degraded by ACE, patients on ACE inhibitors may have increased bradykinin levels that cause hypotension in the recipient. The blood pressure typically returns to normal without intervention.

Immunomodulation Transfusion of allogeneic blood is immunosuppressive. Multiply transfused renal transplant recipients are less likely to reject the graft, and transfusion may result in poorer outcomes in cancer patients and increase the risk of infections. Transfusion-related immunomodulation is thought to be mediated by transfused leukocytes. Leukocyte-depleted cellular products may cause less immunosuppression, although controlled data are unlikely to be obtained as the blood supply becomes universally leukocyte depleted.

INFECTIOUS COMPLICATIONS

The blood supply is initially screened by selecting healthy donors without high-risk lifestyles, medical conditions, or exposure to transmissible pathogens, such as intravenous drug use or visiting malaria endemic areas. Multiple tests performed on donated blood to detect the presence of infectious agents using nucleic acid amplification testing (NAAT) or evidence of prior infections by testing for antibodies to pathogens and sterility of platelet products further reduce the risk of transfusion-acquired infections.

Viral Infections • ***HEPATITIS C VIRUS (HCV)*** Blood donations are tested for antibodies to HCV and HCV RNA. The risk of acquiring HCV through transfusion is now calculated to be approximately 1 in 2,000,000 units. Infection with HCV may be asymptomatic or lead to chronic active hepatitis, cirrhosis, and liver failure.

HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 (HIV-1) Donated blood is tested for antibodies to HIV-1, HIV-1 p24 antigen, and HIV RNA using NAAT. Approximately a dozen seronegative donors have been shown to harbor HIV RNA. The risk of HIV-1 infection per transfusion episode is 1 in 2,000,000. Antibodies to HIV-2 are also measured in donated blood. No cases of HIV-2 infection have been reported in the United States since 1992.

HEPATITIS B VIRUS (HBV) Donated blood is screened for HBV using assays for hepatitis B surface antigen (HbsAg). NAAT testing is not practical because of slow viral replication and lower levels of viremia. The risk of transfusion-associated HBV infection is several times greater than for HCV. Vaccination of individuals who require long-term transfusion therapy can prevent this complication.

OTHER HEPATITIS VIRUSES Hepatitis A virus is rarely transmitted by transfusion; infection is typically asymptomatic and does not lead to chronic disease. Other transfusion-transmitted viruses—TT virus, SEN virus, and GB virus C—do not cause chronic hepatitis or other disease states. Routine testing does not appear to be warranted.

WEST NILE VIRUS (WNV) Transfusion-transmitted WNV infections were documented in 2002. This RNA virus can be detected using NAAT; routine screening began in 2003. WNV infections range in severity from asymptomatic to fatal, with the older population at greater risk.

CYTOMEGALOVIRUS This ubiquitous virus infects ≥50% of the general population and is transmitted by the infected "passenger" WBCs found in transfused PRBCs or platelet components. Cellular components that are leukocyte-reduced have a decreased risk of transmitting CMV, regardless of the serologic status of the donor. Groups at risk for CMV infections include immunosuppressed patients, CMV-seronegative transplant recipients, and neonates; these patients should receive leukocyte-depleted components or CMV seronegative products.

HUMAN T LYMPHOTROPIC VIRUS (HTLV) TYPE 1 Assays to detect HTLV-1 and -2 are used to screen all donated blood. HTLV-1 is associated with adult T cell leukemia/lymphoma and tropical spastic paraparesis in a small percentage of infected persons (Chap. 225e). The risk of HTLV-1 infection via transfusion is 1 in 641,000 transfusion episodes. HTLV-2 is not clearly associated with any disease.

PARVOVIRUS B19 Blood components and pooled plasma products can transmit this virus, the etiologic agent of erythema infectiosum, or fifth disease, in children. Parvovirus B19 shows tropism for erythroid precursors and inhibits both erythrocyte production and maturation. Pure red cell aplasia, presenting either as acute aplastic crisis or chronic anemia with shortened RBC survival, may occur in individuals with an underlying hematologic disease, such as sickle cell disease or thalassemia (Chap. 130). The fetus of a seronegative woman is at risk for developing hydrops from this virus.

Bacterial Contamination The relative risk of transfusion-transmitted bacterial infection has increased as the absolute risk of viral infections has dramatically decreased.

Most bacteria do not grow well at cold temperatures; thus, PRBCs and FFP are not common sources of bacterial contamination. However, some gram-negative bacteria can grow at 1–6°C. *Yersinia*, *Pseudomonas*, *Serratia*, *Acinetobacter*, and *Escherichia* species have all been implicated in infections related to PRBC transfusion. Platelet concentrates, which are stored at room temperature, are more likely to contain skin contaminants such as gram-positive organisms, including coagulase-negative staphylococci. It is estimated that 1 in 1000–2000 platelet components is contaminated with bacteria. The risk of death due to transfusion-associated sepsis has been calculated at 1 in 17,000 for single-unit platelets derived from whole blood donation and 1 in 61,000 for apheresis product. Since 2004, blood banks have instituted methods to detect contaminated platelet components.

Recipients of transfusion contaminated with bacteria may develop fever and chills, which can progress to septic shock and DIC. These reactions may occur abruptly, within minutes of initiating the transfusion, or after several hours. The onset of symptoms and signs is often sudden and fulminant, which distinguishes bacterial contamination from an FNHTR. The reactions, particularly those related to gram-negative contaminants, are the result of infused endotoxins formed within the contaminated stored component.

When these reactions are suspected, the transfusion must be stopped immediately. Therapy is directed at reversing any signs of shock, and broad-spectrum antibiotics should be given. The blood bank should be notified to identify any clerical or serologic error. The blood component bag should be sent for culture and Gram stain.

Other Infectious Agents Various parasites, including those causing malaria, babesiosis, and Chagas' disease, can be transmitted by blood transfusion. Geographic migration and travel of donors shift the incidence of these rare infections. Other agents implicated in transfusion transmission include dengue, chikungunya virus, variant Creutzfeldt-Jakob disease, *A. phagocytophilum*, and yellow fever vaccine virus, and the list will grow. Tests for some pathogens are available, such as *T. cruzi*, but not universally required, whereas others are being developed (*B. microti*). These infections should be considered in the transfused patient in the appropriate clinical setting.

ALTERNATIVES TO TRANSFUSION

Alternatives to allogeneic blood transfusions that avoid homologous donor exposures with attendant immunologic and infectious risks remain attractive. Autologous blood is the best option when transfusion is anticipated. However, the cost-benefit ratio of autologous transfusion remains high. No transfusion is a zero-risk event; clerical errors and bacterial contamination remain potential complications even with autologous transfusions. Additional methods of autologous transfusion in the surgical patient include preoperative hemodilution, recovery of shed blood from sterile surgical sites, and postoperative drainage collection. Directed or designated donation from friends and family of the potential recipient has not been safer than volunteer donor component transfusions. Such directed donations may in fact place the recipient at higher risk for complications such as GVHD and alloimmunization.

Granulocyte and granulocyte-macrophage colony-stimulating factors are clinically useful to hasten leukocyte recovery in patients with leukopenia related to high-dose chemotherapy. Erythropoietin stimulates erythrocyte production in patients with anemia of chronic renal failure and other conditions, thus avoiding or reducing the need for transfusion. This hormone can also stimulate erythropoiesis in the autologous donor to enable additional donation.