PDI, a burden for hospitals and blood centers

A vexing problem for blood centers is the receipt of information after blood collection (most often after shipment and sometimes transfusion, it seems) from either the donor or another source that would seem to disqualify the donor as safe and eligible. This is called post-donation information, or PDI, and often occurs as a result of discussion with others. If it is disqualifying, the blood center must detail the nature of the issue, notify transfusing facilities, and retrieve the component(s) in question, while maintaining confidentiality throughout.

A major source of blood center aggravation stems from the fact that, particularly at high school drawings, old girlfriends (or boyfriends) of the donor call anonymously with accusations about drug use, sexual promiscuity, homosexual relationships, jail time and other “offenses” in order to embarrass or even hurt the donor. Occasionally, it’s a local volunteer who “knows” such and such about him or her. Sometimes, this sort of sexual or drug information is accurate, but in the absence of a reliable source, such as a spouse or parent, it can usually be discounted. A medical officer is usually called upon to make that decision. However other times, it’s a family member with—usually—accurate information, often concerning malarial travel risk. But even malarial travel risk is vastly overemphasized and probably mostly irrelevant.

Nonetheless, many reports go on to result in withdrawals, and sometimes recalls. The authors of the paper, from the headquarters of the American Red Cross Blood Services and the Canadian Blood Services (CBS), carefully characterize the terms ‘recall’ and ‘withdrawal’, which have specific regulatory meaning, and introduce the term ‘component retrieval’ for this process, and then go on to delineate the statistics and categories, infectious and non-infectious of these events. They offer a group of recommendations to approach these events in a better way. The Red Cross noted an annual PDI occurrence rate of 16.3/10,000 donations in 2012, while CBS found a rate of 10.3 to 12.6 per 10,000 over the last four years.

The authors also provide details of the most common reasons for PDI events occurring with the Red Cross and CBS for a combined total of over 8 million donations in a recent interval. Blood collected from donors with a history of cancer in the last 12 months tops the CBS list, followed by malarial travel risk and vCJD travel risk. Outstripping these by a wide margin in the Red Cross data are malarial travel risk and vCJD travel risk, the latter perhaps related to the long-term presence in Europe of U.S. military and their dependents, the kitchens/mess halls of which were provided with British beef during a worrisome period. Men having sex with men and other risk behaviors were also more common in the Red Cross data.

An interesting difference in the approaches of these two large blood provision agencies has to do with the requirements of the respective regulatory agencies. In Canada, the National Advisory Council on Blood and Blood Products does not recommend follow-up for PDI reports of cancer, travel of any kind (malaria and vCJD), tattoos or piercings. For risky behavior, patient testing may be recommended, depending

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Cover photo: Human bone marrow megakaryocyte in the process of forming two small platelets via proplatelet extensions. Visuals Unlimited, Inc.
This issue of PLUS was written by Dr. Robert (Bob) Westphal.

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on the degree of risk after evaluation. In the U.S., the FDA currently requires retrieval of indated components (for any travel); a history of male-male sex, tattoos or piercings, IV drug use (or sex with anyone in these categories). All products, indated or expired, from all ineligible donations back to the beginning of the risk period or the last non-reactive donation (in the case of certain test results) must be retrieved.

One can see from these examples that, especially in the U.S., a very complicated process ensues, much of which seems excessive and irrelevant. Upon such notification by a donor or other caller, and depending on the type of PDI information, units have to be quarantined and returned, information about prior donations and the distribution of those components obtained. Almost immediately, the receiving transfusion facility is notified of the action and asked to gain control of the products in question, return them or indicate their disposition, and report back to the center. The flow of paperwork is heavy, and the odds for mistakes are high. Then decisions have to be made about getting more, or follow-up information, to the hospital and the patient’s physician, who must then decide what to tell the patient or family. In many cases, further investigation after the initial “gain control” letters go out indicates that the unit(s) are acceptable after all. The resulting ill feelings and immense paperwork and time commitments are quite frustrating to all staff involved. In both the U.S. and Canada, over a several-year time period, no cases of transmission of HIV, HCV or HBV have been attributed to any of the units associated with PDI and subsequently retrieved. Similarly, no cases of transmission of cancer or of teratogenic effects of specified medications have been reported, despite the large number of donors who are taking them.

The authors present a detailed analysis of risks and results from actual data obtained from PDI investigations and carefully build a case for a proposed framework for retrievals and patient notifications related to PDI. The regulatory excesses, for which the U.S. is well known, and the large expenditure of resources, time and money occasioned by some of the requirements, could surely be alleviated considerably by careful regulatory review of these recommendations as presented in the framework of Table 3 in the paper. Everyone involved in the collection, testing, administration and transfusion of blood should see this paper.


Double down on platelet contamination!

A lot has been written about bacterial detection strategies in room temperature-stored platelet concentrates, and just about every month, one can find reports of cultures turning positive in the blood center or storage facility just after the unit(s) have been transfused. It is a delicate balance between having safe, non-bacterially contaminated platelets for transfusion and the risk of infecting a patient who—quite likely—is already in precarious clinical condition and usually with reduced immunologic responsiveness, to boot. Some blood centers have increased the volume of sample incubated for culture/bacterial detection, which decreases the infusion size but doesn’t seriously compromise it.

The authors of this paper performed a meta-analysis to evaluate all the current North American data comparing 4 ml vs. 8 ml sample volume associated with detection of contaminated platelets. Results of these studies, when pooled, indicate a higher rate of true-positive culture results and, thus, a statistically significant increase in the detection rate and subsequent interdiction of contaminated units. Broader implementation of this method should definitely reduce the risk of adverse reactions to platelet transfusion…and save some lives.

Bloodless care may benefit patients other than Jehovah’s Witnesses

As further evidenced by the related article in this issue, it is not uncommon to have patients who will not accept allogeneic blood transfusion (ABT). The Jehovah’s Witness faith has more than 8 million members worldwide, and an estimated 1.2 million members in the United States. In addition, there are other people who have personal or religious objections to receiving blood. Many will accept the “minor” fractions, non-red cell containing, such as albumin, gamma globulin, clotting factors and cryoprecipitate. There are several centers and/or physicians who have developed programs to carry such patients through various medical or surgical procedures, including hip replacement, open heart surgery and others. If we agree that it’s better not to have transfusions of blood components, if possible, then there is much to be learned from such programs and centers.

Physicians at the Johns Hopkins Medical Institutions in Baltimore, M.D., established – in June 2012 – such a center, the Bloodless Medicine and Surgery Program, and reported on data for the 297 patients admitted to the program through July 2013. Of these, 197 were medical patients and 100 were surgical patients. Three patients were prospectively excluded from the study when they elected to receive blood, 2 surgical and 1 medical. A control group of surgical patients from the 60,000+ patients admitted during the study period were evaluated, and a propensity score-matched group of 1,157 were chosen to provide a control:test ratio of 4:1, increasing the strength of the analysis. Matching was designed to minimize differences in variables such as age, sex, diabetes, hypertension, obesity, heart disease and other medical conditions. They were not fully matched for type of surgical procedure, since more than 1,900 separate procedures are done at the center.

Those patients in the bloodless surgical group having elective surgery were seen prior to the scheduled operation and asked to begin oral iron therapy (FeSO4), 65 mg of elemental iron 2-3 times/day. Oral and/or IV iron was given to patients with Fe+++ deficiency anemia, and Fe++ and erythropoietin given to those with iron deficiency and chronic renal failure, as were patients anticipating ‘significant’ blood loss. The Bloodless patients were selected on the basis of risk and treated differently, therefore we might expect different outcomes. All blood samples drawn from the bloodless group were collected in pediatric micro-containers, and ICU patients had an in-line reinfusion blood drawing system used via indwelling IV catheters. Since the control group generally had none of these interventions, I think the reader can see where this is going!

Thirty-six (36%) of the 98 bloodless surgical patients had pre-surgical interventions with iron and/or erythropoietin; none of the 467 matched controls did so. Again looking at just the surgical patients, there were no deaths in the bloodless group and 17 in the control group, with a p value of 0.05. Morbidity rates from infection, MI and respiratory problems were not significantly different, but thrombotic events tended toward being more frequent in the control group, p= 0.06.

Looking at comparisons of the entire bloodless group (294 patients), vs. the controls (1,157 patients), illustrates other things. In-hospital death occurred in two ‘bloodless’ patients and in 31 controls, significant at a p value of 0.046. There was a trend, again, in rates of infection overall, with 14 test vs. 88 control group infections, for a p value of 0.08. Hospital length of stay was similar between the groups, and total costs related to the procedure (outpatient pre-treatment for the bloodless group included) were not significantly different, although there was a trend toward lower charges in the group not receiving blood products (p = 0.06). Intra-operative autologous blood salvage was used in 31% of the bloodless surgical patients, vs. only 6% in the standard surgical group. Discharge hemoglobin levels were very similar.

Thus, it seems that preoperative evaluation for patients that identifies and treats underlying causes of anemia would be of benefit for all elective surgery patients. As well, minimizing blood loss to the lab, utilizing intra-operative salvage where indicated, optimizing surgical blood loss, and tolerating lower Hgb levels without transfusion are best for all. For those procedures that aren’t elective, the more ‘urgent’ protocol seen in the article on life-threatening anemia in Jehovah’s Witnesses may be useful. It seems again that less is best, when it comes to transfusion.

Treatment of profound anemia from blood loss in Jehovah’s Witness patients

All of us dealing with the question “When do we pull the transfusion trigger?” have learned a great deal from patients who are Jehovah’s Witnesses, or others who refuse blood transfusion even when faced with significant anemia and major blood loss. Many surgeons began to carefully parse their operative procedures and to develop strategies other than blood transfusion for such patients. The hardest part is knowing just what the risk of mortality is from severe anemia; what age considerations need to be kept in mind? What underlying conditions enhance the risk of death from anemia? What combination of fluids and volume expanders are most effective? How do they differ under alternate circumstances? All of this, along with other reasons, drove long-term searches for stroma-free, red cell free, hemoglobin-based oxygen carriers (HBOC), a labor still not fulfilled to the point of licensure.

The authors of this paper, from the University of Michigan, report on their experience and look at the pertinent literature. They go on to specifically evaluate three strategies for severe anemia in these patients: exogenous erythroid stimulating agents (ESAs), iron supplementation, and hemoglobin-based oxygen carriers (HBOC). Other important points include minimizing phlebotomy and losses from excessive diagnostic testing, as well as careful scrutiny for other treatable causes of anemia, such as B12 deficiency or hypothyroidism. In actuality, more than one mode of treatment is commonly required. The paper includes an excellent diagram for an anemia protocol when a Jehovah’s Witness patient presents with, or develops, a Hgb level < 7 gm/dl. It’s worth cutting out and pasting in your files.

All such patients should start an initial anemia protocol consisting of an ESA, an IV iron preparation and administration of folate and B12, adding Vitamin C, except in cases of renal failure. If the Hgb is <5, it is considered to be critical and treatment with an HBOC is indicated. Availability of these is not guaranteed, and because they are not licensed, specific permission must be obtained from the FDA, the institutional review board and, of course, the patient. Approval is not always guaranteed, nor is availability, but the FDA has allowed for such use under an investigational new drug (IND) protocol. Depending on the clinical situation, respiratory support with high ambient O2 levels may be needed, or helpful.

Several ESAs have been developed over the years, including cross-linked Hgb, polymerized Hgb and conjugated Hgb, but the availability of all of them has been curtailed due to ill effects, in some cases death. One new entry into the field has completed a Phase I safety study and has gone on to a Phase Ib trial in sickle cell patients. It is available for use under an expanded access IND for emergency treatment of Jehovah’s Witnesses. The idea behind the use of these HBOCs is to bridge the gap between the onset of life-threatening anemia and the time required for the ESAs and supplements to contribute to the circulating red cell mass. There also are problems associated with the use of ESAs that has led to their non-licensure in general, such as their vasoactive effects leading to hypertension, coronary artery constriction and myocardial infarction. Levels of methemoglobin, which cannot carry O2, also rise. Hepcidin (a key regulator of the entry of iron into the circulation in mammals; with high hepcidin levels serum iron falls and gut absorption is decreased) levels increase to very high numbers in critically ill trauma patients and are positively correlated with the duration of anemia. A single dose of an ESA can result in a rapid lowering of such levels.

This very readable article is a useful addition to the library of all involved in transfusion medicine.

There are many conditions that require repeated, long-term blood transfusion therapy, including leukemias and other cancers, but chief among are sickle cell disease (SCD) or thalassemia whose patients have lifelong transfusion requirements, without which life would be considerably foreshortened. Alloimmunization results, even in donors carefully screened for possibly offensive antigen exposures, make it difficult to find compatible blood over the years.

Programs designed to limit exposure to red cell antigens not possessed by the patients are very helpful, but their success depends on then finding donors with suitable genotypes in sufficient numbers so as to be able to support such a program. Since these conditions mostly afflict minority racial and ethnic groups in North America, the best support generally comes from donors associated with those groups. However, they are historically underrepresented in blood donor populations in most urban areas of the U.S.

The authors, from Columbia University and the New York Blood Center (NYBC), established a program called PreciseMatch among African-American and Hispanics in 2005, with the goal of increasing donations from them by 150 units per month, focusing on Manhattan, Brooklyn and the Bronx. The coordinators for each borough were tasked with increasing donations from the appropriate groups by 50 units each month. The NYBC collects about 400,000 units annually and distributes tested and processed units to about 200 area hospitals. About 5% of these units are for patients with SCD. The authors detail a large number of informational programs, health expos, church events, street fairs and related educational and social events at schools, clubs and other public places.

In the second year, 2007, they held a series of focus groups to evaluate what problems had been discovered and identify reasons for hindrances. They identified positive motivational factors, as well as negative ones, such as time commitment and convenience. The amount of time, money and staff effort involved in the program was pretty high, though the authors present no specific data on that topic. Another major consideration was the fact that the deferral rates among these new donors were very high. Many in the Latino community accrued deferrals for malarial travel, particularly to the Caribbean and especially the Dominican Republic. In addition, low Hgb levels among African-American women were in the range of 25%, almost all due to iron deficiency, whereas that number in New York Caucasian women is 7%—still a high number. The current average deferral rate at NYBC drives is 16-18%; some minority group drives reported a 50% deferral rate.

Overall, the program—despite a large expenditure of resources—achieved only about 75% of the original goal of 150 units per month. Despite these setbacks, the center believes it has learned a great deal and established relationships in these communities to enable them to continue examining and focusing on this effort.

More platelets cause more adverse events

The Platelet Dose study (PLADO) first reported results in 2010 that examined the ‘transfusion trigger’ question with regard to platelet transfusions in thrombocytopenic patients. Those data led to the currently accepted practice of using a platelet count below 10,000/µl (10^9) as the trigger, except in very special circumstances. The authors have continued this multi-institutional study designed to answer a number of questions about doses, platelet sources (pooled random vs. apheresis), ABO matching, storage duration and recipient characteristics that might affect the frequency of adverse events after platelet transfusion. The patients were divided into high dose (4.4 x 10^11 platelets per meter square body surface area), medium dose (2.2 x 10^11 platelets) and low dose (1.1 x 10^11 platelets) categories; the outcome was the frequency of occurrence of significant bleeding, using WHO criteria. You may recall that there were no significant differences in bleeding between the dosage groups reported in the original study.

The project was further used to evaluate the effects of other product parameters on the occurrence of an adverse event. After exclusions for missing data, and other reasons, there were 5,034 transfusions to 1,102 patients that were evaluated. No HLA-matched platelets were administered in these studies. For an “average sized” person of 1.7 meters square, the low, medium, and high dose infusion volumes of platelet concentrates were 134, 250 and 457 mL respectively. All platelets were leukocyte-reduced. The degree of platelet ABO “match,” platelet source (whole blood vs. apheresis) and storage duration had no effect on the occurrence of an adverse event, the most common of which was fever, which occurred in 6.6% of transfusions, followed by allergic reactions 1.9%, tachycardia 1.8%, and chills or rigors 1.1%. However, platelet dosage was definitely important, with a clear correlation between the number of platelets and occurrence of an adverse event.

Since the results in terms of significant bleeding episodes were equal among all three dosage groups, and the occurrence of adverse reactions, as shown in this study, was highest in the high dose group, it would seem that medium or low dose platelet transfusion doses are superior, including in terms of resources such as money and donor time, to the high dose transfusions. Another factor worth noting is that an increase in the number of donors per transfusion seems to have an effect on risk of an adverse event. Some of this cross-correlates with the effect of the size of the platelet dose, since the higher doses had the highest number/rate of reactions. It may be that the somewhat larger volume of plasma in such transfusions is a confounding event, as well, adding yet another reason to move toward the use of platelet additive solutions in the future.

In the meantime, infusion of leukocyte-reduced platelets, at a dose of 1.1 x 10^11/meter squared and from the least number of donors possible, represents the current best practice.

Two studies (not yet available in print for details) from the same journal are also worth mentioning because they bear on the issue of adverse reactions to transfusions. Febrile non-hemolytic transfusion reactions (FNHTRs) are the commonest in occurrence, and worrisome because of the great amount of discomfort they cause patients, plus the fact that at the inception of such a reaction, it’s impossible to be certain where it is going; that is, in early stages, without additional time and data, it’s almost impossible to tell a “benign” from a more serious reaction. The two papers referenced below both add perspective to this issue.

The first paper deals with FNHTRs in the elderly, and the data are derived from a retrospective study of Medicare databases in the United States. Occurrence of a FNHTR was determined via the ICD-9-CM diagnosis code and the transfusions identified by the recorded procedure and revenue center codes. The authors determined the overall rate of FNHTR in the elderly inpatients of a period in 2011-2012, and then looked at them by age, gender, race, components and number of units transfused. Potential risk factors were identified by multivariate logistic regression analysis.

There were 4,336,338 inpatient transfusion stays for the elderly in this time period, and 2,517 FNHTRs were recorded for a rate of 58 per 100,000 stays. Rates were much higher for red cell and platelet-containing products than for other components, such as plasma only. Higher odds of seeing a reaction were greater for the larger number of units transfused, for women vs. men, for history of a transfusion in the last year, and for both leukemia and lymphoma. Although the data were not available for the abstract, the authors suggest more emphasis on the need to accomplish effective leukocyte reduction (pre-storage) in units of blood components transfused to the elderly.

Of interest, especially since the fact seems to be contradicted by the next paper from Japan, was that the American authors found—at least in their elderly subset of patients—that prior recipient alloimmunization, particularly within 12 months, predisposed to a FNHTR. In the second paper, the authors compared the frequency of adverse transfusion reactions (ATRs) following first transfusions with their frequency after subsequent, later transfusion. They collected two year’s worth of data from five hospitals. As with the Medicare study, this was a retrospective, observational study, and they included red cells (RBCs), fresh frozen plasma (FFP), and platelet concentrate (PC) transfusions given to first-time recipients and to those previously transfused.

Overall, the ATR rate following transfusion of RBCs was 1.08%, FFP 2.84% and PCs 3.34%. On subsequent transfusions, the rates were lower, 0.69%, 1.91%, and 2.75% respectively. First transfusion rates of FNHTRs to RBCs was 0.43%, that of subsequent transfusions 0.23%. For FFP, the rates for allergic reactions were 2.51% the first transfusion and 1.65% subsequently.

Clearly, the reaction rate overall was considerably higher in this second paper, and the rate of reaction in first-time recipients was higher than during subsequent transfusions. It seems unlikely that the definitions of ATRs and FNHTRs differ that much between the respective countries’ institutions. From the abstract, in the study from Japan, one can’t tell if the transfusions occurred during the same, or a subsequent, hospitalization. Likely the sample sizes were much smaller than the several million hospitalizations in the Medicare study, suggesting it may not be possible to really compare these two sets of data. There also are genetic and cultural differences, although that seems less likely to be important than the age and general health of the Japanese patients, who probably were younger, somewhat healthier and with greater immunologic reactivity.

It would be interesting to see the national records for FNHTRs from each country over a broader period of time and what rates are overall on an age-adjusted basis.

TRALI from IVIG

A pretty impressive amount of research dollars and human resources has been expended in efforts to identify the causes of, and reduce the incidence of, what we call transfusion-related acute lung injury, TRALI. As noted in the following article, the incidence has been reduced, but it is still the greatest single cause of death from transfusion of blood products. Much of it has been correlated with elevated levels of Class II HLA antibodies, and likely HNA antibodies, in products with large plasma volumes that come from women with high HLA Ab titers resulting from pregnancy.

The Canadian authors of this paper identified an unusual case that occurred in a woman with common variable immune deficiency, who had been treated with IVIG preparations since 1996. The patient had previously had transfusion reactions (assumed not to be TRALI) after IVIG transfusion, once from one manufacturer’s preparation and once from another. Since then, 2011, she was treated with a third commercial IVIG product and received acetaminophen and diphenhydramine prior to infusion, which was given once a month. On the occasion described, she had a classic pulmonary event consistent with TRALI. She recovered with appropriate treatment, and subsequent transfusions have been accomplished with a different lot number of the product.

Still on TRALI’s trail

An article and an editorial in a recent issue of Transfusion (see References) jointly bring to bear support for a quotation from Galileo, or at least he is purported to have said it: “The aim of science is not to open the door to infinite wisdom, but rather to set a limit to infinite error.” Absolute and ‘forever’ truths are hard to come by.

The authors of the article from Belgium looked for Human Leucocyte Antigen (HLA) and Human Neutrophil Antigen (HNA) antibodies (Abs) in plateletpheresis donors who had been pregnant or previously transfused. Studies have concluded that the Class II and HNA Abs are stronger triggers for TRALI than Class I HLA Abs. TRALI has accounted for about half of the fatalities reported to the U.S. Food and Drug Administration (FDA) from 2005 through 2011. Two studies have shown that plasma from women with HNA Abs is most often implicated, and even though steps have been taken to reduce transfusion of FFP from women, with a subsequent decrease in reported cases, some TRALI cases are still observed. The question has also been raised with regard to FFP or untreated plasma in platelet concentrates in donors, including men, with a history of transfusion.

In the course of one year, of the 3,068 platelet-pheresis donors presenting at the center 1,040 agreed to participate and were questioned with regard to pregnancy history (women) and transfusion history (men and women). There were 947 women and 93 men. Samples were collected for identification of HLA Abs and a sample saved frozen for future DNA testing.

The overall alloimmunization rate was 20.2%. None of the 12 transfused, but nulliparous (no history of pregnancy) women—a total of 322—had detectable Abs. One of the 77 male donors with a history of transfusion tested weakly positive. Of the 513 women who were not transfused, 154 (30%) had detectable Abs. Those who were transfused and pregnant had a rate of almost 36%. The passage of time since the last pregnancy did not seem to reduce the presence of Abs. The authors did not test for HNA Abs.

Although the production of IVIG necessarily includes concentrating the TRALI-responsible antibodies along with everything else in the gamma globulin fraction, the fact is that such products are made from very large numbers of plasma units, thus potentially diluting the reactive culprits. Unfortunately, there were no tests available on this lot of IVIG from the manufacturer, and not all of the lot number in question was retained at the institution. There have been only very scarce reports of TRALI from fractionated blood products, pointing out the need for continued vigilance during all transfusion occurrences.


Continues on next page
The authors of this study believe that a history of transfusion alone is not indicative of the likelihood of Abs, but that a program that repeats testing of each plateletpheresis donor after each pregnancy deserves implementation.

In his accompanying editorial, Dr. AuBuchon, from the Puget Sound Blood Center, uses another wonderful quote from Galileo: “All truths are easy to understand once they are discovered; the point is to discover them.” Although Class II HLA antibodies are believed to be a primary cause of TRALI, they are not the only cause, since cases occur in their absence; he even suggests that perhaps something else is going on, in some cases, that appears to fit the definition, but may act through a totally different mechanism. There are some studies identifying HNA Abs as causing severe TRALI, and even the majority of reported cases; however, a useful test for wide-scale screening is not available, and since almost all of these anti-HNAs occur in pregnant women, current screening for HLA Abs identifies most such risk-inducing plasma. Although donor WBC Abs are thought to be most commonly at fault, it’s also conceivable that recipient Abs are reacting against donor WBCs or fragments in transfused products. He provides a table of seven different mechanisms culminating in the reactions and events we call TRALI.

As Dr. AuBuchon and the other authors point out, we have reduced the rate of TRALI from plasma infusion to close to 1 in 2 million, a level deemed acceptable for post-transfusion HIV infection. That still needs to be attained for plateletpheresis products. But if the true risk of TRALI is as high as has been found in active surveillance studies, we have a long way to go.


Some things aren’t what they seem

“The truth is rarely pure and never simple,” wrote Oscar Wilde in 1895 (The Importance of Being Earnest). Another skeptical comment has it that “a lie gets around the world twice before the truth gets its pants on.” The authors of this paper introduce it (see Reference) with the story of the emperor’s new clothes, another delightful exposure of our human susceptibility to believable falsehoods. Although the first descriptions of IgA-mediated anaphylactic transfusion reactions (ATRs) were not designed as falsehoods, the underlying biological mechanism is probably not what we have always thought. The basic premise was that Ig-A deficient patients develop anti-IgA antibodies, some after a transfusion, that react with donor IgA in plasma-containing blood products. Very expensive rare donor registries have been developed, in part, to identify and stockpile products from healthy donors who are IgA deficient.

In the midst of so many allergic transfusion reactions, which occur commonly although in reduced numbers since leukodepletion of products began, isolating those that are truly anaphylactic can be difficult. Mild allergic reactions, such as flushing, urticaria and itching, are still pretty common (1-3%) in plasma transfusions. However, truly anaphylactic reactions are seen in only approximately 1:50,000 red cell transfusions. Various hemovigilance studies in Canada, the United States, the United Kingdom and Holland have found only limited numbers of plasma from reported IgA anaphylaxis cases to have anti-IgA antibodies. When tested, some such patients have normal levels of IgA.

Additional evidence in support against the role of IgA is the comparative frequency of IgA deficiency in populations and the frequency of anti-IgA. North American studies have identified from 1 per 1,500 to 1 per 1,000 donors in healthy blood donors. In 2011, a total of 21 million blood components were transfused in the U.S.; assuming the frequency of IgA deficiency to be the same in both the donor and recipient populations, one would
The leishmaniases are zoonotic infections caused by several species of intracellular protozoan parasites of the genus *Leishmania*. They are transmitted to humans by the bite of a species of sandflies, and are endemic in many parts of the world, including the Middle East, central Asia, China, the Indian sub-continent, West and East Africa, and parts of Central and South America. Of the four major species of *leishmania*, three are primarily responsible for cutaneous ulcers that can become quite severe and spread locally, causing disfiguring and mutilating facial lesions. The fourth, by *Leishmania donovani*, causes “kala azar”, or visceral leishmaniasis, with predominant involvement of the spleen, liver and lymphatic system. This form is endemic in parts of China, the Indian subcontinent, East Africa, South America, and the Middle East. As with the more fearsome parasite, malaria, the disease is only spread vector to victim by the bite of female sandflies.

Several hundred cases of visceral leishmaniasis have been seen in the United States, in troops returning from World War II, in immigrants from endemic areas and, occasionally, in tourists returning from endemic areas who were bitten by sandflies, especially in beach or marshy areas of those regions. During and after “Desert Storm” and afterwards in the several military ventures that have ensued in the area, including Afghanistan, there have been reported cases in returning U.S. military personnel. The authors of this paper, currently available only as an abstract (see Reference), repeat what has been previously noted, namely that although there are cases reported to have occurred from blood transfusion, these have mostly been seen in infants and children.

They list as a reference a unique case of transfusion-transmitted fatal kala-azar in an Indian infant who acquired this infection within a few days of his birth after receiving blood from his maternal uncle, who was asymptomatic at the time of blood donation but died due to severe kala-azar within three months. The baby developed fever and hepatosplenomegaly within one month of blood transfusion and, in spite of repeated anti-leishmanial therapy, died at the age of seven months.

There are also reported cases in organ transplant recipients, *in utero* from mother to child, and by sexual transmission.

The authors, who are based in Sicily in the far south of Italy, argue in their abstract for special screening of donors or immigrants from endemic areas, screening for *Leishmania* and exclusion for donors who are positive or who are known to have visceral leishmaniasis. For a while, the U.S. screened and deferred donors returning from Iraq and Kuwait who had a history of leishmaniasis. The question is no longer specifically asked. To date, there have been no transfusion-transmitted cases reported in the U.S., probably due to the very low prevalence in the population in general.

**Leishmaniasis and exposed donors**

The leishmaniases are zoonotic infections caused by several species of intracellular protozoan parasites of the genus *Leishmania*. They are transmitted to humans by the bite of a species of sandflies, and are endemic in many parts of the world, including the Middle East, central Asia, China, the Indian sub-continent, West and East Africa, and parts of Central and South America. Of the four major species of *leishmania*, three are primarily responsible for cutaneous ulcers that can become quite severe and spread locally, causing disfiguring and mutilating facial lesions. The fourth, by *Leishmania donovani*, causes “kala azar”, or visceral leishmaniasis, with predominant involvement of the spleen, liver and lymphatic system. This form is endemic in parts of China, the Indian subcontinent, East Africa, South America, and the Middle East. As with the more fearsome parasite, malaria, the disease is only spread vector to victim by the bite of female sandflies.

Several hundred cases of visceral leishmaniasis have been seen in the United States, in troops returning from World War II, in immigrants from endemic areas and, occasionally, in tourists returning from endemic areas who were bitten by sandflies, especially in beach or marshy areas of those regions. During and after “Desert Storm” and afterwards in the several military ventures that have ensued in the area, including Afghanistan, there have been reported cases in returning U.S. military personnel. The authors of this paper, currently available only as an abstract (see Reference), repeat what has been previously noted, namely that although there are cases reported to have occurred from blood transfusion, these have mostly been seen in infants and children.

They list as a reference a unique case of transfusion-transmitted fatal kala-azar in an Indian infant who acquired this infection within a few days of his birth after receiving blood from his maternal uncle, who was asymptomatic at the time of blood donation but died due to severe kala-azar within three months. The baby developed fever and hepatosplenomegaly within one month of blood transfusion and, in spite of repeated anti-leishmanial therapy, died at the age of seven months.

There are also reported cases in organ transplant recipients, *in utero* from mother to child, and by sexual transmission.

The authors, who are based in Sicily in the far south of Italy, argue in their abstract for special screening of donors or immigrants from endemic areas, screening for *Leishmania* and exclusion for donors who are positive or who are known to have visceral leishmaniasis. For a while, the U.S. screened and deferred donors returning from Iraq and Kuwait who had a history of leishmaniasis. The question is no longer specifically asked. To date, there have been no transfusion-transmitted cases reported in the U.S., probably due to the very low prevalence in the population in general.
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CORRECTION: In the Winter 2015 issue of PLUS on page 3 there were two errors. 1. In the article on Ebola, fourth-last sentence should read “But if there is no electricity” 2. In the middle of the first paragraph of the Babesia article, the sentences should have been read “ Nonetheless, from then until 2009, 155 cases of transfusion-transmitted babesiosis have been reported. Half of these were recognized from 2005 to 2009…” We regret the errors.