Transfusion-Transmitted AIDS: A look at the first?/last? 30 years

One hematologist/blood banker saw his first case of AIDS/HIV infection in January, 1981, in a hospital in the central highlands of Haiti. He had no idea, of course, what it was. That same month he saw his first and 30th case of falciparum malaria, but at least he recognized it. In June of that same year, the CDC’s Mortality and Morbidity Weekly Report reviewed four cases of Pneumocystis carinii pneumonia in homosexual men from San Francisco. The occurrence of this rare and unusual disease in such a cluster was very disturbing. About a year later, CDC reported the same occurrence in three individuals with severe hemophilia A, all heterosexual. That same year, a case of AIDS in an infant who had received multiple transfusions at birth for treatment of erythroblastosis fetalis was noted. All of the donors were healthy at the time of donation, but one of them had died of AIDS some months after donating.

Thus began what many of us called the nightmare years of transfusion-associated AIDS (TAA). In December of 1982, a meeting was convened by the CDC and included the federal government’s scientific and regulatory offices (FDA), blood bankers, plasma industry representatives and patient groups. Mitigating strategies were suggested, including surrogate testing for HIV (HBcAb) and low CD4/CD8 T-cell ratios. As described in the October Supplement to Transfusion (see references below), the meeting “…turned into a contentious debate about the existence of AIDS in transfusion recipients and persons with hemophilia…” and no agreement came out of the discussions.

Therefore, in March of 1983, the U.S. Public Health Service issued its recommendations for AIDS prevention, including “as a temporary measure” asking members of groups thus far identified as being at high risk for AIDS not to donate blood or plasma. These groups consisted of what some called the “Four H’s”: homosexual or bisexual men and their sexual partners; Haitians in the U.S.; past or present abusers of injected drugs (heroin); and hemophiliacs and sexual partners of any of the above. These steps led to discrimination against, and agitation among, many people of these targeted groups, and they culminated in some of the most difficult and complicated discussions with donors and others about the risk from mosquitoes, landing in the Haitian capital’s airport, cruise ship trips to the Caribbean and similar concerns. When the virus, then called HTLV-III, was discovered in 1983, scientists began working frantically to develop a screening test, with lots of help from the NIH. When it was approved by the FDA in March 1985, there was great rejoicing among blood bankers and everyone else, but then the problem of at-risk donors seeking testing and the setting up of alternative test sites to keep them from blood donation was recognized. This was confounded in May of that year when Rock Hudson announced that he had AIDS. The public that blood banks dealt with went crazy. One local television station used a blood drop as a graphic for all their AIDS stories. People feared contracting AIDS from donating blood, from insect bites, and from talking with gay men.

Wisely, the CDC worked with local and regional public health offices and blood-testing facilities to establish alternative test sites where people who were thought to be at risk could get free testing and counseling so they would not donate blood to the community blood supply. Nonetheless, times were not as open for recognition and discussion of homosexuality or injected drug use; thus, many at-risk people still sought testing at blood donation sites. Blood centers got involved in the counseling business as well, working with public health officials at meeting events and educational sessions with gay men, teachers’ groups, sports teams, news organizations and others. It was a very busy, sometimes confusing era. The article by Drs. Jay Epstein, Harold Jaffe, Harvey Alter and...
Harvey Klein provides a wonderful summary of detailed events that have profoundly affected the nation’s blood system since the appearance of TAA, including the many current issues of concern. These include vCJD, Chagas’ disease, West Nile Virus, anthrax and bioterrorism, hepatitis E and pandemic respiratory viruses.

In another article in the same issue of Transfusion, Corey Dubin, from the Committee of 10,000, a hemophilia advocacy group formed in the 1980s, and Dr. Don Francis, a CDC advocate of strong federal action at the time, provide a somewhat different perspective. They suggest that prior to the recognition of TAA the increasing occurrence of TA-hepatitis (both hepatitis B and what was then called non-A, non-B hepatitis) provides support that “collective denial” was present in the suppliers of blood and the collectors of commercial plasma and that the increasing occurrence of TA-hepatitis cried out for action even before AIDS was known. In the mid 1970s it was clearly recognized that TA-hepatitis had increased as a cause of death in patients with hemophilia despite the fact that a test for HBsAg had been widely used since 1972.

The development of Factor VIII and Factor IX concentrates by the plasma industry was seen by the hemophilia community and their caregivers as near to a miracle. No more infusions of fresh frozen plasma or of cryoprecipitate, the latter a mainstay of treatment for hemophilia A in the 1960s and early 1970s. Now preventive therapy was available in expensive, but concentrated, form. The plasma industry was heavily invested in the process, but unfortunately was including large amounts of plasma from higher risk, paid donors to augment the yield of immune globulins, another product of the refined fractionation process. The risk of hepatitis, now recognized as mostly hepatitis C, was significant but not so much as to deter the industry, the patients, nor their physicians from making/using it since the risk was felt to be small compared to the wonderful benefit obtained. Little did we know.

Dr. Stramer and Dodd, writing on behalf of the Emerging Infectious Diseases subgroup of the AABB’s Transfusion-Transmitted Diseases Committee, provide an excellent review/summary of infectious disease testing in blood products. They also provide tools for the community at large to surveil, monitor and evaluate emerging infectious agents with an eye towards their potential to be of risk/concern to the blood supply. As examples, they cite concerns about the status of dengue, parvovirus 4, hepatitis E, granulocytic ehrlichiosis, anaplasmosis (formerly monocytes ehrlichiosis), chikungunya, West Nile virus and others. Their article serves to introduce the remaining contents of this first “themed issue” of Transfusion. The articles are grouped as relating to HIV, hepatitis, NAT testing and “other viruses,” and they afford a wide range of useful information on current testing and future directions.

By the end of 2002, about 4,000 patients with hemophilia had died of AIDS. Those who worked through that period have been forever scarred, and we’ve hopefully improved in our approach to taking care of people. Sir Edmund Burke, the prestigious British parliamentarian in the late 1700s, famously said, “You can’t plan the future from the past,” meaning that new times call for new measures. But we should also remember the equally oft-quoted line from Professor George Santayanna, a Spanish philosopher (and poet) who taught at Harvard at the turn of the 20th century: “Those who choose to ignore history are doomed to repeat it.”


Nothing left but the good stuff...

Many of you will remember that when the HIV virus was first isolated, it was called HTLV-III. It was thought to be directly related to two other viruses, HTLV-I and HTLV-II, human T-cell lymphotropic viruses. HTLV-I is associated with adult T-cell leukemia in 2–5% of carriers and with tropical spastic paraparesis at a lower rate of 1–2% in this population. Affected, endemic populations are seen in Japan and surrounding islands, sub-Saharan Africa and parts of the West Indies and South America. It can be transmitted by breast milk, sexual contact, blood transfusion and injected drug use. Since 1988, testing for HTLV-I and -II has been mandatory in the U.S. and many other countries, although no specific disease relationship with HTLV-II has been shown. The latter is most commonly seen in injected drug users in the U.S. Using PCR, the two viruses can be distinguished from one another, but the antibodies, which are the basis of the screening test, reflect the high degree of similarity between the two.

A recent report of transmission of HTLV-I in an emergency transfusion of a severely injured soldier in Afghanistan was published in October 2013 (see reference). In addition, a British evaluation of the efficacy of leukocyte reduction of red cell transfusions in preventing HTLV-I infections, effective reduction of Human Herpes Virus-8 (HHV-8) by leukocyte reduction of blood from 12 patients with Kaposi’s sarcoma, and articles about leukocyte reduction in preventing CMV infection can all be found in the same issue of Transfusion. An editorial from staff at Emory University nicely ties all these together (see reference) and elaborates on the safest strategy for prevention of CMV infection, most particularly in newborns and premature newborns.

HHV-8, and even more commonly CMV, may have a high viral load in the plasma, not just the leukocytes. In the early phase of CMV infection, the plasma contains large amounts of the virus. This diminishes markedly after three to four months. Thus, the combination of serology and leukocyte reduction can be shown to be very safe for the at-high-risk recipients, although it limits the size of the available donor pool. The editorial writers raise the question of whether NAT testing for CMV would add to safety by removing the risk of both converting and reactivating donors, and they point out that effective pathogen reduction would be the most successful and simplest way to prepare the safest blood. What is needed is a safe, effective way of doing pathogen reduction for each of the blood products we use.


Emergency use of Group A plasma

Massive transfusion protocols (MTPs) have been developed at many, if not most, trauma centers to address the trauma-induced coagulopathy that is seen in up to 25% of severely injured patients at the time of presentation. MTPs are designed to restore the rapid depletion of key substances needed for coagulation—clotting proteins and platelets. Since clinical indications call for immediate transfusion, often before even a blood group can be determined, the trend has been to use Group O red cells and AB plasma. But AB donors are generally 4% or less of the donor population, and AB plasma is in high demand. Critical care staff at the Mayo Clinic, Rochester, Minnesota, developed an MTP protocol using Group A plasma and evaluated the results after experience with 254 trauma patients receiving emergency MTP blood.

The authors retrospectively reviewed the data from the 254 patients who received the Group A plasma from 2008–2011. All deaths that occurred prior to transfusion were eliminated. Of the 254 transfused, 35 (14%) received incompatible Group A plasma; 219 (86%) did not. [The 14% were either group B, 10%, or AB, 4%.] In this north central U.S. population, the odds were good of plasma compatibility, since 86% of the time there was no expected plasma incompatibility with such an MTP. Analysis showed that there were no statistically significant differences in the two groups based on age, sex, injury severity scores, or time in the trauma unit. The median number of blood products was similar for each component. Importantly, there were no significant differences in complication rates, including those related to blood transfusion (TRALI, TACO, acute lung injury, ARDS). However, the incompatible group had a trend towards more time on a ventilator.

The discussion of the paper, when presented at an international conference last year, pointed out the risk of drawing conclusions from such small numbers. But, it’s very clear that the authors have demonstrated a way to reduce the tremendous pressure on Group AB plasma for MTPs, certainly laudable, and in their population—as well as in most parts of the United States—the odds are in favor of such a move. Significant titers of anti-B in Group A donors are very uncommon, and a handful of previous, similar studies have shown no ill effects. Group A plasma, however, should not be used emergently in small children or for treatment of Group B or Group AB patients with TTP.

Many experts now feel that the early coagulopathy of trauma includes activation of fibrinolytic activity with destruction of coagulation proteins, as well as consumption of coagulation proteins, and they have added early administration of tranexamic acid to their resuscitation protocols in MTPs. See the Winter 2012 issue of PLUS for more details. Tranexamic acid was not part of the protocol in this study.

More on MTPs and plasma

Researchers from the University of Texas Health Science Center in Houston have developed a new thawed plasma (TP) protocol for use in their massive transfusion protocol (MTP) for severely injured trauma patients (see reference below). When clinically indicated, they would implement the MTP and send a sample to the blood bank for ABO group, Rh type and crossmatch. Immediately, however, 6 Group O red cells, 6 Group AB plasmas and 1 apheresis platelet were delivered to the patient and transfused based on clinical indications. Beginning in 2010, they began to store TP (jumbo AB units from only male donors) in the emergency department (TP-ED) along with the 4 O negative RBCs already stored there. Such units of plasma, usable for 5 days, are returned to the blood bank at day 4 for use in routine patient care to avoid expiration. They retrospectively compared the outcomes of patients who received the TP directly stored in the ED vs. the former cases, those receiving TP kept at the blood bank (TP-BB).

One hundred thirty patients in the TP-BB group and 164 in the TP-ED group were compared. The TP-ED cases had a shorter time lapse from arrival to first plasma transfusion (89 vs. 43 minutes) and were transfused significantly smaller volumes of red cells, plasma and platelets. The authors state that the injury severity and physiologic disturbances were greater in the TP-ED group. In addition to the reduction in overall blood product use, the authors found a 60% decrease in odds for 30-day mortality using multivariate logistic regression analysis (but not by univariate analysis or for mortality at 24 hours). The reason for this would seem to relate to the greater severity of injury and disturbed physiology in the TP-ED group; perhaps the most severe cases in the TP-BB group died before receiving transfusion.

It should be pointed out that the TP-ED patients were prospectively evaluated, but the TP-BB patients were used as retrospective controls. Thus, the evaluations of severity and disturbance were not done by the same people. Even though similar indices were used, it is hard to be certain that the groups are truly comparable. The favorable trend is clear, but a prospective, randomized study needs to be performed to provide convincingly firm data.

Save time, save money, save blood

Weight-bearing joint operations, primarily knee and hip arthroplasty, are increasing in frequency in the western world, which is at least partly due to the increased longevity and body weight seen in these populations. Once something becomes technically relatively easy, it’s amazing how demand for it can increase. The authors (see reference below) undertook a study in their Italian hospital to review the transfusion practices in 600 such patients in order to assess the effectiveness of their pre-operative autologous blood donation (PABD) and post-operative cell salvage (PCS) programs in total knee and total hip arthroplasty (TKA/THA). All operations were performed by a single surgeon and single anaesthesiologist. No tourniquet was used, and average operative times for TKA and THA were 45 and 40 minutes, respectively.

Patients were advised to donate one unit of blood between 2 and 3 weeks pre-operatively, and they could do so only if they were Class 1 or 2 anaesthesia risk and had an Hgb concentration (both men and women) of more than 12.5 g/dl. No erythropoietin was used. Immediately post-op, they were transferred to the recovery room where a transfusion team leader made the decisions about transfusion and PCS re-infusion. Transfusion was triggered by a Hgb less than 8 g/dl or “signs and symptoms of anemia.”

The authors reviewed the records of 600 procedures, 288 TKA and 312 THA. Of these, 38% were men and 62% women. There were a number of complicating and exclusionary factors making for a somewhat difficult analysis, and many patients (such as Jehovah’s Witnesses and initially anemic patients) had to be excluded. Operative blood loss was higher in TKAs, but post-operative blood loss higher in THAs. A total of 182 patients had PABD collection; 157 of these were not used. Patients receiving allogeneic blood were generally sicker and had not undergone PABD. Overall, only 42 of the 461 evaluable patients received any blood transfusion, less than 10%.

The transfusion rates were higher in those who underwent THA and higher in patients who underwent PABD plus PCS.

Although the limitations of a retrospective analysis are clear, the message seems to reinforce the growing belief that the best place to store blood is in the patient’s body and not collect PABD as a routine measure to avoid autologous transfusion.

Give us your hips…

Blood management programs are in place in many hospitals, and much information concerning their effectiveness has been forthcoming. Although we rightfully tout the safety of the volunteer blood supply due to successful screening for a number of very serious transfusion transmissible infections, we are now looking at other concerns that relate to patient health and medical cost, such as the effects of transfusion of blood on hospital stay, overall infection rates, ventilator time and so on. A variety of ways to minimize the amount of blood transfused have become standardized, such as guidelines concerning thresholds for what we call “pulling the transfusion trigger,” an apt phrase since this lifesaving procedure may also be life-threatening.

Patient blood management (PBM) programs have, among others, three factors: the correction of preoperative anemia, minimizing perioperative blood loss, and optimizing the patient’s tolerance of anemia. Since preoperative anemia is associated with postoperative morbidity and mortality, and since it is the strongest predictor of the likelihood of perioperative transfusion, strategies to correct it when present are of great interest. Administration of iron, when indicated, is one way to correct preoperative anemia. Another is the use of preoperative injections of recombinant human erythropoietin (EPO). The authors of this study (see reference) noted several studies in which patients with preoperative Hgb levels of 10–13 g/dL saw a reduction in transfusion by 75% if treated with EPO ahead of time. However, they also noted the adverse events seen in some renal and oncology patients treated with EPO, and thus undertook a large scale study of their own.

They performed a retrospective observational study at a large teaching hospital in Utrecht, the Netherlands, and included all patients (4,568) undergoing total hip arthroplasty (THA) from 1999–2010. They used the same EPO trigger as above, but excluded patients with a preoperative Hgb <10. They evaluated the effect of an EPO protocol, implemented in 2003, as part of a broader PBM strategy. There was a roughly two year transition period after the introduction of the program. The broader strategy included preoperative measurement of Hgb, improved surgical techniques, a transfusion committee review process, intra-operative cell salvage, and education and training on transfusion for staff and students. The preoperative EPO arm, with supplemental iron, was begun in 2003, as noted. Preoperative autologous donation was not a part of the PBM strategy at any time.

Overall, the absolute reduction in allogeneic transfusion in the whole group after introduction of the preoperative EPO program was 17%. In the group with an initial value of 10–13 g/dL of Hgb, it was 25%. In the group with preoperative Hgb > 13 g/dL, the reduction in transfusion was 8%. In the post-intervention period, almost half (46%) of the eligible patients received EPO. The transfusion rate in the EPO group was 14%, whereas in the non-EPO treated patients with HGB between 10 and 13 g/dL, it was 50%. The length of hospital stay in patients receiving the EPO was shorter (mean of 7 days) than in the non-EPO low Hgb group (mean of 10 days).

The authors point out the importance of looking at these results as a part of a multifaceted total blood management program and believe that an institutional awareness of and commitment to good transfusion practices contribute substantially to reducing transfusion rates in patients.

We all know that the best and safest blood donors are those who come to donate on a regular and continuing basis. Their capacity to donate, their understanding of the process, and their regular health and infectious disease evaluations all contribute to the operation of a successful blood program. But donors age, they move around, they become afflicted with the illnesses we are all liable to, and—perhaps more importantly these days—they are often hard at work at one, two, or sometimes three activities to make ends meet. Such a commitment of time and energy to donate has become harder to find and foster in many segments of our population, and most blood centers have turned efforts towards the recruitment of new, younger blood donors to fill the void.

Younger donor audiences have been recruited for donation on high school and college campuses. Young people are, generally, very civic-minded and interested in supporting such an altruistic enterprise. However, the majority of these donors do not return to become committed donors; thus, the system becomes more reliant on young, first-time donors. A number of studies have identified several factors that account for this, most commonly syncope, dizziness, faintness, weakness and lightheadedness. Some have had bad experiences with needle insertion, and some of these have had hematomas or other problems. But the syncopal and pre-syncopal reactions are the most common reason for non-returns in many studies. In studies involving thousands of donors, roughly 64% of donors with no reactions returned but only 40% of those with reactions. Minor reactions led to 14–23% reductions in return rates. Major reactions led to 25 – 49% reductions in return rates.

The authors of this study (see reference) analyzed two-year donor return behavior in new donors who had engaged in pre-donation water consumption, with or without leg muscle activation, compared to controls. These interventions have been proposed to decrease the rate of syncopal/pre-syncopal reactions. They used a series of path analyses to demonstrate the role of donor anxiety in shaping return-donation commitments. They found that anxiety had a direct negative influence on donor intention, that anxiety increased the reports of needle pain, and that pain affected the severity rating of any syncopal or pre-syncopal reactions, contributing as well to decreased donation intention. The authors conclude that donation anxiety plays a central role in future donation behavior. Importantly, donors in the preventive treatment arm did have fewer reactions, even though the same factors were influential on the reaction rate.

The study was performed in groups of college donors with an average age of 20 years, and it is very likely that it holds true in younger, high school donors and perhaps to some degree in older donor groups. The mathematical model of path analysis that they used is of interest. It is a social sciences model that may not be familiar to many practitioners of transfusion medicine/blood banking. An individual’s anxiety about donation, as well as the actual apparent donation process, needs to be considered when assessing ways of improving new donor retention since the former has a significant impact on the latter.

This is the very provocative title of an editorial introducing the October 2013, issue of the Journal of Hemostasis and Thrombosis. The historical sketch that immediately follows (see reference below) deals specifically with frozen plasma (PF24/FP). The editorial points out that the studies of Hippocrates and Galen in anatomy and physiology eventually led to the widespread practice of treating all sorts of maladies and afflictions by bloodletting, usually accomplished through venesection. (Health depended on a balance of the four humors in the body: blood, phlegm, yellow bile and black bile. Purges, cathartics, plasters and bloodletting were used to restore a balance.) This practice persisted for centuries, long after it had been demonstrated to be ineffective, sometimes even harmful. Many older readers will recall the fate of Robin Hood, who fell into the hands of a wicked cousin and under the guise of helping him basically bled him slowly to death.

In the article on frozen plasma, the author points out that despite modern recombinant DNA technology, PF24/FP is the “...most frequently prescribed hemostatic agent” today. This is the same as it was decades ago. Annually, over 300,000 units are transfused in the United Kingdom, and more than 4.4 million in the U.S. Comparatively, the U.S. is using almost three times the number of units per capita as the U.K. With few exceptions, no clinical benefits have been documented in randomized, controlled trials (see Table 1 in reference). In over 70 such trials, the only documented benefits have been in TTP with plasma exchange, prevention of neonatal hemorrhage in neonates, treating thrombocytopenia in early dengue hemorrhagic fever, and priming the bypass pump in cardiac surgery in children. One uncontrolled trial showed a benefit of transfusable plasma in a high ratio to red cells and platelets in massive trauma. Despite this, the use of transfusable plasma remains unchanged or increased.

Probably the most frequent “indication” for plasma transfusion has been an elevated INR, PT or aPTT. Yet there have been many studies evaluating the predictive value of an abnormal PT or aPTT with regard to actual bleeding; they are not predictive of bleeding. In addition, the administration of standard doses of PF24/FP frequently has no corrective effect on an abnormal test. These tests are insensitive to the presence or absence of anticoagulants, such as proteins S and C, which are also decreased in severe liver disease. These tests (INR, PT, aPTT) were developed to evaluate the causes of inherited coagulopathies, not as predictors of bleeding. Thus, the amount of PF24/FP needed to correct such tests may be quite large and not reasonable to administer. Readers are referred to the Winter 2012 issue of PLUS, which offered a review of this topic at a special symposium in Chicago in March that year. Recent guidelines from the AABB recommend using PF24/FP only following massive transfusion after trauma and in patients with coumadin-related intracranial hemorrhage. Some feel that the use of Vitamin K and prothrombin complex concentrates are better for coumadin reversal. People do agree, however, that specific coagulation deficiencies, with attendant bleeding, that have no known available concentrate, such as Factor V, are an indication for PF24/FP. In some parts of the world without available concentrates such use may also be warranted.

Dabigitran and rivaroxaban are not former countries in Central Asia... read on.

Readers of PLUS may recall an article from last winter’s issue concerning the use of warfarin (coumadin) and newer agents used for anticoagulation to prevent thromboembolic phenomena in a variety of circumstances. A Vitamin K antagonist that inhibits synthesis of coagulation Factors II, VII, IX and X, warfarin has been in use for more than 50 years. Much experience with its use has been accumulated. It is orally administered with the dose adjusted to a clinically appropriate level of anticoagulation using the INR—an internationally standardized prothrombin time. It must be monitored regularly and the dose adjusted as needed. Many drugs interact with it in various ways, and much attention to these details is necessary to avoid inadequate therapeutic levels and/or dangerously prolonged effects that can lead to minor or severe bleeding.

The ideal anticoagulant would be one that dissociated its antithrombotic effects from its anticoagulant effects; however, that ideal has not yet been realized. But new, orally active small molecules have been developed that selectively inhibit serine proteases that are active in coagulation. Dabigitran is a direct inhibitor of thrombin, thus interfering with the conversion of fibrinogen to fibrin, the penultimate step to a solid clot formation. Rivaroxaban inhibits activated Factor X (Factor Xa), which converts prothrombin to thrombin, one step before the site of fibrinogen’s conversion to fibrin, the antepenultimate step. Both drugs can be given daily at a fixed dose without the need for regular monitoring of the INR. They also have a shorter half-life, 13 hours for dabigitran and 7–11 hours for rivaroxaban. However, if renal function is diminished (creatinine clearance <30-40 ml/min), the half-life of dabigitran more than doubles. Rivaroxiban is primarily metabolized by the liver, and no dosage adjustments are needed as long as the creatinine clearance is >15–20 ml/min; however, a major published study reduced the dose similarly to that of dabigitran.

Another concern with dabigitran is that at the higher dosing level commonly used in patients less than 80 years old, gastrointestinal (GI) bleeding may occur; overall, GI side effects occurred with increased frequency, compared to warfarin. Dabigitran accumulates in the feces, and the local effect on mucosa is thought to be the cause for GI blood loss. A few selected drugs, some of them used in patients with cardiac problems, may interact adversely with dabigitran, but dosage can usually be adjusted. Rivaroxaban was also associated with some increased GI bleeding, but there are fewer drugs that interact with it metabolically. However, these include protease inhibitors, such as drugs used for the treatment of HIV infection.

Patients with poor compliance with taking their warfarin will possibly do worse on one of these agents, since the duration of effect is much shorter and a thrombotic event is thus somewhat more likely. It should also be noted that in the case of a severe hemorrhage, Vitamin K or FFP has no effect. Prothrombin complex concentrates can reverse the effects of rivaroxaban, but not dabigitran; however, no studies of the use of PCCs or recombinant Factor VIIa have been done with either drug. It should also be noted that the INR or prothrombin time in patients on these drugs can be either hyper-therapeutic, sub-therapeutic or therapeutic but is not a measure of relative drug activity, as it is with warfarin. More specific information and therapeutic guidelines can be found in this excellent review. There are other related drugs, but these two are prototypes of what are called oral direct inhibitors (ODIs). For the majority of patients who have good and adequate anticoagulant control with warfarin-type drugs, the primary benefit of the ODIs is convenience. However, there are no specific antidotes for rapid reversal and broader experience in their use compared to warfarin for all its indications is still being collected.

New Patient Blood Management course posted to SUCCESS!

A new course, “Preoperative Anemia and Anemia Management” is now available for CEU and CME credit on the SUCCESS website. This presentation reviews the significance and prevalence of preoperative anemia. Dr. Irwin Gross will walk students through the elements of a preoperative anemia management program, providing practical advice on testing, treatment, program logistics and reimbursement.

Publications Corner

Recent publications by American Red Cross scientists and physicians:


**Where are we in efforts to unravel the complexity of Rh to guide transfusion decisions?** Nance ST, Lomas-Francis C. *Transfusion* 2013 Sep 8. doi: 10.1111/trf.12406. [Epub ahead of print]


Remember these Websites

- Immunohematology Journal [redcross.org/immunohematology](http://redcross.org/immunohematology)
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