Vaccination of Hematopoietic Stem Cell Transplant Recipients

Recommendations of Centers for Disease Control and Prevention, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation

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BACKGROUND

HSCT[1] is the infusion of hematopoietic stem cells from a donor into a patient who has received chemotherapy, which is usually marrow-ablative. Increasingly, HSCT has been used to treat neoplastic diseases, hematologic disorders, immunodeficiency syndromes, congenital enzyme deficiencies, and autoimmune disorders (e.g., systemic lupus erythematosus or multiple sclerosis) (1-4). Moreover, HSCT has become standard treatment for selected conditions (1,5,6). Data from the International Bone Marrow Transplant Registry and the Autologous Blood and Marrow Transplant Registry indicate that approximately 20,000 HSCTs were performed in North America during 1998 (Statistical Center of the International Bone Marrow Transplant Registry and Autologous Blood and Marrow Transplant Registry, unpublished data, 1998).

HSCTs are classified as either allogeneic or autologous on the basis of the source of the transplanted hematopoietic progenitor cells. Cells used in allogeneic HSCTs are harvested from a donor other than the transplant recipient. Such transplants are the most effective treatment for persons with severe aplastic anemia (7) and offer the only curative therapy for persons with chronic myelogenous leukemia (6). Allogeneic donors might be a blood relative or an unrelated donor. Allogeneic transplants are usually most successful when the donor is a human lymphocyte antigen (HLA)-identical twin or matched sibling. However, for allogeneic candidates who lack such a donor, registry organizations (e.g., the National Marrow Donor Program) maintain computerized databases that store information regarding HLA type from millions of volunteer donors (8-10). Another source of stem cells for allogeneic candidates without an HLA-matched sibling is a mismatched family member (11,12). However, persons who receive allogeneic grafts from donors who are not HLA-matched siblings are at a substantially greater risk for graft- versus-host disease (GVHD) (13). These persons are also at increased risk for suboptimal graft function and delayed immune system recovery (13). To reduce GVHD among allogeneic HSCTs, techniques have been developed to remove T-lymphocytes, the principal effectors of GVHD, from the donor graft. Although the recipients of T-lymphocyte-depleted marrow grafts generally have

[1]For this report, HSCT is defined as any transplantation of blood- or marrow-derived hematopoietic stem cells, regardless of transplant type (e.g., allogeneic or autologous) or cell source (e.g., bone marrow, peripheral blood, or placental/umbilical cord blood). In addition, HSCT recipients are presumed immunocompetent at >24 months after HSCT if they are not on immunosuppressive therapy and do not have graft-versus-host disease (GVHD), a condition that occurs when the transplanted cells recognize that the recipient's cells are not the same cells and attack them.

lower rates of GVHD, they also have greater rates of graft rejection, cytomegalovirus (CMV) infection, invasive fungal infection, and Epstein-Barr virus (EBV)-associated posttransplant lymphoproliferative disease (14).

The patient's own cells are used in an autologous HSCT. Similar to autologous transplants are syngeneic transplants, among whom the HLA-identical twin serves as the donor. Autologous HSCTs are preferred for patients who require high-level or marrow-ablative chemotherapy to eradicate an underlying malignancy but have healthy, undiseased bone marrows. Autologous HSCTs are also preferred when the immunologic antitumor effect of an allograft is not beneficial. Autologous HSCTs are used most frequently to treat breast cancer, non-Hodgkin's lymphoma, and Hodgkin's disease (15). Neither autologous nor syngeneic HSCTs confer a risk for chronic GVHD.

Recently, medical centers have begun to harvest hematopoietic stem cells from placental or umbilical cord blood (UCB) immediately after birth. These harvested cells are used primarily for allogeneic transplants among children. Early results demonstrate that greater degrees of histoincompatibility between donor and recipient might be tolerated without graft rejection or GVHD when UCB hematopoietic cells are used (16-18). However, immune system function after UCB transplants has not been well-studied.

HSCT is also evolving rapidly in other areas. For example, hematopoietic stem cells harvested from the patient's peripheral blood after treatment with hematopoietic colony-stimulating factors (e.g., granulocyte colony- stimulating factor [G-CSF or filgastrim] or granulocyte- macrophage colony-stimulating factor [GM-CSF or sargramostim]) are being used increasingly among autologous recipients (19) and are under investigation for use among allogeneic HSCT. Peripheral blood has largely replaced bone marrow as a source of stem cells for autologous recipients. A benefit of harvesting such cells from the donor's peripheral blood instead of bone marrow is that it eliminates the need for general anesthesia associated with bone marrow aspiration.

GVHD is a condition in which the donated cells recognize the recipient's cells as nonself and attack them. Although the use of intravenous immunoglobulin (IVIG) in the routine management of allogeneic patients was common in the past as a means of producing immune modulation among patients with GVHD, this practice has declined because of cost factors (20) and because of the development of other strategies for GVHD prophylaxis (21). For example, use of cyclosporine GVHD prophylaxis has become commonplace since its introduction during the early 1980s. Most frequently, cyclosporine or tacrolimus (FK506) is administered in combination with other immunosuppressive agents (e.g., methotrexate or corticosteroids) (21). Although cyclosporine is effective in preventing GVHD, its use entails greater hazards for infectious complications and relapse of the underlying neoplastic disease for which the transplant was performed.

Although survival rates for certain autologous recipients have improved(22,23), infection remains a leading cause of death among allogeneic transplants and is a major cause of morbidity among autologous HSCTs (23). Researchers from the National Marrow Donor Program reported that, of 462 persons receiving unrelated allogeneic HSCTs during December 1987-November 1990, a total of 66% had died by 1991 (9). Among primary and

secondary causes of death, the most common cause was infection, which occurred among 37% of 307 patients (9).[2]

Despite high morbidity and mortality after HSCT, recipients who survive long-term are likely to enjoy good health. A survey of 798 persons who had received an HSCT before 1985 and who had survived for >5 years after HSCT, determined that 93% were in good health and that 89% had returned to work or school full time (24). In another survey of 125 adults who had survived a mean of 10 years after HSCT, 88% responded that the benefits of transplantation outweighed the side effects (25).

Immune System Recovery After HSCT

During the first year after an HSCT, recipients typically follow a predictable pattern of immune system deficiency and recovery, which begins with the chemotherapy or radiation therapy (i.e., the conditioning regimen) administered just before the HSCT to treat the underlying disease. Unfortunately, this conditioning regimen also destroys normal hematopoiesis for neutrophils, monocytes, and macrophages and damages mucosal progenitor cells, causing a temporary loss of mucosal barrier integrity. The gastrointestinal tract, which normally contains bacteria, commensal fungi, and other bacteria-carrying sources (e.g., skin or mucosa) becomes a reservoir of potential pathogens. Virtually all HSCT recipients rapidly lose all T- and B-lymphocytes after conditioning, losing immune memory accumulated through a lifetime of exposure to infectious agents, environmental antigens, and vaccines. Because transfer of donor immunity to HSCT recipients is variable and influenced by the timing of antigen exposure among donor and recipient, passively acquired donor immunity cannot be relied upon to provide long-term immunity against infectious diseases among HSCT recipients.

During the first month after HSCT, the major host-defense deficits include impaired phagocytosis and damaged mucocutaneous barriers. Additionally, indwelling intravenous catheters are frequently placed and left in situ for weeks to administer parenteral medications, blood products, and nutritional supplements. These catheters serve as another portal of entry for opportunistic pathogens from organisms colonizing the skin (e.g., coagulase- negative Staphylococci, Staphylococcus aureus, Candida species, and Enterococci) (26,27).

Engraftment for adults and children is defined as the point at which a patient can maintain a sustained absolute neutrophil count (ANC) of >500/mm3 and sustained platelet count of >20,000, lasting >3 consecutive days without transfusions. Among unrelated allogeneic recipients, engraftment occurs at a median of 22 days after HSCT (range: 6-84 days) (9). In the absence of corticosteroid use, engraftment is associated with the restoration of effective phagocytic function, which results in a decreased risk for bacterial and fungal infections. However, all HSCT recipients and particularly allogeneic recipients, experience an immune system dysfunction for months after engraftment. For example, although allogeneic recipients might have normal total lymphocyte counts within >2 months after HSCT, they have abnormal CD4/CD8 T-cell ratios, reflecting their decreased CD4 and

[2]Presently, no updated data have been published.

increased CD8 T-cell counts (21). They might also have immunoglobulin G (IgG)2, IgG4, and immunoglobulin A (IgA) deficiencies for months after HSCT and have difficulty switching from immunoglobulin M (IgM) to IgG production after antigen exposure (26). Immune system recovery might be delayed further by cytomegalovirus infection (28).

During the first >2 months after HSCT, recipients might experience acute GVHD that manifests as skin, gastrointestinal, and liver injury, and is graded on a scale of I-IV (26,29,30). Although autologous or syngeneic recipients might occasionally experience a mild, self-limited illness that is acute GVHD-like (13,31), GVHD occurs primarily among allogeneic recipients, particularly those receiving matched, unrelated donor transplants. GVHD is a substantial risk factor for infection among HSCT recipients because it is associated with a delayed immunologic recovery and prolonged immunodeficiency (13). Additionally, the immunosuppressive agents used for GVHD prophylaxis and treatment might make the HSCT recipient morevulnerable to opportunistic viral and fungal pathogens (32).

Certain patients, particularly adult allogeneic recipients, might also experience chronic GVHD, which is graded as either limited or extensive chronic GVHD (13,33). Chronic GVHD appears similar to autoimmune, connective-tissue disorders (e.g., scleroderma or systemic lupus erythematosus) (34) and is associated with cellular and humoral immunodeficiencies, including macrophage deficiency, impaired neutrophil chemotaxis (35), poor response to vaccination (36-38), and severe mucositis (13). Risk factors for chronic GVHD include increasing age, allogeneic HSCT (particularly those among whom the donor is unrelated or a non-HLA identical family member) (34), and a history of acute GVHD (18,39). Chronic GVHD was first described as occurring >100 days after HSCT but can occur 40 days after HSCT (13). Although allogeneic recipients with chronic GVHD have normal or high total serum immunoglobulin levels (35), they experience long-lasting IgA, IgG, and IgG subclass deficiencies (35,40,41) and poor opsonization and impaired reticuloendothelial function. Consequently, they are at even greater risk for infections (27,33), particularly life-threatening bacterial infections from encapsulated organisms (e.g., *Streptococcus pneumoniae*, *Haemophilus influenzae*, or *Neisseria meningitidis*). After chronic GVHD resolves, which might take years, cell-mediated and humoral immunity function are gradually restored.

HSCT RECIPIENT VACCINATIONS

Antibody titers to vaccine-preventable diseases (e.g., tetanus, polio, measles, mumps, rubella, and encapsulated organisms) decline during the 1-4 years after allogeneic or autologous HSCT (42,43-46) if the recipient is not revaccinated. Clinical relevance of decreased antibodies to vaccine-preventable diseases among HSCT recipients is not immediately apparent because a limited number of cases of vaccine-preventable diseases are reported among U.S. recipients. However, vaccine-preventable diseases still pose risks to the U.S. population. Additionally, evidence exists that certain vaccine-preventable diseases (e.g., encapsulated organisms) can pose increased risk for HSCT recipients (42); therefore, HSCT recipients should be routinely revaccinated after HSCT so that they can experience immunity to the same vaccine-preventable diseases as others (Table 1).

HSCT center personnel have developed vaccination schedules for HSCT recipients (47). One study determined that HSCT center personnel used 3-11 different vaccination schedules per vaccine (47); consequently, the study authors requested national guidelines for doses and timing of vaccines after HSCT to eliminate confusion among HSCT center personnel regarding how to vaccinate their patients. To address this need, an interim vaccination schedule for HSCT recipients was drafted in collaboration with partner organizations, including CDC's Advisory Committee on Immunization Practices. The purpose of the vaccination schedule in these guidelines is to provide guidance for HSCT centers (Table 1). Although limited data were found regarding safety and immunogenicity (e.g., serologic studies of antibody titers after vaccination) among HSCT recipients, no data were found regarding vaccine efficacy among HSCT recipients (e.g., which determine whether vaccinated HSCT recipients have decreased attack rates of disease compared with unvaccinated HSCT recipients). Because certain HSCT recipients have faster immune system recovery after HSCT than others, researchers have proposed that different vaccination schedules be recommended for recipients of different types of HSCT. However, to date, data are too limited to do so. **Therefore, the same vaccination schedule is recommended for all HSCT recipients (e.g., allogeneic, autologous, and bone marrow, peripheral, or UCB grafts) until additional data are published**. In the tables, vaccines have only been recommended for use among HSCT recipients if evidence exists of safety and immunogenicity for those recipients. Vaccination of family members, household contacts, and HCWs are also recommended to minimize exposure of vaccine-preventable diseases among HSCT recipients (Tables 2-4).

RECOMMENDATIONS FOR SPECIFIC VACCINE-PREVENTABLE DISEASES

Streptococcus pneumoniae (pneumococcus)

Information regarding the currently available 23-valent pneumococcal polysaccharide vaccine indicates limited immunogenicity among HSCT recipients. However, because of its potential benefit to certain patients, it should be administered to HSCT recipients at 12 and 24 months after HSCT (42,48,49). No data were found regarding safety and immunogenicity of the 7-valent conjugate pneumococcal vaccine among HSCT recipients; therefore, no recommendation regarding use of this vaccine can be made.

As with adults, pediatric HSCT recipients aged >2 years should be administered the current 23-valent pneumococcal polysaccharide vaccine because the vaccine can be effective. However, this vaccine should not be administered to children aged <2 years because it is not effective among that age population. No data were found regarding safety and immunogenicity of the 7-valent conjugate pneumococcal vaccine among pediatric HSCT recipients; therefore, no recommendation regarding use of this vaccine can be made.

Haemophilus influenzae type b (Hib)

Although no data regarding vaccine efficacy among HSCT recipients were found, Hib conjugate vaccine should be administered to HSCT recipients at 12, 14, and 24 months after HSCT. This vaccine is recommended because the majority of HSCT recipients have low levels of Hib capsular polysaccharide antibodies >4 months after HSCT (50), and

allogeneic recipients with chronic GVHD are at increased risk for infection from encapsulated organisms (e.g., Hib) (51,52). HSCT recipients who are exposed to persons with Hib disease should be offered rifampin prophylaxis according to published recommendations (53) (Appendix).

Recommendations for preventing Hib disease are the same for pediatric or adult HSCT recipients, except that any child infected with Hib pneumonia requires standard precautions with droplet precautions added for the first 24 hours after beginning appropriate antibiotic therapy (53,54). Appropriate pediatric doses should be administered for Hib conjugate vaccine and for rifampin prophylaxis (55) (Appendix).

Varicella zoster virus (VZV)

Live attenuated varicella zoster vaccine is contraindicated among HSCT recipients <24 months after HSCT (56). Use of varicella vaccine among HSCT recipients is restricted to research protocols for recipients >24 months after HSCT who are presumed immunocompetent. Further research is needed to determine the safety, immunogenicity, and efficacy of varicella vaccine among HSCT recipients.

Health care workers, family members, household contacts, and visitors who are healthy and do not have a reported history of varicella infection or who are VZV-seronegative should receive varicella vaccine before being allowed to visit or have direct contact with an HSCT recipient. Ideally, VZV-susceptible family members, household contacts, and potential visitors of immunocompromised HSCT recipients should be vaccinated as soon as the decision is made to perform HSCT. The vaccination dose or doses should be completed >4 weeks before the conditioning regimen begins or >6 weeks (42 days) before the HSCT is performed.

HSCT recipients and candidates undergoing conditioning therapy should avoid contact with any VZV vaccine recipient who experiences a rash after vaccination. When this rash occurs, it usually appears 14-21 days after vaccination (median: 22 days; range: 5-35 days) (personal communication from Robert G. Sharrar, M.D., Merck & Co., Inc.). However, to date, no serious disease has been reported among immunocompromised patients from transmission of varicella vaccine virus, and the varicella vaccine strain is susceptible to acyclovir.

VZV-seronegative HSCT recipients should be administered varicella zoster immune globulin[3] (VZIG) as soon as possible but ideally within 96 hours after close or household contact with a person having either chickenpox or shingles if the HSCT recipient is not immunocompetent (i.e., allogeneic patient <24 months after HSCT, >24 months after HSCT and on immunosuppressive therapy, or having chronic GVHD). Researchers report VZIG administration for VZV exposure as described for HSCT recipients who were VZV-seropositive before HSCT.

[3]VZIG is distributed by FFF Enterprises, Inc., under contract with the American Red Cross, except in Massachusetts where it is distributed by the Massachusetts Public Health Biologic Laboratories (now a unit of the University of Massachusetts). FFF Enterprises, Inc., can be contacted at FFF Enterprises, Inc., 41093 County Center Drive, Temecula, CA 92591. Phone: (800) 522-4448

Because of the high morbidity of VZV-associated disease among severely immunocompromised HSCT recipients and until further data are published, HSCT physicians should administer VZIG to all VZV-seronegative HSCT recipients or candidates undergoing conditioning therapy who are exposed to a VZV vaccinee having a varicella-like rash. Researchers also report VZIG administration for this situation for VZV-seropositive HSCT recipients and candidates undergoing conditioning therapy. These recommendations are made because the vaccinee might be unknowingly incubating wild-type varicella, particularly during the first 14 days after varicella vaccination, and because vaccine-strain VZV has been rarely transmitted by varicella vaccinees with vesicular rashes postvaccination (57).

If VZV-seronegative HSCT recipients or candidates undergoing conditioning therapy are closely exposed to varicella >3 weeks after receiving VZIG, they should be administered another dose of VZIG (58). Researchers also recommend VZIG administration for this condition for VZV-seropositive HSCT recipients and candidates undergoing conditioning therapy.

Recommendations for VZV prevention are the same for allogeneic or autologous recipients. Recommendations for preventing VZV disease among pediatric or adult HSCT recipients are the same, except that appropriate dose adjustments for VZIG should be made for pediatric HSCT recipients (Appendix).

Influenza Virus

Influenza vaccination of family members and close or household contacts is strongly recommended during each influenza season (i.e., October-May) starting the season before HSCT and continuing >24 months after HSCT (59) to prevent influenza exposure among the recipients or candidates. All family members and close or household contacts of HSCT recipients who remain immunocompromised >24 months after HSCT should continue to be vaccinated annually as long as the HSCT recipient's immunocompromise persists (59). Seasonal influenza vaccination is strongly recommended for all HCWs of HSCT recipients (60,61).

If health care workers, family members, or other close contacts of HSCT recipients receive influenza vaccination during an influenza A outbreak, they should receive amantadine or rimantadine chemoprophylaxis for 2 weeks after influenza vaccination while the vaccinee experiences an immunologic response to the vaccine. Such a strategy is likely to prevent transmission of influenza A to HCWs and other close contacts of HSCT recipients, which could prevent influenza A transmission to HSCT recipients themselves. However, if a nosocomial outbreak occurs with an influenza A strain that is not contained in the available influenza vaccine, all healthy family members, close and household contacts, and HCWs of HSCT recipients and candidates should be administered influenza A chemoprophylaxis with amantadine or rimantadine until the end of the outbreak (59).

In 1999, two neuroaminidase inhibitors (zanamivir and oseltamivir) were approved for treatment of influenza, but are not currently approved for prophylaxis[4]. To date, experience is limited regarding use of zanamivir or oseltamivir in the treatment or prophylaxis of influenza among HSCT settings. However, health care workers, family members, or other close contacts can be offered a neuroaminidase inhibitor (e.g., zanamivir or oseltamivir) using the same strategies outlined previously, if a) rimantadine or amantadine cannot be tolerated, b) the outbreak strain of influenza A is amantadine or rimantadine-resistant, or c) the outbreak strain is influenza B (62-65). Zanamivir can be administered to persons aged >12 years, and oseltamivir can be administered to persons aged >18 years. Patients with influenza should be placed under droplet and standard precautions to prevent transmission of influenza to HSCT recipients. HCWs with influenza should be excused from patient care until they are no longer infectious.

Life-long seasonal influenza vaccination is recommended for all HSCT candidates and recipients, beginning during the influenza season before HSCT and resuming >6 months after HSCT (60). Influenza vaccinations administered to HSCT recipients <6 months after HSCT are unlikely to be beneficial and are not recommended (60). HSCT recipients <6 months after HSCT should receive chemoprophylaxis with amantadine or rimantadine during community or nosocomial influenza A outbreaks. These drugs are not effective against influenza B. Additionally, antiviral-resistant strains of influenza can emerge during treatment with amantadine or rimantadine and transmission of resistant strains can occur (66,67). During such outbreaks, HSCT recipients 6-24 months after HSCT, or >24 months after HSCT and still substantially immunocompromised (i.e., receiving immunosuppressive therapy, have had a relapse of their underlying disease, or have GVHD) and who have not yet received a current influenza vaccination, should be vaccinated against influenza immediately. Additionally, to allow sufficient time for the patient to experience an immunologic response to influenza vaccine, chemoprophylaxis with amantadine or rimantadine can be used for these HSCT recipients for 2 weeks after vaccination during a nosocomial or community influenza A outbreak. Influenza A chemoprophylaxis with amantadine or rimantadine has been recommended for all influenza A-exposed HSCT recipients <24 months after HSCT or >24 months after HSCT and substantially immunocompromised regardless of vaccination history, because of their likely suboptimal immunologic response to influenza vaccine (60,61). However, no recommendation regarding such chemoprophylaxis can be made because of lack of data.

To prevent severe disease, early preemptive therapy with amantadine or rimantadine has been reported for HSCT recipients with unexplained acute upper or lower respiratory symptoms during a community or nosocomial outbreak of influenza A (59). However, the effectiveness in preventing influenza-related complications and the safety of this strategy have not been evaluated among HSCT recipients. Therefore, data are insufficient to make a recommendation.

[4]Subsequent to publication of this document, oseltamivir was approved for influenza prophylaxis of persons >13 years of age. See current ACIP statement on influenza vaccination for details.

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TABLE 1. Recommended vaccinations for hematopoietic stem cell transplant* (HSCT) recipients, including both allogeneic and autologous recipients

For these guidelines, HSCT recipients are presumed immunocompetent at ≥24 months after HSCT if they are not on immunosuppressive therapy and do not have graft-versus-host disease (GVHD).

Vaccine or toxoid	Time after HSCT			Rating
	12 months	14 months	24 months	
Inactivated vaccine or toxoid				
Diphtheria, tetanus, pertussis				
Children aged <7 years*	Diphtheria toxoid-tetanus toxoid-pertussis vaccine (DTP) or diphtheria toxoid-tetanus toxoid (DT)†	DTP or DT	DTP or DT	BIII
Children aged ≥7 years§	Tetanus-diphtheria toxoid (Td)	Td	Td	BII
Haemophilus influenzae type b (Hib) conjugate¶	Hib conjugate	Hib conjugate	Hib conjugate	BII
Hepatitis (HepB)**	HepB	HepB	HepB	BIII
23-valent pneumococcal polysaccharide (PPV23)††	PPV23	—	PPV23	BIII
Hepatitis A§§	Routine administration not indicated			Not rated because of limited data
Influenza¶¶	Lifelong, seasonal administration, beginning before HSCT and resuming at ≥6 months after HSCT			BII
Meningococcal***	Routine administration not indicated			Not rated because of limited data
Inactivated polio (IPV)†††	IPV	IPV	IPV	BII
Rabies§§§	Routine administration not indicated			Not rated because of limited data
Lyme disease	Routine administration not indicated; limited data regarding safety, efficacy, or immunogenicity among HSCT recipients			Not rated because of limited data
Live-attenuated vaccine				
Measles-mumps-rubella (MMR)¶¶¶ ****††††	—	—	MMR	BIII
Varicella vaccine §§§§	Contraindicated for HSCT recipients			EIII
Rotavirus vaccine	Not recommended for any person in the United States¶¶¶¶			EII

TABLE 1. (*Continued*) Recommended vaccinations for hematopoietic stem cell transplant* (HSCT) recipients, including both allogeneic and autologous recipients

* Studies report that an HSCT recipient can be primed if the donor has had primary vaccination series. Studies also report that a recipient's antibody titer before HSCT might affect the titer 1 year after HSCT (**Source**: Lum LG. Kinetics of immune reconstitution after human marrow transplantation. Blood 1987;69[2]:369–80). No data were found regarding safety and immunogenicity of pertussis vaccination among HSCT recipients.

† DT should be used whenever a contraindication exists to pertussis vaccination.

§ HSCT recipients should be revaccinated with tetanus-diphtheria toxoids every 10 years, as routinely recommended for all adolescents and adults (**Sources**: CDC. Diphtheria, tetanus, and pertussis: recommendations of vaccine use and other prevention measures; recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1991;40[No. RR-10]:1–28; and CDC. Use of vaccines and immunoglobulin in persons with altered immunocompetence: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1993;42[No. RR-4]:1–18).

¶ Hib conjugate vaccine is recommended for HSCT recipients of any age (**Sources**: CDC. Recommendations for use of *Haemophilus* b conjugate vaccines and a combined diphtheria, tetanus, pertussis, and *Haemophilus* b vaccine: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1993;42[No. RR-13]:1–15; and CDC. Use of vaccines and immunoglobulin in persons with altered immunocompetence: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1993;42[No. RR-4]:1–18).

** Hepatitis B vaccination is recommended for all susceptible persons aged ≤18 years and for adults who have risk factors for hepatitis B virus infection (**Sources**: CDC. Hepatitis B virus: a comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination; recommendations of the Immunization Practices Advisory Committee [ACIP]. MMWR 1991;40[No. RR-13]:1–25; and CDC. Notice to readers: update; recommendations to prevent hepatitis B virus transmission—United States. MMWR 1995;44[30]:574–5). ACIP hepatitis B vaccination recommendations indicate that high doses (40 µg/dose) are recommended for adult dialysis patients and other immunocompromised adults (**Source**: CDC. Notice to readers: update; recommendations to prevent hepatitis B virus transmission—United States. MMWR 1995;44[30]:574–5). No data were found regarding immunocompromised children and their response to higher doses of vaccine. Postvaccination testing for antibody to hepatitis B surface antigen is recommended 1–2 months after the third vaccine dose to ensure protection among immunocompromised persons (**Source**: CDC. Notice to readers: update; recommendations to prevent hepatitis B virus transmission—United States. MMWR 1995;44[30]:574–5). Persons who do not respond to the primary vaccine series should complete a second 3-dose series.

†† The 23-valent pneumococcal polysaccharide vaccine might not be protective against pneumococcal infection among HSCT recipients. The second dose of vaccine is not a booster dose, but provides a second chance for immunologic response among persons who failed to respond to the first dose (**Source**: Guinan EC, Molrine DC, Antin JH, et al. Polysaccharide conjugate vaccine responses in bone marrow transplant patients. Transplant 1994;57[5]:677–84). Adjunctive antibiotic prophylaxis against encapsulated organisms, including pneumococcal disease, is recommended for allogeneic recipients with chronic GVHD (**Source**: Bortin MM, Horowitz MM, Gale RP, et al. Changing trends in allogeneic bone marrow transplantation for leukemia in the 1980s. JAMA 1992; 268[5]:607–12). No data were found regarding safety and immunogenicity of the 7-valent conjugate pneumococcal vaccine among HSCT recipients; therefore, no recommendation regarding use of this vaccine can be made.

§§ No data were found regarding immunogenicity, safety, and efficacy of hepatitis A vaccine among HSCT recipients. Researchers report that hepatitis A vaccination can be used for investigational use among HSCT recipients aged ≥24 months at ≥12 months after HSCT and who are at increased risk for hepatitis A or its adverse consequences (e.g., persons with chronic liver disease, including chronic GVHD, and children living in areas with consistently elevated hepatitis A incidence) (**Source**: CDC. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1999;48[No. RR-12]:1–37).

¶¶ Children aged <9 years receiving influenza vaccination for the first time require two doses. Children aged ≤12 years should receive only split-virus influenza vaccine. Persons aged >12 years can receive whole- or split-virus vaccine. ACIP's and the American Academy of Pediatrics' dosing schedule should be used (**Sources**: American Academy of Pediatrics. Influenza. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2000:351–9; and CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 2000;49[No. RR-3]:1–38). For optimal influenza prevention, both vaccination and influenza chemoprophylaxis should be used among HSCT recipients.

*** Administration of meningococcal vaccine should be evaluated for HSCT recipients who live in endemic areas or areas experiencing outbreaks (**Source**: CDC. Control and prevention of meningococcal disease and control and prevention of serogroup C meningococcal disease: evaluation and management of suspected outbreaks. MMWR 1997;46[No. RR-5]:1–21). However, meningococcal vaccine immunogenicity and efficacy among HSCT recipients have not been studied.

††† Inactivated polio virus vaccine is immunogenic among HSCT recipients, although no data were found regarding efficacy and more data are needed regarding optimal methods and timing of immunization (**Sources**: Henning KJ, White MH, Sepkowitz KA, Armstrong D. National survey of immunization practices following allogeneic bone marrow transplantation. JAMA 1997;277[14]:1148–51; and CDC. Poliomyelitis prevention in the United States: introduction of a sequential vaccination schedule of inactivated poliovirus vaccine followed by oral poliovirus vaccine; recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1997;46[No. RR-3]:1–25).

TABLE 1. (*Continued*) Recommended vaccinations for hematopoietic stem cell transplant* (HSCT) recipients, including both allogeneic and autologous recipients

§§§ Clinicians can administer preexposure rabies vaccine to HSCT recipients with potential occupational exposures to rabies (**Source**: CDC. Human rabies prevention—United States, 1999: recommendations of the Advisory Committee on Immunization Practices [ACIP] MMWR 1999;48[No. RR-1]:1–21; and published erratum, MMWR 1999;48[1]:16). However, the safety and immunogenicity of rabies vaccination among HSCT recipients has not been studied. Preexposure rabies vaccination should probably be delayed until 12–24 months after HSCT. Administration of rabies vaccine with human rabies immunoglobulin postexposure can be administered anytime after HSCT as indicated. Existing ACIP and American Academy of Pediatrics guidelines for postexposure human rabies immunoglobulin and vaccine administration should be followed, which include administering 5 doses of rabies vaccine administered on days 0, 3, 7, 14, and 28 postexposure (**Sources**: American Academy of Pediatrics. Rabies. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics;2000:475–82; and CDC. Human rabies prevention—United States, 1999: recommendations of the Advisory Committee on Immunization Practices [ACIP] MMWR 1999;48[No. RR-1]:1–21; published erratum, MMWR 1999;48[1]:16).

¶¶¶ The first dose of measles-mumps-rubella vaccine should be administered ≥24 months after HSCT if the HSCT recipient is presumed immunocompetent. The second measles-mumps-rubella dose is recommended 6–12 months later (BIII); however, the benefit of a second dose among HSCT recipients has not been evaluated. During outbreaks, the second dose can be administered 4 weeks after the first dose (**Source**: CDC. Use of vaccines and immunoglobulin in persons with altered immunocompetence: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1993;42[No. RR-4]:1–18).

**** The half-life of intravenous immunoglobulin is decreased among HSCT recipients, but its effect on vaccine immunogenicity has not been evaluated. ACIP's and the American Academy of Pediatrics' recommendations regarding intervals between administration of immunoglobulin preparations for various indications and vaccines containing live measles virus should be used (**Sources**: American Academy of Pediatrics. Measles. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2000:385–96; CDC. Measles, mumps, and rubella—vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1998;47[No. RR-8]:1–48; and CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1994;43[No. RR-1]:1–38).

†††† Use of live vaccines (e.g., measles-mumps-rubella) is indicated only among immunocompetent persons and is contraindicated for recipients after HSCT who are not presumed immunocompetent (**Sources**: CDC. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1996;45[No. RR-11]:1–36; and CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1994;43[No. RR-1]:1–38). Further research is needed to determine the safety, immunogenicity, and efficacy of varicella vaccine among HSCT recipients.

§§§§ To protect HSCT recipients from varicella exposure, all varicella-susceptible health-care workers, family members, and close contacts of the recipient should be vaccinated against varicella (**Source**: American Academy of Pediatrics. Varicella-zoster infections. In: Pickering LK, ed. 2000 red book: report of the committee on Infectious diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics;2000:624–38).

¶¶¶¶ **Source**: CDC. Withdrawal of rotavirus vaccine recommendation. MMWR 1999;48[43]:1007.

Additional Notes: All indicated nonlive vaccines should be administered to HSCT recipients regardless of HSCT type or presence of GVHD. Live-attenuated vaccines, (e.g., measles-mumps-rubella, varicella, Bacillus Calmette-Guérin, yellow fever, and oral typhoid vaccines) should not be administered to any HSCT recipient with active GVHD or immunosuppression (**Source**: CDC. Role of BCG [Bacillus of Calmette and Guérin] vaccine in the prevention and control of tuberculosis in the United States: a joint statement by the Advisory Council for the Elimination of Tuberculosis and the Advisory Committee on Immunization Practices. MMWR 1996;45[No. RR-4]:1–18). To date, no adverse events have been reported (e.g., exacerbation of GVHD) among vaccinated HSCT recipients. However, data regarding immunization among HSCT recipients are limited and further studies are needed to evaluate safety, efficacy, and immunogenicity of the proposed HSCT immunization schedule. Use of combination vaccines is encouraged (**Source**: CDC. Combination vaccines for childhood immunization: recommendations of the Advisory Committee on Immunization Practices [ACIP], the American Academy of Pediatrics [AAP], and the American Academy of Family Physicians [AAFP]. MMWR 1999;48[No. RR-5]:1–15). No contraindications to simultaneous administration of any vaccines exist, except cholera and yellow fever. Adverse events after vaccination should be reported promptly to the Vaccine Adverse Event Reporting System (VAERS), P.O. Box 1100, Rockville, MD 20849-1100. Forms and information can be obtained from VAERS ([800] 822-7967). If the HSCT recipient has lapsed immunizations after HSCT (i.e., has missed one or more vaccine doses), the immunization schedule does not have to be restarted. Instead, the missing vaccine dose should be administered as soon as possible or during the next scheduled clinic appointment.

Table 2. Vaccinations for family, close contacts, and health-care workers (HCWs) of hematopoietic stem cell transplantation (HSCT) recipients*

Vaccine	Recommendations for use	Rating
Hepatitis A†	Routine vaccination is recommended for persons at increased risk for hepatitis A or its adverse consequences (e.g., persons with chronic liver disease or persons traveling to hepatitis A-endemic countries) and for children aged ≥24 months living in areas with consistently elevated hepatitis A incidence.†	BII
Influenza§ ¶	Household contacts — Vaccination is strongly recommended during each influenza season (i.e., October–May) beginning in the season before the transplant and continuing to ≥24 months after HSCT. All household contacts of immunocompromised HSCT recipients should be vaccinated annually as long as these conditions persist.	AI
	HCWs and home caregivers — Annual vaccination is strongly recommended during each influenza season.	AI
Polio**	Vaccination is not routinely recommended for adults but should be administered when polio vaccination is indicated according to published Advisory Committee on Immunization Practices guidelines; when polio vaccine is administered, inactivated polio vaccine should be used.	AI
Measles-mumps-rubella††	Vaccination is recommended for all persons who are aged ≥12 months and who are not pregnant or immunocompromised.	AI
Rotavirus§§	Contraindicated because intussusception has been reported among infants during the first 1–2 weeks after rotavirus vaccination with substantially increased frequency.	EII
Varicella¶¶	Vaccination should be administered to all susceptible HCWs, household contacts, and family members who are aged ≥12 months and who are not pregnant or immunocompromised. When varicella vaccination is administered to persons aged ≥13 years, 2 doses are required, administered 4–8 weeks apart.	AIII

* This vaccination schedule refers only to vaccine-preventable diseases that are spread person-to-person.

† **Source**: CDC. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1999;48(No. RR-12):1–37.

§ Children aged <9 years receiving influenza vaccination for the first time require 2 doses. Children aged ≤12 years should receive only split-virus influenza vaccine. Persons aged >12 years can receive whole- or split-virus vaccine (**Sources**: CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 2000;49[No. RR-3]:1–38; and CDC. Immunization of health care workers: recommendations of the Advisory Committee on Immunization Practices [ACIP] and the Hospital Infection Control Practices Advisory Committee. MMWR 1997;46[No. RR-18]:1–42).

¶ If HCWs, family members, or other close contacts of HSCT recipients receive influenza vaccination during an influenza A outbreak, they should also receive amantadine or rimantadine chemoprophylaxis for 2 weeks after the influenza vaccination (BI) while the vaccinee develops an immunologic response to the vaccine. However, if a nosocomial outbreak occurs with an influenza A strain that is not contained in the available influenza vaccine, HCWs, family members, and other close contacts of HSCT recipients and candidates should be administered influenza A chemoprophylaxis with amantadine or rimantadine until the end of the outbreak (**Source**: CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 2000;49[No. RR-3]:1–38) (BIII). HCWs, family members, or other close contacts can be offered a neuroaminidase inhibitor (e.g., zanamivir or oseltamivir) using the same strategies outlined previously, if one or more of the following exists: a) rimantadine or amantadine cannot be tolerated; b) the outbreak strain of influenza A is amantadine- or rimantadine-resistant; or c) the outbreak strain is influenza B (**Sources**: Monto AS, Robinson DP, Herlocher ML, Hinson JM Jr, Elliott MJ, Crisp A. Zanamivir in the prevention of influenza among healthy adults: a randomized controlled trial. JAMA 1999;282[1]:31–5; Hayden FG, Atmar RL, Schilling M, et al. Use of the selective oral neuraminidase inhibitor oseltamivir to prevent influenza. New Engl J Med 1999;341[18]:1336–43; Hayden FG, Gubareva L, Klein T, et al. Inhaled zanamivir for preventing transmission of influenza in families [Abstract LB-2]. In: Final program, abstracts and exhibits addendum, 38th Interscience Conference on Antimicrobial Agents and Chemotherapy. Washington, DC: American Society for Microbiology, 1991:1; and CDC. Neuraminidase inhibitors for treatment of influenza A and B infections. MMWR 1999;48[No. RR-14]:1–10) (BI). Zanamivir can be administered to persons aged ≥12 years, and oseltamivir can be administered to persons aged ≥18 years.

****Caution**: Vaccine-strain polio virus in oral polio vaccine can be transmitted person-to-person; therefore, oral polio vaccine administration is contraindicated among household contacts of immunocompromised persons. If oral polio vaccine is inadvertently administered to a household contact of an HSCT recipient, ACIP's and the American Academy of Pediatrics' recommendations should be followed to minimize close contact with the immunocompromised person for 4–6 weeks after vaccination (**Sources**: American Academy of Pediatrics. Poliovirus infections. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2000:465–70; CDC. Immunization of health care workers: recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Hospital Infection Control

Table 2. (*Continued*) Vaccinations for family, close contacts, and health-care workers (HCWs) of hematopoietic stem cell transplantation (HSCT) recipients*

Practices Advisory Committee. MMWR 1997;46[No. RR-18]:1–42; and CDC. Poliomyelitis prevention in the United States: introduction of a sequential vaccination schedule of inactivated poliovirus vaccine followed by oral poliovirus vaccine; recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1997;46[No. RR-3]:1–25). Although vaccine-associated paralytic poliomyelitis has not been reported among HSCT recipients after exposure to household contacts inadvertently vaccinated with oral polio vaccine, inactivated polio vaccine should be used among family members, close contacts, and HCWs to avoid person-to-person transmission of vaccine-strain polio virus (**Source**: CDC. Poliomyelitis prevention in the United States: introduction of a sequential vaccination schedule of inactivated poliovirus vaccine followed by oral poliovirus vaccine; recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1997;46[No. RR-3]:1–25).

[††] No evidence exists that live-attenuated vaccine-strain viruses in measles-mumps-rubella vaccine have ever been transmitted from person-to-person, except rubella vaccine virus from a nursing mother to her infant (**Source**: CDC. Measles, mumps, and rubella—vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1998;47[No. RR-8]:1–48).

HCWs, family members, close contacts and visitors who do not have a documented history of varicella-zoster infection or who are seronegative should receive this vaccination before being allowed to visit or have direct contact with an HSCT recipient (AIII). Ideally, varicella-zoster–susceptible HCWs, family members, household contacts, and potential visitors of immunocompromised HSCT recipients should be vaccinated as soon as the decision to perform an HSCT is made. The vaccination dose or doses should be completed ≥4 weeks before the conditioning regimen begins or ≥6 weeks (42 days) before contact with the HSCT recipient is planned (BIII). If a varicella vaccinee develops a postvaccination rash within 42 days of vaccination, the vaccinee should avoid contact with HSCT recipients until all rash lesions are crusted or the rash has resolved (Sources**: CDC. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1996;45[No. RR-11]:1–36; and CDC. Immunization of health care workers: recommendations of the Advisory Committee on Immunization Practices [ACIP] and the Hospital Infection Control Practices Advisory Committee. MMWR 1997;46[No. RR-18]:1–42).

TABLE 3. Vaccinations for hematopoietic stem cell transplant (HSCT) recipients traveling to areas endemic for selected vaccine-preventable diseases

Vaccine	Recommendations for use	Rating
Bacillus of Calmette and Guérin (live-attenuated vaccine)	Use of live-attenuated vaccine is contraindicated among HSCT recipients at <24 months after HSCT and among all persons who are immunocompromised.* No data were found regarding use among HSCT recipients.	EIII
Cholera	Vaccination is not indicated. No data were found regarding safety and immunogenicity among HSCT recipients.†	DIII
Hepatitis A	No data were found regarding immunogenicity, safety, or efficacy of hepatitis A vaccine among HSCT recipients; therefore, intramuscular immunoglobulin use is preferred for hepatitis A prophylaxis among HSCT recipients. However, administration of intramuscular immunoglobulin does not replace avoidance behaviors (e.g., careful selection of food and water).§ Researchers recommend that hepatitis A vaccination be evaluated for investigational use among HSCT recipients aged ≥24 months; however, no recommendation can be made because of limited data.	Not rated because of limited data
Japanese B encephalitis	No data were found regarding safety, immunogenicity, or efficacy among HSCT recipients.¶	Not rated because of limited data
Lyme disease	No data were found regarding safety, immunogenicity, or efficacy among HSCT recipients.	Not rated because of limited data
Meningococcal vaccine	Vaccine should be administered to HSCT recipients traveling to endemic areas or to areas experiencing outbreaks.** However, meningococcal vaccine immunogenicity and efficacy have not been studied among HSCT recipients.	Not rated because of limited data
Plague	No data were found regarding safety, immunogenicity, or efficacy among HSCT recipients.††	Not rated because of limited data
Polio (inactivated polio vaccine only)	Booster dose can be administered as indicated.§§	CIII
Rabies	Researchers recommend that administration of a preexposure series be evaluated for persons at ≥12 months after HSCT if they anticipate travel to endemic areas.¶¶ However, no data were found regarding safety, immunogenicity, or efficacy among HSCT recipients.	Not rated because of limited data
Typhoid, oral (live-attenuated vaccine)	Use of oral typhoid vaccine (live-attenuated strain) is contraindicated among HSCT recipients at <24 months after HSCT and among those who are immunocompromised.*** No data were found regarding safety, immunogenicity, or efficacy among HSCT recipients.	EIII
Typhoid (intramuscular)	No data were found regarding safety, immunogenicity, or efficacy among HSCT recipients.	Not rated because of limited data
Yellow fever (live-attenuated vaccine)	Use of live-attenuated vaccine is contraindicated among HSCT recipients at <24 months after HSCT and among all immunocompromised persons.††† No data were found regarding safety, immunogenicity, or efficacy among HSCT recipients.	EIII

* **Source**: CDC. Role of BCG [Bacillus of Calmette and Guérin] vaccine in the prevention and control of tuberculosis in the United States: a joint statement by the Advisory Council for the Elimination of Tuberculosis and the Advisory Committee on Immunization Practices. MMWR 1996;45(No. RR-4):1–18.

† **Source**: CDC. Recommendations of the Immunization Practices Advisory Committee: cholera vaccine. MMWR 1988;37(40):617–8; 623–4.

§ **Source**: CDC. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1999;48(No. RR-12):1–37.

¶ **Source**: CDC. Inactivated Japanese encephalitis virus vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1993;42(No. RR-1):1–15.

** **Source**: CDC. Control and prevention of meningococcal disease and control and prevention of serogroup C meningococcal disease: evaluation and management of suspected outbreaks. MMWR 1997;46(No. RR-5):1–21.

TABLE 3. (*Continued*) Vaccinations for hematopoietic stem cell transplant (HSCT) recipients traveling to areas endemic for selected vaccine-preventable diseases

†† **Source**: CDC. Prevention of plague: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1996;45(No. RR-14):1–15.

§§ **Source**: CDC. Poliomyelitis prevention in the United States: introduction of a sequential vaccination schedule of inactivated poliovirus vaccine followed by oral poliovirus vaccine; recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1997;46(No. RR-3):1–25.

¶¶ **Source**: CDC. Human rabies prevention—United States, 1999: recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR 1999;48(No. RR-1):1–21; published erratum, MMWR 1999;48(1):16.

***Source**: CDC. Typhoid immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1994;43(No. RR-14):1–7.

††† **Source**: CDC. Yellow fever vaccine: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 90;39(No. RR-6):1–6.

Additional Note: Specific advice for international travelers, including information regarding endemic diseases by country, is available through CDC's automated travelers' hotline at (404) 332-4559; by facsimile at (404) 335-4565; on the Internet at <http://www.cdc.gov>; and by file transfer protocol at <ftp.cdc.gov>.

TABLE 4. Use of passive immunization for hematopoietic stem cell transplant (HSCT) recipients exposed to vaccine-preventable diseases

Preparation	Recommendations for Use	Rating
Cytomegalovirus immunoglobulin	Not recommended for prophylaxis among HSCT recipients because of its lack of efficacy.*	DI
Hepatitis B immunoglobulin	Immunocompromised persons who have percutaneous or permucosal exposure to hepatitis B virus should receive 2 doses administered 1 month apart. For immunocompetent persons, the need for postexposure prophylaxis depends on the vaccination history and antibody to hepatitis B surface antigen response status of the exposed person.†	CIII
Human rabies immunoglobulin	Should be administered with rabies vaccine at anytime after HSCT as indicated for postexposure rabies prophylaxis. Existing Advisory Committee on Immunization Practices guidelines for postexposure should be followed, with 5 doses of rabies vaccine administered on days 0, 3, 7, 14, and 28 postexposure.§	CIII
Respiratory syncytial virus immunoglobulin¶	Because of high rates of case fatality from respiratory syncytial virus pneumonia among HSCT recipients, HSCT physicians can administer HSCT recipients with upper or lower respiratory infection preemptive therapy with a high titer of neutralizing antibodies to prevent severe disease and death until controlled trials can be performed.**	CIII
Respiratory syncytial virus monoclonal antibody	Physicians can use respiratory syncytial virus monoclonal antibody†† investigationally as preemptive therapy (Appendix).	Not rated because of limited data
Tetanus immunoglobulin	Postexposure vaccination should be administered with or without tetanus immunoglobulin as indicated for tetanus exposure§§ that occurs anytime after HSCT.	CIII
Varicella-zoster immunoglobulin¶¶	Ideally, should be administered to HSCT recipients ≤96 hours after close contact with a person with varicella or shingles if the HSCT recipient is at a) <24 months after HSCT or b) ≥24 months after HSCT and still immunocompromised. Administration can extend the varicella incubation period from 10–21 days to 10–28 days. If the HSCT recipient experiences a varicella-zoster virus-like rash after contact with or exposure to a person with varicella or herpes zoster, antiviral drug therapy should be administered until ≥2 days after all lesions have crusted.***	AII
Intramuscular immunoglobulin	Should be administered to hepatitis A-susceptible HSCT recipients who anticipate hepatitis A exposure, (e.g., during travel to endemic areas) and for postexposure prophylaxis as indicated.††† Should also be administered after measles exposure among HSCT recipients who were not vaccinated against measles after HSCT.§§§	BIII
Intravenous immunoglobulin¶¶¶	Can be administered to HSCT recipients with severe hypogammaglobulinemia (immunoglobulin G < 400 mg/dl) ≤100 days after HSCT to prevent bacterial infections**** (Appendix).	CIII

* **Source**: Boeckh M, Bowden R. Cytomegalovirus infection in marrow transplantation. In: Buckner CD, ed. Technical and biological components of marrow transplantation. Boston, MA: Kluwer Academic Publishers, 1995:97–136.

† **Source**: CDC. Immunization of health care workers: recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Hospital Infection Control Practices Advisory Committee. MMWR 1997;46(No. RR-18):1–42.

§ **Sources**: American Academy of Pediatrics. Rabies. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics;2000:475–82; and CDC. Human rabies prevention—United States, 1999: recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR 1999;48(No. RR-1):1–21; published erratum, MMWR 1999;48(1):16.

TABLE 4. (*Continued*) Use of passive immunization for hematopoietic stem cell transplant (HSCT) recipients exposed to vaccine-preventable diseases

¶ Researchers recommend substituting respiratory syncytial virus immunoglobulin for intravenous immunoglobulin for HSCT recipients on replacement intravenous immunoglobulin therapy during respiratory syncytial virus season (i.e., November–April) (**Source**: American Academy of Pediatrics. Respiratory syncytial virus. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics;2000:483–7) (CIII). However, no data were found demonstrating safety and efficacy of respiratory syncytial virus immunoglobulin use among HSCT recipients.

§§ **Source**: CDC. Diphtheria, tetanus, and pertussis: recommendations of vaccine use and other prevention measures; recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1991;40(No. RR-10):1–28.

¶¶ If intravenous immunoglobulin replacement therapy (>250 mg/kg) has been administered <2 weeks before varicella or zoster rash exposure, varicella-zoster immunoglobulin administration is probably not required. Varicella-zoster immunoglobulin is distributed by the American Red Cross, except in Massachusetts, where it is distributed by the Massachusetts Public Health Biologic Laboratories (now a unit of the University of Massachusetts) (**Source**: CDC. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1996;45[No. RR-11]:1–36).

*** **Source**: CDC. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1996;45(No. RR-11):1–36.

††† **Source**: CDC. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1999;48(No. RR-12):1–37.

§§§ **Sources**: CDC. Measles, mumps, and rubella—vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1998;47(No. RR-8):1–48; and Eibl MM, Wedgwood RJ. Intravenous immunoglobulin: a review. Immunodeficiency Reviews 1989;1:1–42.

¶¶¶ When administered, serum immunoglobulin G levels should be monitored regularly (e.g., every 2 weeks).

****Sources**: Antman KH, Rowlings PA, Vaughn WP, et al. High-dose chemotherapy with autologous hematopoietic stem cell support for breast cancer in North America. J Clin Oncol 1997;15(5):1870–9; and Wolff SN, Fay JW, Herzig RH, et al. High-dose weekly intravenous immunoglobulin to prevent infections in patients undergoing autologous bone marrow transplantation or severe myelosuppressive therapy. Ann Intern Med 1993;118(12):937–42.

Additional Notes: Intravenous immunoglobulin can be obtained from the American Red Cross Blood Services, although shortages occasionally occur. Physicians who have difficulty obtaining urgently needed intravenous immunoglobulin and other immunoglobulin products are advised to contact any of the following:

- American Red Cross Customer Service Center, (800) 261-5772;
- Alpha Therapeutic Corporation, (800) 421-0008;
- Baxter Healthcare Corporation, (847) 940-5955;
- Bayer Pharmaceutical Division, (800) 288-8370;
- Aventis Behring Customer Support, (800) 683-1288;
- Novartis Pharmaceuticals Corporation, (973) 781-8300, or the Intravenous Immunoglobulin Emergency Hotline, (888) 234-2520; or
- Immune Deficiency Foundation, (800) 296-4433.

Physicians who are unable to obtain intravenous immunoglobulin for a licensed indication from one of these sources should contact the Product Shortage Officer at the Food and Drug Administration's Center for Biologics Evaluation and Research, Office of Compliance, (301) 827-6220, for assistance. Patients with immunoglobulin E anti-immunoglobulin A antibodies are at high risk for experiencing anaphylaxis from immunoglobulin administration (**Source**: Burks AW, Sampson HA, Buckley RH. Anaphylactic reactions after gamma globulin administration in patients with hypogammaglobulinemia. New Engl J Med 1986;314[9]:560–4). Therefore, persons with immunoglobulin A deficiency should not be administered standard immunoglobulin preparations (DIII; BIII). However, researchers report that use of immunoglobulin A-depleted immunoglobulin preparations can be used with caution in these persons (**Sources**: Burks AW, Sampson HA, Buckley RH. Anaphylactic reactions after gamma globulin administration in patients with hypogammaglobulinemia. New Engl J Med 1986;314[9]:560–4; Siberry GK, Iannone R, eds. Harriet Lane handbook: a manual for pediatric house officers. 15th ed.; St. Louis, MO: Mosby, Inc., 2000:339;739; and Stiehm ER. Human intravenous immunoglobulin in primary and secondary antibody deficiencies [Review]. Pediatr Infect Dis J 1997;16[7]:696–707).

APPENDIX

Dosing Charts for Preventing Opportunistic Vaccine-Preventable Infections Among Hematopoietic Stem Cell Transplant Recipients

I. Preventive regimens for adult or adolescent hematopoietic stem cell transplant (HSCT) recipients

Pathogen: Varicella-zoster virus

Indication	First choice	Alternatives
Prevention of varicella-zoster virus disease after exposure among adult or adolescent HSCT recipients who are at <24 months after HSCT or who are at ≥24 months after HSCT and on immunosuppressive therapy or have chronic graft-versus-host disease: Ideally, administer prophylaxis within 96 hours (preferably, within 48 hours) after close contact with a person who has chickenpox or shingles	Varicella-zoster immunoglobulin, 5 vials (1.25 ml each or 625 units total) intramuscularly (AII)	None

Pathogen: Influenza

Indication	First choice	Alternatives
Prevention of influenza A or B among adult or adolescent HSCT recipients	Lifelong annual seasonal (i.e., October–May) influenza vaccination starting before HSCT and restarting 6 months after HSCT (BIII); whole- or split-virus influenza vaccine, 0.5 ml/dose intramuscularly	None
Prophylaxis and preemptive treatment among all HSCT recipients during community and nosocomial outbreaks of influenza A	Rimantadine, 100 mg by mouth 2 times/day (CIII)	Amantadine, 100 mg by mouth 2 times/day (CIII)

Notes: Rimantadine dose should be reduced for patients with impaired renal function or for severely impaired hepatic function. Amantadine dose should be reduced for renal impairment.

Pathogen: *Streptococcus pneumoniae*

Indication	First choice	Alternatives
Prevention of pneumococcal disease among adult or adolescent HSCT recipients	23-valent pneumococcal polysaccharide vaccine at 12 and 24 months after HSCT (BIII)	None

Note: Penicillin-resistant *Streptococcus pneumoniae* is increasing in the United States.

Pathogen: *Haemophilus influenzae* type b

Indication	First choice	Alternatives
Prevention of invasive *Haemophilus influenzae* type b (Hib) disease among adult or adolescent HSCT recipients	Hib conjugate vaccine administered at 12, 14, and 24 months after HSCT (BII)	None
Generally, HSCT recipients who are household contacts of a person with Hib disease should be administered rifampin prophylaxis* (BIII); however, prophylaxis is not needed for adult or adolescent HSCT recipients who are household contacts of a person with Hib disease if all household contacts aged <4 years are fully vaccinated	Rifampin 600 mg by mouth daily for 4 days (BIII)	

* **Source**: American Academy of Pediatrics. *Haemophilus influenzae* infections. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics;2000:262–72.

II. Preventive regimens for pediatric hematopoietic stem cell transplant (HSCT) recipients

Pathogen: Varicella-zoster virus

Indication	First choice	Alternatives
Prevention of varicella-zoster virus disease after exposure among pediatric HSCT recipients who are at <24 months after HSCT or who are at ≥24 months after HSCT and on immunosuppressive therapy or have chronic graft-versus-host disease: Ideally, administer prophylaxis within 96 hours (preferably, within 48 hours) after close contact with a person who has chickenpox or shingles	Varicella-zoster immunoglobulin, 125 units (1.25 ml)/10 kg (22 lbs) of body weight administered intramuscularly; maximum dose, 625 units or 5 vials (AII); doses administered as follows: Body weight (kg) — Dose — Number of vials 0–10 — 125 units — 1 10.1–20 — 250 units — 2 20.1–30 — 375 units — 3 30.1–40 — 500 units — 4 >40 kg — 625 units — 5	Limited data demonstrate that a 1-week course of high-dose acyclovir might prevent varicella

Pathogen: Influenza

Indication	First choice	Alternatives
Prevention of influenza A and B among pediatric HSCT recipients	Lifelong annual seasonal (i.e., October–May) influenza vaccination before HSCT and resuming ≥6 months after HSCT (BIII); doses administered as follows: Age — Number of doses — Type of influenza vaccine 6–35 mo — 0.25 ml — Split-virus* 3–8 years — 0.5 ml — Split-virus* 9–12 years — 0.5 ml — Split-virus >12 years — 0.5 ml — Whole- or split-virus	None
Prophylaxis and preemptive treatment of influenza A among pediatric HSCT recipients during nosocomial or community influenza A outbreaks	Rimantadine, for children aged 1–9 years, 5 mg/kg/day once daily or divided in 2 doses (CIII); maximum daily dose, 150 mg; for children aged ≥10 years (weight, <40 kg), 5 mg/kg/day by mouth, divided in 2 doses; for children aged ≥10 years (weight, ≥40 kg), 100 mg by mouth 2 times/day	Amantadine, for children aged 1–9 years, 5 mg/kg/day; maximum daily dose, 150 mg; for children aged ≥10 years (weight, <40 kg), 5 mg/kg/day by mouth, divided in 2 doses; for children aged ≥10 years (weight, ≥40 kg), 100 mg by mouth 2 times/day; maximum daily dose, 200 mg

* Children aged <9 years receiving influenza vaccination for the first time require 2 doses of vaccine spaced ≥1 months apart.

Notes: Neither rimantadine nor amantadine are Federal Drug Administration-approved for children aged <1 year. Rimantadine and amantadine doses should be reduced for patients with impaired renal function.

Pathogen: *Streptococcus pneumoniae*

Indication	First choice	Alternatives
Prevention of pneumococcal disease among pediatric HSCT recipients	23-valent pneumococcal polysaccharide vaccine at 12 and 24 months after HSCT (BIII)	None

Notes: The 23-valent pneumococcal polysaccharide vaccine should not be administered to children aged <2 years because of lack of efficacy (DI). Penicillin-resistant *Streptococcus pneumoniae* is increasing in the United States.

II. Preventive regimens for pediatric hematopoietic stem cell transplant (HSCT) recipients (Continued)

Pathogen: *Haemophilus influenzae* type b

Indication	First choice	Alternatives
Prevention of invasive *Haemophilus influenzae* type b (Hib) disease among pediatric HSCT recipients	Hib conjugate vaccine administered at 12, 14, and 24 months after HSCT (BII)	None
Generally, pediatric HSCT recipients who are household contacts of a person with Hib disease should be administered rifampin prophylaxis* (BIII); however, prophylaxis is not needed for pediatric HSCT recipients who are household contacts of a person with Hib disease if all household contacts aged <4 years are fully vaccinated	Rifampin, administered as follows: Age — Dose 0–1 mo — 10 mg/kg by mouth daily for 4 days >1 mo — 20mg/kg by mouth daily for 4 days Maximum dose, 600 mg/day (BIII)	None

* **Source**: American Academy of Pediatrics. *Haemophilus influenzae* infections. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics;2000:262–72.