meet the need for CCP and build a robust inventory of frozen and liquid CCP. The report details the two-phase approach to the implementation of CCP production, which first relied on a manual process to quickly begin collections and distributions of CCP and transitioned to an automated process to boost the volume of operations and inventory.

Between April 2 and May 17, 2020, the center

produced 1,330 CCP products collected from 619 unique CCP donors (299 females, 320 males; 432 [69.8%] first-time and 187 [30.2%] repeat donors). During the manual phase, the center produced an average of 18 CCP products per day and collected from an average of 11 donors. This increased to an average of 25 CCP products per day from 25 donors during the automated phase. The center was able to fill a backlog of patient orders and build an inventory less than 4 weeks after initiating the project, but the authors noted that there was a progressive loss of donors and products throughout the process.

Based on their center's experience, the authors identified several deficits and gaps in sustaining the blood supply. They concluded that there is an urgent need for reliable, real-time data on national blood products inventory and usage down to the regional level. They also noted that the current single-supplier inventory model is not suitable for disasters.

The authors also outlined potential corrections to these challenges. For example, they propose that the federal government develop mechanisms to streamline donor recruitment, testing and new product development in the event of a similar pandemic. They also emphasized the importance of funding to develop pathogen-reduction technology and the development of standing federal protocols to allow rapid deployment of convalescent plasma.



Sickle Cell Gene Therapy Unlikely to Impact AML Risk

The acute myeloid leukemia (AML) diagnosis in a patient who had previously been treated with an investigational gene therapy for sickle cell disease (SCD) is "very unlikely" to be related to the viral vector used in the treatment, according to the manufacturer, Bluebird Bio. The company paused phase 1/2 and phase 3 studies of its betibeglogene autotemcel (Lentiglobin) gene therapy in February following the diagnosis due to concern that the BB305 lentiviral vector (LVV) may have triggered the disease.

According to Bluebird Bio, multiple independent analyses have confirmed that vector insertion in the AML cells from this patient took place in the *VAMP4* gene, or vesicle-associated membrane protein 4. The company noted that *VAMP4* itself has no known role in the development of AML or with any cellular process related to cancer. Additional analysis determined that the insertion into the *VAMP4* gene had no impact on gene expression or gene regulation nor caused any disruption of nearby genes.

Furthermore, independent analysis also showed that this patient had significant chromosomal abnormalities and mutations in the *RUNX1* and *PTPN11* genes that are typically associated with the development of AML. Based on these data, Bluebird Bio believes that the case of AML is very unlikely related to the BB305 LVV.

An investigation into an additional case in which a treated patient developed myelodysplastic syndrome (MDS) is ongoing to determine if the clinical findings meet the criteria to be classified as a case of MDS and, if so, whether betibeglogene autotemcel played any role. ■

CALENDAR

April

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Improving Apheresis Over the Years

Miquel Lozano, MD, PhD

We have improved apheresis through what we have learned about physiological changes resulting from the procedure and the pathophysiology of the diseases we are treating. In addition, adding prophylactic measures and incorporating medications and technical aids have improved apheresis outcomes.

Miquel Lozano, MD, PhD, is the chief of the hemotherapy section at the University Hospital Clinic of Barcelona and an associate professor of medicine at the University of Barcelona. Lozano also serves as the president of the European Society for Hemapheresis and the editor-in-chief for *Vox Sanguinis*. His areas of interest include transfusion medicine, apheresis procedures and congenital and acquired platelet function disorders, and his research has focused on the development and applications of new therapies in transfusion medicine and apheresis. *AABB News* recently spoke to Lozano about his career and his thoughts about transfusion medicine and apheresis.

New types of treatments are using apheresis as the starting point of the therapy, so more attention has been focused on apheresis.

AABB NEWS: **HOW HAS THE PROCEDURE OF APHERESIS CHANGED IN THE PAST FEW DECADES?**

Lozano: In a word: enormously! We have better characterized the changes in the physiology of the apheresis procedures and improved the knowledge of the pathophysiology of the diseases that we were treating, so we have been able to introduce prophylactic measures to improve the tolerability of the procedure and incorporated drug treatments that have improved the outcome of the treatments. One case in point is plasma exchange. In our center, in the early 1980s, a review of 744 procedures found adverse effects in 18.04% of the procedures. Twenty years later, we have reduced the figure to around 2% thanks to the prophylactic measures that we have introduced. In addition, technical aids have improved the procedures. In recent years, apheresis units have implemented ultrasonography for accessing peripheral veins for the apheresis processes and avoiding the need to place a central venous catheter. In our case, we implemented it in 2020. In 2019, we had to place a central venous catheter in 30% of patients to collect hematopoietic progenitors cells for transplantation. In 2020, the figure decreased to 9%.

AABB NEWS: **ARE THERE ANY COMPONENTS OR SUBSTANCES BEING COLLECTED VIA APHERESIS THAT NO ONE WOULD HAVE EXPECTED TO COLLECT THAT WAY 10 YEARS AGO?**

Lozano: More than collecting new components or substances, what has changed is the reasons for which we are collecting those components now. For instance, we have been collecting mononuclear cells from non-mobilized donors for many years, but only very rarely. In the last 5 years, the number of collections has increased exponentially because we have begun using those autologous mononuclear cells for cellular therapies such as chimeric antigen receptors (CAR) T-cell therapies or to prepare dendritic cells. Our center is currently collecting mononuclear cells for five different types of CAR-T therapies — to treat lymphomas, lymphoblastic leukemias and multiple myeloma.

AABB NEWS: **APHERESIS HAS BEEN THE SUBJECT OF INCREASED RESEARCH AND ATTENTION RECENTLY. WHY DO YOU THINK THIS IS?**

Lozano: As I mentioned earlier, new types of treatments are using apheresis as the starting point of the therapy, so more attention has been focused on apheresis.

AABB NEWS: **IN YOUR OPINION, WHAT ARE THE MOST PROMISING AREAS OF RESEARCH IN APHERESIS?**

Lozano: I think a promising area is the application of extracorporeal photoapheresis to treat some conditions for which this treatment might have a role based on the pathophysiology of the disorders.

AABB NEWS: **WHAT NEW USES FOR APHERESIS ARE IN THE WORKS?**

Lozano: There are new indications that are being explored that might have a great impact in the future. For instance, the role of plasma exchange in the treatment of Alzheimer disease. The results of a randomized controlled trial have suggested a beneficial effect of the plasma exchange using albumin as a replacement solution in slowing the progression of the disease. New studies are needed to confirm these findings.

AABB NEWS: **HOW HAS YOUR ROLE EVOLVED OVER TIME?**

Lozano: My role has certainly changed since I started working in apheresis in the early 90s. Starting with a more direct role in patient care and research, my responsibilities now include management and teaching. But I keep trying to maintain my contact with patients.

AABB NEWS: **WHAT IS ONE PROFESSIONAL EXPERIENCE YOU HAD THAT NOBODY KNOWS ABOUT?**

Lozano: Probably that I collaborated in a program funded by the United States Centers for Disease Control and Prevention to increase blood safety and optimize the clinical use of blood in Kazakhstan, Kyrgyzstan and Ukraine between 2013 and 2016. I made friendships there that continue to this day. ■

Barbara Bryant Named Head of Transfusion Medicine Department at NIH Clinical Center

Barbara Bryant, MD, has been named the National Institutes of Health (NIH) Clinical Center's next chief of the Department of Transfusion Medicine. As chief, Bryant oversees the agency's Center for Cellular Engineering, as well as a blood collecting facility, transfusion service, diagnostic testing laboratories, and research and advanced training programs.

Bryant is a former member of the AABB Board of Directors whose four decades of service also include 17 years of working in a blood bank prior to entering medical school and completing her fellowship training in transfusion medicine/blood banking at NIH. Bryant later served as professor and vice-chair of the Department of Pathology, medical director of Transfusion Medicine and Apheresis, medical director of the Pathology Department Quality Management, and the director of the Academy of Master Clinicians at the University of Texas Medical Branch (UTMB). Most recently, Bryant was

an adjunct professor at UTMB and the president/owner of Transfusion Medicine Solutions, LLC.

In addition to her service to AABB, Bryant has been a member of the FDA's Blood Product Advisory Committee and co-chair of the FDA's Advisory Committee on Blood and Tissue Safety and Availability working group. Bryant is also the current past president of the South Central Association of Blood Banks.

Bryant began her new role in January. She succeeds Harvey Klein, MD, who retired in 2019 after serving 36 years as chief of the department, and Cathy Cantilena, MD, who served as acting chief following Klein's departure. ■

Western Kentucky Regional Blood Center CEO Janet Howard Recognized for 40 Years of Service

The Western Kentucky Regional Blood Center recently recognized Janet Howard, MT(ASCP)SBB, the blood center's CEO, for 40 years of service. Howard began working part-time at Western Kentucky in 1981 after completing a medical technology program. She told *AABB News*, "As a tech for 41 years, I have never wavered in the belief of the importance of MTs, MLTs and all of the other specialties in the laboratory. It is hard to believe I have been in this profession for as long as I have — it truly doesn't seem that long!"

Although her fear of making a potentially deadly mistake in labeling blood led to her fear of working at the blood bank, Howard was working there full time within 6 months and was recommended as director in 1988. "When I talk to students both in high school and college, I tell them to not be afraid to jump into something, even if it is scary," she added. "In my internship, Blood Bank was the most 'feared' section

because of the potential harm a mistake could cause. When I came to Western KY Regional Blood Center, I felt it was rather ironic that I had to face this fear… Not only did I face it but I embraced it!" she said. "That is what I try to tell young people as they find their career path in life."

She said that working at the blood center is never boring, with new challenges presented to staff regularly. She worked through the AIDS epidemic in the 1980s, September 11 and hepatitis C testing and is now contending with the COVID-19 pandemic. Howard added that she has no desire to retire because the career has become a passion for her, and she described the people with whom she works as wonderful.

"AABB is an excellent resource for anyone in our profession," added Howard. "Not only does it keep us up-to-date, but the guidance AABB gives on all aspects of blood banking is invaluable." Howard has been an AABB member since 1989.

PEP Volunteer Spotlight

Tina S. Ipe
Division Director of Transfusion Medicine at the University of Arkansas for Medical Sciences; Associate Professor in the Department of Pathology and Laboratory Medicine

How long have you been an AABB member?

I became an AABB member while I was a resident at the Hospital of the University of Pennsylvania in 2011.

In which AABB volunteer activities are you currently active? In which have you participated?

I attended my first AABB Annual Meeting in 2011, where I was awestruck by the educational sessions and people I met. My mentor and sponsor, Dr. Deborah Sesok-Pizzini, helped me navigate through the meeting by introducing me to other thought leaders and change agents in the field. My involvement in volunteer activities was spearheaded by another colleague, Dr. Jill Adamski, with whom I co-chaired the Communications Committee at the American Society for Apheresis (ASFA). We submitted educational proposals and abstracts on behalf of the ASFA committee for AABB annual meetings. This served as a springboard for many volunteer opportunities within AABB, such as the Apheresis Committee, on which I continue to serve as a member. I became an AABB assessor in 2013. Serving as a volunteer assessor enabled me to work with incredibly talented and knowledgeable AABB staff members such as Christopher Bocquet, Nancy Shotas, Frances Ivestor and other assessors worldwide. Because of my interest in global population health and transfusion medicine, I participate as one of the co-chairs for the Research Subcommittee of the Global Transfusion Forum. Other committees that I serve on include the AABB BB/TS Standards Committee and the Annual Meeting Education Committee (AMEC).

What motivates you to volunteer?

Volunteering makes me a more learned physician. Every day, because of my interactions on committees, my knowledge is continually expanded. I constantly learn about new regulations, new medical advancements and new workflow process enhancements with each of my interactions, both locally and internationally. In addition, I get to contribute to causes that matter to me, such as transfusion medicine and apheresis, global health, and diversity, equity, access and inclusion.

I would be remiss not to mention the many AABB staff members who have guided me through volunteering opportunities, such as Arnold McKinnon, Eduardo Nunes and Sharon Carayiannis. And the mentorship of other physicians such as Drs. Beth Shaz, Gay Wehrli, Quentin Eichbaum and Michael Murphy.

How has your volunteer work affected your professional work?

My professional work is a natural extension of the many skills and knowledge that I have obtained from volunteering in AABB committees. I also have developed a broad network of AABB colleagues, both physicians and technical staff, whose experience I can draw from when I do not have the answers.

What have you learned from volunteering with AABB? And what advice would you give to someone interested in volunteering?

I will quote Forest Gump regarding my volunteering with AABB as it has been "like a box of chocolates." I never knew what to expect next, but it has been an excellent opportunity with many happy surprises.

Dive into volunteering. Introduce yourself to individuals such as Arnold McKinnon, who is AABB's Volunteer Engagement Manager, and express your interest. If you fail at your first attempt to get into a committee, brush yourself off and try again.

What is your favorite genre of music?

I cannot say I have a favorite genre because I do like it all. And my musical genre changes with my mood and who is in the car with me as I listen to all types of music, from heavy metal to bluegrass to pop. ■

AABB Launches new Leadership and Management Collection

AABB launched its new Leadership and Management Collection in March to provide resources to current and next generation professionals and cultivate effective leadership strategies. The program comprises 31 resources taken from annual meeting sessions, book chapters and eCasts. Experts from AABB's Leadership & Administrative Subsection reviewed and selected all of the resources included in the program to ensure their relevance and compiled them into a single collection, which is broken down into three areas: managing resources, leading staff and best practices. Participants can earn continuing education credits: physicians up to 37.75 credits and others up to 39 credits. Additional information — including registration fees and an overview of the content — is available on the AABB website under Education > Courses. ■

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