Blood is a drug: think twice!

When we take our messages to the general public about the need for blood, we emphasize its lifesaving—and life-sustaining—properties, as well we should. To be able to take the blood of one person and give it to a critically ill patient, in surgery, in the emergency room, in the maternity ward, in the nursery, on the battlefield...these are pretty special, pretty important and pretty dramatic things. But we often forget that blood is a drug, a potentially dangerous drug. The FDA, decades ago, perhaps as early as 1972 declared that blood was indeed a drug, and by so stating drew the collection, testing, processing, distribution and transfusion of blood products under its jurisdiction. Manufacturers of these drugs must follow the Code of Federal Regulations (CFR) as they apply to pharmaceutical manufacturers, and their Good Manufacturing Practices (GMPs). Each donation and its components is, thus, a “batch” in drug terms; donors are, in a way, our basic reagents from which we produce blood products.

Unlike chemicals, however, donors may be unaware, or forget, or (rarely) tell untruths about their personal or medical history, information that might put a patient at risk. Thus, we have developed very extensive, and expensive, screening procedures for donors, and tests to evaluate the safety of their blood for transfusion so as to prevent transmission of infectious disease wherever possible and to eliminate antibodies or other harmful moieties from the products. In spite of all these efforts, extensive and expensive as they are, bad things sometimes happen. Patients may have reactions to blood components, depending on the patient population and levels of hospital staff attentiveness, perhaps 2–3% of the time. Some of these may be very severe. Some are life-threatening. Occasionally, maybe two dozen times a year in the United States, they are fatal. We tell ourselves that the overall benefits of transfusion far outweigh the risks and liabilities, and that is true. But given the limits of our screening and testing capabilities, we are stuck with causing a measurable degree of harm, every day, every month, every year, right?

Wrong! There is still a lot we can do, or perhaps a better way to say it is, there is less we can do. That’s right: do more by doing less, or, to be more specific, do more good (reduce harm) by giving less blood. Dr. Mark Yazer and his colleagues at the University of Pittsburgh Medical Center did not invent the idea of Total Blood Management (TBM), but their recent paper in Transfusion (see reference below) is a recent—and elegant—summation of the concept. In their words, “...TBM represents a strategy aimed at improving and streamlining the diagnosis and management of anemia, thrombocytopenia and coagulopathy with a focus on reducing or eliminating the need for allogeneic transfusions.” From this statement, one can see that a critical part of such a program is having clear and widely accepted definitions of what, exactly, constitutes the appropriate transfusion trigger for levels of hemoglobin, platelets and coagulation factors. Certain flexibilities, based on individual patient and clinical considerations, are important to the success of a TBM program, as well as having a “change specialist,” a quality-improvement liaison between the TBM task force and the executive authority of the medical institution.

Evidence-based medical decision-making has been the topic of a large number of publications, symposia and conferences
in recent years, and many evidence-based transfusion triggers have been described in various reports. (See, for example, this past fall’s edition of PLUS, which describes these as they relate to the use of plasma products.) The authors describe here a simple method of affixing a warning screen to orders for red cells or plasma that embed an evidence-based criterion in the electronic-ordering system that allows the physician to check his/her patient’s lab value against the “evidence” that such a transfusion is needed or would be beneficial. The physician makes the decision to transfuse, but the TBM system provides them with guidance. Thus, it also provides a teaching tool, and a means of specific feedback to groups or individuals concerning their judgment about transfusion needs. Audit of transfusion practice based on institutionally agreed “transfusion triggers” provides a powerful tool for implementing appropriate change. Prescriber education and audit are critical to the success of the program.

Minimizing allogeneic transfusions through this program also provides the institution with a means for reducing or completely eliminating the use of preoperative autologous donations, a practice increasingly thought to be of almost no benefit and occasionally the cause of actually increasing the perceived need for allogeneic blood transfusion. Some have said for years that the best place to store blood is in the human body, free of preservatives, bacterial contamination risks, identification mistakes and, thus, transmissible pathogens. They also encouraged the appropriate use of perioperative autotransfusion, or cell salvage, as a means of reducing both allogeneic and preoperative autologous transfusion. Finally, by obtaining preoperative blood tests—and ensuring they were viewed by the clinicians—some weeks ahead of elective surgical procedures, they determined that just over a quarter of such patients were anemic, thus providing a mechanism to identify and potentially treat such patients with means other than allogeneic red cell transfusion prior to the planned procedure.

A presentation on this same topic was given at the most recent annual AABB meeting by Dr. Steven Frank, an anesthesiologist from Johns Hopkins University Hospital representing their TBM program, a report which we hope we’ll see soon in widely available form.


**Stem cell transplantation without transfusion?**

You’ve got to be kidding, right? How can anyone possibly go through the process of blood disease and marrow ablation, then receive a hematopoietic stem cell transplant (HSCT), and not get any red blood cell transfusions in the next several weeks? From the mere observance that there are already three question marks in a row in this little article, one might conclude that a little skepticism is in order, right? (Make it four!) But members of the bone marrow transplant program at the University of Ottawa noted that just that very thing occurs in a small number of patients.

Larger RBC transfusion requirements have been associated with reduced survival in HSCT and an increase in adverse effects, such as TRALI, infectious disease transmission and serious transfusion reactions, as well as immune modulation effects, including delayed wound healing and an increase in postoperative infections. And many things contribute to an increase in red cell transfusion requirements, such as patient age, marrow ABO mismatch and unrelated stem cell donors. Another confounding factor is that the many transplantation centers across the North American and other continents have different levels of “transfusion trigger” thresholds, often with modulations based on the patients’ symptoms, as well.

Of 555 patients recently undergoing HSCT at the Ottawa Hospital for whom total transfusion records were available, the authors found 59 who did not receive any red cell transfusions in the first 30 days following the procedure and compared them to the others to identify factors relevant to their transfusion status. The majority of the patients were recipients of an autologous transplant, but analysis showed that not to be a relevant factor. Comparing the transfused-in-first-30-days group to the non-transfused one, no significant differences (p<0.05) were found related to age, conditioning regimen, source of stem cells, or graft source (autologous vs. allogeneic). Those patients with no transfusions in the first 30 days post-transplant were more likely to have a higher pre-transplant hemoglobin level, be male, have early stage...
In a recent article in Transfusion Medicine, staff at the Center for Biologics Evaluation and Research (CBER) of the FDA (see reference on next page) reported on the use of the Centers for Medicare and Medicaid Services (CMS) very large data base to evaluate the numbers and characteristics of transfused blood components in this specific elderly population and the occurrence of certain adverse reactions. The special usefulness of their study is that it reports these data based on outpatient transfusion experiences among elderly patients, data which may come up missing in our usual calculations based on what happens in hospitals. This study focused upon the serious, acute, non-infectious complications of blood transfusion. Just about half of the transfusion-related fatalities reported to the FDA over the six fiscal years from 2005 through 2010 were due to TRALI, and another 24% were due to acute hemolytic transfusion reactions; thus, it seemed fitting to take a closer look at the affected population transfused outside of the inpatient hospital setting with regard to those two items.

Although the number of HSCT recipients not transfused in the first 30 days post-procedure is relatively small, on the order of 10%, the identification of clinical factors thus associated may help to develop strategies to reduce the cost and toxicity of HSCT. The authors note that an association between red cell transfusion and adverse outcomes after HSCT has been reported in previous studies, but that it has not been clear whether such transfused patients are sicker and require more blood, or whether the red cell transfusions themselves are contributing to an adverse outcome. This question often arises in looking at the effects of blood transfusion in a number of studies in seriously ill patients. There is an ongoing prospective clinical trial underway that randomizes HSCT patients into two groups with transfusion triggers of 70 g/L (7.0 g/dl) vs. 90 g/L, with the goal of whether increased red cell transfusion leads to worse outcomes following HSCT.

It is fascinating that blood transfusion, viewed as a near-miraculous scientific achievement in the last century, and rightly so, has become something we are coming to see as a risk as we find more and more uses—if not needs—for blood transfusion. It’s somewhat reminiscent of the old adage to the effect that “...a strength overused can become a weakness.”

Perhaps there can be too much of a good thing.


**FDA identifies potential transfusion complications**

In a recent article in Transfusion Medicine, staff at the Center for Biologics Evaluation and Research (CBER) of the FDA (see reference on next page) reported on the use of the Centers for Medicare and Medicaid Services (CMS) very large data base to evaluate the numbers and characteristics of transfused blood components in this specific elderly population and the occurrence of certain adverse reactions. The special usefulness of their study is that it reports these data based on outpatient transfusion experiences among elderly patients, data which may come up missing in our usual calculations based on what happens in hospitals. This study focused upon the serious, acute, non-infectious complications of blood transfusion. Just about half of the transfusion-related fatalities reported to the FDA over the six fiscal years from 2005 through 2010 were due to TRALI, and another 24% were due to acute hemolytic transfusion reactions; thus, it seemed fitting to take a closer look at the affected population transfused outside of the inpatient hospital setting with regard to those two items.

Although a retrospective claims-based study has drawbacks, the numbers of Medicare-funded outpatient transfusion visits (255,119 in 2007 and 283,297 in 2008) are such as to provide some power to the analysis. In these two years, 0.9 and 1.0%, respectively, of the Medicare population had an outpatient transfusion visit. Among the roughly 85% of these visits in which the transfused blood components were quantified, the number of units per blood recipient in the year were 4.0 and 4.1, respectively. In these two years, 85 and 84% were RBCs only, 6.5 and 6.6% were RBCs and platelets, plasma transfusion alone occurred in 4.7 and 4.4%, and platelets only occurred in
3.1 and 2.9%. The mean number of units per Medicare claim, which I assume to be transfusion episode, averaged about 2 for RBCs, 1.2–1.3 for LR plateletpheresis, and 2.7 for FFP.

The study identified a total of 15 cases of TRALI in the two-year period, 8 in 2007 and 7 in 2008, with the TRALI diagnosis recorded on the same outpatient visit or as an inpatient the same day or the next. Overall rates of TRALI thus were 3.1 and 2.6 per 100,000 in 2007 and 2008. The rates of TRALI for all red cell transfusions were 1.5 and 1.1 per 100,000 in those respective years. LR-RBCs had a rate of 0.8 and 1.4 in the two respective years. The TRALI rate when RBCs and platelets were given in the same visit was 13.1. No TRALI occurred in the small group of FFP-only transfusions, about 9,000 per year; however, the highest TRALI rates observed, 36.4 per 100,000, were seen in very small groups (2,748 and 3,559) of patients receiving both irradiated LR-RBCs and irradiated LR platelets. These data suggest that blood processing can affect TRALI rates: namely, LR reduces the rates and irradiation seems to increase them, especially pre-storage irradiation of components, including red cells. Irradiation can damage RBC membranes, affecting their membrane integrity and elasticity, which leads to leakage of potassium ions and lactic dehydrogenase, enhancing in vitro hemolysis. Similar effects may yet be found in platelets that are irradiated. There was no examination of the commonly noted occurrence of TRALI as a result of anti-HLA or neutrophil antibodies associated with multiparous women donors.

The data regarding the occurrence of ABO incompatibility in these same groups is similarly analyzed by year and by type of component. The rates are slightly higher than those of TRALI, but demonstrate that it is still a rare transfusion-related event. The rates in patients receiving irradiated products, the numbers of which were small overall (see tables in the article), were remarkable at 44.0 per 100,000 for irradiated LR-RBCs.

Perhaps, the authors suggest, blood group testing errors are more common in elderly patients with malignant conditions and transplant procedures. It is also worth considering that the extra handling involved in irradiating products and then returning them to inventory might lead to an increase in clerical errors.

Since these data were based on very large administrative databases, they have several sources of potential error, including recording errors, record losses, accuracy of component products recorded and other issues. Nonetheless, such databases hold a great deal of useful information relating to a number of adverse transfusion events that can be obtained and analyzed to improve our understanding of such events and hopefully add to our capacity to prevent them.

Guidelines from Britain

From “across the pond,” as is sometimes said, comes an extended and thorough paper with guidelines regarding the management of acute transfusion reactions. The British Society of Haematology, an eminent scientific organization that publishes the British Journal of Haematology, has a British Committee for Standards in Haematology (BCSH), and their guidelines on acute transfusion-reaction management were recently published in that journal (see reference below).

The article describes the approach to a patient who develops adverse symptoms/signs while undergoing transfusion, an approach that includes recommendations with regard to initial recognition, establishing the likely cause, treatment, investigations, planning future transfusion and reporting on the event within the hospital and to appropriate hemovigilance organizations.

Although acute non-hemolytic febrile or allergic transfusion reactions (ATRs) are a common complication of transfusion and often result in little or no morbidity, prompt recognition and management are essential. The serious hazards of transfusion hemovigilance organization (SHOT) receives 30–40 reports of anaphylactic reactions each year. Other serious complications of transfusion, such as acute hemolysis, bacterial contamination, TRALI or TACO may commonly present, initially, with features similar to ATRs. The authors, therefore, include these standard ISBT definitions in their discussions, particularly regarding recognition and management.

There are about 10 pages of recommendations and discussions, more than can be thoroughly covered in this article, but several things stand out and deserve emphasis here. The very first recommendation states: “All patients should be transfused in clinical areas where they can be directly observed, and where staff is trained in the administration of blood components and the management of transfused patients, including the emergency management of anaphylaxis.” There is some concern that this is not always the case in all of our patient-care facilities. The second recommendation says: “The recognition and immediate management of ATR should be incorporated into local transfusion policies and there should be mandatory training requirements for all clinical and laboratory staff involved in the transfusion process.” These strike me as being of particular importance, particularly the emphasis in the discussion concerning direct monitoring of patients who are in coma or who are unable, for any reason, to report symptoms to the staff.

The paper continues with recommendations about having patients report anything in the next 24 hours that might be important, what to do if symptoms develop, how to manage mild reactions, and then goes on to discuss the various presenting features of acute reactions with increased severity, defining specific signs and symptoms in detail and proceeding to their appropriate management. There is a useful and detailed flow chart and an excellent table listing severe reaction symptoms and the specifics of investigations to be carried out.

In addition to this clinical information, the next section provides details concerning the laboratory investigation of ATRs—and note that in this paper ATR refers to all acute reactions, not simply anaphylactic ones as one might infer from the abbreviation. This section is followed by one dealing with the management of such patients who subsequently require transfusion, including the lack of clear evidence for the use of antipyretics or NSAIDs. They have a section on ATRs in children and neonates, in whom they are less easily recognized, but probably occur more frequently, and close with a section on the importance of reporting on reactions to the hospital transfusion service, transfusion committee and the regional blood center. The cases are then to be reported to the SHOT hemovigilance team. Of especial interest is the fact that moderate and severe ATRs are considered serious adverse reactions, and, as such, there is a legal requirement to report them to the regulatory authority in the UK. In the United States, some of this is done voluntarily, and is required for all deaths; however, it seems likely there are more occurrences that should become part of our database for improving care in the area of blood transfusion.

Too much of a bad thing

Careful studies have generally agreed that the normal life span of adult human red blood cells is 120 days, and that cells die in a predictably linear age-based curve; that is, there is very little “random” destruction, perhaps 0.06–0.4 % per day. This number has been confirmed with many different types of methods, most accurately including various radioactive labeling techniques. This translates to a linear loss curve of 0.83 % per day, although we often speak of losing “about” 1% per day. In some mammals, the random destruction rate is much higher, perhaps related to a greater degree of blood loss, physical trauma and possibly other reasons.

Thus, generally when we talk about hemolysis, we are talking about a rate of destruction greater than 1% a day. The term “hyperhemolysis” was first used to describe severe hemolytic anemia (usually intravascular lysis) associated with immune and non-immune hemolytic anemias. From the early 1990s it was used to describe a life-threatening hemolytic transfusion reaction (HTR) in sickle cell disease (SCD) wherein the hemoglobin level fell below the pre-transfusion level of the patient, the implication being that the patient’s own red cells were being destroyed along with the transfused red cells. This, then, is a hyperhemolytic transfusion reaction (HHTR). It may also be seen in patients with SCD with infections due to malarial parasites, babesia or mycoplasma; G6PD deficiency; and autoimmune hemolytic anemia.

Dr. George Garratty, certainly one of the world’s experts on hemolytic transfusion reactions, discusses HHTR in a recent editorial in Transfusion Medicine and notes that other workers in the field have published information indicating the syndrome can occur in patients with thalassemia and also in patients without hemoglobinopathies. In commenting on the previous article on hyperhemolysis in a pregnant woman with dyserythropoietic anemia, Dr. Garratty notes that he believes we are rediscovering an old phenomenon, using new terms and definitions.

In answer to the question, “What is the cause of HHTRs?” he feels we don’t have a single, simple working explanation. Most—but not all—of the cases have been described in patients with SCD. The various hypotheses of why this is so include “bystander” lysis, suppression of erythropoiesis, “acute painful episodes,” macrophage hyperactivity, and excessive eryptosis [red cell apoptosis, programmed cell death]. Some of these fit nicely with what is known about some of the unusual characteristics of SCD, such as increased alloimmunization to a variety of antigens (red cells, white cells, platelets, plasma proteins); increased production of autoantibodies and hyperactive macrophages; and abnormal red cell membranes sensitive to reactive lysis. But many of the characteristics in SCD patients with HHTRs are not present in these other populations reported to have HHTRs.

In the same edition of Transfusion Medicine containing Garratty’s editorial, are descriptions of two cases of HHTR occurring in patients without SCD. The several recent reports of HHTR in patients without SCD lead Garratty to conclude that we need new hypotheses to explain these reactions or come to the conclusion that the events being seen in patients without SCD just aren’t the same thing. The occurrence of the phenomenon is a frightening thing for all involved, especially the patient reported in the article from the Netherlands summarized on the next page.

Garratty G. What do we mean by “hyperhemolysis” and what is the cause? Transfusion Medicine, 2012; 22; 77-79.

Erratum in: Transfusion Medicine, 2012; 22; 239
Life-threatening hemolysis: a case report

Ordinarily, we would not devote a review, even a brief one, to a single case report in PLUS; however, this one is very dramatic and provocative, and it leads into a discussion (see preceding article) by Dr. George Garratty that explores some of the issues related to this unusual phenomenon of hyperhemolytic transfusion reactions (HHTRs). The report comes from Dr. Bank and colleagues from the University of Leiden and the Sanquin Blood Supply Foundation in Leiden, The Netherlands. Sanquin Blood Supply Foundation is responsible for the blood supply in the Netherlands, and is affiliated with the Universities of Leiden, Amsterdam and others in the Netherlands. HHTRs are uncommon, but not rare; the congenital dyserythropoietic anemias (CDA) are definitely rare, but as with other rare occurrences, methodical exploration of the CDAs has led to insights into genetic mechanisms governing red cell production and metabolism. Although there are at least three different subtypes of CDA, they all require long-term transfusion support, which in turn leads to concerns about iron overload, splenectomy and perhaps bone marrow transplantation. The unusual complication of an HHTR in a pregnant woman with rare CDA led to this report.

This 33-year-old woman had type 1 CDA, and she was also a carrier for Factor V Leiden and Protein C deficiency, the latter two promoting factors for thrombosis. She previously had lost five pregnancies, common in Factor V Leiden cases, but had a healthy 5-year-old son. The patient was chronically anemic, but not transfused; however, she had received blood at a regional hospital twice before her admission at 6 months gestation to the Leiden Hospital. On admission, she had a slightly rapid pulse and an enlarged spleen. Her hemoglobin level (Hgb) was 6.3 g/dl and she had evidence of hemolysis. She had a weakly positive DAT two weeks before, but now it was negative and it remained negative during the rest of her pregnancy. Anti-Jka was detected, induced by, or boosted by, her recent transfusions. Fetal ultrasound was normal. In order to keep her Hgb level between 4.8 to 6.4 g/dl she required 3–4 units of Jk(a–) red cells per week.

Despite aspirin and low-molecular-weight heparin, she developed jugular vein thrombosis, related to the IV catheter placement (as well as her inherited coagulation protein abnormalities) with Staph. aureus septicemia and heart failure during the 32nd week of pregnancy. Even though she received more frequent transfusions, her Hgb could not be raised above 6.4 g/dl. The size of her spleen increased. At 34 weeks of pregnancy she delivered vaginally a healthy son.

She persisted in her transfusion-resistant hemolysis and anemia and her DAT became positive again, both with anti-IgG and anti-C3d; she now also was found to have 2 new antibodies (anti-Lua and anti-Kpa). All of this occurred despite the use of high-dose IVIG and interferon-alpha, both thought to perhaps moderate her hemolysis, which persisted throughout the many DAT-negative weeks as well as those following DAT-positivity. Two months after delivery, she was still very anemic and underwent splenectomy. She recovered completely, required no further transfusions and one week after splenectomy was discharged with an Hgb of 9.0 g/dl and no evidence of hemolysis. She has been maintained on an iron chelator and has been continuing her normal activities.

There are no clear cut criteria to define the HHTR, nor are its mechanisms well-understood. When defined by the fact that post-transfusion Hgb levels are lower than those pre-transfusion, with evidence of hemolysis, the authors feel that this patient fits the criteria. Dr. Garratty agrees in his accompanying editorial (see preceding article). In an early paper from 2004, Petz and Garratty describe hyperhemolysis as the destruction of cells by an antibody against an antigen that is not an unmodified basic component of the red cell membrane.

Strange happenings! “There are more things in heaven and earth, Horatio, than are dreamt of in your philosophy.” (From “Hamlet”, Act 1, Scene 5, William Shakespeare)

Most people have not seen many patients with TTP, thrombotic thrombocytopenic purpura, but it is talked about a lot at blood bank meetings and written about fairly often, probably because it has remained a mystery to most of us since it was first described by Eli Moschcowitz in 1924. In spite of the title above, this will not be a definitive explanation of the process and its cause(s), but the paper that prompts this summary is really interesting, and seems to take us another step further down the road to understanding TTP, which perhaps might improve our care of these patients.

TTP is classically defined, as per Moschcowitz, as a pentad of symptoms, although in many—if not most—cases, some of them are absent.

- Thrombocytopenia with bruising/purpura
- Microangiopathic hemolytic anemia—anemia, jaundice and fragmented, chewed up RBCs noted on the peripheral smear (schistocytes)
- Fluctuating neurological symptoms, including altered mental status, hallucinations, headaches, bizarre behavior, difficulty speaking, stroke
- Renal failure of varying degrees, but of rapid onset fever
- Fever

There are other causes of thrombocytopenia with microangiopathic hemolysis, but most are more easily identified as to causation. In earlier reviews, such as one in 1966 of 272 patients, most were women, and the mortality rate approached 90%. The mortality rate now is considerably better than that, but many deaths occur. Unregulated von Willebrand Factor (VWF)-dependent thrombosis seems to be the mechanism in both congenital and acquired cases.

VWF is made and released by vascular endothelial cells in the form of ultra-large multimers (UL) of VWF. ADAMTS13 is an enzyme that cleaves these UL-VWFs, and a deficiency of this function results in abnormal levels of circulating UL VWF. This, in turn, binds to platelets which clump up, initiating microvascular thrombi in small arteriolar vessels, causing many of the symptoms, and through which pulses of red cells under pressure are forced, leading to fragmentation. So the theory goes, and there is considerable evidence for it. But, clinical remission can be achieved in patients with an acute TTP episode despite persistence of low levels of ADAMTS13, suggesting other factors are in play.

It is also known that beta2-glycoprotein I (B2GPI) interacts with VWF in a glycoprotein Ib binding state. Given the fact that active VWF multimers are present in TTP, the authors wondered if B2GPI might have an active role in the disease process. Indeed, they found that there are lower levels of it in TTP patients, both acutely and in remission. They observed a direct correlation with levels of ADAMTS13 (both were low) and an inverse relationship between the degree of VWF activation and B2GPI; i.e., low levels of the glycoprotein were seen when high levels of activated VWF were present. They demonstrated that B2GPI can block platelet adhesion to the VWF strings produced by endothelial cells by directly binding to the VWF, suggesting that this glycoprotein may protect from the effects of hyperactive VWF multimers by inhibiting its interaction with platelets.

This is a very complex paper that discusses the physical chemistry of these experiments and of the known biology of the various molecules at play here in much greater detail. The authors also point out that there is a wide variation of B2GPI levels in normal individuals, and that overlap is noted between plots of measurements of the protein in acute phase patients, patients in remission and healthy controls. However, in each of seven patients with paired acute-remission samples, it is clear that remission levels are greater in each case. Further work will pursue this in more detail, and will help define whether or not B2GPI might play a role in the treatment of this unusual but devastating disease, now treated basically with plasma exchange.

The “Endurance” and our patients

On the cover of one of this year’s Immunohematology issues there is a fabulous and historic photograph that is a whole story unto itself, but not for this particular issue of PLUS. The photo shows a three-masted sailing ship, all sails furled or dangling, tattered, from the forward shrouds. The ship is seen from about 200 yards away, trapped in a sea of Antarctic ice, frozen clusters of which loom over the foreground, and which eventually crushed the ship, the Endurance, which had transported Ernest Shackleton and his exploring crew into the Antarctic at the time of World War I. Through incredible effort, and some luck, they all survived.

This particular issue of the journal concerns itself with sickle cell disease (SCD) and the transfusion of patients afflicted with it. The relationship of the cover with the topic of SCD has to do with the immovable, inflexible rigidity of ice, which in its more common and friendlier form of water is flexible, functional and useful for our needs. Red cells with SS hemoglobin cause a myriad of problems for patients when they give up their oxygen molecules and become rigid, misshapen, and inflexible. In efforts to break the sickling cycle and improve oxygenation, we transfuse these patients with other people’s red cells, and we transfuse them as well to replace the often rapid destruction of their own cells.

Dr. Geralyn Meny, most recently with the American Red Cross Blood Center in Philadelphia and currently Director of Transfusion Medicine, Department of Pathology, UT Health Science Center at San Antonio, organized a whole issue of Immunohematology with authors from several specialized centers for managing SCD to describe their transfusion-management protocols for patients with SCD. Institutions represented by the assembled authors include Johns Hopkins Medical Institutions, St. Louis Children’s Hospital and the Missouri-Illinois American Red Cross Blood Services, Children’s Hospital in Boston, Children’s National Medical Center, Children’s Hospital and Research Center of Oakland, The Atlanta Sickle Cell Consortium, and the Children’s Hospital of Philadelphia.

In her Introduction, Dr. Meny notes that estimates are that SCD affects about 90–100,000 Americans, about 1/500 African American births and 1/36,000 Hispanic American births. Improved therapy in infants (ages 0–3 years) has led to reduced mortality rates of about 68% in that group; however, overall life expectancy is estimated to range between 53–60 years, considerably below the national average. She asks what role red cell transfusion plays in the care of SCD patients and wonders if we are doing all we can, and should do, to minimize the complications of such transfusion.

Acute hemolysis, chronic anemia, the acute “chest syndrome,” stroke, and painful sickling crises with bone infarcts and growth disturbances are among the symptoms that patients
One of the things that emerges is the increasing role of molecular testing in managing the transfusion needs of SCD patients. Molecular genotyping is often performed on all African American donors based on optional self-selection during the registration and screening phase of donation. Others perform it on all, or a selection of, frequently repeating donors. Some centers are involved in research regarding the utility of non-myelo-ablative hematopoietic stem cell therapy in patients with crippling or life-threatening disease. Others are examining their patients for factors that may predispose them to iron overload disease and the role of molecular matching to retard this process by the use of erythrocytapheresis in selected donors.

The seven reports and the editorial in this issue are rich with historical perspective, operational suggestions and ideas for further pursuit and future use. If you haven’t seen this issue and would like to have it, you may contact Sandra Nance of the American Red Cross Blood Services at immuno@redcross.org.

Meny GM. Transfusion protocols for patients with sickle cell disease: working toward consensus? Immunohematology 2012; vol. 28, Number 1:1–2.
Immunohematology Journal

The American Red Cross publishes Immunohematology quarterly. This peer-reviewed journal covers recent research findings of interest to those in the field of transfusion medicine. Submit subscription requests and manuscripts to immuno@redcross.org. Issues more than one year old can be accessed at no charge at redcrossblood.org/immunohematology.

Publications Corner

Recent publications by American Red Cross scientists and physicians:


**Steele WR, High PM, Schreiber GB.** AIDS knowledge and beliefs related to blood donation in U.S. adults: results from a national telephone survey. *Transfusion* 2012; 52:1277–89.

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