Blood Safety

Mary E. Chamberland,* Jay Epstein,† Roger Y. Dodd,‡ David Persing,§ Robert G. Will,¶ Alfred DeMaria, Jr.,# Jean C. Emmanuel, Beatrice Pierce,†† and Rima Khabbaz***
*Centers for Disease Control and Prevention, Atlanta, Georgia, USA; †Food and Drug Administration, Washington, D.C., USA; ‡American Red Cross, Washington, D.C., USA; §Western General Hospital, Edinburgh, Scotland; ¶The Mayo Clinic, Rochester, Minnesota, USA; #Massachusetts Department of Public Health, Boston, Masschusetts, USA; **World Health Organization, Geneva, Switzerland; and ††National Hemophilia Foundation, New York, New York, USA

The blood supply in industrialized countries is safer than ever. However, blood (a human tissue) is a natural vehicle for transmission of infectious agents. In recent years, numerous pathogens have emerged in the United States and worldwide with the potential to affect the safety of the blood supply.

International Movement of Infectious Agents

Movement of transfusable blood and blood components between countries is relatively uncommon. However, infectious agents can cross international borders through immigration or travel. For example, malaria is an important problem in much of the world, with an estimated 300 to 500 million cases per year. On average, 1,000 cases are reported each year in the United States, most in persons who travel to malaria-endemic areas. Only a small number of cases (approximately three per year) are transmitted by exposure to infected blood products. Current measures (which temporarily defer donors with a history of origin in a malarious country, clinical malaria, or travel to malaria-endemic areas) appear to be effective. Similarly, Chagas disease, a vector-borne disease caused by the parasite *Trypanosoma cruzi,* is endemic in parts of Central and South America and Mexico, where infected persons can transmit the disease through transfusion. The immigration of millions of persons from *T. cruzi*–endemic areas and increased international travel have raised concerns about the potential for transfusion-transmitted Chagas disease. Five cases of *T. cruzi* transmission from transfusions have been reported in North America. Recent seroprevalence studies showed that approximately 0.1% of blood donors likely to have been born in or have traveled to disease-endemic countries were seropositive for *T. cruzi*. Moreover, American Red Cross studies of recipients of *T. cruzi*–seropositive blood and blood products showed no evidence of transmission. Finally, variant forms of recognized pathogens can potentially affect the safety of the blood supply. Current serologic tests do not consistently detect HIV-1 group O infections, which are common in some West and Central African countries but very rare (two cases) in the United States. Efforts are under way to modify existing serologic tests to improve detection of group O strains without compromising sensitivity for the predominant group M viruses. As an interim measure, the Food and Drug Administration has recommended that donors at increased risk for HIV-1 group O on the basis of residence and risk exposure be deferred from donating blood or plasma.

Creutzfeldt-Jakob Disease and Blood Safety

Risk for transmission by transfusion is poorly characterized for a number of emerging agents. One of these is Creutzfeldt-Jakob disease (CJD), a rare, fatal neurodegenerative disease believed to be caused by an abnormal form of prion protein. CJD has been transmitted iatrogenically through human pituitary-derived growth hormones, human dura mater grafts, corneal transplants, and contaminated surface electroencephalogram electrodes and neurosurgical instruments. Incubation was as long as 30 years in some cases. Concerns regarding bloodborne transmission of the CJD agent derive primarily from laboratory studies, including animal models, which suggest such a potential. However, no proven cases of blood transmission are reported in humans, and accumulating epidemiologic information (surveillance, follow-up of recipients of blood from donors who subsequently developed CJD, and case-control data) indicates that the risk (if any) for transmission of CJD by blood products is extremely small. At present, CJD is considered a remote, theoretical risk.

In March 1996, health officials in the United Kingdom announced that the agent responsible for the decade-old bovine spongiform encephalopathy epizootic might have spread to humans. As of March 1998, 24 persons have been reported with this apparently new variant form of CJD (nvCJD). The possibility of nvCJD transmission through the blood supply has been debated. Currently, this risk is theoretical. However, because the infectious agent of nvCJD is new in humans, it may present risks that differ from those of classic CJD. In addition, important differences have been noted in the two diseases. For example, human spleen and tonsil tissues contain abnormal prion protein in nvCJD but not in classic CJD. In view of this uncertainty, U.K. health officials have undertaken a conservative approach, including 1) withdrawal of blood products donated by persons subsequently confirmed or strongly suspected to have nvCJD; 2) discontinuation of the use of British plasma in plasma-derived products; and 3) consideration of leukodepletion of all blood donations, in view of experimental studies suggesting that B lymphocytes may play a role in the development of scrapie.

Tick-Borne Agents and Transfusion Risk

In the United States, the most commonly reported transfusion-associated tickborne infection is babesiosis. At least 21 reported cases of babesiosis, mostly caused by *Babesia microti* but also by the more recently recognized WA1-type *Babesia* parasite, have been transmitted by transfusion of blood from asymptomatic infected blood donors. With the expansion of deer populations (natural host of *B. microti*) in the northeastern United States, the incidence of transfusion-transmitted babesiosis may increase. The tick vector and animal reservoir of the *Babesia* more recently found in the northwestern and western United States remain to be defined. The parasite survives blood-banking conditions and is transmissible by transfusion of red blood cells and platelet concentrates. Although babesiosis classically causes a febrile illness with hemolytic anemia, infection can also cause chronic asymptomatic or mildly symptomatic parasitemia. Recent studies suggest that untreated persons have evidence of *B. microti* DNA for longer periods, despite mild or absent symptoms, and may transmit infection for months or possibly longer. The potential for transmission of other tick-borne agents is unclear. Like babesiosis, Lyme disease or ehrlichiosis (caused by an obligate intracellular gram-negative rickettsia) may be asymptomatic or mildly symptomatic; spirochetemia or rickettsemia can precede prodromal symptoms by 24 to 72 hours, making transmission by transfusion a possibility. One case of transfusion-transmitted Rocky Mountain spotted fever has been reported.

Summary

Since blood is a biologic product, it is unlikely that the risk for transfusion-transmitted infection will ever be reduced to zero. The approach to emerging infections associated with transfusion of blood and blood products includes assessing the transmissibility of the agent by this route; developing effective prevention strategies, including screening tests and donor deferral policies; improving viral and bacterial inactivation procedures; and surveillance for known, as well as emerging and poorly characterized, transfusion-transmitted agents. Vigilance is needed to help ensure proper balance between safety and the availability of blood. Finally, vigilance needs to extend to the developing world, where the basic elements to reduce transfusion-transmitted infections and systems of disease surveillance are often not available.