The American Red Cross initiated a comprehensive hemovigilance program in 2003 to monitor complications of blood donation and transfusion in its 35 regional blood centers across the United States. Each year, regional blood centers evaluate more than 200 cases of suspected transfusion-transmitted infections, take immediate action to prevent transfusion of other blood components collected from the involved donors, and perform additional investigations and testing to identify the source of infection. Among the infectious agents monitored by the American Red Cross Hemovigilance Program is Babesia microti, the primary cause of human babesiosis in the United States.

B. microti is an intraerythrocytic parasite endemic to the Northeast and upper Midwest. Published studies indicate that B. microti increasingly poses a blood safety risk. An American Red Cross Hemovigilance Program study described the donor and recipient characteristics of suspected transfusion-transmitted B. microti cases reported between 2005 and 2007.

Please see next page

Photo: Intraerythrocytic Babesia organism: As the parasite leaves the erythrocyte, it causes significant damage to the erythrocyte membrane, including perforations, protrusions, and inclusions. The exact mechanism for hemolysis, however, remains poorly characterized.
Symptoms can be nonspecific, mimicking many systemic infectious diseases, and include fever, chills, myalgias, fatigue, and jaundice caused by hemolytic anemia. Babesiosis is transmitted primarily through the bite of an infected tick, typically *Ixodes* spp., although occasionally transmission occurs via transfusion of blood products collected from asymptomatic infected donors. More than 50 transfusion-related cases have been reported in the United States. This report describes a transfusion-acquired case of babesiosis caused by *B. microti* in a resident of Los Angeles County, California.

Field mice are a common host for the Babesia vector in the United States.

Suspected transfusion-transmitted *Babesia* infections were reported by transfusion services or were discovered through recipient-tracing investigations of prior donations from donors with a positive test for *B. microti* in a serologic study. Follow-up samples from involved donors were tested by *Babesia*-specific immunofluorescence assay, Western blot, and/or real-time polymerase chain reaction analysis. Eighteen definite or probable *B. microti* infections, including five fatalities, were identified in transfusion recipients, 16 from hospital-reported cases and two through serologic lookback studies. Thirteen recipients were 61 to 84 years old and two were 2 years old or younger. Two recipients had sickle cell disease and four were known to be asplenic, including one with sickle cell disease. Seventeen antibody-positive donors were implicated; 11 (65%) were residents in *Babesia*-endemic areas, while four (24%) nonresident donors had a history of travel to endemic areas.

The researchers concluded that transfusion-transmitted *B. microti* can be a significant cause of transfusion-related morbidity and mortality, especially in infant, elderly, and asplenic blood recipients. These data demonstrate the need for interventions, in both endemic and nonendemic areas of the United States, to reduce patient risk.

**CASE STUDY: TRANSFUSION-TRANSMITTED BABESIOSIS**

Babesiosis is an infection of red blood cells (RBCs) caused by various species of the protozoan genus *Babesia*. Most human infections reported in the United States are attributed to *B. microti* and occur most frequently in the Northeast and less commonly in the Midwest. Infrequently, babesiosis cases have been documented in California and Washington; however, these cases were caused by local *Babesia*-like isolates, including *B. duncani* and a *B. divergens*-like parasite. *B. microti* infection is often asymptomatic but can potentially be severe and even fatal, especially in the elderly, asplensics, and other immunosuppressed persons.

Symptoms can be nonspecific, mimicking many systemic infectious diseases, and include fever, chills, myalgias, fatigue, and jaundice caused by hemolytic anemia.

Babesiosis is transmitted primarily through the bite of an infected tick, typically *Ixodes* spp., although occasionally transmission occurs via transfusion of blood products collected from asymptomatic infected donors. More than 50 transfusion-related cases have been reported in the United States. This report describes a transfusion-acquired case of babesiosis caused by *B. microti* in a resident of Los Angeles County, California.

Cattle are the most common host for the *Babesia* vector in Europe.
CASE STUDY: TRANSFUSION-TRANSMITTED BABESIOSIS, CONT.

Table 1

Results of serologic testing and PCR analyses of specimens collected from a California resident with babesiosis and donors of packed red blood cells, 2007*

<table>
<thead>
<tr>
<th>Specimen source</th>
<th>Residence</th>
<th>Date of transfusion</th>
<th>Date of specimen collection</th>
<th>PCR</th>
<th>IFA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>California</td>
<td>Feb 12</td>
<td>Feb 26</td>
<td>Positive</td>
<td>&lt;8</td>
</tr>
<tr>
<td>Donor 1</td>
<td>Maine</td>
<td>Jan 1</td>
<td>Feb 20</td>
<td>___</td>
<td>64</td>
</tr>
<tr>
<td>Donor 2</td>
<td>Maine</td>
<td>Jan 1</td>
<td>Feb 26</td>
<td>___</td>
<td>256</td>
</tr>
<tr>
<td>Donor 3</td>
<td>California</td>
<td>Jan 22</td>
<td>Feb 21</td>
<td>___</td>
<td>&lt;8</td>
</tr>
<tr>
<td>Donor 4</td>
<td>California</td>
<td>Jan 23</td>
<td>Feb 22</td>
<td>___</td>
<td>&lt;8</td>
</tr>
<tr>
<td>Donor 5</td>
<td>California</td>
<td>Jan 24</td>
<td>Feb 21</td>
<td>___</td>
<td>&lt;8</td>
</tr>
<tr>
<td>Donor 6</td>
<td>California</td>
<td>Jan 24</td>
<td>Feb 21</td>
<td>___</td>
<td>&lt;8</td>
</tr>
</tbody>
</table>

*IFA, immunofluorescent antibody.
†Involving blood products from specified donor.
‡<8 is considered a negative titer for total B. microti antibody.
*IFA tests conducted at the Centers for Disease Control and Prevention Reference Diagnostic Laboratory.
†PCR test performed at the Los Angeles County Public Health Laboratory.
‡Serologic testing results obtained from peripheral smear and confirmed at the Los Angeles County Public Health Laboratory.

The Case

On February 12, 2007, a 58-year-old man with metastatic esophageal cancer was admitted to an acute care facility for evaluation of hematemesis and normocytic anemia. The initial examination showed he had hypotension without fever, joint swelling, headaches, or rash. Laboratory evaluation showed a hemoglobin concentration of 8.4 mg/dL, a platelet count of 71,000/mm³, and a leukocyte count of 3.5 x 10³/mm³ with 19% bands. Results of liver function tests showed mild elevations in levels of aspartate transaminase (202 mg/dL), alanine transaminase (33 mg/dL), and total bilirubin (0.7 mg/dL). An abnormal blood cell count prompted a manual differential count. Babesia spp. was identified on a peripheral smear and subsequently confirmed at the Los Angeles County Public Health Laboratory. The result of PCR analysis performed by a commercial laboratory was positive and highly specific for B. microti DNA, a result confirmed by the Centers for Disease Control and Prevention (CDC) (Table 1). The commercial laboratory also performed indirect fluorescent antibody (IFA) testing for B. microti and found both acute and convalescent specimens to be negative. Confirmatory testing at CDC corroborated the negative result for the acute specimen but showed the convalescent specimen, collected 8 days after onset, to be positive for B. microti, with a total antibody titer of 64. The patient was treated with azithromycin and atovaquone for 7 days, given 2 blood transfusions for anemia, and discharged in stable condition on February 16, 2007. Before admission, the patient had visited an oncology clinic numerous times for treatment related to his esophageal cancer: radiation therapy in October 2006, 3 chemotherapy courses from October 2006 through February 2007, and blood transfusions in January 2007. The patient received 6 units of packed red blood cells (PRBCs) and 2 units of fresh frozen plasma (FFP) over several clinic visits on January 1 and January 22–24, 2007. The patient was in Salt Lake City, Utah, from January 13 through January 20, 2007; however, because of poor health, he did not engage in any outdoor activities. At least a year before his admission in 2006, the patient visited an undeveloped property near Klamath Falls, Oregon, where he spent time outdoors. He could not recall ever incurring a tick bite, seeing ticks, or having any animal contact.

Table 1 summarizes the serologic and PCR results for specimens collected from the patient and 6 PRBC donors. The PRBC units came from 2 blood banks: 1 in Maine (2 units) and 1 in California (4 units). A blood donor from Maine tested positive for B. microti by IFA, with a total antibody titer 256, but tested negative for B. microti by PCR. Testing of specimens from the remaining PRBC donors yielded negative results. Specimens from FFP donors were not tested because of the low risk for Babesia spp. transmission associated with plasma products.

The implicated donor was a 49-year-old male resident of Maine, where babesiosis is less common than in other states in the northeast. For example, whereas Maine typically reports <12 cases annually, Rhode Island has reported up to 51 cases.5 However, the donor resided in the southern coastal region of the state, where Maine’s cases are concentrated.6 He frequent tick-infested areas and is likely to have become infected in late August 2006, when he sought treatment for fever, chills, weight loss, and fatigue and was tested for various infections, including Lyme disease and ehrlichiosis. At that time, he was not tested for babesiosis. His health improved without a specific diagnosis or treatment, and he remained asymptomatic, but he evidently was parasitemic when he donated blood on December 20, 2006. Blood products from this donation were included in the transfusion the patient received on January 1, 2007. Between October 2005 and the blood donation on December 20, 2006, the donor made 3 donations. All other recipients of blood products from this donor were residents of Maine. They were notified of the need for serologic testing; none were reported to be infected (V. Rea, pers. comm.).
Conclusions

Babesiosis was documented in a man with metastatic cancer who resided in an area nonendemic for *B. microti*. On the basis of laboratory and epidemiologic information, we concluded that the patient acquired the infection via transfusion of infected PRBCs donated in a disease-endemic area thousands of miles away. The 12-day period from donation to transfusion was within the maximum 35 days that *B. microti* has been known to remain viable in refrigerated blood.7

The period from time of transfusion exposure until positive smear was ≈6 weeks; incubation periods for transfusion-related cases have ranged from weeks to many months (B. Herwaldt, pers. comm.). We had tentatively hypothesized that the patient might have acquired the infection in Oregon, where he spent substantial time outdoors, but remained asymptomatic until he became ill with cancer; however, we rejected this hypothesis because human cases of babesiosis have never been documented in Oregon (or in Utah where the man also visited) and because infections acquired in western states are more likely to be caused by local *Babesia* agents.

This case demonstrates that, even among transfused patients who show atypical symptoms of babesiosis, the possibility of infection should be considered if they have received blood products from disease-endemic areas and display abnormal blood cell counts, such as low iron and low leukocyte counts. Generalized debilitation associated with cancer and chemotherapy may have masked *Babesia*-related symptoms in this patient and undermined his immune response.

This case also underscores the widening seasonal and geographic boundaries of babesiosis. Tick-borne babesiosis usually peaks from July through September 4, but because asymptomatic *Babesia* infection can persist for months to years, especially in untreated persons 7,8, transfusion-associated infection can occur throughout the year. Geographic limitations in babesiosis are virtually erased by the mobility of donors and blood products.

The blood bank involved in this case has blood collection centers throughout southern California and the East Coast. Medical evaluation for babesiosis in both febrile and afebrile transfusion recipients should include a Giemsa-stained thin blood smear, an acute serologic evaluation by IFA testing and a convalescent serologic evaluation by IFA testing taken 4–6 weeks apart 9, and PCR evaluation of whole blood. The varied clinical spectrum of babesiosis makes its detection in blood donors challenging.

This case exemplifies the limitations in screening healthy asymptomatic donors for babesiosis. Available screening tests to detect *Babesia* spp. postdonation are not cost-effective and have inadequate sensitivity.7,11 Nucleic acid testing and inactivation procedures may provide useful options for detecting *Babesia* spp. in the future.7,11 Until effective screening procedures are available, however, diagnosis of babesiosis in blood donors will continue to be based primarily on clinical observation.

References


A NOVEL PARVOVIRUS B19 GENOTYPE 3 ISOLATE FOUND IN U.S. PLASMA DONATION

Parvovirus B19 (B19V) is a pathogen frequently identified in human plasma donations through the detection of nucleic acids. Three B19V genotypes have been defined based on isolates having greater than 10% divergence in overall DNA sequence. B19V Genotype 3 is a rarely occurring genotype that has been detected primarily in Ghana with sporadic reports in Brazil and France, but has not been previously reported in North America.

In this study, a polymerase chain reaction assay was developed with broad specificity for B19V detection. The performance of this assay was assessed by testing approximately 440,000 clinical samples representing more than 81,000 individual donors. Determinations of B19V titer, DNA sequence, and antibody concentrations were performed on samples of interest. This assessment identified a series of 8 plasma donations spanning 28 days from a single donor in the United States infected with B19V Genotype 3 as confirmed by DNA sequence analysis. The B19V titer of this series of donations showed virus titers that peaked at greater than 10(11) IU/mL. The virus titer decreased significantly over the next several donations coinciding with an increase in immunoglobulin M (IgM) levels. The immunoglobulin G levels also increased but lagged approximately 7 days behind the IgM levels. This study is the first report of a B19V Genotype 3 detected from a plasma donor located in the United States. Although the data are consistent with recent reports suggesting low incidence for this genotype, they indicate its increasing relevance among blood and plasma donors.


BABESIA MICROTI LIFE CYCLE

The Babesia microti life cycle involves two hosts, which includes a rodent, primarily the white-footed mouse, Peromyscus leucopus, and a tick in the genus, Ixodes. During a blood meal, a Babesia-infected tick introduces sporozoites into the mouse host. Sporozoites enter erythrocytes and undergo asexual reproduction (budding). In the blood, some parasites differentiate into male and female gametocytes, although these cannot be distinguished at the light microscope level. The definitive host is the tick. Once ingested by an appropriate tick, gametocytes unite and undergo a sporogonic cycle resulting in sporozoites. Transovarial transmission (also known as vertical, or hereditary, transmission) has been documented for “large” Babesia spp. but not for the “small” Babesiae, such as B. microti. Humans enter the cycle when bitten by infected ticks. During a blood meal, a Babesia-infected tick introduces sporozoites into the human host. Sporozoites enter erythrocytes and undergo asexual replication (budding). Multiplication of the blood stage parasites is responsible for the clinical manifestations of the disease. Humans are, for all practical purposes, dead-end hosts, and there is probably little, if any, subsequent transmission that occurs from ticks feeding on infected persons. However, human to human transmission is well recognized to occur through blood transfusions.

AABB ISSUES NEW TRANSFUSION-TRANSMITTED BABESIA BULLETIN

The AABB issued Association Bulletin #09-06 providing members with the latest information on how to manage patients, donors and blood components in the event of known or suspected cases of transfusion-transmitted Babesia. The bulletin, which was developed by the AABB Transfusion-Transmitted Diseases Babesia Work Group, also includes educational materials for clinicians about the epidemiology of Babesia, a chart that describes approaches to investigation of transfusion-transmitted Babesia used by several blood centers operating in endemic areas, and a summary of available interventions which could reduce transfusion transmission of the disease.

For more information, please go to aabb.org

Babesia parasites resemble Plasmodium falciparum; however Babesia has several distinguishing features: the parasites are pleomorphic (vary in shape and size), can be vacuolated, and do not produce pigment.
Deferred travel to malaria-endemic areas excludes many blood donors in the United States. Most transfusion-transmitted malaria is associated with lengthy residence in malaria-endemic areas rather than routine travel. This study compared the impact of existing deferral requirements to the risk that a presenting donor with malaria travel history harbors malaria parasites under current and hypothetical alternate regulations.

Deferred donors from 6 blood centers were sampled to estimate a national cohort of donors deferred annually for malaria travel to different geographic regions. Risk for malaria infection after travel to each region and distribution of incubation periods for each malaria species were estimated for U.S. travelers. Region-specific travel risks were used to estimate the risk that a presenting blood donor with malaria travel history harbors malaria parasites under current and hypothetical alternate regulations.

Travel to Africa presents risk for malaria infection greater than 1000 times that of travel to malaria-endemic parts of Mexico, yet Mexico accounts for more than 10 times as many deferred donors. Shortening the deferral period from 12 to 3 months for travelers to Mexico increases the risk of collecting a contaminated unit by only 1 unit per 57 years (sensitivity analysis, 1 every 29-114 years), at annual gain of more than 56,000 donations. This study provided the first systematic appraisal of the
IN BLOOD DONORS DEFERRED

U.S. requirements for donor qualification regarding travel to malarial areas. Consideration should be given to relaxing the guidelines for travel to very-low-risk areas such as Mexico.


MALARIA AT A GLANCE

247 million people in the world contracted malaria in 2006.
650 million people are at risk.
880,000 died from the disease.
1,505 malaria cases were reported in the United States in 2007.
1 year is how long travelers to a malaria endemic area are deferred from donating blood after returning to the United States.
3 years is how long residents of malaria risk areas are deferred from donating blood.
3 years after treatment is how long those diagnosed with malaria are deferred from donating blood, as long as they remain symptom free.
<1 per 1 million is the rate of transfusion-transmitted malaria in the United States.

Source: WHO, CDC, FDA
The goal of this study was to assess transfusion reactions arising from prestorage-pooled platelet (PSPP) infusions compared with apheresis single-donor platelets (SDPs) and poststorage-pooled, whole blood-derived random-donor platelets (RDPs). Over an 18 month span, the transfusion reaction records of patients receiving platelet (PLT) infusions were retrospectively reviewed at two academic, tertiary care hospitals. Chi-square analysis was used for statistical comparisons; significance was a p value of less than 0.05. For the two sites, 10,251 prestorage-leukoreduced PLT products were infused including 4731 PSPPs, 3999 SDPs, and 1521 RDPs.

Of the total infusions, 0.91% (93/10,251) were associated with a transfusion reaction. The aggregate transfusion reaction rate was 0.89% (42/4,731) for PSPPs, 0.75% (30/3,999) for SDPs, and 1.38% (21/1,521) for RDPs. There were no significant differences in total reaction rate between PSPPs and the other PLT products (p > 0.05).

Allergic transfusion reactions were the most common adverse event for PLT products evaluated (63/10,251; 0.61%) and febrile reactions were second most common (27/10,251; 0.26%). There were 2 suspected cases of sepsis (1 associated with PSPP and 1 associated with RDP; both culture negative) and 1 case of volume overload associated with RDP infusion. There were no significant differences in aggregate allergic or febrile reaction rates among the 93 PLT products evaluated (p > 0.05). No reports of transfusion-related acute lung injury or hemolysis were noted.

The researchers concluded that there was no difference in reaction rates observed among PSPPs and the other PLT products. They found that the transfusion reactions occurring in this population were not dependent on the type of PLT product infused.

Over the past 20 years, the molecular bases of almost all the major blood group antigens have been determined. This research has enabled development of deoxyribonucleic acid (DNA) based methods for determination of blood group genotype. One application of these DNA-based methods has been for the determination of fetal blood group in pregnancies where the fetus is at risk from Hemolytic Disease of the Fetus and Newborn (HDFN).

Professor David Anstee, Director of the Bristol Institute for Transfusion Services, explained that the replacement of all conventional serological methods for pre-transfusion testing by molecular methods is not straightforward. He contends that matching beyond ABO and Rh(D) type is unnecessary for the majority of transfusion recipients and that the minority (<10%) of untransfused patients at risk of alloimmunization who would benefit from more extensively blood group matched blood cannot be identified reliably. The study found that even if a method to identify individuals most likely to make alloantibodies were available, this would not of itself guarantee the provision of extensively phenotype matched blood for these patients because this is determined by the size and racial composition of blood donations available for transfusion.

However, routine use of DNA-based extended phenotyping to provide optimally matched donations for patients with pre-existing antibodies or patients with a known predisposition to alloimmunization, such as those with sickle cell disease, will become more common. While DNA-based blood group typing provides a valuable adjunct to traditional methods of ABO and Rh(D) typing, it is not expected to replace these conventional means.

RESEARCHERS LOOK AT BLOOD USE IN THE AMBULATORY SETTING AMONG U.S. ELDERLY

A study conducted by the Food and Drug Administration (FDA) Office of Biostatistics and Epidemiology, Center for Biologics Evaluation and Research analyzed blood use in the ambulatory setting by U.S. elderly Medicare beneficiaries who were 65 years old or older during 2001.

As the U.S. population ages and delivery of healthcare in outpatient settings is on the rise, ambulatory blood utilization is expected to increase.

The researchers noted that there is currently a lack of broad population-based studies detailing ambulatory blood utilization patterns among the US elderly.

This descriptive cross-sectional study of ambulatory blood utilization in institutional outpatient settings used Medicare administrative data (5% sample of enrollees) for calendar year 2001. Blood use was identified by either the presence of recorded blood units or the procedure code(s) for transfusion of whole blood or red blood cells.

Among 1,368,368 elderly Medicare beneficiaries analyzed, 7,054 (0.52%) had blood transfusion in institutional outpatient settings, and 34,186 (2.50%) had blood transfusion in the inpatient setting. Of 10,705 institutional outpatient claims with blood use quantified in this cohort of elderly Medicare beneficiaries, the top 10 principal diagnoses using the largest quantities of blood accounted for 66.3% of total blood units transfused. Nine of these 10 principal diagnoses were either for anemias or neoplasms and accounted for 64% of total blood units transfused. (51% and 13% respectively)

This population-based study suggests that most of the ambulatory blood utilization among U.S. elderly is for diagnoses of anemias and neoplasms rather than procedures, providing information on ambulatory blood utilization patterns which may be used to better understand the reasons for transfusion in the ambulatory setting as blood use is expected to grow.


SCIENTISTS DISCUSS WAYS TO FURTHER IMPROVE ALLOGENEIC BLOOD TRANSFUSION OUTCOMES

As the risks of allogeneic blood transfusion (ABT) transmitted viruses were reduced to exceedingly low levels in the United States, transfusion-related acute lung injury (TRALI), hemolytic transfusion reactions (HTRs), and transfusion-associated sepsis (TAS) have emerged as the leading causes of ABT-related deaths.

Since 2004, preventive measures for TRALI and TAS have been implemented, but their implementation remains incomplete. Infectious causes of ABT-related deaths currently account for less than 15% of all transfusion-related mortality, but the possibility remains that a new transfusion-transmitted agent causing a fatal infectious disease may emerge in the future.

Aside from these established complications of ABT, randomized controlled trials comparing recipients of non-white blood cell (WBC) reduced versus WBC-reduced blood components in cardiac surgery have documented increased mortality in association with the use of non-WBC reduced ABT. The authors concluded that ABT-related mortality can be further reduced by universally applying the policies of avoiding prospective donors alloimmunized to WBC antigens from donating plasma products, adopting strategies to prevent HTRs, WBC-reducing components transfused to patients undergoing cardiac surgery, reducing exposure to allogeneic donors through conservative transfusion guidelines, and avoiding product pooling, and implementing pathogen-reduction technologies to address the residual risk of TAS as well as the potential risk of the next transfusion-transmitted agent to emerge in the future.

NEW FACET OF DIAMOND-BLACKFAN ANEMIA FOUND

Diamond-Blackfan anemia (DBA) is an inherited bone marrow failure syndrome characterized by anemia, congenital abnormalities, and cancer predisposition. Small ribosomal subunit genes RPS19, RPS24, and RPS17 are mutated in approximately one-third of patients. In this study, researchers used a candidate gene strategy combining high-resolution genomic mapping and gene expression microarray in the analysis of 2 DBA patients with chromosome 3q deletions to identify RPL35A as a potential DBA gene. Sequence analysis of a cohort of DBA probands confirmed involvement of RPL35A in DBA. shRNA inhibition shows that Rpl35a is essential for maturation of 28S and 5.8S rRNAs, 60S subunit biogenesis, normal proliferation, and cell survival.

Analysis of pre-rRNA processing in primary DBA lymphoblastoid cell lines demonstrated similar alterations of large ribosomal subunit rRNA in both RPL35A-mutated and some RPL35A wild-type patients, suggesting additional large ribosomal subunit gene defects are likely present in some cases of DBA. These data demonstrate that alterations of large ribosomal subunit proteins cause DBA and support the hypothesis that DBA is primarily the result of altered ribosomal function. The results also establish that haploinsufficiency of large ribosomal subunit proteins contributes to bone marrow failure and potentially cancer predisposition.


ANEMIA IS ASSOCIATED WITH GREATER RISKS IN HEART DISEASE PATIENTS

A study in the journal Congestive Heart Failure found that anemia in patients with chronic heart failure is associated with a significantly increased risk of death. The findings also showed that anemia is associated with a poorer degree of left ventricular function and a lower left ventricular ejection fraction, an objective measure of cardiac function.

The aim of this study was to assess the impact of anemia on the clinical outcomes of chronic heart failure (CHF) by a meta-analysis and systemic review of published literature. Twenty published English-language articles were selected from Medline, PubMed, and ISI Database. Clinical data were extracted, pooled, and analyzed with a fixed- or random-effects model.

A total of 97,699 patients with CHF were identified from the published studies. Meta-analysis of these studies indicated that anemia is associated with a higher risk for death (relative risk [RR], 1.66; P<.0001). In addition, anemic patients had more advanced New York Heart Association class (III or IV; RR, 1.35; P<.0001) and lower left ventricular ejection fraction (weight mean difference, 0.53; P<.0001) than nonanemic patients.

The researchers found that their systemic review also revealed that the severity of anemia is closely related to the rate of mortality and hospitalization for heart failure. Anemia was associated with an increased risk of mortality and rate of hospitalization for heart failure. The study concluded that anemia is an independent risk factor for adverse outcomes in patients with CHF.

Neutrophils are highly specialized innate effector cells that have evolved for killing pathogens. Human neonates have a common multifactorial syndrome of neutrophil dysfunction that is incompletely characterized and contributes to sepsis and other severe infectious complications.

In this study, researchers identified a novel defect in the antibacterial defenses of neonates: inability to form neutrophil extracellular traps (NETs).

NETs are lattices of extracellular DNA, chromatin, and antibacterial proteins that mediate extracellular killing of microorganisms and are thought to form via a unique death pathway signaled by nicotinamide adenine dinucleotide phosphate (NADPH) oxidase–generated reactive oxygen species (ROS).

They found that neutrophils from term and preterm infants fail to form NETs when activated by inflammatory agonists—in contrast to leukocytes from healthy adults. The deficiency in NET formation is paralleled by a previously unrecognized deficit in extracellular bacterial killing.

The study found that the generation of ROSs did not complement the defect in NET formation by neonatal neutrophils, as it did in adult cells with inactivated NADPH oxidase, demonstrating that ROSs are necessary but not sufficient signaling intermediaries and identifying a deficiency in linked or downstream pathways in neonatal leukocytes. Impaired NET formation may be a critical facet of a common developmental immunodeficiency that predisposes newborn infants to infection.

STUDY FINDS MODERATE EXPOSURE TO ALLOGENEIC BLOOD PRODUCTS IS NOT ASSOCIATED WITH REDUCED LONG-TERM SURVIVAL AFTER CORONARY DISEASE SURGERY

Some studies have suggested that blood transfusion has an adverse effect on long-term health, mainly through immune modulation and tumor promotion. To further assess this concern, researchers performed a prospective observational study with the hypothesis that after taking perioperative risk factors relevant to long-term survival into account, patients undergoing coronary artery surgery who receive a perioperative allogeneic blood transfusion have worse long-term survival than those who do not.

The health outcomes of 1,841 consecutive subjects who had isolated nonemergency first-time coronary artery surgery and who survived more than 60 days after surgery were determined by record linkage. The association between length of survival, blood products transfused, and risk factors for long-term survival at entry to the study were determined by Cox proportional hazards regression.

A total of 1,062 subjects were transfused. Of these, 266 subjects died during a mean follow-up of 8.1 yr. Of subjects who were transfused, 27% had a new malignant condition recorded on the death certificate, compared with 43% who were not transfused. Older age, cerebrovascular disease, use of a mammary graft, chronic pulmonary disease, renal dysfunction, reduced left ventricular function, and preoperative anemia were predictive of reduced long-term survival. There was no association between transfusion of blood products and long-term survival.

The researchers concluded that patients who have undergone coronary artery surgery and who have received moderate amounts of blood as part of responsible and conservative management should be reassured that they are unlikely to experience a reduction in long-term survival.


REMEMBER THESE WEBSITES

Immunohematology Journal
redcross.org/en/immunohematology
Reimbursement
redcross.org/hospitals/reimbursement
PLUS
Fall 2009, Volume Three, Issue Four

A SYNOPSIS OF THE 2008 NHLBI/NIH GUIDELINES ON THE CLINICAL AND LABORATORY DIAGNOSIS OF VON WILLEBRAND DISEASE

Von Willebrand factor (VWF) mediates blood platelet adhesion and accumulation at sites of blood vessel injury, and also carries coagulation factor VIII (FVIII) that is important for generating procoagulant activity.

Von Willebrand disease (VWD) is the most common inherited bleeding disorder. VWD reflects deficiency or defects of VWF that may also cause decreased FVIII. It may also occur less commonly as an acquired disorder (acquired von Willebrand syndrome).

An article in the American Journal of Hematology briefly summarizes selected features of the March 2008 evidence-based clinical and laboratory diagnostic recommendations from the National Heart, Lung, and Blood Institute (NHLBI) Expert Panel for assessment for VWD or other bleeding disorders or risks. Management of VWD is also addressed in the NHLBI guidelines, but is not summarized in the journal article. The VWD guidelines are available at the NHLBI Web site www.nhlbi.nih.gov/guidelines/vwd


RESOURCES AVAILABLE

What If I Need Blood? is a brochure which answers commonly asked questions and explains the transfusion options for patients.

The second edition of Practice Guidelines for Blood Transfusion: A Compilation of Peer-Reviewed Literature is a concise transfusion medicine resource, providing guidelines for some of the more commonly encountered clinical situations.

A Guide to American Red Cross Reference Laboratory Services is a guide describing the many services offered by the American Red Cross Immunohematology Reference Laboratories.