blood® Editorial

Introduction to a review series on transfusion medicine

In their review in this journal for the 50th anniversary of the American Society of Hematology (ASH), Alter and Klein underscored that "the beginning of the modern era of blood transfusion coincided with World War II and the resultant need for massive blood replacement."[1] Initially focused mainly on laboratory activity aimed at testing blood donors and processing blood and its components, transfusion medicine has progressively evolved to become a clinically oriented discipline.[2] This evolution has been characterized by continued innovation that has made blood transfusion increasingly useful.[3] Nowadays, blood transfusions represent one of the most common procedures for patients in the hospital.[4] According to the American Red Cross, ~36 000 U of red blood cells (RBCs), 7000 U of platelets, and 10 000 U of plasma are transfused daily in the United States.[5] Despite continuous improvements, blood transfusion still involves risks and, therefore, the implementation of best transfusion practices and guidelines is of fundamental importance in clinical practice.[6] The review series in this issue of *Blood* primarily provides an update on prevention, diagnosis, and treatment of transfusion reactions for practicing physicians. In addition, this series illustrates how genomics and big data analytics are also impacting this area of medicine.

The reviews in this series include the following:

- Connie M. Westhoff, "Blood group genotyping"
- Christopher A. Tormey and Jeanne E. Hendrickson, "Transfusion-related red blood cell alloantibodies: induction and consequences"
- Ruchika Goel, Aaron A. R. Tobian, and Beth H. Shaz, "Non-infectious transfusion-associated adverse events and their mitigation strategies"
- John W. Semple, Johan Rebetz, and Rick Kapur, "Transfusion-associated circulatory overload and transfusion-related acute lung injury"
- Michael P. Busch, Evan M. Bloch, and Steven Kleinman, "Prevention of transfusion-transmitted infections"

In the first review, Westhoff illustrates the innovation in the field, summarizing the evolving use and applications of genotyping for RBC and platelet blood group antigens. Conventional blood typing by antibody-based methods has been useful for decades but has significant limitations; consequently, routine RBC typing for transfusion has been essentially limited to ABO and RhD determination. Blood group genotyping uses single-nucleotide polymorphisms (SNPs) in genes encoding human blood group antigens and DNA arrays for their evaluation. The advantages of this approach have already been shown in several areas, including prenatal medicine, transplantation settings, and prevention of alloimmunization in patients with sickle cell disease. Although DNA-based genotyping is clearly advantageous compared with antibody-based methods, DNA arrays can interrogate only a limited number of known SNPs. By contrast, next-generation sequencing (NGS) can interrogate the whole exome or genome, and is continuously improving in terms of instruments and costs. In Westhoff's view, NGS is likely soon to become a tool for immunohematology reference laboratories.

In the second review, Tormey and Hendrickson examine alloantibody formation in response to transfused blood products, a complication that remains a clinically significant problem. They focus on alloimmunization to non-ABO blood group antigens, also known as RBC antigens. Alloantibody formation may have significant clinical consequences, including delayed hemolytic or serologic reactions and difficulties in locating compatible blood for alloimmunized individuals. In addition, alloantibodies can also be clinically significant in settings like pregnancy and hematopoietic stem cell transplantation. To prevent alloimmunization in patients with sickle cell disease, matching for some blood group antigens is now recommended, and DNA-based RBC typing has already become the primary method for extended RBC typing in some institutions.[7]

The Biomedical Excellence for Safer Transfusion (BEST) Collaborative has reported that transfusion reactions occur in up to 1 in 100 transfusions.[4] In the third review, Goel, Tobian, and Shaz focus on features of the most common noninfectious transfusion-associated adverse events, and discuss definitions, diagnostic criteria, treatment, and mitigation strategies. The most common noninfectious reactions include allergic reactions, ranging from mild urticarial lesions to anaphylaxis, and febrile nonhemolytic reactions that occur during or shortly after transfusion. Many countries now have national hemovigilance systems for monitoring, reporting, and analyzing transfusion-associated adverse events with the aim of making blood transfusion increasingly safer. To further improve hemovigilance, vein-to-vein databases are being created and big data applications are being implemented to enable management and analysis of the huge quantities of digital information that accumulate.[8] Although the use of big data in transfusion medicine will hopefully improve patient blood management, Goel et al emphasize that the single best modality for preventing transfusion-associated adverse events is avoiding an unnecessary transfusion. To minimize the hazards related to the administration of blood products, clinicians are expected to follow best transfusion practices that focus

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on transfusing the right product to the right patient at the right time.

In the fourth review, Semple, Rebetz, and Kapur examine transfusion-associated circulatory overload (TACO) and transfusion-related acute lung injury (TRALI). Both TACO and TRALI are syndromes of acute respiratory distress that occur within 6 hours of blood transfusion and demonstrate infiltrates on a chest radiograph indicative of the presence of pulmonary edema. TACO and TRALI are life-threatening transfusion reactions, and specific therapies are unfortunately lacking. For TACO, supportive measures may include the use of diuretics, oxygen, and intubation, whereas preventive strategies are available for TRALI.

In the final review, Busch, Bloch, and Kleinman discuss the prevention of transfusion-transmitted infections. The classic transfusion-transmitted infectious agents include hepatitis B virus, HIV, human T-cell lymphotropic virus type I/II, and hepatitis C virus (HCV). The recognition that HIV and HCV are transmissible by blood significantly contributed to making transfusion medicine increasingly focused on patient care.[2] Research in this field has provided reliable tests for detecting virus-specific antibodies, antigens, and nucleic acid sequences, so that risks per blood transfusion unit are now <1 in 1 000 000 in the United States and other high-income countries. Agents of recent transfusion-transmitted concern include West Nile virus, Zika virus, and *Babesia microti*. Busch et al analyze these emerging infectious diseases, previous false alarms, and current approaches to surveillance and response. They also underline the need for global blood-safety programs, as the high level of transfusion safety in high-income countries has not been matched so far in most low- to middle-income countries.

I hope that these articles will help *Blood* readers improve their knowledge of the optimal use of blood products and the management of transfusion reactions.

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