Transfusion-associated bacterial sepsis: a concise review

S.J. Wagner and D. Lieby

Key Words: transfusion-associated sepsis, bacterial contamination of blood

Although sepsis from bacterial contamination of blood is reported as an infrequent event in transfusion medicine, outcomes may be severe or fatal and therefore are an issue of concern. Sources of contaminating bacteria include donor bacteremia, skin, containers and other disposables, and the environment.

Estimates of the frequency of component contamination vary greatly depending on the measure employed. The recognized measures are (1) fatalities from confirmed cases of transfusion-associated sepsis, (2) bacterial contamination associated with febrile transfusion reactions, and (3) bacterial culturing of blood components. The frequency of fatalities attributable to sepsis has been estimated at 1 per 6 million units transfused. However, the actual frequency of fatalities may be greater due to underreporting and failure to recognize cases of transfusion-related sepsis. Bacterial contamination associated with febrile transfusion reactions has been reported to occur in 1 per 1,700 pools of whole blood-derived platelet concentrates, representing approximately 1 per 10,000 individual units. For single donor platelets, febrile reactions have been associated with bacterial sepsis in roughly 1 per 20,000 units. Definitive studies involving contamination of components include a second culture of the sample to rule out false positives. A study by Leiby et al. using this confirmatory criteria estimated that on average, there was 1 contaminated unit per 1,670 recently outdated platelets. However, all of the contaminated units contained levels of organisms too low (< 10 CFU/mL) to be thought a risk for sepsis on transfusion. Another study estimated that the incidence of platelet contamination was roughly 1 in 300 units, although only one-half of initially positive cultures could be confirmed by subsequent testing. Estimates of contamination of red cell components by culture method have varied from none to 1 per 500 units.

Low levels of bacteria initially present in contaminated red cell and platelet units may proliferate during storage to levels of $10^2$–$10^8$ CFU/mL or more, and severe clinical reactions seem to be associated with levels of about $10^6$ CFU/mL or more. The majority of cases of sepsis from platelet transfusions have occurred in units stored for 3 or more days. The organisms involved in contamination often reflect the unique blood bank storage conditions of the component. For example, aerobic organisms capable of room temperature proliferation are involved in sepsis from platelet transfusions. Because many different strains favor these conditions, it is not surprising that a great variety of organisms have been implicated in sepsis from platelets. Nevertheless, the common skin bacterium, Staphylococcus epidermidis, has been recovered from roughly 25 percent of these events. Other implicated organisms listed in decreasing order of prevalence include salmonella, cholerasuis, Serratia marcescens, Staphylococcus aureus, Bacillus cereus, Streptococcus viridans group, Escherichia coli group A beta-hemolytic streptococci, Enterobacter cloacae, and others.

Organisms implicated in sepsis from red cells are usually distinguished by their ability to proliferate at 1°–6°C. The species most frequently reported causing sepsis is Yersinia enterocolitica, an iron-requiring enteric, gram negative, psychrophile. It has been identified in approximately 50 percent of the cases. Other organisms include Pseudomonas species (most notably P. fluorescens, which is identified in approximately 25% of all cases), Enterobacter cloacae, Escherichia coli, and Campylobacter jejuni.

Although Yersinia is known to cause gastroenteritis, only one-third of the donors involved in transmission of the organism recall diarrhea (8–30 days prior to dona-
tion, although some have diarrhea postdonation). Thus, infected individuals are typically asymptomatic at the time of blood donation. Most cases of transfusion-associated *Yersinia* have involved red cell units stored for more than 25 days. A majority of the reported cases have resulted in death. In vitro, the organism proliferates exponentially in red cell units with doubling times ranging from 18–20 hours after an initial 1–2 week lag phase. Stationary phase is typically reached after 25 days in deliberately inoculated units; this correlates well with the age of units implicated in *Yersinia* sepsis.1

When a patient develops clinical signs suggestive of sepsis, the transfusion should be stopped and a gram stain and culture of both the patient’s blood and the blood bag should be performed. The unit should be inspected for visible signs of clots, hemolysis, or abnormal color. In addition, it is useful to type the organism(s) recovered from the patient and the blood bag for confirmatory purposes. Other components from the donation that is under investigation should be quarantined and may be cultured if the implicated component is not available.

In addition to proper selection and cleaning of the phlebotomy site, a number of interventions have been proposed to reduce the incidence of transfusion-associated bacterial sepsis. These include a reduction of the storage time of components, inclusion of antibiotics in the collection set, leukoreduction of blood components, bacterial inactivation, and testing. Further reduction in the storage time of red cells or platelets is logistically difficult and could affect the availability of blood components. Because of the risk for adverse reactions from antibiotics (e.g., hypersensitivity, etc.), the risk-to-benefit ratio for their inclusion in collection sets is not favorable. In vitro studies have demonstrated that leukoreduction has little effect on the levels of bacteria in platelets.1 In contrast, the use of leukoreduction filters in red cell units deliberately inoculated with *Yersinia* has been shown to inhibit the proliferation of the organism during storage.1 However, because of the virulence properties of *Yersinia*, it is not clear that spiking studies adequately reflect the outcome that would otherwise be obtained from leukoreducing naturally infected blood.7 Photochemicals such as the psoralens and near-UV light have been used experimentally to inactivate a wide range of bacterial species in platelet concentrates without apparent damage to the in vitro properties of platelets.8 Significant work remains to be done in order to fully evaluate this technology.

Several methods for detecting the presence of bacteria have been proposed, including gram stain, acridine orange stain, cessation of platelet swirling, visual inspection of the red cell container and segment colors, pH and glucose levels, automated bacterial culturing, measurement of bacterial ribosomal RNA, and immunological and polymerase chain reaction (PCR) testing.9 In general, gram stain, platelet swirling, differential color of red cells, and pH and glucose determinations lack the sensitivity to reliably detect at least $10^5$ CFU/mL in contaminated components. PCR tests have been developed for specific organisms, but a test capable of detecting the great variety of strains that have been implicated in transfusion-associated sepsis has not been devised. A procedurally complex test utilizing a universal chemiluminescent probe for a ubiquitous ribosomal RNA sequence has been used to detect bacteria in red cells and platelets at the $10^4$ CFU/mL level;10 further development appears to be halted. Other more refined nucleic acid–based methods for bacterial detection are under development, and application of automated bacterial culture methods for detection are currently being investigated. There is potential for the application of these techniques to yield simple, rapid, sensitive, unambiguous, and cost-effective test procedures for bacteria in blood.

**References**


Stephen J. Wagner, PhD, Product Development Dept., Holland Laboratory, American Red Cross Blood Services, 15601 Crabbs Branch Way, Rockville, MD 20855; David Lieby, PhD, Transmissible Disease Dept., Holland Laboratory, Rockville, MD.

Manuscripts:
The editorial staff of Immunohematology welcomes manuscripts pertaining to blood group serology and education for consideration for publication. We are especially interested in case reports, papers on platelet and white cell serology, scientific articles covering original investigations, and papers on the use of computers in the blood bank. Deadlines for receipt of manuscripts for the March, June, September, and December issues are the first weeks in October, January, April, and July, respectively. Instructions for scientific articles and case reports can be obtained by phoning or faxing a request to Mary H. McGinniss, Managing Editor, Immunohematology, at (301) 299-7443, or see “Instructions for Authors” in Immunohematology, issue No. 1, of the current year.

IMMUNOHEMATOLOGY IS ON THE WEB!
http://biomed.redcross.org/immunohematology/

For more information or to send an e-mail message to the editor: dmallory@usa.redcross.org