Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

CHAPTER 66

Transfusion Transmitted Diseases

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Transfusion transmitted diseases (TTD) can be caused by viruses, protozoa and prions. A comprehensive, but not all-inclusive, list of potentially TTDs can be found in Table 66.1. While bacteria are transmitted by transfusion, it is usually the products of the bacteria in the donor product (endotoxin) rather than the transfer of infectious bacteria that are the cause of posttransfusion bacteria-related complications. For this reason, bacterial contamination of blood products and methods to limit and detect bacteria in platelet products are discussed in Chapters 59 and 17 of this book, respectively.

Mitigation of transfusion transmission of infectious agents is largely based on donor selection and donor testing in the US, and around the world. Donor selection and testing also occupy individual chapters in this text, including Chapter 5, and Chapters 11–16. Indeed, these strategies have been greatly effective in lowering the residual risk of TTDs in the US, as shown in Figure 66.1. Finally, pathogen-reduction

TABLE 66.1 Potential Transfusion Transmitted Agents

Viruses
- Hepatitis A virus
- Hepatitis B virus
- Hepatitis C virus
- Hepatitis D virus
- Hepatitis G virus
- TTV and SEN-V
- Human Immunodeficiency Virus (HIV)
- Human T-cell lymphotropic virus (HTLV) 1 and 2
- Cytomegalovirus (CMV)
- Epstein-Barr virus (EBV)
- Human herpes virus (HHV)-8
- Lymphocytic Choriomeningitis (LCMV)
- Severe acute respiratory syndrome (SARS)
- Parvovirus B19
- West Nile Virus
- Monkeypox virus
- Viral hemorrhagic fevers
- Simian foamy virus (SFV)
- Chikungunya
- Anaplasma

Protozoa
- *Plasmodium* spp. (malaria)
- *Trypanosoma cruzi* (Chagas' disease)
- *Toxoplasma gondii* (toxoplasmosis)
- *Babesia microti/divergens* (babesiosis)
- *Leishmania* spp. (leishmaniasis)

Prions
- Transmissible spongiform encephalopathies (Creutzfeldt-Jakob disease and others)

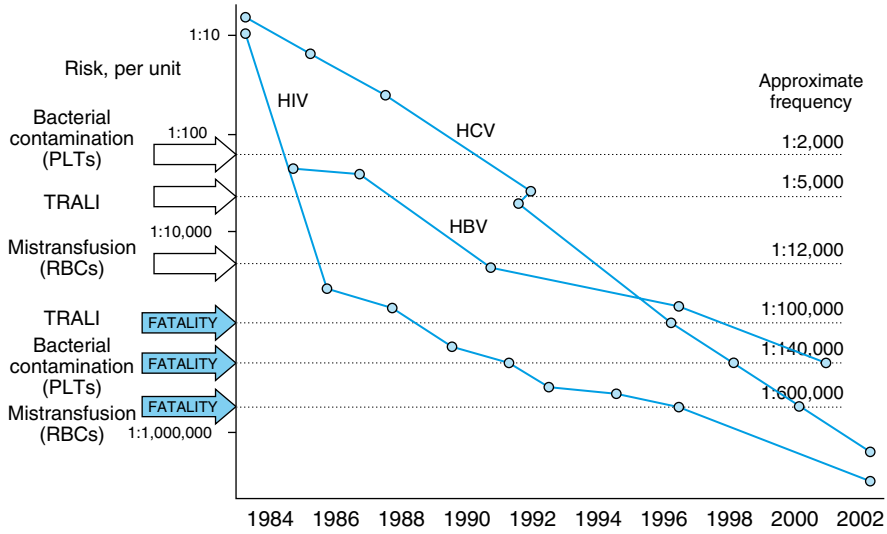

FIGURE 66.1 Comparison of transfusion risks and their evolution over time. HBV hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; PLTs, platelets; RBCs, red blood cells; TRALI = transfusion related acute lung injury; From AuBuchon JP. (2004). Emily Cooley Memorial Award. Managing change to improve transfusion safety. *Transfusion* **44**, 1377–1383.

or -inactivation technologies have the potential to eliminate virtually all TTD, though these technologies are only approved for use for platelets and plasma, and then only outside of the US.

Hepatitis Viruses: The hepatitis viruses include hepadnaviruses, flaviviruses and picornaviruses, which have all been reported to be transmitted through transfusion, and result in inflammation of the liver as the primary clinical manifestation (other viruses and agents result in hepatitis but it is not the primary disease), with symptoms of jaundice, dark urine, hepatomegaly, anorexia, malaise, fever, nausea, abdominal pain and vomiting. Hepatitis B and hepatitis C, which are transmitted parenterally (i.e. through contact with blood and other body fluids), are the typical hepatitis viruses transmitted through transfusion, but hepatitis A (HAV), which is traditionally transmitted through the fecal–oral route, has rarely been transmitted when sufficient amounts of virus are present.

Hepatitis A: HAV in the *Picornaviridae* family, usually results in a mild, self-limited disease with a mortality rate of less than 0.2%. Hepatitis A does not result in chronic infection. The virus is typically transmitted through the fecal–oral route, resulting in foodborne outbreaks. Prophylaxis can be provided through immune serum globulin, and prevention through vaccination is available. The seropositivity rate in the US is approximately 33%.

As most individuals are quite ill during the viremic phase of HAV infection, they most often will not be feeling well enough to donate blood, or will be deferred due to fever or sickness. The risk of transfusion transmitted hepatitis A is less than 1 case

per million transfused products. Solvent-detergent processes used to make pathogen-reduced plasma from plasma pooled products fail fully to inactivate the non-enveloped HAV, and as a result transmission has occurred. This has resulted in additional inactivation steps and testing for HAV in products manufactured from large pools of plasma. In addition, recipients of pooled plasma products (e.g. hemophilia patients) should receive the hepatitis A vaccine.

Hepatitis B: Hepatitis B virus (HBV) is a DNA virus and member of the *Hepadnavidae* family, which is transmitted parenterally, sexually and perinatally. In the US (prevalence 5.6%) and other low-prevalence countries, most infections are horizontal from adult to adult; in countries with a high prevalence of HBV, both horizontal and vertical (i.e. perinatal) infections occur. Widespread vaccination of infants and high-risk adults has resulted in a decreased incidence of the disease (from 260,000 new infections/year to 60,000/year in the US). In addition, hepatitis B immune globulin is available for post-exposure prophylaxis, or for infants born to infected mothers. TT-HBV may result in either an acute infection with subsequent clearance of the virus and immunity, or chronic infection with persistence of viral replication. Chronic infection may resolve with the development of immunity or may reactivate, resulting in further acute disease.

Acute Infection: The incubation period is usually 60–150 days. Most individuals are asymptomatic, but 30–50% of infected persons $\geq$ 5 years of age will experience jaundice, fever, loss of appetite, nausea, vomiting and abdominal pain, and 0.5–1% of infected individuals, usually $\geq$ 60 years of age, will have a fulminant acute infection resulting in death. Serologic results in acutely infected adults demonstrate HBsAg positive, anti-HBc positive, IgM anti-HBc positive, and anti-HBs negative. The formation of anti-HBs and the disappearance of HBsAg indicate development of immunity without further clinical disease.

Chronic Infection: The likelihood of chronic infection is related to the age of the patient at the time of infection, such that 90% of persons who were infected in infancy, yet only 6% of persons who were infected after age 5 develop chronic disease. Chronic infection may be asymptomatic, while some individuals will develop severe and fatal disease from cirrhosis and hepatocellular carcinoma. Extrahepatic manifestations, which most often result from cryoglobulinemia, include rashes, arthritis, vasculitis and glomerulonephritis. Serologic results in patients with chronic active hepatitis demonstrate HBsAg positive, anti-HBc positive, IgM anti-HBc negative, and anti-HBs negative. Treatment for chronic infection includes interferon, lamivudine, adefovir, and additional antiviral medications.

Risk of Transfusion Transmission: In the US, with the current use of testing for HBsAg and anti-HBc, the estimated residual risk of HBV transmission is 1 : 205,000 among *repeat* donors, or 1 : 144,000 among *all* donors, in the absence of nucleic acid testing (NAT). These estimates depend on assumptions, extrapolations and reporting of posttransfusion infection. Transfusion transmitted HBV may either be under-reported or over-reported, as many cases of posttransfusion HBV infection may have not been contracted through transfusion (one report found only 1 in 59 cases could be unequivocally linked to transfusion).

NAT testing for HBV has been implemented in some countries where the prevalence is especially high. In the US, the minipool approach to NAT has the same sensitivity as the most recent generation of serologic tests for HBsAg, as HBsAg rises to high titers very quickly and at approximately the same time as HBV DNA (i.e. minipool NAT testing does not significantly decrease the window period).

Hepatitis D: The infectious form of hepatitis D is coated with HBsAg, and therefore hepatitis D is only infectious in the presence of active HBV infection. Co-infection with hepatitis D and B results in more serious disease than infection with hepatitis B alone. Current measures to detect infectivity for HBV also target the elimination of hepatitis D from transfusion transmission.

Hepatitis C: Hepatitis C is an RNA virus in the *Flaviviridae* family and is parenterally transmitted, especially through blood transfusions (prior to testing) and intravenous drug use. In the 1970s, 10% of blood transfusion recipients had evidence of hepatitis C infection. With the use of the current NAT testing, risk is estimated at 1 : 1.4 million products or less. The incidence of new infections in the US has declined from 240,000 per year in the 1980s to 19,000 per year in 2006 (http://www.cdc.gov/hepatitis/HCV.htm). The current seroprevalence in the US is 1.8% overall and 79% in intravenous drug users.

Acute Infection: Acute infection with hepatitis C virus (HCV) is asymptomatic in 80% of patients. Approximately 20% will have symptoms (fever, jaundice, loss of appetite, fatigue and nausea) of acute infection after an incubation period of 7–8 weeks.

Chronic Infection: Chronic infection develops in 75–85% of infected individuals, with cirrhosis developing in 20–30% (after an average of 20 years) and hepatocellular carcinoma (after an average of 30 years). HCV is the leading indication for liver transplantation in the US. Current treatment for chronic infection includes interferon and ribavirin.

Risk of Transfusion Transmission: With the use of current enzyme immunoassay tests and NAT, the current risk is less frequently than 1 : 1.4 million donations. A positive test result for HCV antibodies in a donor requires a "lookback" per the FDA, to locate, notify, test and, if appropriate, treat recipients of products donated previously by the same donor, at a time when they did not test positive for HCV either because of having not yet acquired the infection or having markers of infection below the limits of test detection (http://www.fda.gov/cber/gdlns/hcvlkbk.htm). The yield of lookback has been very low since the implementation of NAT testing *circa* 2000.

Hepatitis E: Hepatitis E results in a self-limited hepatitis, and is typically transmitted by the fecal–oral route. The hepatitis E virus is found predominantly in tropical countries. Rare cases of transfusion-transmitted hepatitis E have recently been reported.

Hepatitis G: Hepatitis G is common in the normal population; 3–15% of normal individuals have antibodies to hepatitis G, and viral RNA is detected in 1–3%. The virus is transfusion transmitted, demonstrated by a high prevalence of infection in multiply transfused individuals. Currently, no disease is associated with this virus, and thus no testing is required.

TTV and SEN-V: TTV and SEN-V are widely distributed and are transmissible by transfusion, but currently there is little evidence that they cause disease in recipients. Therefore, testing strategies to mitigate transfusion transmission of these viruses is not warranted.

Retroviruses: Retroviruses are RNA viruses with the presence of viral particle-associated reverse transcriptase and a unique replication cycle. The virus particles attach to the cell membrane and subsequently enter the host cell, then the reverse transcriptase enzyme copies viral RNA into cDNA (complementary double-stranded DNA) and the cDNA is then integrated into the host cell's genome. Subsequent transcription, processing and translation of viral genes are mediated by the host cell enzymes. Particles then bud from the cell membrane and infect other cells. In addition, the virus can spread by fusion of infected and uninfected cells, or by replication of the integrated viral DNA during mitosis or meiosis.

Human Immunodeficiency Virus: Human immunodeficiency virus (HIV) is a lentivirus, which is a subgroup of the retrovirus family. HIV-1 was discovered in 1983, and the first test was licensed for donor screening in 1985. HIV transmission by intravenous administration of infected blood products is highly efficient. Of hemophiliacs treated with Factor VIII in the early 1980s, 50% were infected; 100% of those who received more than 500,000 units of Factor VIII were infected. In the San Francisco area in 1982, the risk of HIV was ~1 : 100 transfused products.

HIV infection can be transmitted through sexual contact, childbirth, breast-feeding and parenteral exposure to blood. The CDC reported that in 2006 in the US the highest incidence of new disease was in male African Americans, aged 25–44, who had male-to-male sex; of new infections, 50% were from male-to-male sex, 33% from high-risk heterosexual contact, and 13% from intravenous drug use (http://www.cdc.gov/hiv/).

HIV-1 and HIV-2 infection both cause AIDS. The HIV-1 family is divided into main (M), outlier (O) and non-M, non-O (N) groups. Group M has 11 distinct subtypes or clades (A–K). In the US, clade B is almost exclusively prevalent. The greatest genetic diversity is in central Africa. Group O is most common in Cameroon and surrounding West African countries (where it represents 1–2% of HIV infections). Group O infection in the US is very rare, and is usually found in immigrants. Previous generations of HIV antibody assays did not reliably detect group O, but current assays have increased sensitivity to group O and other unusual variants. Still, the FDA continues to recommend permanent deferral of blood donors who were born, resided or traveled in West Africa since 1977, or who has had sexual contact with someone who fulfills these criteria. HIV-2 is also rare in the US (one infected donor identified out of 7.2 million donations), with no reported cases of HIV-2 transfusion transmission in the US.

Infection: Approximately 60% of acute HIV infections result in a non-specific flu-like illness with an incubation period of 2–4 weeks. The acute infection resolves in weeks to a few months, resulting in an asymptomatic period that may last years. During this period the HIV viremia persists, and the number of CD4+ lymphocytes (the primary target of HIV) gradually declines. This loss of CD4+ lymphocytes results in opportunistic infections, and in addition there are direct viral effects on multiple organs; these together result in death after, on average, 8–10 years. The course of the disease has changed dramatically with the advent of potent antiretroviral therapy,

which has greatly prolonged survival. However, these medications do not eradicate HIV, and have multiple side-effects. Moreover, resistant viral strains have developed which add to the difficulty in treating HIV-infected patients.

Risk of Transfusion Transmission: Current testing for HIV infection in blood donors includes serologic assays for antibodies to HIV-1/HIV-2 and by minipool NAT. The current estimates of HIV transmission are less frequently 1 : 2 million products tested, with expected (but unmeasurable) frequencies approximating 1 : 5 to 1 : 8 million products transfused (US). Identification of persons who have received blood products from donors who are later found to test positive for HIV (referred to as "lookback") is mandated by the FDA (CFR 610.46).

Human T-cell Lymphotropic Virus: Human T-cell lymphotropic virus (HTLV) is transmitted by transfusion. HTLV-1 predominately infects CD4+ lymphocytes while HTLV-2 infects preferentially CD8+ lymphocytes, and to a lesser extent infects CD4+ lymphocytes, B lymphocytes and macrophages. The seroprevalence in blood donors in the US is approximately 10–20 per 100,000 donors. The primary modes of transfusion are vertical transmission from mother to child, secondary to breast feeding (the infection rate declined from 30% to 3% with the discontinuation of infected mother breast-feeding), sexual transmission and parenteral exposure (intravenous drug use).

Infection: Most HTLV infections are asymptomatic, but there is a 2–4% risk of disease that may develop up to 40 years after infection. HTLV-1 is associated with a CD4+ lymphoma, adult T-cell leukemia/lymphoma (ATLL). The risk of ATLL in individuals infected at birth is 4% in their lifetime, with a lower risk in those infected during adulthood (i.e. those who acquire HTLV from transfusion). ATLL has a high mortality rate within 1 year of disease onset. HTLV-1 and HTLV-2 are associated with tropical spastic paraparesis (also known as HTLV-1 associated myelopathy [HAM]; TSP), which is a slowly progressive myelopathy characterized by spastic paraparesis of the lower extremities, hyperreflexia, and bowel and bladder symptomatology. The risk of TSP is about 2% in HTLV-1 positive individuals, with a similar or lower risk in HTLV-2 positive individuals. Other diseases associated with HTLV-1 or HTLV-2 infection include lymphocytic pneumonitis, uveitis, polymyositis, arthritis, bronchitis, dermatitis, and other infectious syndromes.

Risk of Transfusion Transmission: RBCs, platelets and whole blood, but not fresh frozen plasma, have resulted in seroconversion of transfusion recipients. Products stored for greater than 7 days before transfusion are less likely to transmit the virus. In the US, seroconversion rates in individuals who receive seropositive cellular components have been reported from 14% to 30%. In a lookback study of recipients from 1999 to 2005 from the ARC, only 38 donors seroconverted in that timeframe; these individuals donated 31 cellular components. None of the four alive recipients who agreed to testing for HTLV was seropositive. The risk of transfusion transmission is estimated to be 1 per 3 million products transfused.

Herpesviruses: The herpesviruses have double-stranded DNA, and express viral enzymes that participate in DNA synthesis and nucleic acid metabolism; the viral

DNA synthesis and packaging is confined to the host cell nucleus, the infected cell is destroyed during active viral replication, and the virus is capable of latency indefinitely. CMV is the herpesvirus that is most relevant to transfusion medicine, but other leukocytotropic herpesviruses (EBV, HHV-6, HHV-7 and HHV-8) may also contaminate blood products.

Cytomegalovirus: Cytomegalovirus (CMV) is transmitted through transfusion and HPC and solid-organ transplantation. CMV transmission in the community is usually through close contact with a person shedding CMV. The seroconversion rate in blood donors is approximately 1%/year (rates of up to 13%/year in adolescents have been reported). Prevalence ranges from 40 to 90%; the rate increases with age, and is higher in lower socioeconomic groups, urban areas and developing countries. Approximately 50% of US blood donors are CMV seropositive.

Infection: Immunocompetent individuals have a mild self-limited disease course, with fever, malaise, hepatosplenomegaly and rash. The immune response does not eliminate the virus, but the virus becomes latent in the peripheral blood leukocytes. Transplacental infection in 5–15% of infected infants results in intrauterine growth retardation, deafness, mental retardation, blindness and thrombocytopenic bleeding. Infection in immunocompromised patients (including premature infants, recipients of solid-organ or HPC transplantation, and AIDS patients) can lead to pneumonitis, hepatitis, retinitis and multisystem organ failure, which may result in death. Treatment of CMV infection includes antivirals such as ganciclovir, cidofovir and foscarnet.

CMV infection can be detected through anti-CMV antibodies, CMV antigenemia assay (which uses immunostaining to identify and quantitate peripheral blood leukocytes containing CMV proteins), and CMV PCR. PCR has allowed earlier detection of CMV, and has largely replaced the need for the CMV antigenemia assay.

Risk of Transfusion Transmission: Leukocytes are the primary mode of transfusion transmission of CMV, and therefore leukoreduction greatly decreases the risk of CMV transmission. Transfusion can lead to active CMV infection in a recipient by transfusion transmitted CMV where a seronegative recipient is transfused with a CMV-infected product; reactivated CMV infection where a CMV-seropositive recipient experiences reactivation of their latent infection after transfusion of a CMV-negative product; and CMV superinfection, when a seropositive recipient contracts a new strain of CMV from a CMV-positive product. Transfusion transmitted CMV is an important cause of morbidity and mortality in immunocompromised patients: 13–37% of immunocompromised patients, including low birth-weight neonates, will contract CMV from transfusion of unscreened and unleukoreduced blood products. Up to 4% of recipients who receive seronegative blood products have acquired CMV, and up to 3% of recipients who receive leukoreduced blood products have acquired CMV, based on a number of different reported studies. Indications for CMV-safe products, defined as leukoreduced and/or anti-CMV negative, are reviewed in Chapter 38.

Epstein Barr Virus: Epstein Barr virus (EBV) is associated with a variety of diseases, including infectious mononucleosis, Burkitt's lymphoma and nasopharyngeal carcinoma. EBV infection is usually through infected saliva. Acute infection in

children is asymptomatic, or characterized by a sore throat and enlarged lymph nodes. Acute infection in adults results in infectious mononucleosis with fever, tonsillar infection, enlarged lymph nodes, hematologic and immunologic abnormalities, hepatitis or other organ involvement. EBV infects B lymphocytes, where it remains latent. Occasional cases of posttransfusion EBV infection have been reported, but screening for EBV is not performed because of the high prevalence of seropositivity (90%) and because donors with active infection (infectious mononucleosis) are usually symptomatic. Leukoreduction may prevent or decrease the risk of transfusion transmission.

HHV-8: HHV-8 (also known as Kaposi's Sarcoma Herpesvirus) is associated with Kaposi's sarcoma, primary effusion lymphoma and multicentric Castleman's disease. HHV-8 is primarily transmitted through sexual contact. The incidence in US blood donors is 2.4%. One study in the US demonstrated a 0.082% risk of seroconversion per transfused component. A study in Uganda, where the HHV-8 seroprevalence rate is approximately 40%, showed the seroconversion rate after transfusion with a seropositive product to be 2.8%. Proposed methods to reduce the risk of transfusion transmission include leukoreduction, donor testing and pathogen reduction.

Other Viruses:

Parvovirus B19: Infection with parvovirus B19 usually results in asymptomatic or mild symptoms of rash, vomiting, aching joints and limbs, fatigue and malaise (erythema infectiosum or fifth disease). Infection in sickle cell disease and thalassemia patients may result in aplastic crisis. In immunocompromised individuals (especially HIV-positive individuals), parvovirus infection may result in aplastic anemia. Infection during pregnancy may result in severe fetal anemia or malformation in the infants. The seropositivity rate in blood donors is 30–60%. It is transmitted either through release of virus from the upper respiratory tract, or parenterally. Viremia appears within the first week and persists for 1–2 weeks; chronic infection does not occur. Rare cases of transfusion transmission through blood products have been reported. Parvovirus is not destroyed by solvent-detergent treatment or heat inactivation. Because of seroconversion in recipients of solvent-detergent treated plasma, additional viral inactivation steps as well as NAT testing were implemented for plasma that would be pooled and used to manufacture plasma derivatives.

West Nile Virus: West Nile virus (WNV) is a flavivirus that is primarily transmitted through mosquitoes, with birds as the intermediate host. WNV first appeared in the US in New York in 1999, and rapidly expanded its geographic area within 3 years. Transfusion transmission resulted in 23 infections in 2002 during an outbreak in the US where 4156 individuals were infected and there were 284 fatalities.

Infection: Infection is often asymptomatic, and does not result in chronic infection with viremia persisting less than 28 days. The incubation period is approximately 3–14 days followed by a range of symptoms including mild fever, headache, rash, eye pain, vomiting, lymphocytopenia, muscle weakness, flaccid paralysis, poliomyelitis and peripheral demyelination. Approximately 1 in 150 infections results in severe

neurologic disease, especially in those over the age of 50 years. Prevention is through avoiding mosquitoes and mosquito bites.

Risk of Transfusion Transmission: After the documentation of transfusion transmission in 2002, WNV NAT testing was implemented in 2003. Minipool NAT testing only resulted in seven transfusion-transmission cases in 2003–2004. These breakthrough cases resulted in a combination of minipool NAT testing during the non-season coupled with more sensitive individual donor NAT testing in epidemic locations during epidemic times. This testing strategy has resulted in no documented WNV transfusion since the change in testing.

Protozoa:

***Plasmodium* spp. (Malaria):** There are four known *Plasmodium* species that result in malaria in humans: *P. falciparum*, *P. malariae*, *P. vivax* and *P. ovale*. The incubation periods range from 12–30 days, depending on the species. *P. falciparum* results in the most serious infection, which can be fatal, compared to the other species. Transmission to humans is through the mosquito, with the lifecycle split between the mosquito and humans. The merozoite form infects the RBCs, where it replicates, resulting in the RBC bursting and releasing organisms into the blood to infect other RBCs. Infection usually lasts for 1–2 years, but can last for up to 30 years in the case of *P. malariae*.

Infection: Malarial infection results in fever, chills, headache, hemolytic anemia and splenomegaly. Diagnosis is through examination of thick- and thin-blood smears. A variety of medications are used for prophylaxis or treatment of malaria.

Risk of Transfusion Transmission: The risk of malaria is 0.25 cases per million transfusions. Symptoms of infection include fever, chills, headache and hemolysis, and occur a week to several months after transfusion. Transfusion transmitted infection is rarely fatal, and usually results from transmission of *P. falciparum*. Prevention of malarial transmission is through donor deferral, which requires that persons who have had malaria in the preceding 3 years are deferred, travelers to endemic areas are deferred a year, and immigrants of endemic areas are deferred for 3 years after leaving the area. Malarial risk areas are available through the CDC website (http://www.cdc.gov/malaria/risk_map/).

***Trypanosoma Cruzi* (Chagas' Disease):** Chagas' disease is confined mainly to Mexico and South and Central America, with increased prevalence in the southern US from immigrants from endemic areas. It is transmitted to humans through the bite of the reduvid bugs, and the lifecycle is split between the two hosts. Acute infections are asymptomatic or mild. Rarely, the site of entry evolves into an erythematous nodule called a chagoma; this may be accompanied by fever and hepatosplenomegaly. Younger children may develop acute myocarditis or meningioencephalitis. Acute infection resolves without treatment, but lifelong low-level parasitemia persists. Of chronically infected individuals, 20–40% develop cardiac or gastrointestinal symptoms years to decades later. Transmission through transfusion is the second major source of human infection, especially in endemic areas. Seven cases of transfusion transmission in the

US and Canada have been reported. The FDA licensed a screening test for antibodies to *T. cruzi* in blood donors in 2006. Testing of about 65% of the US blood supply has demonstrated that 1 : 25,000–35,000 donors are confirmed positive, with the majority of infected donors in Florida and California.

***Toxoplasma Gondii* (Toxoplasmosis):** Infection with *T. gondii* occurs in up to 95% of adults in some countries. Cats and mice are intermediate hosts. Acute infection in healthy individuals is usually asymptomatic, but infection in immunocompromised individuals can result in severe disease with CNS involvement, myocarditis and pneumonia. Congenital infection can give rise to serious complications, including liver, CNS disease, abortion or stillbirth. Acute infection resolves with antibody formation, but the organism remains latent in leukocytes. Transmission by transfusion has been documented in immunocompromised individuals. Prevention of transfusion transmission appears possible by leukoreduction, but this has not been evaluated.

***Babesia Microti/Divergens* (Babesiosis):** *Babesia microti* in North America and *B. divergens* in Europe are transmitted by tick bite. Symptoms of babesiosis range from mild to severe illness with a hemolysis and fever, and infection lasting more than a year can occur. RBCs are the site of replication. More than 50 cases of transfusion transmission of babesiosis have occurred in the US, with an estimated risk of up to 1 in 1000 in parts of Connecticut. Furthermore, PCR studies reveal that ~1 in 1800 donors in Connecticut are parasitemic. Transfusion transmitted disease occurs with fever developing 1–4 weeks after transfusion; this may be associated with chills, headache, hemolysis, hemoglobinuria and, rarely, life-threatening hemolytic anemia, renal failure and coagulopathy. Asplenic, elderly or severely immunocompromised patients are at risk for more severe infection. Donor selection is currently used to prevent transfusion transmission, including not collecting blood in areas where the disease vectors are endemic during the spring and summer months. Future strategies to prevent disease transmission, especially in high-risk areas, potentially include serologic or NAT testing.

***Leishmania* spp. (Leishmaniasis):** There are three forms of leishmaniasis: cutaneous, mucocutaneous and visceral (kala-azar). The organism is transmitted through the bite of sandflies, with each *Leishmania* species restricted to a particular *Phlebotomus* species. The reservoir for the organism includes rodents and small wild mammals. The lifecycle is split between the sandfly and the mammal. In the human the organism invades the reticuloendothelial system, where it replicates and then is released back into the blood. Parasitemia is generally transient and of low levels, and therefore the risk of transfusion transmission is low. Outside of the US, transfusion transmission of *L. donovani*, which causes visceral leishmaniasis, has been reported. Veterans who served in the Persian Gulf are deferred from donating for 1 year upon leaving.

Prions: Prion disease results from the benign form of the prion protein (PrP) changing to an insoluble protease-resistant form (PrP^{Sc}), which leads to the formation of plaques in the brain.

Transmissible Spongiform Encephalopathies (Creutzfeldt-Jakob Disease): Bovine spongiform encephalopathy (BSE) was initially described in cattle in the UK in 1986. BSE was transmitted through the food chain through meat or bone meal. A ban on ruminant protein in cattle feed has resulted in decreased incidence of BSE. In 1995, BSE was transmitted to humans through the food chain and resulted in variant Creutzfeldt-Jakob disease (vCJD) in the UK. vCJD differs from classical CJD by an earlier age of onset, slower disease progression, and higher levels of PrP^{Sc} in the brain. The disease presents with behavioral changes and dysasthesia, and progresses to cerebellar ataxia, dementia and death in 7–38 months. The majority of cases of vCJD have appeared in the UK, but there have also been reports in other European countries. At least four cases of transfusion transmission of vCJD have occurred in the UK. It is estimated that transfusion transmission by donors who develop vCJD within several years of donation is about 14% for recipients who survive longer than 5 years posttransfusion. Prevention includes deferral for donors who have resided in the UK or Europe for over 6 months, and the use of filters to remove prions; these remove approximately half the infectivity.

Other Emerging Infections: There are numerous potentially emerging infections (Dengue fever, SARS, influenza, LCMV) which require continuous surveillance of the blood supply and evaluations of interventions.

Recommended Reading

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