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- **PBM IN PEDIATRIC PATIENTS**
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Technology Enables Issuing Blood at the Point of Care

Computerized blood issue systems combine software and hardware to ensure that units of blood go to the correct patient.

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AABB's Newest White Paper Examines Balancing Supply and Demand for Blood

The paper is meant to be useful for both the blood community and the public and explores how to ensure sufficient collections without creating unneeded surpluses.

16

New Technologies Hold Promise for Transfusion Medicine

Methods to identify high quality donors, simplify blood draws and predict ideal donation intervals are in development.
This issue of AABB News focuses on innovations that are advancing our work in blood banking, transfusion medicine and biotherapies. As we all struggle with the unknowns of the novel coronavirus outbreak, we may need these new technologies in place even sooner than we expected, as this rapidly evolving situation requires us to reevaluate what we do and how we do it. We may no longer be able to afford a 5-day platelet. We may need better ways to predict which patients will need a transfusion in order to better manage our inventory (and our donors).

The first feature article in the issue, which begins on page 8, discusses electronic remote blood issue and how it has increased efficiency and reduced costs where it has been implemented. The second feature, starting on page 16, provides a glimpse into some of the new technologies in development that may help us improve our work. These innovations include a machine learning model that can predict personalized inter-donation intervals, a robot that uses ultrasound to improve the accuracy of venipuncture and a microfluidics device that could help identify donors with “high-quality” blood that lasts longer in storage and in circulation.

Meeting the Needs of the Community

AABB’s uniform goal is to meet the needs of our members, the larger blood and biotherapies communities, and the patients we serve. At present, disruptions caused by the novel coronavirus outbreak are triggering a great deal of consternation, particularly with respect to the blood supply. AABB remains committed to supporting blood centers and transfusion services during this challenging time, so they can continue their work providing lifesaving products and services to their patients uninterrupted. To aid in this effort, we have made a number of resources available. Visit our website at www.aabb.org to access our new Coronavirus Resources web page, our COVID-19 outbreak planning checklist, key messages for use in discussing the coronavirus with blood donors, patients and the public, and other valuable resources.

I hope that this challenge allows us to find ways of staying connected virtually — and to stick with them.

Beth Shaz, MD
AABB President
The series provides a thorough overview of blood banking and transfusion medicine 101 through 22 on-demand eCasts in four subject areas:

- Industry Review/Overview
- Blood Banking Fundamentals
- Transfusion Medicine Fundamentals
- Regulatory/Compliance Deep Dive

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Register online at AABB.org/Blood101 today.
Robert Carden, PhD, CEO, Commonwealth Transfusion Foundation (CTF); Gavin Evans, executive director of the Global Blood Fund (GBF); John Armitage, MD, CEO, Oklahoma Blood Institute; and Christine Bales, BS, MT(ASCP)I, CQA(ASQ), vice president, Consulting and Global Services, AABB, recently traveled to Dar es Salaam, Tanzania, for feasibility and design work on a study at the Tanzania National Blood Transfusion Services comparing two methods of measuring donor hemoglobin levels. In an operational experiment expected to have global implications, the investigation — commissioned and led by the Virginia-based CTF — will assess whether switching from the qualitative copper sulfate donor hemoglobin screening method to a quantitative method would result in a net increase in donors by avoiding inappropriate deferrals. The study will also evaluate the financial implications of replacing copper sulfate screening with a quantitative screening method. In Tanzania and many other resource-limited countries, the cost of devices and consumables is considered prohibitive. Prior research indicates that when opportunity costs are considered, quantitative screening is actually more cost effective than copper sulfate.
CTF is a non-profit, private foundation whose mission is to inspire and champion research and education that optimizes clinical outcomes in transfusion medicine and assures a safe and sustainable blood supply for the United States. GBF is a 501(c)(3) organization registered in both the U.S. and the United Kingdom that provides money, equipment, training and other forms of support to more than 40 countries in Africa, Asia, Eastern Europe, the Middle East, Latin America and the Caribbean. AABB has engaged in ongoing, collaborative efforts for many years to improve transfusion care in resource-limited countries, including Tanzania, through the President’s Emergency Plan for AIDS Relief (PEPFAR) program.

Asante Sana means “Thank the Donor” in Swahili. The NBTS team with Magdalena Lyimo, Program Manager, NBTS, Armitage, Lelo Balyima, Abdu Juma, NBTS, and Bales.
Don Siegel, PhD, MD, is a professor of pathology and laboratory medicine at the University of Pennsylvania, where he is also the founding and current director of the Division of Transfusion Medicine and Therapeutic Pathology. He is the director of the University of Pennsylvania blood bank, the apheresis/infusion unit, the hematopoietic stem cell laboratory and a National Institutes of Health T32-supported ACGME-accredited transfusion medicine fellowship program. He also directs the Clinical Cell and Vaccine Production GMP facility within his division; this facility has manufactured more than 3,000 cellular products that have been administered to more than 1,000 patients — including the first genetically-modified cellular therapy product approved by the Food and Drug Administration and licensed to Novartis (Kymriah), as well as the first CRISPR-edited cells administered to patients in the United States.

An Early-Career NBF Grant

After a clinical pathology residency and transfusion medicine fellowship at Penn, Siegel stayed on to begin his faculty career in 1991, and soon received a National Blood Foundation early-career Scientific Research Grant for his study, Biology of Human Warm Autoimmune Hemolytic Anemia. In this study, Siegel developed and applied a new method known as phage display for producing monoclonal antibodies to red blood cells in vitro without the need for B cell immortalization. After completing the study, Siegel became an NBF Scholar. According to Siegel, this grant played an important role in starting his academic career, which has included contributions to clinical translation, such as the development of novel CART T cells for clinical trials and the training of a new generation of researchers in transfusion medicine. Siegel has worked on local, national and international levels in clinical service, basic and applied research and education. He has also participated in every AABB annual meeting throughout the past 31 years, by speaking at education sessions and presenting his original research. Notably, 18 of Siegel’s trainees have been awarded NBF grants of their own.

An Educator Begins Sharing His Expertise

Siegel first began teaching in the transfusion medicine fellowship program at Penn in 1991 and became the program’s director in the late 1990s. Since then, he has successfully renewed the program’s T32 training grant for five additional 5-year terms. The clinical program, which prepares MD and MD/PhD trainees for clinical and research careers in transfusion medicine, has been ranked the best in the country by U.S. News and World Report. Many graduates of the program have pursued careers in academic medicine and continued conducting grant funded research, and many hold prestigious positions at an academic blood bank, blood center, associated clinical laboratory or pharmaceutical company, or within the Food and Drug Administration.

The Antibody Phage Display Method

Siegel succeeded in cloning human alloantibodies to cell surface antigens — such as those on red blood cells and platelets — based on his pioneering use of antibody phage display.

The ability to clone human alloantibodies from peripheral blood enabled Siegel to study autoantibodies produced by patients with immune thrombocytopenia (ITP) and thrombotic thrombocytopenic purpura (TTP). Subsequently, he was able to demonstrate the clonal nature of the B-cell response in ITP on a genetic level and, eventually, to create the first and only authentic murine model of TTP.

Method Goes Beyond Transfusion Medicine

Siegel’s work using phage display approaches to discover and characterize antibodies extends beyond
transfusion medicine, into dermatology, infectious disease and biotherapies — specifically CART cells. According to Siegel, his most meaningful work began when the friend who had taught him phage display was diagnosed with medullary thyroid cancer (MTC), a deadly disease for which the most effective treatments have only ever prolonged the life of those with metastatic disease about a year. Siegel recently began developing a CART-cell therapy to treat the disease, and in a span of 2 ½ months, in collaboration with two of his former transfusion medicine fellows at Penn, discovered an MTC target, developed an antibody fragment to it using phage display, incorporated the fragment into a human CART cell and demonstrated that the engineered cells could kill the MTC cells in vitro. Although Siegel’s friend died before he could receive the therapy, a clinical trial of the treatment is scheduled to begin later this year. Siegel is also working to extend this work to provide novel immunotherapies for veterinary patients. He created a 40 billion member canine antibody display library from which canine antibodies can be isolated, and he and a colleague at the Penn Vet School are using it to create canine checkpoint inhibitors and CART cells.

This early work on phage display also led to numerous discoveries in seemingly disparate areas, including the human immune response to the RhD antigen, new methods for phenotyping red cells and antibody-mediated autoimmune diseases. A special 2005 issue of Transfusion on the NBF Scientific Research Grant Program contained an article, “Developing phage display tools for use in transfusion medicine,” that detailed Siegel’s early work. In the article, Siegel discussed the need for immunohematology methods that enabled the study of human antibody repertoires at the molecular level, and since 1996, he has taught these methods annually to 16 international students per year in a 2-week laboratory course at Cold Spring Harbor Laboratory in New York.

**A Cell Therapy Program Begins at Penn**

Siegel played an important role in developing the cell therapy program at Penn. In 1999, when Carl June, MD, had just arrived at Penn to start developing the program, Siegel convinced him to situate it in his pathology department within transfusion medicine, rather than as an independent institute with a separate set of faculty running an unconnected cell collection unit and laboratory. Siegel believes that such novel cell therapy programs should be associated with blood banks, apheresis units and hematopoietic stem cell labs, where transfusion professionals can share the clinical and regulatory expertise they have gained on collecting and manipulating human cells throughout the past 50 years.

Penn’s cell therapy program went on to complete numerous first-in-human trials, including the first use of lentivirus in humans, the first zinc finger nuclease gene-edited HIV-patient cells that rendered the cells HIV-resistant, the first successfully-administered CART cells, and, most recently, the first CRISPR-edited T cells for treating myeloma and sarcoma — the T cells are designed to resist tumor suppression through checkpoint inhibition. This CRISPR work was published last month in the journal Science.

**An NBF Awardee Receives Numerous Honors**

Siegel was recently selected as one of 20 Penn faculty (out of more than 2000 candidates) to serve as a founding member of the Penn Medicine Academy of Master Clinicians. As a member of the research team that brought CART cells to the clinic, he and seven others at Penn received the Leukemia & Lymphoma Society’s 2020 Robert de Villiers Spiral of Life Award earlier this month. In 2018, Siegel was honored with the American Society for Apheresis’ Francis S. Morrison, MD, Memorial Lectureship and the Gift of Life Award from the Ree Wynn Foundation for his work on TTP. AABB awarded Siegel and his coauthors the 2016 Research Innovation in Scientific Excellence (RISE) Award for the best original article published in Transfusion for their work creating the first and only murine model of TTP. Siegel has also received numerous teaching awards from his institution.