Emerging Infectious Disease in Transfusion Medicine

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After reading this article, the reader should understand the different viruses, bacteria, and other agents that can contaminate the blood bank supply.

**Blood Banking exam 60402** questions and corresponding answer form are located after the “Your Lab Focus” section on p. 507.

Emergence of new infectious diseases raises concern about the safety of the blood supply in the United States.

This article will briefly review these emerging and enduring transfusion-transmitted infections.

This article also reviews the different procedures and tests that blood banks implement to screen for these infections.

This millennium, we have seen the emergence of new infectious diseases. The West Nile virus (WNV) was first detected in North America in the summer of 1999; SARS became a world health emergency in winter/spring 2002/2003; and an outbreak of the monkeypox virus, the first in North America, was detected in the spring of 2003.1

The emergence of these new infectious diseases raises concerns about the safety of our blood supply. More than 20 million units of blood components are transfused into approximately 4 million people yearly in the United States.2

It has been repeatedly stated that the current United States blood supply is the safest it has ever been. This has been accomplished by careful elimination of high-risk donors through the donor questionnaire and by advances in serologic and nucleic acid testing (NAT). Because the transmission frequency of infectious agents classically associated with transfusion, such as HIV and HCV, has markedly decreased, new viral agents and non-viral agents have received more attention.

**Viruses**

**West Nile Virus**

West Nile virus is a flavivirus transmitted via mosquitoes, with humans as incidental vectors. West Nile virus has created an epidemic in the United States since its introduction in New York City in 1999 with a steady movement towards the western United States. West Nile virus infection is usually asymptomatic; however, disease severity increases with patient age and with immunocompromised state, ranging from a mild febrile illness to meningitis and death.

The maximum risk of WNV transmission during an epidemic is estimated at 10 to 15 per 10,000 blood units transfused.1 In 2002, multiple cases of WNV transmission through blood transfusions were confirmed.3 Beginning in June 2003, pooled NAT was implemented to screen all donations for WNV. Of the first 2.2 million donations screened with NAT, 777 units were found positive for WNV (personal communication, Sue Stramer, PhD, November 2003; see also reference 4).

**Severe Acute Respiratory Syndrome**

Severe acute respiratory syndrome (SARS), a febrile respiratory illness caused by a novel coronavirus, was first recognized in China and has caused outbreaks throughout the world. It is unknown whether SARS can be transmitted via blood transfusions; however, the virus has been detected in blood and has been shown to replicate within mononuclear cells of peripheral blood.4

Safeguards have been implemented to protect the blood supply from this new virus, including the exclusion of febrile/symptomatic donors and deferral of donors who
have been exposed or traveled to specific areas during endemic periods.5

**Orthopoxviruses and Other Viruses**

Interest in orthopoxviruses (smallpox, vaccinia, and monkeypox) has increased following the potential bioterrorism threat of smallpox and subsequent defensive vaccinations with vaccinia, and by the recent monkeypox outbreak in the United States.6 In order to prevent possible transfusion-transmission, individuals who have received the vaccinia vaccine or have come in close contact with a vaccine recipient are temporarily deferred from blood donation.7 Those naturally infected by any of these viruses would be presumed to be symptomatic and would thus be deferred by the screening process.

The viral agents classically associated with transfusion-transmission include human immunodeficiency virus (HIV), hepatitis C virus (HCV), hepatitis B virus (HBV), and HTLV I/II. The risk of transfusion-transmission of HIV has been virtually eliminated. Prior to antibody testing of donated blood, from 1978-1982, the risk of HIV transmission peaked at 1.1% per unit transfused.2 Today, with the use of classic serologic tests and NAT implementation in 1999, the risk of HIV transmission is estimated at 1 in 2,135,000 units, or less.8 Cases of apparent HIV transmission from NAT negative units have been reported and are attributed to donations obtained during the window period (viremic phase prior to laboratory detection) of HIV infection in the donor, now estimated at 10 to 15 days. Hepatitis C virus (HCV) has also experienced a dramatic decline with NAT testing, with a reduction of the window period from 70 days to approximately 10 days. The current risk of HCV transmission with NAT implementation is 1 in 1,935,000 units, or less. Nucleic acid testing is currently not performed for hepatitis B virus (HBV) but its incidence continues to decrease. The current estimated risk for HBV transmission is approximately 1 in 205,000 units.9

Immunosuppressed patients are susceptible to additional viral agents, including cytomegalovirus (CMV), Ebstein-Barr virus (EBV), and parvovirus B19. Prevention of EBV transfusion-transmission, especially in the most susceptible, EBV-naïve pediatric liver transplant patients, may be accomplished by leukoreduction of cellular products.10 Prevention of CMV transfusion transmission is largely accomplished by transfusing CMV-seronegative or leukoreduced units.11 There is currently no mandatory testing performed for parvovirus B19; however, possible mechanisms for inactivation are being considered.8

**Bacteria**

Bacterial contamination of blood components continues to be a serious complication of transfusion, accounting for >10% of transfusion-associated fatalities from 1985 to 1999.12 The risk of receiving a unit with bacterial contamination is higher than the rates of viral transmission, and is estimated to be approximately 1 in 5 million RBC units and 1 in 100,000 units of single-donor and pooled platelets.

The clinical manifestations range from simple fever to sepsis and death. Bacterial infection carries a high mortality, ranging from 20% with platelet units to 70% with RBC units. Fatality rates are estimated at 1 in 8 million for RBC units and 1 in 500,000 for single-donor and pooled platelets.

Organisms implicated include gram-positive *Staphylococcus* and *Streptococcus* spp. and gram-negative *Escherichia coli*, *Serratia*, and *Enterobacter* spp.13 *Yersinia enterocolitica* is classically associated with bacterial contamination of RBC units. Gram-negative organisms are associated with a higher risk of fatality for both RBC and platelet transfusions.

Many methods can be employed to prevent transfusion of bacteria-contaminated blood products. Conventional methods include improved donor skin disinfection, the continued use of sterile bags and disinfection of equipment, and deferral of ill, bacteremic donors through the donor questionnaire, and exclusion of individuals with signs/symptoms of infection or recent dental/medical procedures. The use of single donor platelets in contrast to platelet concentrate pools has been shown to decrease the risk of septic transfusion reactions.14

A bulletin issued November 1, 2003 by the American Association of Blood Banks (AABB) describes new guidelines for detection and limitation of bacterial contamination, including phlebotomy diversion, increased use of apheresis platelets, and bacterial detection through bacterial culture or other methods.15 A new standard from the AABB to limit bacterial contamination of platelet products required implementation by either the blood center or hospital transfusion service by March 2004. This added layer of protection requires that every unit be tested prior to transfusion.

**Parasites and Tick-Borne Pathogens**

Chagas disease, caused by protozoan parasite *Trypanosoma cruzi*, is endemic in areas of Mexico, Central America, and South America. The disease is usually self-limited and is followed by an asymptomatic phase that can persist for decades with detectable antibody titers and low-level parasitemia. Seroprevalence rates in the United States range from 1/500 to 1/9,500 differing by geographic regions. There have been 9 cases of transfusion-transmitted Chagas disease reported in North America, with immunocompromised patients showing greater susceptibility for fulminant disease.16 Risk estimates for transfusion-transmission of *T. cruzi* are not available.17

Malaria is caused by mosquito-transmitted intracellular parasites from the genus *Plasmodium* that infect red blood cells. These parasites are endemic in tropical and subtropical regions, and unlike *T. cruzi*, there is no significant, chronically infected population within the United States. Malaria infection in the United States is usually associated with donor travel.
into endemic areas with few cases acquired within the United States. Transfusion-transmitted malaria is well documented with more than 100 cases reported. There are no tests approved for blood supply screening and prevention is dependent on deferral of donors who have traveled to endemic areas.18

Tick-borne infectious diseases include babesiosis caused by an intracellular protozoan Babesia spp., ehrlichiosis caused by Ehrlichia chaffeensis and a separate unknown agent from Ehrlichia spp., Lyme disease caused by spirochete Borrelia burgdorferi, and Rocky Mountain spotted fever (RMSF) caused by the bacterium Rickettsia rickettsii. There have been more than 20 cases of transfusion-transmitted babesiosis and 1 case each of RMSF and ehrlichiosis.19 There have been no reported cases of transfusion-transmitted Lyme disease. There are currently only limited methods in place for prevention of transfusion transmission of these agents. There are no screening laboratory tests available, and screening questions identifying exposure to ticks do not seem effective in identifying seropositive donors.

**Prion Agents**

Creutzfeldt-Jakob disease (CJD) and variant Creutzfeldt-Jakob disease (vCJD) are fatal neurodegenerative diseases or transmissible spongiform encephalopathies (TSE) caused by prion agents. Central to the pathophysiology of these diseases is the prion protein (PrP) which exists naturally (PrP0) but can transform into a pathologic form (PrPSc) in the presence of another pathologic PrP.20

There is a familial transmission of CJD; however, most cases are sporadic with a few possible iatrogenic cases transmitted through neural tissue transplantation. Variant Creutzfeldt-Jakob disease is thought to result from human ingestion of the bovine spongiform encephalopathy (BSE) agent with greater than 100 cases reported worldwide, with a majority of cases reported in the UK.21

There are no known human cases of prion disease transmission through blood transfusions, and PrPSc was not detected in theuffy coat from 1 vCJD patient.22 However, infectivity of blood and blood components have been shown in laboratory rodents infected with TSE,23 and that BSE and scrapie (prion agent found in sheep) can be transmitted through blood transfusions.24

Current guidelines include deferral of individuals who have a family history of CJD, a history of neural graft transplantation, and who have resided or traveled to the UK and/or Europe, including United States military personnel, for a total of 6 months or more.25

**Conclusion**

As described above, the United States blood supply has reached an unprecedented level of safety through the detection and exclusion of infected donors and units. However, society would prefer a blood supply with “zero risk,” and steps toward a pathogen-free blood supply continue to be explored, including new technologies for inactivation of infective agents.26-27 This “zero risk” comes at an enormous cost; the implementation of minipool NAT for HIV and HCV is estimated to cost between $1.27-11.2 million per quality-adjusted life-year saved.28,29

In addition to monetary costs, donor deferrals continue to reduce the already limited donor pool; it is estimated that the deferral guidelines implemented to protect against vCJD has eliminated 3% to 5% of the donor population.30 The advancement toward a pathogen-free blood supply should be balanced by cost-effectiveness.

Finally, there is the question of the theoretical emerging pathogen. How do we defend the blood supply against a truly emerging infective agent? A close look at the West Nile virus scenario demonstrates the following: the first suspected case of transfusion-transmitted WNV was discovered on August 30, 2002; NAT testing for WNV was initiated on June 2003; and by August 2003, 329 WNV positive units were removed from the blood supply.

As this example shows, there is a system in place to combat possible emerging transfusion-transmitted infections. This framework, along with a constant vigilance, has shown to be an effective defense against emerging and existing pathogens.

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