A New Look at “Massive Transfusion”

Massive transfusion has been defined for a long time as the receipt of 10 units or more of blood in a 24 hr. period, but does not necessarily define life-threatening critical bleeding. The authors (see references) note that the phrase “ultramassive transfusion” (UMT) has come into being and although it has not been strictly defined it is being used to describe transfusion episodes that substantially exceed the previous definition. For this study (from 11 hospitals in 6 countries), it is defined as 20 or more units of red cells over two consecutive days. The group reviewed historical data from older studies which suggested that in the 1980s and 1990s survival rates from UMT gradually increased. However, the more units received, the lower the survival rates. They also noted that a small percentage of patients having UMT use a very high percentage of units given for trauma resuscitation.

From 2009-2013, they retrospectively found 1975 patients in their hospitals who met UMT criterion, and they studied 1360 patients in detail. They grouped the patients into seven diagnostic categories, such as cardiac surgery, solid organ transplant, general medicine, general surgery, obstetrics, trauma, and other. In the first week, these patients (all together) used a total of 120,000 blood components, an average of 35 red cell units, 30 plasma units and 7 platelet equivalent doses (roughly 30-35 platelet units). Overall survival for the entire group was about 60% at 30 days. Among the subgroup who received 60 or more units over 2 consecutive days, survival was 48% at 30 days. The highest odds for non-survival were in the trauma group, about 40% at 30 days; the highest odds for survival were in the organ transplant group, about 80% at 30 days. No information is provided on the use of tranexamic acid, use of tranexamic acid (increasingly used in traumatic hemorrhage) nor cryoprecipitate.

An accompanying editorial from staff at Johns Hopkins has several comments on this study. They note that this study illustrates that all UMT patients are not the same, that there is a huge difference in survival based on the underlying category of the patient. Those with trauma perhaps have much more significant tissue injury with concomitant greater systemic activation of coagulation and of fibrinolysis. Thus, many UMT patients have very good odds for long term survival and useful life. Despite the many studies documenting adverse effects associated with transfusion, blood does save lives and that it is prudent to continue UMT.

They make a very interesting observation about the ratio of plasma, platelets, and red cells, transfused in the study. The estimated ratio from summary statistics is 0.86/1.2/1, and if one
considers that a plateletpheresis unit contains roughly 1 unit of plasma the ratio becomes 1.06/1.2/1. This is close to a balanced ratio of reconstituted whole blood. In a study of their own, to be published in *Anesthesiology*, these authors noted that hospital acquired infections and deep vein thrombosis were 4-5 times more common in high dose transfusion patients, perhaps related to transfusion-related immune modulation, and that the incidence of TACO and congestive heart failure are increased.

They close by noting that blood saves lives. With all the emphasis on restrictive transfusion thresholds and “less is more”, they suggest that sometimes “more is more” and the signs in our hospital elevators saying “give blood, save lives” are for real.


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**When Does A Equal AB?**

Shortages of frozen plasma for use in trauma patients have long been with us. Many of our hospitals have kept “in case” inventories of group AB plasma on hand at all times, and in varying numbers, for use in emergency treatment of trauma patients since the units can be given to any recipient without concern for the ABO group of the recipients’ red cells. Since group AB donors are only about 4% of the U.S. population, this is a situation impossible to maintain. Add to this the fact that an AABB standard now requires (since January, 2014) that plasma or whole blood for allogeneic transfusion should be obtained only from male donors or from females lacking HLA antibodies from pregnancy so as to avoid the occurrence of TRALI, many cases of which are related to such antibodies.

In this article (see reference), the authors developed a survey that was sent to 121 U.S. Level 1 trauma centers. The survey is presented in the article, and the main focus of it was to identify the use of AB and A plasma with regard to emergent transfusion in the hospitals. There were 61 responses, a 50% rate which is generally considered useful. Of these, 97% kept thawed plasma on hand for emergency use. Five hospitals (9%) used AB only; 17 (32%) used A only; 14 (26%) used AB and A only; and, the remainder kept various combinations, including group O. Thirty-four hospitals, 63%, stated they used group A plasma in the initial resuscitation of patients with unknown ABO group. Of these 34, 21 (62%) had no limit on the number of such units that could be transfused (group A units). Almost 80% of these respondents did NOT titer the anti-B in the thawed group A plasma units. Half of these centers had implemented this policy in the past year.

In sum, the majority of Level 1 Trauma Centers maintain thawed plasma inventories and use group A plasma for trauma patients of unknown ABO group. Most centers do not limit the amount of group A plasma and do not titer the anti-B. This study did not incorporate information from smaller or rural hospitals, but it seems fair to say that as more and more experience with this practice accumulates it will be adopted pretty much universally.

Avoiding Heartbreak in Sickle Cell Disease Can Get Tough

But alloimmunized patients with SCD have worse survival rates than SCD patients without that complication. Depending on antigens involved, their frequency or rarity, providing totally compatible blood is very difficult, and the selection of donors/units to avoid the “most likely” antibodies is not always possible. The authors of this study, from Atlanta, Washington, D.C., and Connecticut, (see references) wrote this report using 5 heart-breaking stories of young people with severe SCD to illustrate the concept that RBC alloimmunization contributes to death in SCD.

Details of each story are beyond the scope of this brief note, but those who have cared for such patients can likely imagine the agonies of the caregivers as well as the even worse agonies of the patients, who died after innumerable complications, multiple transfusion reactions and an inability to find any compatible blood, even internationally. The authors use these stories to illustrate the fact that some SCD patients die due to alloimmunization and the consequences associated with the difficulty in obtaining compatible blood.

In a separate article (see references), authors from high level red cell reference laboratories in the United States, England, Germany, Israel, and Finland collaborated on an article reviewing international rare donor panels on behalf of the International Society of Blood Transfusion (ISBT). They provide some details of their own reference panels and discuss the commitment of resources to this effort. The leadership of ISBT has convened a working party to support the WHO International Rare Donor Panel in an effort to get countries to submit their donors’ phenotype or genotype information to be catalogued in the database. Countries are asked to keep their lists updated and to supply a product when requested. Some donor blood types are extremely scarce around the world so having a protocol that having a protocol to identify and recruit such donors is very important. They also point out that patients in need of such units need to be managed appropriately so that blood is used properly.


Children with sickle cell disease (SCD) and those who care for them, have many difficulties in their lives. For the patients, these “difficulties” include frequent medical visits, hospitalizations, severe painful crises, life-threatening respiratory events, bone infarcts, splenic sequestration, skin ulcers and other things that all add up to lots of misery and lots of blood transfusions. Red cell transfusion is a mainstay of treatment for the many events that occur, and many of those with severe SCD and frequent transfusions rapidly develop alloantibodies, making it difficult, sometimes, to find compatible blood.

Studies have shown that over a ten year period such frequently transfused patients had high levels of alloimmunization: 29% of pediatric patients and 47% of adults. However, in that particular study only 4% of the patients reported experiencing a hemolytic transfusion reaction (HTR), and only 1 patient died from that. Delayed HTRs may go unrecognized. The recent advent of complete blood group information based on DNA determination has affected that to some degree and is considered the best way to try to avoid such alloimmunization through careful donor selection and dedicated donor panels for each patient. By keeping the patients Hgb at 10 gm/dl and aiming for a Hgb S concentration of 30% or less in the circulation, some things are avoided. Still, many patients prone to such complications (and not all equally are) still fall prey to acute chest syndromes, strokes and other effects of SSD.
Our current climate of anxiety, current ever since September 11, 2001, has resulted in untold expenditures for “security” in the billions, probably trillions of dollars globally, each year; yet we are not calm, and nor are we secure. In the arena of transfusion medicine we continue to experience explosions of heretofore unheard of diseases, all too many of which are transfusion-transmissable. Strange apparitions in the form of “new” organisms remind us that on our secure islands of modern civilization bad things are still washing ashore. The vectors are many, and certainly include our own species.

An article last year in the NEJM, written by Drs. Ed Snyder, Susan Stramer and Richard Benjamin reviewed some of these in a call to develop/approve new and available pathogen inactivation techniques for all blood products so as to avoid the problem of appearance of a new organism, transfusion transmission of said organism, research to develop a test, getting it approved, and then implemented.

These sorts of infectious disease crises occur around the world, often in circumstances and places where technology and public health are not available to notice, identify and cope with them, much as occurred with the great plagues of medieval times, the influenza pandemic and HIV. The occurrence of SARS (severe acute respiratory syndrome), MERS (the Middle East Respiratory Syndrome) and the recent West African Ebola outbreak are reminders of our human frailties and of the patchiness of the systems we have in place to deal with such things.

In this article (see reference), the authors describe the work of the Commission on a Global Health Risk Framework for the Future, which was initiated in the spring of 2015. Leadership provided by the U.S. National Academy of Medicine for establishing an international oversight group of leaders in business, science and government. Meetings were held around the world over several weeks with a variety of experts from governments, industries, health care and with the World Bank, World Health Organization, and the United Nations.

The article is well worth reading, and reviews the recommendations of this effort with regard to pandemic preparedness, strengthening of public health, improving global and regional systems to deal with such events, and accelerating research and development in the various fields. The commission feels its recommendations provide a comprehensive framework for dealing with infectious disease crises. They see a great need to strengthen WHO capabilities and to improve coordination with the rest of the UN system and the World Bank. Public health infrastructure needs to be further strengthened and educated, right down to the lowest levels, and even in failed states. Acceptance and funding of these initiatives will be difficult. Some people (such as this writer, who spent several years on the biological fringes of counter-terrorism) feel that there is plenty of money available for human security, but it needs some re-focusing. Political figures currently note the grave risks we have been ignoring by not dealing with our failing national infrastructure—roads, bridges, weakened local disaster response activities. Our international infrastructure for epidemic outbreaks, both prevention and management of, is similarly in need of major repair.

Among physicians who do not have patients who regularly require platelets, some are very concerned that thrombocytopenic bleeding will occur at less than “normal” platelet counts, say $100 \times 10^9$ platelets. In many hospitals it is the norm to treat such patients prophylactically if any surgical or other invasive intervention is planned. These are procedures such as epidural anesthesia or diagnostic lumbar puncture, central IV line placement, and bronchoscopy with or without alveolar lavage. Due to an absence of good data, expert opinion, previous operator experience and “word of mouth” anecdotes are summoned for decision making. For leukemia patients, several prospective trials have established $10 \times 10^9/L$ as the threshold for prophylactic platelet transfusion. But published recommendations include, for example, thresholds of $20 \times 10^9$ for central line placements and $80 \times 10^9$ for epidural anesthesia.

The authors of this study (see reference) retrospectively identified 150 consecutive patients with platelet counts of not more than $100 \times 10^9$ who underwent bronchoscopy or bronchoscopy with alveolar lavage in the past few years. Patients with gross hemoptysis or transbronchial lung biopsy were excluded. Sixty-five percent of 89 patients with platelet counts $< 50 \times 10^9$ received prophylactic transfusion, whereas only 8% of patients with counts above $50 \times 10^9$ did so. Not all patients who received platelets had a rise in the count, and at the time of bronchoscopy 15 patients had counts $< 20 \times 10^9$. Of the 63 patients who received platelet transfusions before bronchoscopy, 54 of them had platelet counts $> 20 \times 10^9$.

Of these 150 patients with “low” platelet counts, some transfused and some not, only 1 patient had bleeding that fit the British Thoracic Service criteria of “mild bleeding”, defined as the continuous suctioning of blood from the airways with spontaneous cessation. That patient’s platelet count was $61 \times 10^9$. It isn’t clear whether all patients had broncho-alveolar lavage, and some patients already had some bleeding on admission. But the point seems to be that in real-life bronchoscopy experience, there is no evidence that a platelet count of $< 20 \times 10^9$ necessitates, on its own, preoperative platelet transfusion, and perioperative bleeding seems unrelated to the platelet count.


Hepatitis E Virus in U.S. Blood Donors

Hepatitis E virus (HEV) is a spherical, non-enveloped single-stranded RNA virus about 32-34 nanometers in diameter. Being non-enveloped makes it resistant to current viral inactivation processes for transfusable products. It has at least 5 genotypes. It is found pretty much around the world. Humans are natural hosts for the virus: other primates, cows, pigs, sheep and goats are as well. These animals have a high prevalence of antibodies in some parts of the world and may be a source of zoonotic infections in humans. HEV is transmitted primarily through the fecal-oral route and is commonly shared as a water-borne infection and is the major cause of non-A, non-hepatitis around the world.

In recent years tests for HEV antibodies (IgM and IgG) have allowed for large serological surveys in many parts of the world and offered some surprising results. HEV infections account for up to 50% of acute, sporadic hepatitis in highly endemic areas such as the Middle East, North Africa, China, India, Pakistan, and West Africa. In North America, HEV antibodies have been found in much higher rates than anticipated.

This study in almost 19,000 U.S. blood donors from 6 geographic areas showed the highest prevalence of antibodies (predominantly IgG) to be in the Northeast (10%) and Midwest (12.5%).

Overall, the U.S. average prevalence was 7.7%, with the lowest areas being the South Central and Southeast regions. Prior U.S. surveys have found a wide range of antibody prevalence, depending on age and location. These have varied from 3-4% to 9-10%. An outbreak of HEV among pig farmers in the Netherlands in the last decade, and
Oh, No! Not Another One!

Life is full of incredible happenings, not a lot are pleasant, but it’s a wise person who can learn from them. Thanks to some folks from Rhode Island (see reference), we can all learn from the following story. As you likely know, Rhode Island is right in the middle of an area heavily endemic for tick-bite transmitted infections from black-legged ticks, *Ixodes scapularis*.

A 78 y/o woman suffered a ventricular fibrillation cardiac arrest which occurred out of the hospital. She was then admitted and underwent cardiopulmonary bypass 3 days later. She received 7 units of red blood cells and 2 units of pre-pooled platelets. All components were leukoreduced during their preparation. She was transferred to an inpatient cardiac rehab unit and 3 days later returned to the regular medical floors with fever (104°F), chills, dyspnea (O₂ saturation of 86%), and cough. Chest X-ray showed atelectasis in the left lower lobe and a pleural effusion. She was treated for pneumonia. The next day she worsened and was transferred to the ICU. Neutrophils seen on blood smear showed inclusion bodies consistent with morulae, and she was switched to treatment with oral doxycycline. She went home 1 month after her cardiac arrest.

The patient tested positive for *A. phagocytophilum*, 2 weeks after return to the general medical floor. Her admission sera did not react, and the patient denied any outdoor or animal exposure. There were no intra-erythrocytic parasites found, such as *Babesia microti*. The patient was transfused 10 days before the onset of symptoms.

In addition to the rather miraculous outcome for this patient, a few other things come to mind. The leukoreduction filters in this case were specifically for in-line reduction of leukocytes for platelet products, and they differ from red cell leukodepletion filters in their composition. The residual number of granulocytes in such units is very low; most of the residual leukocytes are mononuclear cells. There currently are no licensed test kits for screening donors or their donated products for human granulocytic anaplasmosis, nor for ehrlichiosis, either.

A final observation about this case is that the diagnosis was suspected when a live human being who knows how to look at blood smears did so. In many situations with abnormal CBCs, red cell problems, white cell problems and even some platelet problems can be diagnosed or suspected by the trained eye that will never occur using only automated processors as they currently exist.

**References**


As we’ve all noted, just when you think you have your work organized; you’ve brought order to your files, updated your work space, finished training new staff and revising the work manuals, along comes something else. This something else recently has been concerns about what are we going to do about the outbreak of Zika virus infection, which has erupted in this hemisphere in the past year, and in the past few months has actually reached the shores of the United States.

Zika is another arthropod-borne arbovirus, a Flavivirus like its cousins dengue and chikungunya, both of which are relatively recent arrivals in the northern parts of the Western hemisphere. Zika was first isolated in a Rhesus monkey in 1947, in the Zika forest of Uganda; hence its name. For the next 65+ years, it was responsible only for sporadic cases in Africa and Asia. The most common symptoms are similar to those of dengue and chikungunya; rash, fever, conjunctivitis and arthralgias. It has more recently been found in French Polynesia, islands south of Hawaii and near the equator, far west of Ecuador and northeast of Australia where a case of Zika-related Guillain-Barre syndrome was reported in 2013. Tahiti is in these islands, and among other shared experiences they now tell us of efforts to inactivate Zika virus in human plasma (see reference 1).

As just about everyone has read, it erupted in northeastern Brazil early last year, and has been associated with increased births of microcephalic infants who were stillborn, as well as from placentas and amniotic fluid, and identified in those older patients with Guillain-Barre.

The virus has been transmitted sexually from men to both men and women, and during the Polynesian outbreak was found in 2.8% of samples from asymptomatic blood donors. It has also been isolated from urine, in addition to blood and semen. Cases of Zika from travel have been documented in symptomatic patients from around the United States, from California, Florida, Texas and Vermont. Not all infected patients are symptomatic. The virus has been found to persist for some weeks in semen, but clear cut data on blood persistence are not currently known. It has been shown that most of the infections are asymptomatic, so a history-taking intervention with potential blood donors who have traveled to recognizably known areas of Zika are not much help.

With the exception of sexual and blood—blood contact, it can only be transmitted by the bite of an infected mosquito, some of which, A. aegyptii, have been present in southern areas of the U.S. for some time. The geographic distribution of this species has moved northerly quite a bit in recent decades, likely related to global warming. A cousin, A. albopictus, can winter over much further north in this country, and is now found all the way north into New England and as far north and west as southern Minnesota and Wisconsin. If the virus gains a foothold in this country it could spread considerably if left to its own devices. It now covers virtually all of Mexico, Central America, the Caribbean and most of South America.

Although the virus can be shown to be inactivated in plasma using amotosalen and UV-A illumination, similar to its cousins, dengue, chickungunya and West Nile viruses, (see reference 1) we know that red cell transfusions have not been able, so far, to tolerate such treatments.

Anemia is common in patients admitted for elective surgery, occurring in anywhere from 5% to 75% of elective procedures, depending on the patient population. Age, economic status, previous medical history and other factors all exert an effect on patients' health and hemoglobin levels. Not only is preoperative anemia an independent risk factor for perioperative morbidity and mortality, it is a strong predictor that perioperative transfusion will take place, and this in itself brings a risk of morbidity, including lung injury, renal failure, increased sepsis and risks of hemolysis and transfusion reactions. And transfusion costs a lot of money, with estimates of perioperative transfusion costs ranging from $1.6M to $6M per hospital per year. Half of the 21 million blood components transfused per year in the U.S. are administered perioperatively.

The perioperative evaluation and treatment of anemia is one of the pillars of patient blood management (PBM), which has been a “hot topic” for several years now. There are numerous articles about how it works, and it has been very clearly shown to lower hospital blood use, improve patient outcomes and reduce costs. Many, if not most, large university hospitals/medical centers have implemented such programs, or are in the process of doing so.

One article (see references) from the Duke University Medical Center describes how they went about planning, developing and implementing just such a program, described as their Perioperative Anemia Clinic (PAC). Their planning began 3 years ago this summer (2013) and their clinic opened a year later. Since the launch of their program, they have screened 175 patients scheduled for joint surgery, 25 of whom were referred to the PAC, and only one of these required transfusion. The program is effectively spreading to other services.

They elaborate in detail the 7 steps they identified in developing their PAC including target populations, financial modeling, anemia definitions, treatment algorithms, and integration with their electronic health record system. They adopted the protocol published a few years ago by Goodnough, et al. (see references) and fit it to their institutional needs. The actual operations of the clinic are especially interesting, as there often is a need to involve other specialists or departments to deal with the various types/causes of anemia. There may be referrals to primary care, gastroenterology, hematology, nephrology and then monitoring of the various interventions. Such interventions may include iron therapy—oral and/or intravenous, erythropoietin treatment, folic acid, surgery for gastrointestinal lesions, the evaluation of renal failure, and other concerns.

The authors present a table describing the net value of their anemia clinic after 1 year and project it to a 5 year value looking at the decrease in transfusions and associated costs, as well as the revenues gained from their infusion and treatment centers, and project at least a $2.7M value at 5 years. Of course the morbidity, mortality and stress of the patients involved cannot be measured but is a primary motivation for carrying out this development process.

In addition there is an elegant flow chart/algorithm that outlines the whole approach to the evaluation of preoperative anemia and diagnostic and therapeutic steps to take along the way. If you have not gotten involved with such a project at your institution, you might want to look closely at this article.

Time to Review Your MSBOS? Read This!

It is very expensive to provide blood transfusions in our hospitals these days, and very costly to do so outside of our regular facilities. Running a hospital blood bank requires maintaining a standard inventory of blood groups based on need, testing of both donor and recipient blood, maintaining proper temperatures for various products, record keeping for all, and adequate 24 hour staffing to handle daily work requirements. The costs of blood, of reagents for testing blood, for salaries and benefits, and for laboratory equipment to carry this all out are considerable. Significant decreases in blood usage have occurred with improved transfusion criteria based on solid evidence. In some ways this has allowed blood transfusion services to look at some other aspects of saving money—and blood.

Physicians at the University of Pittsburgh (see reference) have been using the maximum surgical blood ordering schedule (MSBOS) for many years. This is an institution-specific list of commonly performed surgical procedures that suggests the amount and degree of pre-transfusion testing to be performed. Having such a tool, the hospital transfusion service is able to predict, in general, what the surgical blood needs will be for that day. For many patients having procedures that usually require no blood, the minimum is a type and screen (T and S) to identify blood group and type and to identify any alloantibodies. The objective of this study was to determine what percentage of red cells issued to the OR were returned unused and to determine how often all of the issued units for any given patient were returned untransfused.

To do so, they collected data over a consecutive 4 week period in 2014 and retrospectively looked at the type of procedure; the extent of pre-transfusion testing recommended by the MSBOS; the number of units issued, returned or transfused; and, the number of times red cells were ordered during the case by the surgical team. Only patients who were eligible for red cells issued solely based on an electronic cross-match (current and confirmed ABO and Rh result and with no current or historical red cell antibodies) were included in the retrospective analysis. This information was compared to the institution’s MSBOS.

There were 1350 surgical procedures in which 439 patients had a T&S performed. At least 1 unit was issued to 215/439 cases (49%). To these 215, 742 red cell units were issued and 537 (72%) of these units were returned. In 152 of these 215 (71%) cases all of the red cells for each case were returned. In the surgical categories in the study, the percentage of returned red cells varied from 38-93%. The authors calculated usage rates for the 9 major surgical categories in their institution (e.g., cardiothoracic, neurological, orthopedic, general, etc.) In neurosurgery, for example, the unused proportion was 94%, and in 93% of the cases all of the issued units were returned. In all categories, when stratified by the MSBOS recommendations, the unused proportion and the percent of cases where all were returned was very high.

Thus, most of the red cells issued per patient were consistent with the MSBOS, but most of them were returned. Some of this may relate to the fact that not all MSBOS are “up to date”; that is, recent experience has generally led to less red cell use in most categories. Some hospitals are reviewing their schedules. In addition, it’s likely that house staff order pre-operative blood based on the MSBOS, and the more experienced surgeon might know he needed less in some cases. This suggests the need to involve experienced members of the surgical staff in updating the institution’s MSBOS to reflect more current practices.

**Preserving Platelet Function with Antioxidants**

Considerable sums are spent these days by mortal creatures on efforts to live longer and to stave off serious life-threatening events such as cancer and heart disease by ingesting “healthy anti-oxidants”, things such as green tea, cranberries, blueberries, blackberries, russet potatoes, beans, pecans and walnuts, all of which are good, healthy and nutritious foods. All living things are mortal, which is to say all are time-limited with regard to normal function and life span. The process by which this happens is called apoptosis, a process of cellular death that occurs in multi-celled organisms, of which we are one. Detectable changes at a cellular level include bleb formation, nuclear fragmentation and chromatin condensation, chromosomal DNA fragmentation and RNA decay. Billions of our cells die each day in this fashion. Most are safely replenished.

During storage *ex vivo*, platelets undergo structural and chemical changes that affect their effectiveness and safety when transfused to humans. They acquire activation markers and fail to respond normally to platelet activation signals. They also become activated and release prothrombotic and inflammatory cytokines which can cause serious transfusion reactions. Because of these losses from these platelets, they don’t respond anywhere nearly as effectively when performing as hemostatic agents. Enter physician scientists from The University of Rochester School of Medicine and Dentistry (see reference).

Resveratrol is a naturally occurring antioxidant found in grapes, peanuts and red wine. It is well known for its cardio-protective, anti-inflammatory and antioxidant activity and is currently under investigation in 75 different clinical trials for its beneficial actions, including in obesity, diabetes and Alzheimer’s disease. It damps platelet aggregation and thromboxane production in vitro, but nothing is known about its effects on stored platelets. Under carefully controlled laboratory conditions, human platelets were collected as usual, treated with resveratrol and stored under standard conditions (room temperature) for 5 days and then were evaluated in the laboratory.

Resveratrol persists in plasma stored at room temperature, but it is rapidly metabolized by the liver. It is a naturally occurring plant product with minimal toxicity at high doses. The dosage used in this platelet study was well within the levels used pharmaceutically or in current nutritional supplements. Thus its beneficial effects persist during storage, but IV administration is non-toxic and it is rapidly removed from the circulation.

Resveratrol treated platelets released less thromboxane B2 and prostaglandin E2 during storage when compared to control platelets; both of these are released during storage and are pro-inflammatory and prothrombotic agonists. As is already known, the control platelets in this study have diminished responses to ADP or collagen alone, and the authors found they also lose their ability to spread on fibrinogen. Treatment with resveratrol improved the ability of the platelets to aggregate and spread, and resveratrol modestly reduced apoptosis during storage. The authors used an *in vitro* method of transfusion and thromboelastography and found that clot strength was improved with the resveratrol-stored platelets compared to conventional ones. They demonstrated (in an *in vivo* mouse model) a longer half-life subsequent to transfusion, as well.

These studies demonstrate that such platelets have decreased release of inflammatory mediators while preserving platelet function and survival after transfusion. More work needs to be done, of course, to more fully investigate the mechanisms of action of this agent, and to determine appropriate approaches to demonstrate safety and efficacy in humans.

The Red Cross is pleased to annually host the Graham A. Jamieson Memorial Lecture in Blood Research. This year Dr Jerry Sandler, Medical Director, Transfusion Service of MedStar Georgetown University Hospital presented “Changing Practices in Hospital Transfusion Services (1968-2016)”. This informative talk was enjoyed by more than 100 attendees and was followed by lively discussion and networking among many of the leading experts in transfusion medicine.

From left to right: Richard Schubert, former President and CEO of the American Red Cross, Dr. Steven Wagner head of the Red Cross Research blood program and Dr. Jerry Sandler, Professor of Medicine and Pathology, Georgetown University School of Medicine.

### Publications Corner

Recent publications by American Red Cross scientists and physicians:


**First example of an FY*01 allele associated with weakened expression of Fya on red blood cells.** Arndt PA, Horn T, Keller JA, Heri SM, Keller MA. Immunohematology. 2015;31(3):103-7.