CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

October 20, 2000 / Vol. 49 / No. RR-10

MMWR™
MORBIDITY AND MORTALITY
WEEKLY REPORT

Recommendations and Reports

Inside: Continuing Education Examination

Guidelines for Preventing Opportunistic Infections Among Hematopoietic Stem Cell Transplant Recipients

Recommendations of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Disease Control and Prevention (CDC)
Atlanta, GA 30333

The *MMWR* series of publications is published by the Epidemiology Program Office, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30333.

SUGGESTED CITATION

Centers for Disease Control and Prevention. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients: recommendations of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation. MMWR 2000;49(No. RR-10):[inclusive page numbers].

Contents

Contents — Continued

Contents — Continued

Abbreviations Used in This Publication

ANC	absolute neutrophil count
BAL	bronchoalveolar lavage
CDA	chlorodeoxyadenosine
CJD	Creutzfeldt-Jakob disease
CMV	cytomegalovirus
CRV	community-acquired respiratory virus
DNA	deoxyribonucleic acid
EBV	Epstein-Barr virus
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
G-CSF	granulocyte colony-stimulating factor (filgastrim)
GM-CSF	granulocyte-macrophage colony-stimulating factor (sargramostim)
GVHD	graft-versus-host disease
HCW	health-care worker
HEPA filter	high-efficiency (>90%) particulate air filter
Hib	*Haemophilus influenzae* type b
HIV	human immunodeficiency virus
HLA	human lymphocyte antigen
HSCT	hematopoietic stem cell transplant; for this report, includes all blood- and marrow-derived hematopoietic stem cell transplants
HSV	herpes simplex virus
HTLV	human T-lymphotropic virus
IgA	immunoglobulin A
IgG	immunoglobulin G
IgM	immunoglobulin M
IVIG	intravenous immunoglobulin
LAF	laminar air flow
LD	Legionnaires' disease
LRI	lower respiratory infection
MIC	minimum inhibitory concentration
MRSA	methicillin-resistant *Staphylococcus aureus*
nvCJD	new variant Creutzfeldt-Jakob disease
OI	opportunistic infection
PCP	*Pneumocystis carinii* pneumonia
PCR	polymerase chain reaction
PZA/RIF	pyrazinamide/rifampin
RNA	ribonucleic acid
RSV	respiratory syncytial virus
TB	*Mycobacteria tuberculosis*
TMP-SMZ	trimethoprim-sulfamethasaxole
TST	tuberculin skin test
UCB	umbilical cord blood
URI	upper respiratory infection
VRE	vancomycin-resistant *Enterococcus*
VZIG	varicella-zoster immunoglobulin
VZV	varicella-zoster virus

The following CDC staff members prepared this report:

Clare A. Dykewicz, M.D., M.P.H.
Harold W. Jaffe, M.D., Director
Division of AIDS, STD, and TB Laboratory Research
National Center for Infectious Diseases

Jonathan E. Kaplan, M.D.
Division of AIDS, STD, and TB Laboratory Research
National Center for Infectious Diseases
Division of HIV/AIDS Prevention — Surveillance and Epidemiology
National Center for HIV, STD, and TB Prevention

in collaboration with
the Guidelines Working Group Members from CDC,
the Infectious Disease Society of America,
and the American Society of Blood and Marrow Transplantation

Clare A. Dykewicz, M.D., M.P.H., Chair
Harold W. Jaffe, M.D.
Thomas J. Spira, M.D.
Division of AIDS, STD, and TB Laboratory Research
William R. Jarvis, M.D.
Hospital Infections Program
National Center for Infectious Diseases, CDC

Jonathan E. Kaplan, M.D.
Division of AIDS, STD, and TB Laboratory Research
National Center for Infectious Diseases
Division of HIV/AIDS Prevention — Surveillance and Epidemiology
National Center for HIV, STD, and TB Prevention, CDC

Brian R. Edlin, M.D.
Division of HIV/AIDS Prevention—Surveillance and Epidemiology
National Center for HIV, STD, and TB Prevention, CDC

Robert T. Chen, M.D., M.A.
Beth Hibbs, R.N., M.P.H.
Epidemiology and Surveillance Division
National Immunization Program, CDC

Raleigh A. Bowden, M.D.
Keith Sullivan, M.D.
Fred Hutchinson Cancer Research Center
Seattle, Washington

David Emanuel, M.B.Ch.B.
Indiana University
Indianapolis, Indiana

David L. Longworth, M.D.
Cleveland Clinic Foundation
Cleveland, Ohio

Philip A. Rowlings, M.B.B.S., M.S.
International Bone Marrow Transplant Registry/
Autologous Blood and Marrow Transplant Registry
Milwaukee, Wisconsin

Robert H. Rubin, M.D.
Massachusetts General Hospital
Boston, Massachusetts
and
Massachusetts Institute of Technology
Cambridge, Massachusetts

Kent A. Sepkowitz, M.D.
Memorial-Sloan Kettering Cancer Center
New York, New York

John R. Wingard, M.D.
University of Florida
Gainesville, Florida

Additional Contributors

John F. Modlin, M.D.
Dartmouth Medical School
Hanover, New Hampshire

Donna M. Ambrosino, M.D.
Dana-Farber Cancer Institute
Boston, Massachusetts

Norman W. Baylor, Ph.D.
Food and Drug Administration
Rockville, Maryland

Albert D. Donnenberg, Ph.D.
University of Pittsburgh
Pittsburgh, Pennsylvania

Pierce Gardner, M.D.
State University of New York at Stony Brook
Stony Brook, New York

Roger H. Giller, M.D.
University of Colorado
Denver, Colorado

Neal A. Halsey, M.D.
Johns Hopkins University
Baltimore, Maryland

Chinh T. Le, M.D.
Kaiser-Permanente Medical Center
Santa Rosa, California

Deborah C. Molrine, M.D.
Dana-Farber Cancer Institute
Boston, Massachusetts

Keith M. Sullivan, M.D.
Fred Hutchinson Cancer Research Center
Seattle, Washington

Guidelines for Preventing Opportunistic Infections Among Hematopoietic Stem Cell Transplant Recipients

Recommendations of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation

Summary

CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation have cosponsored these guidelines for preventing opportunistic infections (OIs) among hematopoietic stem cell transplant (HSCT) recipients. The guidelines were drafted with the assistance of a working group of experts in infectious diseases, transplantation, and public health. For the purposes of this report, HSCT is defined as any transplantation of blood- or marrow-derived hematopoietic stem cells, regardless of transplant type (i.e., allogeneic or autologous) or cell source (i.e., bone marrow, peripheral blood, or placental or umbilical cord blood). Such OIs as bacterial, viral, fungal, protozoal, and helminth infections occur with increased frequency or severity among HSCT recipients. These evidence-based guidelines contain information regarding preventing OIs, hospital infection control, strategies for safe living after transplantation, vaccinations, and hematopoietic stem cell safety. The disease-specific sections address preventing exposure and disease for pediatric and adult and autologous and allogeneic HSCT recipients. The goal of these guidelines is twofold: to summarize current data and provide evidence-based recommendations regarding preventing OIs among HSCT patients. The guidelines were developed for use by HSCT recipients, their household and close contacts, transplant and infectious diseases physicians, HSCT center personnel, and public health professionals. For all recommendations, prevention strategies are rated by the strength of the recommendation and the quality of the evidence supporting the recommendation. Adhering to these guidelines should reduce the number and severity of OIs among HSCT recipients.

INTRODUCTION

In 1992, the Institute of Medicine (*1*) recommended that CDC lead a global effort to detect and control emerging infectious agents. In response, CDC published a plan (*2*) that outlined national disease prevention priorities, including the development of guidelines for preventing opportunistic infections (OIs) among immunosuppressed persons. During 1995, CDC published guidelines for preventing OIs among persons infected with human immunodeficiency virus (HIV) and revised those guidelines during 1997 and 1999 (*3–5*). Because of the success of those guidelines, CDC sought to determine the need for expanding OI prevention activities to other immunosuppressed populations. An informal survey of hematology, oncology, and infectious disease specialists at transplant centers

and a working group formed by CDC determined that guidelines were needed to help prevent OIs among hematopoietic stem cell transplant (HSCT)* recipients.

The working group defined OIs as infections that occur with increased frequency or severity among HSCT recipients, and they drafted evidence-based recommendations for preventing exposure to and disease caused by bacterial, fungal, viral, protozoal, or helminthic pathogens. During March 1997, the working group presented the first draft of these guidelines at a meeting of representatives from public and private health organizations. After review by that group and other experts, these guidelines were revised and made available during September 1999 for a 45-day public comment period after notification in the *Federal Register*. Public comments were added when feasible, and the report was approved by CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation. The pediatric content of these guidelines has been endorsed also by the American Academy of Pediatrics. The hematopoietic stem cell safety section was endorsed by the International Society of Hematotherapy and Graft Engineering.

The first recommendations presented in this report are followed by recommendations for hospital infection control, strategies for safe living, vaccinations, and hematopoietic stem cell safety. Unless otherwise noted, these recommendations address allogeneic and autologous and pediatric and adult HSCT recipients. Additionally, these recommendations are intended for use by the recipients, their household and other close contacts, transplant and infectious diseases specialists, HSCT center personnel, and public health professionals.

Using These Guidelines

For all recommendations, prevention strategies are rated by the strength of the recommendation (Table 1) and the quality of the evidence (Table 2) supporting the recommendation. The principles of this rating system were developed by the Infectious Disease Society of America and the U.S. Public Health Service for use in the guidelines for preventing OIs among HIV-infected persons (*3–6*). This rating system allows assessments of recommendations to which adherence is critical.

BACKGROUND

HSCT 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) (*7–10*). Moreover, HSCT has become standard treatment for selected conditions (*7,11,12*). 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

*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.

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 (*13*) and offer the only curative therapy for persons with chronic myelogenous leukemia (*12*). 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 (*14–16*). Another source of stem cells for allogeneic candidates without an HLA-matched sibling is a mismatched family member (*17,18*). 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) (*19*). These persons are also at increased risk for suboptimal graft function and delayed immune system recovery (*19*). 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 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 (*20*).

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 (*21*). 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 (*22–24*). 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 (*25*) 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 (*26*) and because of the development of other strategies for GVHD prophylaxis (*27*). 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) (*27*). 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 (*28,29*), infection remains a leading cause of death among allogeneic transplants and is a major cause of morbidity among autologous HSCTs (*29*). 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 (*15*). Among primary and secondary causes of death, the most common cause was infection, which occurred among 37% of 307 patients (*15*).*

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 (*30*). 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 (*31*).

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*) (*32,33*).

*Presently, no updated data have been published.

Engraftment for adults and children is defined as the point at which a patient can maintain a sustained absolute neutrophil count (ANC) of >500/mm^3 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) (*15*). 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 increased CD8 T-cell counts (*27*). They might also have immunoglobulin G (IgG)$_2$, IgG$_4$, and immunoglobulin A (IgA) deficiencies for months after HSCT and have difficulty switching from immunoglobulin M (IgM) to IgG production after antigen exposure (*32*). Immune system recovery might be delayed further by CMV infection (*34*).

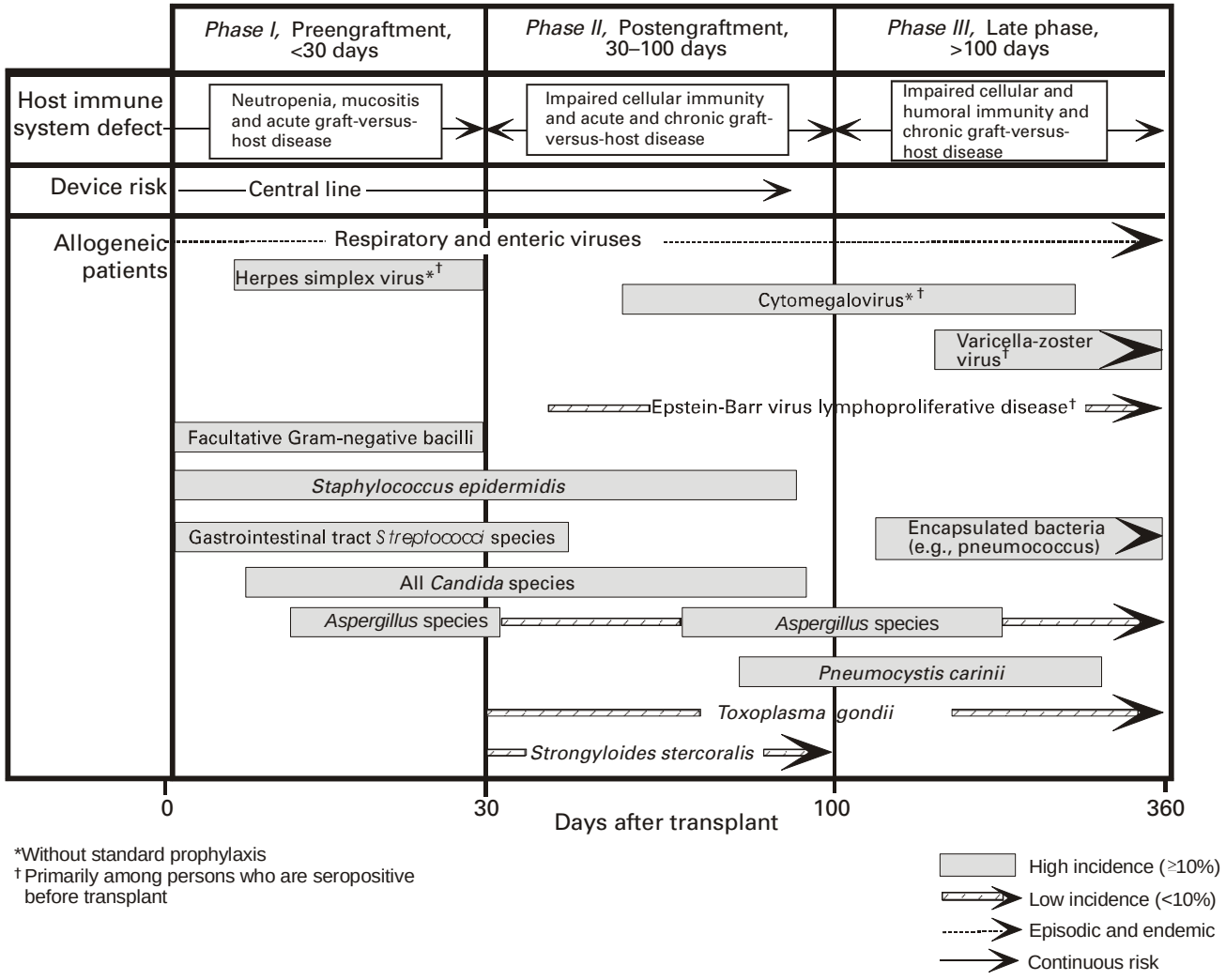
During the first ≥2 months after HSCT, recipients might experience acute GVHD that manifests as skin, gastrointestinal, and liver injury, and is graded on a scale of I–IV (*32,35,36*). Although autologous or syngeneic recipients might occasionally experience a mild, self-limited illness that is acute GVHD-like (*19,37*), 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 (*19*). Additionally, the immunosuppressive agents used for GVHD prophylaxis and treatment might make the HSCT recipient more vulnerable to opportunistic viral and fungal pathogens (*38*).

Certain patients, particularly adult allogeneic recipients, might also experience chronic GVHD, which is graded as either limited or extensive chronic GVHD (*19,39*). Chronic GVHD appears similar to autoimmune, connective-tissue disorders (e.g., scleroderma or systemic lupus erythematosus) (*40*) and is associated with cellular and humoral immunodeficiencies, including macrophage deficiency, impaired neutrophil chemotaxis (*41*), poor response to vaccination (*42–44*), and severe mucositis (*19*). 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) (*40*), and a history of acute GVHD (*24,45*). Chronic GVHD was first described as occurring >100 days after HSCT but can occur 40 days after HSCT (*19*). Although allogeneic recipients with chronic GVHD have normal or high total serum immunoglobulin levels (*41*), they experience long-lasting IgA, IgG, and IgG subclass deficiencies (*41,46,47*) and poor opsonization and impaired reticuloendothelial function. Consequently, they are at even greater risk for infections (*32,39*), particularly life-threatening bacterial infections from encapsulated organisms (e.g., *Stre. pneumoniae*, *Ha. influenzae*, or *Ne. meningitidis*). After chronic GVHD resolves, which might take years, cell-mediated and humoral immunity function are gradually restored.

Opportunistic Pathogens After HSCT

HSCT recipients experience certain infections at different times posttransplant, reflecting the predominant host-defense defect(s) (Figure). Immune system recovery for HSCT recipients takes place in three phases beginning at day 0, the day of transplant.

FIGURE. Phases of opportunistic infections among allogeneic HSCT recipients



Phase I is the preengraftment phase (<30 days after HSCT); phase II, the postengraftment phase (30–100 days after HSCT); and phase III, the late phase (>100 days after HSCT). Prevention strategies should be based on these three phases and the following information:

- **Phase I, preengraftment.** During the first month posttransplant, HSCT recipients have two critical risk factors for infection — prolonged neutropenia and breaks in the mucocutaneous barrier resulting from the HSCT preparative regimens and frequent vascular access required for patient care. Consequently, oral, gastro-intestinal, and skin flora are sources of infection. Prevalent pathogens include *Candida* species, and as neutropenia continues, *Aspergillus* species. Additionally, herpes simplex virus (HSV) reactivation can occur during this phase. During preengraftment, the risks for infection are the same for autologous or allogeneic patients, and OIs can appear as febrile neutropenia. Although a recipient's first fever during preengraftment is probably caused by a bacterial pathogen, rarely is an organism or site of infection identified. Instead, such infections are usually treated preemptively or empirically (*48*) until the neutropenia resolves (*49*). Growth factors can be administered during phase I to decrease neutropenia duration and complications (e.g., febrile neutropenia) (*50*).

- **Phase II, postengraftment.** Phase II is dominated by impaired cell-mediated immunity for allogeneic or autologous recipients. Scope and impact of this defect for allogeneic recipients are determined by the extent of GVHD and its immunosuppressive therapy. After engraftment, the herpes viruses, particularly CMV, are critical pathogens. At 30–100 days after HSCT, CMV causes pneumonia, hepatitis, and colitis and potentiates superinfection with opportunistic pathogens, particularly among patients with active GVHD. Other dominant pathogens during this phase include *Pneumocystis carinii* and *Aspergillus* species.

- **Phase III, late phase.** During phase III, autologous recipients usually have more rapid recovery of immune system function and, therefore, a lower risk for OIs than do allogeneic recipients. Because of cell-mediated and humoral immunity defects and impaired reticuloendothelial system function, allogeneic patients with chronic GVHD and recipients of alternate donor allogeneic transplants are at risk for certain infections during this phase. Alternate donors include matched unrelated, UCB, or mismatched family-related donors. These patients are at risk for infections that include CMV, varicella-zoster virus (VZV), EBV-related posttransplant lymphoproliferative disease, community-acquired respiratory viruses (CRV), and infections with encapsulated bacteria (e.g., *Ha. influenzae* and *Stre. pneumoniae*). Risk for these infections is approximately proportional to the severity of the patient's GVHD during phases II and III. Patients receiving mismatched allogeneic transplants have a higher attack rate and severity of GVHD and, therefore, a higher risk for OIs during phases II and III than do patients receiving matched allogeneic HSCTs. In contrast, patients undergoing autologous transplantation are primarily at risk for infection during phase I.

Preventing infections among HSCT recipients is preferable to treating infections. However, despite recent technologic advances, more research is needed to optimize health outcomes for HSCT recipients. Efforts to improve immune system reconstitution, particularly among allogeneic transplant recipients, and to prevent or resolve the immune dysregulation resulting from donor-recipient histoincompatibility and GVHD remain

substantial challenges for preventing recurrent, persistent, or progressive infections among HSCT patients.

BACTERIAL INFECTIONS

General Recommendations

Preventing Exposure

Because bacteria are carried on the hands, health-care workers (HCWs) and others in contact with HSCT recipients should routinely follow appropriate hand-washing practices to avoid exposing recipients to bacterial pathogens (AIII).

Preventing Disease

Preventing Early Disease (0–100 Days After HSCT). Routine gut decontamination is not recommended for HSCT candidates (51–53) (DIII). Because of limited data, no recommendations can be made regarding the routine use of antibiotics for bacterial prophylaxis among afebrile, asymptomatic neutropenic recipients. Although studies have reported that using prophylactic antibiotics might reduce bacteremia rates after HSCT (51), infection-related fatality rates are not reduced (52). If physicians choose to use prophylactic antibiotics among asymptomatic, afebrile, neutropenic recipients, they should routinely review hospital and HSCT center antibiotic-susceptibility profiles, particularly when using a single antibiotic for antibacterial prophylaxis (BIII). The emergence of fluoquinolone-resistant coagulase-negative *Staphylococci* and *Es. coli* (51,52), vancomycin-intermediate *Sta. aureus* and vancomycin-resistant *Enterococcus* (VRE) are increasing concerns (54). Vancomycin should not be used as an agent for routine bacterial prophylaxis (DIII). Growth factors (e.g., GM-CSF and G-CSF) shorten the duration of neutropenia after HSCT (55); however, no data were found that indicate whether growth factors effectively reduce the attack rate of invasive bacterial disease.

Physicians should not routinely administer IVIG products to HSCT recipients for bacterial infection prophylaxis (DII), although IVIG has been recommended for use in producing immune system modulation for GVHD prevention. Researchers have recommended routine IVIG* use to prevent bacterial infections among the approximately 20%–25% of HSCT recipients with unrelated marrow grafts who experience severe

*Since November 1997, the United States has had a shortage of intravenous immunoglobulin (IVIG) (**Source:** CDC. Availability of immune globulin intravenous for treatment of immune deficient patients—United States, 1997–1998. MMWR 1999:48[8];159–162). Physicians who have difficulty obtaining IVIG should contact the following sources:

- 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 IVIG Emergency Hotline, (888) 234-2520; or
- Immune Deficiency Foundation, (800) 296-4433.

Physicians who are unable to obtain IVIG 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.

hypogamma-globulinemia (e.g., IgG < 400 mg/dl) within the first 100 days after transplant (CIII). For example, recipients who are hypogammaglobulinemic might receive prophylactic IVIG to prevent bacterial sinopulmonary infections (e.g., from *Stre. pneumoniae*) (*8*) (CIII). For hypogammaglobulinemic allogeneic recipients, physicians can use a higher and more frequent dose of IVIG than is standard for non-HSCT recipients because the IVIG half-life among HSCT recipients (generally 1–10 days) is much shorter than the half-life among healthy adults (generally 18–23 days) (*56–58*). Additionally, infections might accelerate IgG catabolism; therefore, the IVIG dose for a hypogammaglobulinemic recipient should be individualized to maintain trough serum IgG concentrations >400–500 mg/dl (*58*) (BII). Consequently, physicians should monitor trough serum IgG concentrations among these patients approximately every 2 weeks and adjust IVIG doses as needed (BIII) (Appendix).

Preventing Late Disease (>100 Days After HSCT). Antibiotic prophylaxis is recommended for preventing infection with encapsulated organisms (e.g., *Stre. pneumoniae*, *Ha. influenzae*, or *Ne. meningitidis*) among allogeneic recipients with chronic GVHD for as long as active chronic GVHD treatment is administered (*59*) (BIII). Antibiotic selection should be guided by local antibiotic resistance patterns. In the absence of severe demonstrable hypogammaglobulinemia (e.g., IgG levels < 400 mg/dl, which might be associated with recurrent sinopulmonary infections), routine monthly IVIG administration to HSCT recipients >90 days after HSCT is not recommended (*60*) (DI) as a means of preventing bacterial infections.

Other Disease Prevention Recommendations. Routine use of IVIG among autologous recipients is not recommended (*61*) (DII). Recommendations for preventing bacterial infections are the same among pediatric or adult HSCT recipients.

Recommendations Regarding *Stre. pneumoniae*

Preventing Exposure

Appropriate care precautions should be taken with hospitalized patients infected with *Stre. pneumoniae* (*62,63*) (BIII) to prevent exposure among HSCT recipients.

Preventing Disease

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 (*64–66*) (BIII). 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.

Antibiotic prophylaxis is recommended for preventing infection with encapsulated organisms (e.g., *Stre. pneumoniae* , *Ha. influenzae* , and *Ne. meningitidis*) among allogeneic recipients with chronic GVHD for as long as active chronic GVHD treatment is administered (*59*) (BIII). Trimethoprim-sulfamethasaxole (TMP-SMZ) administered for *Pneumocystis carinii* pneumonia (PCP) prophylaxis will also provide protection against pneumococcal infections. However, no data were found to support using TMP-SMZ prophylaxis among HSCT recipients solely for the purpose of preventing *Stre. pneumoniae* disease. Certain strains of *Stre. pneumoniae* are resistant to TMP-SMZ and penicillin. Recommendations for preventing pneumococcal infections are the same for allogeneic or autologous recipients.

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 (BIII). However, this vaccine should not be administered to children aged <2 years because it is not effective among that age population (DI). 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.

Recommendations Regarding *Streptococci viridans*

Preventing Exposure

Because *Streptococci viridans* colonize the oropharynx and gut, no effective method of preventing exposure is known.

Preventing Disease

Chemotherapy-induced oral mucositis is a potential source of *Streptococci viridans* bacteremia. Consequently, before conditioning starts, dental consults should be obtained for all HSCT candidates to assess their state of oral health and to perform any needed dental procedures to decrease the risk for oral infections after transplant (*67*) (AIII).

Generally, HSCT physicians should not use prophylactic antibiotics to prevent *Streptococci viridans* infections (DIII). No data were found that demonstrate efficacy of prophylactic antibiotics for this infection. Furthermore, such use might select antibiotic-resistant bacteria, and in fact, penicillin- and vancomycin-resistant strains of *Streptococci viridans* have been reported (*68*). However, when *Streptococci viridans* infections among HSCT recipients are virulent and associated with overwhelming sepsis and shock in an institution, prophylaxis might be evaluated (CIII). Decisions regarding the use of *Streptococci viridans* prophylaxis should be made only after consultation with the hospital epidemiologists or infection-control practitioners who monitor rates of nosocomial bacteremia and bacterial susceptibility (BIII).

HSCT physicians should be familiar with current antibiotic susceptibilities for patient isolates from their HSCT centers, including *Streptococci viridans* (BIII). Physicians should maintain a high index of suspicion for this infection among HSCT recipients with symptomatic mucositis because early diagnosis and aggressive therapy are currently the only potential means of preventing shock when severely neutropenic HSCT recipients experience *Streptococci viridans* bacteremia (*69*).

Recommendations Regarding *Ha. influenzae* type b

Preventing Exposure

Adults with *Ha. influenzae* type b (Hib) pneumonia require standard precautions (*62*) to prevent exposing the HSCT recipient to Hib. Adults and children who are in contact with the HSCT recipient and who have known or suspected invasive Hib disease, including meningitis, bacteremia, or epiglottitis, should be placed in droplet precautions until 24 hours after they begin appropriate antibiotic therapy, after which they can be switched to standard precautions. Household contacts exposed to persons with Hib disease and who also have contact with HSCT recipients should be administered rifampin prophylaxis according to published recommendations (*70,71*); prophylaxis for household contacts of

a patient with Hib disease are necessary if all contacts aged <4 years are not fully vaccinated (BIII) (Appendix). This recommendation is critical because the risk for invasive Hib disease among unvaccinated household contacts aged <4 years is increased, and rifampin can be effective in eliminating Hib carriage and preventing invasive Hib disease (*72–74*). Pediatric household contacts should be up-to-date with Hib vaccinations to prevent possible Hib exposure to the HSCT recipient (AII).

Preventing Disease

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 (BII). This vaccine is recommended because the majority of HSCT recipients have low levels of Hib capsular polysaccharide antibodies ≥4 months after HSCT (*75*), and allogeneic recipients with chronic GVHD are at increased risk for infection from encapsulated organisms (e.g., Hib) (*76,77*). HSCT recipients who are exposed to persons with Hib disease should be offered rifampin prophylaxis according to published recommendations (*70*) (BIII) (Appendix).

Antibiotic prophylaxis is recommended for preventing infection with encapsulated organisms (e.g., *Stre. pneumoniae*, *Ha. influenzae*, or *Ne. meningitidis*) among allogeneic recipients with chronic GVHD for as long as active chronic GVHD treatment is administered (*59*) (BIII). Antibiotic selection should be guided by local antibiotic-resistance patterns. Recommendations for preventing Hib infections are the same for allogeneic or autologous recipients. 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 (*62,70*) (BIII). Appropriate pediatric doses should be administered for Hib conjugate vaccine and for rifampin prophylaxis (*71*) (Appendix).

VIRAL INFECTIONS

Recommendations Regarding Cytomegalovirus

Preventing Exposure

HSCT candidates should be tested for the presence of serum anti-CMV IgG antibodies before transplantation to determine their risk for primary CMV infection and reactivation after HSCT (AIII). Only Food and Drug Administration (FDA) licensed or approved tests should be used. HSCT recipients and candidates should avoid sharing cups, glasses, and eating utensils with others, including family members, to decrease the risk for CMV exposure (BIII).

Sexually active patients who are not in long-term monogamous relationships should always use latex condoms during sexual contact to reduce their risk for exposure to CMV and other sexually transmitted pathogens (AII). However, even long-time monogamous pairs can be discordant for CMV infections. Therefore, during periods of immunocompromise, sexually active HSCT recipients in monogamous relationships should ask partners to be tested for serum CMV IgG antibody, and discordant couples should use latex condoms during sexual contact to reduce the risk for exposure to this sexually transmitted OI (CIII).

After handling or changing diapers or after wiping oral and nasal secretions, HSCT candidates and recipients should practice regular hand washing to reduce the risk for CMV exposure (AII). CMV-seronegative recipients of allogeneic stem cell transplants from CMV-seronegative donors (i.e., R-negative or D-negative) should receive only leukocyte-reduced or CMV-seronegative red cells or leukocyte-reduced platelets (<1 x 10^6 leukocytes/unit) to prevent transfusion-associated CMV infection (*78*) (AI). However, insufficient data were found to recommend use of leukocyte-reduced or CMV-seronegative red cells and platelets among CMV-seronegative recipients who have CMV-seropositive donors (i.e., R-negative or D-positive).

All HCWs should wear gloves when handling blood products or other potentially contaminated biologic materials (AII) to prevent transmission of CMV to HSCT recipients. HSCT patients who are known to excrete CMV should be placed under standard precautions (*62*) for the duration of CMV excretion to avoid possible transmission to CMV-seronegative HSCT recipients and candidates (AIII). Physicians are cautioned that CMV excretion can be episodic or prolonged.

Preventing Disease and Disease Recurrence

HSCT recipients at risk for CMV disease after HSCT (i.e., all CMV-seropositive HSCT recipients, and all CMV-seronegative recipients with a CMV-seropositive donor) should be placed on a CMV disease prevention program from the time of engraftment until 100 days after HSCT (i.e., phase II) (AI). Physicians should use either prophylaxis or preemptive treatment with ganciclovir for allogeneic recipients (AI). In selecting a CMV disease prevention strategy, physicians should assess the risks and benefits of each strategy, the needs and condition of the patient, and the hospital's virology laboratory support capability.

Prophylaxis strategy against early CMV (i.e., <100 days after HSCT) for allogeneic recipients involves administering ganciclovir prophylaxis to all allogeneic recipients at risk throughout phase II (i.e., from engraftment to 100 days after HSCT). The induction course is usually started at engraftment (AI), although physicians can add a brief prophylactic course during HSCT preconditioning (CIII) (Appendix).

Preemptive strategy against early CMV (i.e., <100 days after HSCT) for allogeneic recipients is preferred over prophylaxis for CMV-seronegative HSCT recipients of seropositive donor cells (i.e., D-positive or R-negative) because of the low attack rate of active CMV infection if screened or filtered blood product support is used (BII). Preemptive strategy restricts ganciclovir use for those patients who have evidence of CMV infection after HSCT. It requires the use of sensitive and specific laboratory tests to rapidly diagnose CMV infection after HSCT and to enable immediate administration of ganciclovir after CMV infection has been detected. Allogeneic recipients at risk should be screened ≥1 times/week from 10 days to 100 days after HSCT (i.e., phase II) for the presence of CMV viremia or antigenemia (AIII).

HSCT physicians should select one of two diagnostic tests to determine the need for preemptive treatment. Currently, the detection of CMV pp65 antigen in leukocytes (antigenemia) (*79,80*) is preferred for screening for preemptive treatment because it is more rapid and sensitive than culture and has good positive predictive value (*79–81*). Direct detection of CMV-DNA (deoxyribonucleic acid) by polymerase chain reaction (PCR) (*82*) is very sensitive but has a low positive predictive value (*79*). Although CMV-DNA PCR is less sensitive than whole blood or leukocyte PCR, plasma CMV-DNA PCR is useful

during neutropenia, when the number of leukocytes/slide is too low to allow CMV pp65 antigenemia testing.

Virus culture of urine, saliva, blood, or bronchoalveolar washings by rapid shell-vial culture (*83*) or routine culture (*84,85*) can be used; however, viral culture techniques are less sensitive than CMV-DNA PCR or CMV pp65 antigenemia tests. Also, rapid shell-viral cultures require ≥48 hours and routine viral cultures can require weeks to obtain final results. Thus, viral culture techniques are less satisfactory than PCR or antigenemia tests. HSCT centers without access to PCR or antigenemia tests should use prophylaxis rather than preemptive therapy for CMV disease prevention (*86*) (BII). Physicians do use other diagnostic tests (e.g., hybrid capture CMV-DNA assay, Version 2.0 [*87*] or CMV pp67 viral RNA [ribonucleic acid] detection) (*88*); however, limited data were found regarding use among HSCT recipients, and therefore, no recommendation for use can be made.

Allogeneic recipients ≤100 days after HSCT (i.e., during phase II) should begin preemptive treatment with ganciclovir if CMV viremia or any antigenemia is detected or if the recipient has ≥2 consecutively positive CMV-DNA PCR tests (BIII). After preemptive treatment has been started, maintenance ganciclovir is usually continued until 100 days after HSCT or for a minimum of 3 weeks, whichever is longer (AI) (Appendix). Antigen or PCR tests should be negative when ganciclovir is stopped. Studies report that a shorter course of ganciclovir (e.g., for 3 weeks or until negative PCR or antigenemia occurs) (*89–91*) might provide adequate CMV prevention with less toxicity, but routine weekly screening by pp65 antigen or PCR test is necessary after stopping ganciclovir because CMV reactivation can occur (BIII).

Presently, only the intravenous formulation of ganciclovir has been approved for use in CMV prophylactic or preemptive strategies (BIII). No recommendation for oral ganciclovir use among HSCT recipients can be made because clinical trials evaluating its efficacy are still in progress. One group has used ganciclovir and foscarnet on alternate days for CMV prevention (*92*), but no recommendation can be made regarding this strategy because of limited data. Patients who are ganciclovir-intolerant should be administered foscarnet instead (*93*) (BII) (Appendix). HSCT recipients receiving ganciclovir should have ANCs checked ≥2 times/week (BIII). Researchers report managing ganciclovir-associated neutropenia by adding G-CSF (*94*) or temporarily stopping ganciclovir for ≥2 days if the patient's ANC is <1,000 (CIII). Ganciclovir can be restarted when the patient's ANC is ≥1,000 for 2 consecutive days. Alternatively, researchers report substituting foscarnet for ganciclovir if a) the HSCT recipient is still CMV viremic or antigenemic or b) the ANC remains <1,000 for >5 days after ganciclovir has been stopped (CIII) (Appendix). Because neutropenia accompanying ganciclovir administration is usually brief, such patients do not require antifungal or antibacterial prophylaxis (DIII).

Currently, no benefit has been reported from routinely administering ganciclovir prophylaxis to all HSCT recipients at >100 days after HSCT (i.e., during phase III). However, persons with high risk for late CMV disease should be routinely screened biweekly for evidence of CMV reactivation as long as substantial immunocompromise persists (BIII). Risk factors for late CMV disease include allogeneic HSCT accompanied by chronic GVHD, steroid use, low CD4 counts, delay in high avidity anti-CMV antibody, and recipients of matched unrelated or T-cell–depleted HSCTs who are at high risk (*95–99*). If CMV is still detectable by routine screening ≥100 days after HSCT, ganciclovir should be continued until CMV is no longer detectable (AI). If low-grade CMV antigenemia (<5 positive cells/slide) is detected on routine screening, the antigenemia test should be repeated in 3 days

(BIII). If CMV antigenemia indicates ≥5 cells/slide, PCR is positive, or the shell-vial culture detects CMV viremia, a 3-week course of preemptive ganciclovir treatment should be administered (BIII) (Appendix). Ganciclovir should also be started if the patient has had ≥2 consecutively positive viremia or PCR tests (e.g., in a person receiving steroids for GVHD or who received ganciclovir or foscarnet at <100 days after HSCT). Current investigational strategies for preventing late CMV disease include the use of targeted prophylaxis with antiviral drugs and cellular immunotherapy for those with deficient or absent CMV-specific immune system function.

If viremia persists after 4 weeks of ganciclovir preemptive therapy or if the level of antigenemia continues to rise after 3 weeks of therapy, ganciclovir-resistant CMV should be suspected. If CMV viremia recurs during continuous treatment with ganciclovir, researchers report restarting ganciclovir induction (*100*) or stopping ganciclovir and starting foscarnet (CIII). Limited data were found regarding the use of foscarnet among HSCT recipients for either CMV prophylaxis or preemptive therapy (*92,93*).

Infusion of donor-derived CMV-specific clones of CD8+ T-cells into the transplant recipient is being evaluated under FDA Investigational New Drug authorization; therefore, no recommendation can be made. Although, in a substantial cooperative study, high-dose acyclovir has had certain efficacy for preventing CMV disease (*101*), its utility is limited in a setting where more potent anti-CMV agents (e.g., ganciclovir) are used (*102*). Acyclovir is not effective in preventing CMV disease after autologous HSCT (*103*) and is, therefore, not recommended for CMV preemptive therapy (DII). Consequently, valacyclovir, although under study for use among HSCT recipients, is presumed to be less effective than ganciclovir against CMV and is currently not recommended for CMV disease prevention (DII).

Although HSCT physicians continue to use IVIG for immune system modulation, IVIG is not recommended for CMV disease prophylaxis among HSCT recipients (DI). Cidofovir, a nucleoside analog, is approved by FDA for the treatment of AIDS-associated CMV retinitis. The drug's major disadvantage is nephrotoxicity. Cidofovir is currently in FDA phase 1 trial for use among HSCT recipients; therefore, recommendations for its use cannot be made.

Use of CMV-negative or leukocyte-reduced blood products is not routinely required for all autologous recipients because most have a substantially lower risk for CMV disease. However, CMV-negative or leukocyte-reduced blood products can be used for CMV-seronegative autologous recipients (CIII). Researchers report that CMV-seropositive autologous recipients be evaluated for preemptive therapy if they have underlying hematologic malignancies (e.g., lymphoma or leukemia), are receiving intense conditioning regimens or graft manipulation, or have recently received fludarabine or 2-chlorodeoxyadenosine (CDA) (CIII). This subpopulation of autologous recipients should be monitored weekly from time of engraftment until 60 days after HSCT for CMV reactivation, preferably with quantitative CMV pp65 antigen (*80*) or quantitative PCR (BII).

Autologous recipients at high risk who experience CMV antigenemia (i.e., blood levels of ≥5 positive cells/slide) should receive 3 weeks of preemptive treatment with ganciclovir or foscarnet (*80*), but CD34+-selected patients should be treated at any level of antigenemia (BII) (Appendix). Prophylactic approach to CMV disease prevention is not appropriate for CMV-seropositive autologous recipients. Indications for the use of CMV prophylaxis or preemptive treatment are the same for children or adults.

Recommendations Regarding EBV

Preventing Exposure

All transplant candidates, particularly those who are EBV-seronegative, should be advised of behaviors that could decrease the likelihood of EBV exposure (AII). For example, HSCT recipients and candidates should follow safe hygiene practices (e.g., frequent hand washing [AIII] and avoiding the sharing of cups, glasses, and eating utensils with others) (*104*) (BIII), and they should avoid contact with potentially infected respiratory secretions and saliva (*104*) (AII).

Preventing Disease

Infusion of donor-derived, EBV-specific cytotoxic T-lymphocytes has demonstrated promise in the prophylaxis of EBV-lymphoma among recipients of T-cell–depleted unrelated or mismatched allogeneic recipients (*105,106*). However, insufficient data were found to recommend its use. Prophylaxis or preemptive therapy with acyclovir is not recommended because of lack of efficacy (*107,108*) (DII).

Recommendations Regarding HSV

Preventing Exposure

HSCT candidates should be tested for serum anti-HSV IgG before transplant (AIII); however, type-specific anti-HSV IgG serology testing is not necessary. Only FDA-licensed or -approved tests should be used. All HSCT candidates, particularly those who are HSV-seronegative, should be informed of the importance of avoiding HSV infection while immunocompromised and should be advised of behaviors that will decrease the likelihood of HSV exposure (AII). HSCT recipients and candidates should avoid sharing cups, glasses, and eating utensils with others (BIII). Sexually active patients who are not in a long-term monogamous relationship should always use latex condoms during sexual contact to reduce the risk for exposure to HSV as well as other sexually transmitted pathogens (AII). However, even long-time monogamous pairs can be discordant for HSV infections. Therefore, during periods of immunocompromise, sexually active HSCT recipients in such relationships should ask partners to be tested for serum HSV IgG antibody. If the partners are discordant, they should consider using latex condoms during sexual contact to reduce the risk for exposure to this sexually transmitted OI (CIII). Any person with disseminated, primary, or severe mucocutaneous HSV disease should be placed under contact precautions for the duration of the illness (*62*) (AI) to prevent transmission of HSV to HSCT recipients.

Preventing Disease and Disease Recurrence

Acyclovir. Acyclovir prophylaxis should be offered to all HSV-seropositive allogeneic recipients to prevent HSV reactivation during the early posttransplant period (*109–113*) (AI). Standard approach is to begin acyclovir prophylaxis at the start of the conditioning therapy and continue until engraftment occurs or until mucositis resolves, whichever is longer, or approximately 30 days after HSCT (BIII) (Appendix). Without supportive data from controlled studies, routine use of antiviral prophylaxis for >30 days after HSCT to prevent HSV is not recommended (DIII). Routine acyclovir prophylaxis is not indicated for

HSV-seronegative HSCT recipients, even if the donors are HSV-seropositive (DIII). Researchers have proposed administration of ganciclovir prophylaxis alone (*86*) to HSCT recipients who required simultaneous prophylaxis for CMV and HSV after HSCT (CIII) because ganciclovir has in vitro activity against CMV and HSV 1 and 2 (*114*), although ganciclovir has not been approved for use against HSV.

Valacyclovir. Researchers have reported valacyclovir use for preventing HSV among HSCT recipients (CIII); however, preliminary data demonstrate that very high doses of valacyclovir (8 g/day) were associated with thrombotic thrombocytopenic purpura/hemolytic uremic syndrome among HSCT recipients (*115*). Controlled trial data among HSCT recipients are limited (*115*), and the FDA has not approved valacyclovir for use among recipients. Physicians wishing to use valacyclovir among recipients with renal impairment should exercise caution and decrease doses as needed (BIII) (Appendix).

Foscarnet. Because of its substantial renal and infusion-related toxicity, foscarnet is not recommended for routine HSV prophylaxis among HSCT recipients (DIII).

Famciclovir. Presently, data regarding safety and efficacy of famciclovir among HSCT recipients are limited; therefore, no recommendations for HSV prophylaxis with famciclovir can be made.

Other Recommendations

HSV prophylaxis lasting >30 days after HSCT might be considered for persons with frequent recurrent HSV (CIII) (Appendix). Acyclovir can be used during phase I for administration to HSV-seropositive autologous recipients who are likely to experience substantial mucositis from the conditioning regimen (CIII). Antiviral prophylaxis doses should be modified for use among children (Appendix), but no published data were found regarding valacyclovir safety and efficacy among children.

Recommendations Regarding VZV

Preventing Exposure

HSCT candidates should be tested for the presence of serum anti-VZV IgG antibodies (AIII). However, these tests are not 100% reliable, particularly among severely immunosuppressed patients. Researchers recommend that a past history of varicella accompanied by a positive titer is more likely to indicate the presence of immunity to VZV than a low positive titer alone. All HSCT candidates and recipients, particularly those who are VZV-seronegative, should be informed of the potential seriousness of VZV disease among immunocompromised persons and advised of strategies to decrease their risk for VZV exposure (*116–122*) (AII).

Although researchers report that the majority of VZV disease after HSCT is caused by reactivation of endogenous VZV, HSCT candidates and recipients who are VZV-seronegative, or VZV-seropositive and immunocompromised, should avoid exposure to persons with active VZV infections (*123*) (AII). HCWs, 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 VZV vaccination before being allowed to visit or have direct contact with an HSCT recipient (AIII). 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 (BIII).

HSCT recipients and candidates undergoing conditioning therapy should avoid contact with any VZV vaccine recipient who experiences a rash after vaccination (BIII). When this rash occurs, it usually appears 14–21 days after VZV 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 VZV vaccine virus, and the VZV vaccine strain is susceptible to acyclovir.

All HSCT recipients with VZV disease should be placed under airborne and contact precautions (*62*) (AII) to prevent transmission to other HSCT recipients. Contact precautions should be continued until all skin lesions are crusted. Airborne precautions should be instituted 10 days after exposure to VZV and continued until 21 days after last exposure or 28 days postexposure if the patient received varicella-zoster immunoglobulin (VZIG)* (*62*) (AI) because a person infected with VZV can be infectious before the rash appears.

Preventing Disease

VZIG. VZV-seronegative HSCT recipients should be administered 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) (AII). Researchers report VZIG administration for VZV exposure as described for HSCT recipients who were VZV-seropositive before HSCT (CIII).

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 (BIII). Researchers also report VZIG administration for this situation for VZV-seropositive HSCT recipients and candidates undergoing conditioning therapy (CIII). 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 VZV vaccinees with vesicular rashes postvaccination (*121*).

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 (*120*) (BIII). Researchers also recommend VZIG administration for this condition for VZV-seropositive HSCT recipients and candidates undergoing conditioning therapy (CIII).

*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) (*19*). FFF Enterprises, Inc., can be contacted at

FFF Enterprises, Inc.
41093 County Center Drive
Temecula, CA 92591
Phone: (800) 522-4448

Antiviral Drugs. Any HSCT recipient or candidate undergoing conditioning therapy who experiences a VZV-like rash (particularly after exposure to a person with wild-type varicella or shingles) should receive preemptive intravenous acyclovir until ≥2 days after all lesions have crusted (BIII) (Appendix). Any HSCT recipient or candidate undergoing conditioning therapy who experiences a VZV-like rash after exposure to a VZV vaccinee with a rash should be administered intravenous acyclovir preemptively to prevent severe, disseminated VZV disease (BII). Acyclovir should be administered until 2 days after all lesions have crusted.

Long-term acyclovir prophylaxis to prevent recurrent VZV infection (e.g., during the first 6 months after HSCT) is not routinely recommended (*124–126*) (DIII); however, this therapy could be considered for use among HSCT recipients with severe, long-term immunodeficiency (CIII). When acyclovir resistance occurs among patients, HSCT physicians should use foscarnet for preemptive treatment of VZV disease (*127*) (BIII). Researchers report valacyclovir use for preventing HSV among HSCT recipients (CIII). However, preliminary data demonstrate that very high doses of valacyclovir (8 g/day) were associated with thrombotic thrombocytopenic purpura/hemolytic uremic syndrome among HSCT recipients (*115*). Controlled trial data regarding HSCT recipients are limited (*115*), and the FDA has not approved valacyclovir for use among HSCT recipients. Physicians wishing to use valacyclovir among HSCT recipients with renal impairment should exercise caution and decrease doses as needed (BIII) (Appendix). No data were found demonstrating safety and efficacy of preemptive treatment of famciclovir against herpes zoster among HSCT recipients. Consequently, no recommendation for its use can be made.

Live-Attenuated VZV Vaccine. VZV vaccine use is contraindicated among HSCT recipients <24 months after HSCT (*128*) (EIII). Use of VZV 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 VZV vaccine among HSCT recipients.

Other Recommendations

An inactivated VZV vaccine has been used investigationally among HSCT recipients (*129*); however, more studies are needed before a recommendation regarding its use can be made. 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 (AIII) (Appendix).

Recommendations Regarding CRV Infections: Influenza, Respiratory Syncytial Virus, Parainfluenza Virus, and Adenovirus

Preventing Exposure

Preventing CRV exposure is critical in preventing CRV disease (*130,131*). To prevent nosocomial CRV transmission, HSCT recipients and their HCWs should always follow HSCT infection control guidelines (AIII). To minimize the risk for CRV transmission, HCWs and visitors with upper respiratory infection (URI) symptoms should be restricted from

contact with HSCT recipients and HSCT candidates undergoing conditioning therapy (AIII). At a minimum, active clinical surveillance for CRV disease should be conducted on all hospitalized HSCT recipients and candidates undergoing conditioning therapy; this clinical surveillance should include daily screening for signs and symptoms of CRV (e.g., URI or lower respiratory infection [LRI]) (AIII). Viral cultures of asymptomatic HSCT candidates are unlikely to be useful. HSCT recipients with URI or LRI symptoms should be placed under contact precautions to avoid transmitting infection to other HSCT candidates and recipients, HCWs, and visitors until the etiology of illness is identified (*62*) (BIII). Optimal isolation precautions should be modified as needed after the etiology is identified (AIII). HSCT recipients and candidates, their family members and visitors, and all HCWs should be informed regarding CRV infection control measures and the potential severity of CRV infections among HSCT recipients (*130–140*) (BIII). Physicians have routinely conducted culture-based CRV surveillance among HSCT recipients; however, the cost effectiveness of this approach has not been evaluated.

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 (*141*) (AI) 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 (*141*) (AI). Seasonal influenza vaccination is strongly recommended for all HCWs of HSCT recipients (*142,143*) (AI).

If HCWs, 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 (BI) 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 (*141*) (BIII).

In 1999, two neuroaminidase inhibitors (zanamivir and oseltamivir) were approved for treatment of influenza, but are not currently approved for prophylaxis. To date, experience is limited regarding use of zanamivir or oseltamivir in the treatment or prophylaxis of influenza among HSCT settings. However, 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 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 (*144–147*) (BI). 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 (AIII) to prevent transmission of influenza to HSCT recipients. HCWs with influenza should be excused from patient care until they are no longer infectious (AIII).

Preventing Disease

HSCT physicians should determine the etiology of a URI in an HSCT recipient or candidate undergoing conditioning therapy, if possible, because respiratory syncytial

virus (RSV), influenza, parainfluenza, and adenovirus URIs can progress to more serious LRI, and certain CRVs can be treated (BIII). Appropriate diagnostic samples include nasopharyngeal washes, swabs or aspirates, throat swabs, and bronchoalveolar lavage (BAL) fluid. HSCT candidates with URI symptoms at the time conditioning therapy is scheduled to start should postpone their conditioning regimen until the URIs resolve, if possible, because certain URIs might progress to LRI during immunosuppression (*131,133,137,138*) (BIII).

Recommendations Regarding Influenza. 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 (*142*) (BIII). Influenza vaccinations administered to HSCT recipients <6 months after HSCT are unlikely to be beneficial and are not recommended (*142*) (DII). HSCT recipients <6 months after HSCT should receive chemoprophylaxis with amantadine or rimantadine during community or nosocomial influenza A outbreaks (BIII). 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 (*148,149*). 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 (BIII). 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 (CIII). 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 (*142,143*). 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 URI or LRI symptoms during a community or nosocomial outbreak of influenza A (*141*). 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.

Neuroaminidase inhibitors (zanimivir and oseltamivir), intravenous and aerosol ribavirin, and combination drug therapy (e.g., rimantadine or amantadine with ribavirin or interferon) (*143,150–153*) have been proposed for investigational, preemptive treatment to prevent severe influenza disease among HSCT recipients. However, because of lack of data, no recommendation for use of these strategies among HSCT recipients can be made.

Recommendations Regarding RSV. Respiratory secretions of any hospitalized HSCT candidate or recipient who experiences signs or symptoms of CRV infection should be tested promptly by viral culture and rapid diagnostic tests for RSV (BIII). If two diagnostic samples taken ≥2 days apart do not identify a respiratory pathogen despite persistence

of respiratory symptoms, BAL and further testing are advised (BIII). This testing is critical because of the high morbidity and case fatality of RSV disease among HSCT recipients (*154,155*). HSCT recipients, particularly those who are preengraftment and at highest risk for severe RSV pneumonia, should have their illness diagnosed early (i.e., during RSV URI), and their illness should be treated aggressively to prevent fatal RSV disease (BIII).

Although a definitive, uniformly effective preemptive therapy for RSV infection among HSCT recipients has not been identified, certain strategies have been proposed, including use of aerosolized ribavirin (*155,156*), RSV antibodies (i.e., passive immunization with high RSV-titered IVIG or RSV immunoglobulin) in combination with aerosolized ribavirin (*137,157*), and RSV monoclonal antibody (*158*). Clinical trials are currently underway to evaluate the efficacy of these strategies. No recommendation regarding the optimal method for RSV prevention and preemptive therapy can be made because of limited data. Further, current data do not support use of intravenous ribavirin for preemptive therapy for RSV pneumonia among HSCT recipients (*60*) (DIII), and no commercially licensed vaccines against RSV are currently available.

Recommendations Regarding Parainfluenza Virus and Adenovirus. Immunoprophylaxis, chemoprophylaxis, and preemptive treatment for parainfluenza virus and adenovirus infections among HSCT recipients have been proposed (*159,160*). However, no recommendation can be made in these guidelines because of insufficient data. No commercially licensed vaccines against parainfluenza or adenovirus are currently available.

Other Disease Prevention Recommendations

The recommendations for preventing CRV infections and their recurrence are the same for allogeneic or autologous recipients. Generally, these recommendations apply to children or adults (*161–164*), but with appropriate adjustments in antiviral drug and influenza vaccine doses for children (Appendix).

For pediatric HSCT recipients and candidates aged >6 months, annual seasonal influenza vaccination is recommended HSCT (BIII). Children aged <9 years who are receiving influenza vaccination for the first time require two doses administered ≥1 months apart (AI). Healthy children who receive influenza vaccination for the first time might not generate protective antibodies until 2 weeks after receipt of the second dose of influenza vaccine. Therefore, during an influenza A outbreak, pediatric recipients aged <9 years, ≥6 months after HSCT, and receiving their first influenza vaccination, should be administered ≥6 weeks of influenza A chemoprophylaxis after the first dose of influenza vaccine (*141*) (BIII) (Appendix). Amantadine and rimantadine are not FDA-approved for children aged <1 year (*141,161*) (DIII).

To prevent RSV disease, researchers report substituting RSV-IVIG for IVIG during RSV season (i.e., November–April) for pediatric recipients (i.e., children aged <18 years) who receive routine IVIG therapy (*164*) (i.e., those with hypogammaglobulinemia) (CIII) (Appendix). Other researchers report that pediatric recipients with RSV can be considered for preemptive therapy (e.g., during URI or early LRI) with aerosolized ribavirin (CIII), although this therapy remains controversial (*164*) (Appendix). Droplet and contact precautions for the duration of illness are required for pediatric recipients for the duration of adenovirus (*62*) (AIII).

FUNGAL INFECTIONS

General Recommendations

Preventing Exposure

Limited data were found that demonstrate to what extent preventing fungal exposures is effective in preventing infection and disease. However, HSCT recipients and candidates undergoing conditioning therapy have been advised to avoid contact with certain areas and substances, including foods, that might increase a patient's risk for fungal exposures (CII). Specific precautions have included avoiding areas of high dust exposure (e.g., excavation sites, areas of building construction or renovation, chicken coops, and caves), occupations involving soil, and foods that contain molds (e.g., blue cheese).

Preventing Disease

Growth factors (e.g., GM-CSF and G-CSF) shorten the duration of neutropenia after HSCT (*165*); however, no data were found that indicate which growth factors effectively reduce the attack rate of invasive fungal disease. Therefore, no recommendation for use of growth factors solely for prophylaxis against invasive fungal disease can be made.

Topical antifungal drugs, which are applied to the skin or mucosa (e.g., nystatin or clotrimazole), might reduce fungal colonization in the area of application. However, these agents have not been proven to prevent generation of locally invasive or disseminated yeast infections (e.g., candidiasis) or mold infections (e.g., aspergillosis) and are not recommended for their prophylaxis (DII). Performing fungal surveillance cultures is not indicated for asymptomatic HSCT recipients (*166,167*) (DII), but cultures should be obtained from symptomatic HSCT recipients (BIII).

Recommendations Regarding Yeast Infections

Preventing Exposure

Invasive candidiasis is usually caused by dissemination of endogenous *Candida* species that have colonized a patient's gastrointestinal tract (*168*). Consequently, methods of preventing exogenous yeast exposure usually do not prevent invasive yeast infections after HSCT. However, because *Candida* species can be carried on the hands, HCWs and others in contact with HSCT recipients should follow appropriate hand-washing practices to safeguard patients from exposure (AIII).

Preventing Disease

Allogeneic recipients should be administered fluconazole prophylaxis to prevent invasive disease with fluconazole-susceptible *Candida* species during neutropenia, particularly among centers where *Can. albicans* is the predominant cause of invasive fungal disease preengraftment (AI) (Appendix). Because candidiasis occurs during phase I (*169*), fluconazole (400 mg/day by mouth or intravenously) should be administered (*169,170*) from the day of HSCT until engraftment (AII). However, fluconazole is not effective against

certain *Candida* species, including *Can. krusei* (*171*) and *Can. glabrata* and is, therefore, not recommended for their prevention (DI). Further studies are needed to determine the optimal duration of fluconazole prophylaxis. Preliminary studies have reported that low-dose fluconazole prophylaxis (100–200 mg/day by mouth) among neutropenic patients has variable efficacy in preventing candidiasis (*172*). Therefore, this therapy is not recommended for HSCT recipients (DII). Oral, nonabsorbable antifungal drugs, including oral amphotericin B (500 mg suspension every 6 hours), nystatin, and clotrimazole troches, might reduce superficial colonization and control local mucosal candidiasis, but have not been demonstrated to reduce invasive candidiasis (CIII).

Other Recommendations

HSCT candidates with candidemia or invasive candidiasis can safely receive transplants (*173*) if a) their infection was diagnosed early and treated immediately and aggressively with amphotericin B or alternatively with appropriate doses of fluconazole if the organism is susceptible; and b) evidence of disease control is reported (e.g., by serial computed tomography scans) before the transplant (BIII). Such patients should continue receiving therapeutic doses of an appropriate antifungal drug throughout phase I (BII) and until a careful review of clinical, laboratory, and serial computed tomography scans verifies resolution of candidiasis (BII).

Because autologous recipients generally have an overall lower risk for invasive fungal infection than allogeneic recipients, certain autologous recipients do not require routine antiyeast prophylaxis (DIII). However, researchers recommend administering antiyeast prophylaxis to a subpopulation of autologous recipients with underlying hematologic malignancies (e.g., lymphoma or leukemia) and who have or will have prolonged neutropenia and mucosal damage from intense conditioning regimens or graft manipulation, or have received fludarabine or 2-CDA recently (BIII). Recommendations regarding preventing invasive yeast infections among pediatric or adult HSCT recipients are the same, except that appropriate dose adjustments for prophylactic drugs should be made for pediatric recipients (Appendix).

Recommendations Regarding Mold Infections

Preventing Exposure

Nosocomial mold infections among HSCT recipients result primarily from respiratory exposure to and direct contact with fungal spores (*174*). Ongoing hospital construction and renovation have been associated with an increased risk for nosocomial mold infection, particularly aspergillosis, among severely immunocompromised patients (*175–177*). Therefore, whenever possible, HSCT recipients who remain immunocompromised should avoid hospital construction or renovation areas (AIII). When constructing new HSCT centers or renovating old ones, hospital planners should ensure that rooms for HSCT patients have an adequate capacity to minimize fungal spore counts through use of

- high-efficiency (>90%) particulate air (HEPA) filtration (*140,178,179*) (BIII);
- directed room airflow (i.e., positive air pressure in patient rooms in relation to corridor air pressure) so that air from patient rooms flows into the corridor (*180*) (BIII);

- correctly sealed rooms, including correctly sealed windows and electrical outlets (*140*) (BIII);
- high rates of room air exchange (i.e., >12 air changes/hour) (*140,178*) (BIII); and
- barriers between patient care and renovation or construction areas (e.g., sealed plastic) that prevent dust from entering patient care areas and that are impermeable to *Aspergillus* species (*175,179*) (BIII).

Additionally, HSCT centers should be cleaned with care, particularly after hospital renovation or construction, to avoid exposing HSCT recipients and candidates to mold spores (*174,176*) (BIII).

Preventing Disease

No regimen has been reported to be clearly effective or superior in preventing aspergillosis, and therefore, no recommendation can be made. Further studies are needed to determine the optimal strategy for aspergillosis prevention. Moderate-dose (0.5 mg/kg/day) amphotericin B (*181–184*), low-dose (0.1–0.25 mg/kg/day) amphotericin B (*185–187*), intranasal amphotericin B spray (*188*), lipid formulations of amphotericin B (*182,189*), and aerosolized amphotericin B (*190*) have been administered for aspergillosis prophylaxis, but data are limited regarding the safety and efficacy of these formulations among HSCT recipients. Additionally, itraconazole capsules are not recommended for fungal prophylaxis among HSCT recipients (*191*) (DII) for three reasons. First, itraconazole capsules are poorly absorbed gastrointestinally, particularly among patients who are fasting (*192*) or receiving cytotoxic agents (*193*). Second, persons taking itraconazole capsules do not achieve steady-state serum levels for 2 weeks (*188,194*), and when achieved, these levels are lower than the average *Aspergillus* species minimum inhibitory concentration (MIC) among HSCT recipients (*195*). Third, itraconazole has adverse interactions with other drugs (e.g., antiepileptics, rifampin, oral hypoglycemics, protease inhibitors, vinca alkaloids, cyclosporine, methylprednisolone, and warfarin-like anticoagulants) (*196*). Trials assessing the efficacy of the recently licensed cyclodextrin oral solution and intravenous formulations of itraconazole in preventing invasive fungal disease among HSCT recipients are in progress; however, no recommendations regarding its use for *Aspergillus* species infection prophylaxis can be made. For HSCT recipients whose respiratory specimens are culture positive for *Aspergillus* species, acute invasive aspergillosis should be diagnosed presumptively (*197*) and treated preemptively and aggressively (e.g., with intravenous amphotericin) (AIII).

The risk for aspergillosis recurrence has been high among allogeneic recipients with preexisting invasive aspergillosis. Previously, allogeneic HSCTs were avoided among persons with uncontrolled, proven aspergillosis. However, HSCT center personnel have recently reported successful allogeneic or autologous HSCT among a limited number of persons who have had successfully treated, prior invasive pulmonary aspergillosis (*198–200*). Because of limited data, no recommendations regarding strategies for preventing aspergillosis recurrence can be made.

PROTOZOAL AND HELMINTHIC INFECTIONS

Recommendations Regarding PCP

Preventing Exposure

Although a possible cause of PCP is reactivation of latent infection among immunocompromised persons, cases of person-to-person transmission of PCP have been reported (*201–206*). Generally, standard precautions should be used for patients with PCP (*62*) (BIII), but researchers have reported patients with PCP being isolated (*201,204*) and contact precautions being used if evidence existed of person-to-person transmission in the institution (CIII). This subject remains controversial, and until further data are published, HSCT recipients should avoid exposure to persons with PCP (*62*) (CIII).

Preventing Disease and Disease Recurrence

Physicians should prescribe PCP prophylaxis for allogeneic recipients throughout all periods of immunocompromise (*207*) after engraftment. Prophylaxis should be administered from engraftment until 6 months after HSCT (AII) for all patients, and >6 months after HSCT for the duration of immunosuppression for those who a) are receiving immunosuppressive therapy (e.g. prednisone or cyclosporine) (AI), or b) have chronic GVHD (BII). However, PCP prophylaxis can be initiated before engraftment if engraftment is delayed (CIII). Researchers report an additional 1- to 2-week course of PCP prophylaxis before HSCT (i.e., day –14 to day –2) (CIII).

Preferred PCP prophylaxis is TMP-SMZ (AII); however, if TMP-SMZ is administered before engraftment, the associated myelosuppression could delay engraftment, and patients might experience sensitivity to the drug. Every effort should be made to keep such patients on the drug, including assessment of desensitization therapy, although data regarding this technique among HSCT recipients are limited. For patients who cannot tolerate TMP-SMZ, physicians can choose to use alternative PCP prophylaxis regimens (e.g., dapsone) (*208*) (BIII). Use of aerosolized pentamidine (*209*) is associated with the lowest PCP prevention rates and should only be used if other agents cannot be tolerated. Atovaquone is a possible alternative drug for PCP prophylaxis among dapsone-intolerant persons with HIV infection (*210*); however, no recommendation regarding use of atovaquone among HSCT recipients can be made because of lack of data. Although data are limited, concomitant use of leucovorin (folinic acid) and TMP-SMZ is not recommended (*211,212*) (DIII). A patient's history of PCP should not be regarded as a contraindication to HSCT (*213*) (DIII).

Recurrent PCP among HSCT recipients is rare; however, patients with continued immunosuppression should remain on PCP prophylaxis until their immunosuppression is resolved (AI). The regimen recommended for preventing toxoplasmosis recurrence among HSCT recipients (i.e., TMP-SMZ) will also prevent PCP recurrence.

Other Recommendations

PCP prophylaxis should be considered for autologous recipients who have underlying hematologic malignancies (i.e., lymphoma or leukemia), are receiving intense conditioning regimens or graft manipulation, or have recently received fludarabine or 2-CDA

(*207,214*) (BIII). PCP prophylaxis should be administered ≥6 months after HSCT if substantial immunosuppression or immunosuppressive therapy (e.g., steroids) persists (CIII). Use of PCP prophylaxis among other autologous recipients is controversial (CIII). Generally, indications for PCP prophylaxis are the same among children or adults, but pediatric doses should be used (Appendix).

Recommendations Regarding *Toxoplasma gondii*

Preventing Exposure

All HSCT recipients should be provided information regarding strategies to reduce their risk for *Toxoplasma* species exposure. Researchers report that potential donors for allogeneic HSCT be tested for *To. gondii* antibodies (*215,216*) by using FDA-licensed or -approved screening tests that include IgG antibody testing because *To. gondii* has been reported to be transmitted by leukocyte transfusion (*217*) and HSCT (*218,219*) (CIII).

Preventing Disease and Disease Recurrence

Because most toxoplasmosis among HSCT recipients is caused by disease reactivation, researchers report that candidates for allogeneic HSCT can be tested for IgG antibody to determine whether they are at risk for disease reactivation after HSCT (*215,216,218*) (CIII). However, the value of such testing is controversial because a limited number of patients who were seronegative for *To. gondii* pretransplant experienced the infection posttransplant (*220*). If testing is performed, only FDA-licensed or -approved screening tests should be used.

Researchers recommend toxoplasmosis prophylaxis for seropositive allogeneic recipients with active GVHD or a prior history of toxoplasmic chorioretinitis (*221,222*), but data demonstrating efficacy are limited (CIII). The optimal prophylactic regimen for toxoplasmosis among HSCT recipients has not been determined, but a proposed drug is TMP-SMZ (BII), although allogeneic recipients have experienced break-through clinical disease despite TMP-SMZ prophylaxis (*218*). For patients who are TMP-SMZ–intolerant, a combination of clindamycin, pyramethamine, and leucovorin can be substituted for *To. gondii* prophylaxis (Appendix). After therapy for toxoplasmosis, HSCT recipients should continue receiving suppressive doses of TMP-SMZ or an alternate regimen for the duration of their immunosuppression (BIII) (Appendix).

Other Recommendations

Recipients of autologous transplants are at negligible risk for toxoplasmosis reactivation (*218*). No prophylaxis or screening for toxoplasmosis infection is recommended for such patients (DIII). Indications for toxoplasmosis prophylaxis are the same among children or adults, but pediatric doses should be used among children (Appendix).

Recommendations Regarding *Strongyloides stercoralis*

Preventing Exposure

Allogeneic recipients should avoid contact with outhouses and cutaneous exposure to soil or other surfaces that might be contaminated with human feces (*223*) (AIII). Allogeneic recipients who work in settings (e.g., hospitals or institutions) where they could be

exposed to fecal matter should wear gloves when working with patients or in areas with potential fecal contamination (AIII).

Preventing Disease and Disease Recurrence

Travel and residence histories should be obtained for all patients before HSCT to determine any exposures to high-risk areas (e.g., such moist temperate areas as the tropics, subtropics, or the southeastern United States and Europe) (*223*) (BIII). HSCT candidates who have unexplained peripheral eosinophilia or who have resided in or traveled to areas endemic for strongyloidiasis, even during the distant past, should be screened for asymptomatic strongyloidiasis before HSCT (BIII). Serologic testing with an enzyme-linked immunosorbent assay is the preferred screening method and has a sensitivity and specificity of >90% (*223,224*) (BIII). FDA-licensed or -approved screening tests should be used. Although stool examinations for strongyloidiasis are specific, the sensitivity obtained from ≥3 stool examinations is 60%–70%; the sensitivity obtained from concentrated stool exams is, at best, 80% (*223*). A total of ≥3 stool examinations should be performed if serologic tests are unavailable or if strongyloidiasis is clinically suspected in a seronegative patient (BIII).

HSCT candidates whose screening tests before HSCT are positive for *Strongyloides* species, and those with an unexplained eosinophilia and a travel or residence history indicative of exposure to *Strongyloides stercoralis* should be empirically treated before transplantation (*225,226*), preferably with ivermectin (BIII), even if seronegative or stool-negative (Appendix).

To prevent recurrence among HSCT candidates with parasitologically confirmed strongyloidiasis, cure after therapy should be verified with ≥3 consecutive negative stool examinations before proceeding with HSCT (AIII). Data are insufficient to recommend a drug prophylaxis regimen after HSCT to prevent recurrence of strongyloidiasis. HSCT recipients who had strongyloidiasis before or after HSCT should be monitored carefully for signs and symptoms of recurrent infection for 6 months after treatment (BIII).

Other Recommendations

Hyperinfection strongyloidiasis has not been reported after autologous HSCT; however, the same screening precautions should be used among autologous recipients (BIII). Indications for empiric treatment for strongyloidiasis before HSCT are the same among children or adults except for children weighing <15 kg, for whom the preferred drug is thiabendazole (BIII) (Appendix).

Recommendations Regarding *Trypanosoma cruzi*

Preventing Exposure

HSCT physicians should be aware that *Trypanosoma cruzi*, the etiologic agent of Chagas' disease, can be transmitted congenitally, through blood transfusion (*227*), and possibly through HSCT. Additionally, treatment for persons infected with *Tr. cruzi* is not always effective, even during the acute stage of infection (*227*). Therefore, potential donors who were born, received a blood transfusion, or ever lived for ≥6 months in a Chagas' disease endemic area (e.g., parts of South and Central America and Mexico) should be screened serologically for anti-*Tr. cruzi* serum IgG antibody (*228*) (BIII). Persons who lived <6 months in a Chagas'-endemic area but who had high-risk living

conditions (e.g., having had extensive exposure to the Chagas' disease vector — the reduviid bug — or having lived in dwellings with mud walls, unmilled logs and sticks, or a thatched roof) should also be screened for evidence of *Tr. cruzi* infection (BIII). Because Chagas' disease can be transmitted congenitally, researchers report that any person with extensive multigenerational maternal family histories of cardiac disease (e.g., cardiomegaly and arrhythmias) should be screened serologically for serum IgG anti-*Tr. cruzi* antibodies (*227*) (CIII). To decrease the risk for misdiagnosis by false-positive or false-negative serologic tests, *Tr. cruzi* screening should consist of ≥2 conventional serologic tests (e.g., enzyme immunoassay, indirect hemagglutination, indirect fluorescent antibody) or ≥1 conventional serologic tests, followed by a confirmatory serologic test (e.g., radioimmunoprecipitation assay) (*229*) (BIII). Persons with active Chagas' disease should not serve as HSCT donors (DIII). Researchers also recommend deferral of HSCT donation for a past history of Chagas' disease (CIII).

Preventing Disease

HSCT candidates who are at risk for being infected with *Tr. cruzi* should be screened for serum IgG anti-*Tr. cruzi* antibody (*228*) (BIII). *Tr. cruzi* seropositivity is not a contraindication to HSCT (*228,230*). However, if an acute illness occurs in a *Tr. cruzi*-seropositive HSCT recipient, particularly during neutropenia, *Tr. cruzi* reactivation should be included in the differential diagnosis (*230*) (BIII). Researchers have proposed use of beznidazole or nifurtimox for preemptive therapy or prophylaxis of recurrent *Tr. cruzi* among seropositive HSCT recipients (*230,231*), but insufficient data were found to make a recommendation.*

Other Recommendations

Recommendations are the same for autologous or allogeneic recipients. However, recurrence of Chagas' disease is probably less likely to occur among autologous recipients because of the shorter duration of immunosuppression. Recommendations are the same among children or adults.

HOSPITAL INFECTION CONTROL

Room Ventilation

HSCT center personnel should follow published guidelines for hospital room design and ventilation (*140,180*) (BIII). HSCT centers should also prevent birds from gaining access to hospital air-intake ducts (*140,174*) (AII). All allogeneic recipients should be placed in rooms with >12 air exchanges/hour (*232,233*) and point-of-use HEPA filters that are capable of removing particles ≥0.3 µm in diameter (*140,178,180,233*) (AIII). Correct filtration is critical in HSCT centers with ongoing construction and renovation (*179*). When portable HEPA filters are used as adjuncts to the primary ventilation system, they must be placed centrally in patient rooms so that space is available around all surfaces to allow free air circulation (BIII). The need for environmental HEPA filtration for autologous recipients has not been established. However, HEPA-filtered rooms should

*For additional information regarding the epidemiology of Chagas' disease, contact CDC/National Center for Infectious Diseases/Division of Parasitic Diseases, (770) 488-7760.

be evaluated for autologous recipients if they experience prolonged neutropenia, a substantial risk factor for nosocomial aspergillosis (CIII).

A laminar air flow (LAF) room contains filtered air that moves in parallel, unidirectional flow — the air enters the room from one wall and exits the room on the opposite wall (*232*). Although LAF has been demonstrated to protect patients from infection during aspergillosis outbreaks related to hospital construction (*234,235*), the value of routine LAF room use for all HSCT recipients is doubtful because substantial overall survival benefit has not been reported (*236*). During 1983, LAF rooms were preferred for allogeneic recipients with aplastic anemia and HLA-identical sibling donors because use of regular rooms was associated with a mortality rate that was approximately four times higher than for those recipients treated in LAF rooms (*237*). However, the survival of aplastic anemia HSCT recipients during the late 1990s exceeds that reported during the early 1980s, and no studies have been done to determine whether HSCT recipients with aplastic anemia still have an improved survival rate when treated in an LAF room. Therefore, HSCT centers need not construct LAF rooms for each HSCT recipient. Use of LAF rooms, if available, is optional (CII).

Hospital rooms should have directed airflow so that air intake occurs at one side of the room and air exhaust occurs at the opposite side (*140*) (BIII). Each hospital room should also be well-sealed (e.g, around windows and electrical outlets) (*140*) (BIII). To provide consistent positive pressure in the recipient's room, HSCT centers should maintain consistent pressure differentials between the patient's room and the hallway or anteroom at >2.5 Pa (i.e., 0.01 inches by water gauge) (*232,233*) (BIII). Generally, hospital rooms for HSCT recipients should have positive room air pressure when compared with any adjoining hallways, toilets, and anterooms, if present.

Anterooms should have positive air pressure compared with hallways (*180*). An exception is the HSCT recipient with an active disease that has airborne transmission (e.g., pulmonary or laryngeal *Mycobacteria tuberculosis* [TB] or measles). These HSCT patients should be placed in negative isolation rooms (*62*) (BIII), and a room with an anteroom is recommended for such patients (*180*) (BIII).

Whenever possible, HSCT centers should have self-closing doors to maintain constant pressure differentials among the HSCT recipients' room and anterooms, if available, and hallways (*233*) (BIII). To enable the nursing staff to observe the HSCT recipient even when the doors are closed, windows can be installed in either the door or the wall of the HSCT recipient's room (*233*) (CIII).

HSCT centers should provide backup emergency power and redundant air-handling and pressurization systems to maintain a constant number of air exchanges and room pressurization in the center when the central ventilation system is shut off for maintenance and repair (*238*) (BIII). Additionally, infection control personnel should work with maintenance personnel to develop protocols to protect HSCT centers at all times from bursts of mold spores that might occur when air-handling systems are restarted after routine maintenance shut-downs (BIII).

Construction, Renovation, and Building Cleaning

Construction and Renovation

Hospital construction and renovation have been associated with an increased risk for nosocomial fungal infection, particularly aspergillosis, among severely immunocompromised patients (*175,176*). Therefore, persons responsible for HSCT center

construction or renovation should consult published recommendations regarding environmental controls during construction (*239,240*) (AIII).

Whenever possible, HSCT recipients, HCWs, and visitors should avoid construction or renovation areas (*240*) (AIII). Also, equipment and supplies used by HSCT recipients or their HCWs should not be exposed to construction or renovation areas (*240*). When planning for construction or renovation, the HSCT center should include plans for intensified aspergillosis-control measures (AIII). Construction and renovation infection control planning committees should include engineers, architects, housekeeping staff, infection control personnel, the director of the HSCT center, the administration, and safety officers (*241*) (BIII).

When constructing new HSCT centers, planners should ensure that patient rooms will have adequate capacity to minimize fungal spore counts by following room ventilation recommendations. During outdoor construction and demolition, the intake air should be sealed (BIII), if possible; if not, filters should be checked frequently. Additionally, to protect HSCT patient care areas during fire drills and emergencies, weather stripping should be placed around stairwell doors, or alternatively, the stairwell air should be filtered to the level of safety of the adjacent hospital air (BIII). False ceilings should be avoided whenever possible (*174*) (BII). If use of false ceilings cannot be avoided, the area above false ceilings should be vacuumed routinely to minimize dust and, therefore, fungal exposure to patients (*174*) (BIII).

During hospital construction or renovation, hospitals should construct rigid, dustproof barriers with airtight seals (*242*) between patient care and construction or renovation areas to prevent dust from entering patient care areas; these barriers (i.e., sealed drywall) should be impermeable to *Aspergillus* species (*140,175,176,179,240*) (BIII). If impervious barriers cannot be created around the construction or renovation area, patients should be moved from the area until renovation or construction is complete and the area has been cleaned appropriately (*176*) (BIII). HSCT centers should direct pedestrian traffic occurring near construction or renovation areas away from patient care areas to limit the opening and closing of doors or other barriers that might cause dust dispersion, entry of contaminated air, or tracking of dust into patient areas (*140*), particularly those in the HSCT center (*176*) (BIII). If possible, specific corridors, entrances, and exits should be dedicated to construction use only (*240*). An elevator to which patients do not have access also should be dedicated to construction use only (*240*). Construction workers, whose clothing might be contaminated with *Aspergillus* species spores, should use the construction elevator and avoid contact with patients, patient care areas, other elevators, and nonconstruction areas (BIII).

Hospital construction or renovation areas should have negative air pressure relative to that in adjacent patient care areas, if no contraindications exist for such pressure differential (*140,176,179,240,242*) (BIII). Ideally, air from the construction or renovation areas should be exhausted to the outside of the hospital (*176*) (BIII) or if recirculated, it should be HEPA-filtered first (BIII).

Researchers have proposed that HSCT recipients wear the N95 respirator to prevent mold exposure during transportation near hospital construction or renovation areas (CIII) because the N95 respirators are regarded as effective against any aerosol. However, to be maximally effective, N95 respirators must be fit-tested and all users must be trained. With correct personnel fit-testing and training, N95 respirators reliably reduce aerosol exposure by 90%. Without fit-testing and training, aerosol exposure would be reduced but not necessarily by 90% (*243*). For patients who cannot use or tolerate an

N95 respirator, researchers have proposed using the powered air purifying respirator (*244,245*), which can be used by patients in wheelchairs. Limitations of the powered air purifying respirator include its cost and that it is not appropriate for young children and infants. General limitations of using respirators are that no commercially available respirator, including N95, has been tested specifically for its efficacy in reducing exposure to *Aspergillus* species in hospital construction or renovation areas, and no studies have been done that assess the usefulness and acceptability of using respirators among HSCT recipients. Standard surgical masks provide negligible protection against mold spores and are not recommended for this indication (DIII).

Newly constructed or renovated areas should be cleaned before patients are allowed to enter them (*140,176*) (AIII). Decontamination of fungal-contaminated areas that cannot be extracted and replaced should be done using copper-8-quinolate (*179*) (BIII). Also, areas above false ceilings located under or adjacent to construction areas should be vacuumed (*174*) (BIII). Additionally, the ventilation, direction of airflow, and room pressurization should be tested and correctly adjusted before patients are allowed to enter (BIII).

Cleaning

HSCT centers should be cleaned ≥1 times/day with special attention to dust control (BIII). Exhaust vents, window sills, and all horizontal surfaces should be cleaned with cloths and mop heads that have been premoistened with an FDA- or Environmental Protection Agency (EPA)-registered hospital disinfectant (BIII). Thorough cleaning during and after any construction activity, including minor renovation projects, is critical (BIII).

HSCT center personnel should prohibit exposures of patients to such activities as vacuuming or other floor or carpet vacuuming that could cause aerosolization of fungal spores (e.g., *Aspergillus* species) (*140*) (AIII). Accordingly, doors to patient rooms should be closed when vacuuming HSCT center corridors. All vacuum cleaners used in the HSCT center should be fitted with HEPA filters. An FDA- or EPA-registered disinfectant (*246,247*) should be used daily for environmental disinfection and when wet vacuuming is performed in the HSCT center (BIII). If an HSCT center provides care for infants, phenolic disinfectants can be used to clean the floors only if the compound is diluted according to the product label; but phenolic compounds should not be used to clean basinets or incubators (*246*) (DIII).

Water leaks should be cleaned up and repaired as soon as possible but within 72 hours to prevent mold proliferation in floor and wall coverings, ceiling tiles, and cabinetry in and around all HSCT patients care areas (BIII). If cleanup and repair are delayed ≥72 hours after the water leak, the involved materials should be assumed to contain fungi and handled accordingly. Use of a moisture meter to detect water penetration of walls should be used whenever possible to guide decision-making (*238*) (BIII). For example, if the wall does not have <20% moisture content ≥72 hours after water penetration, it should be removed (BIII). Design and selection of furnishings should focus on creating and maintaining a dust-free environment. Flooring and finishes (i.e., wall coverings, window shades, and countertops) used in HSCT centers should be scrubbable, nonporous, easily disinfected, and they should collect minimal dust (BIII).

Isolation and Barrier Precautions

HSCT center personnel should follow published guidelines for hospital isolation practices, including CDC guidelines for preventing nosocomial infections (*62,140,248*) (AIII).

However, the efficacy of specific isolation and barrier precautions in preventing nosocomial infections among HSCT recipients has not been evaluated.

HSCT recipients should be placed in private (i.e., single-patient) rooms (BIII). If contact with body fluids is anticipated, standard precautions should be followed (AIII). These precautions include hand washing and wearing appropriate gloves, surgical masks or eye and face protection, and gowns during procedures and activities that are likely to generate splashes or sprays of blood, body fluids, secretions or excretions, or cause soiling of clothing (*62*). When indicated, HSCT recipients should also be placed on airborne, droplet, or contact precautions in addition to standard precautions (*62*) (AIII). Careful observation of isolation precautions is critical in preventing transmission of infectious agents among HSCT recipients, HCWs, visitors, and other HSCT recipients. Physicians are cautioned that HSCT recipients might have a prolonged or episodic excretion of organisms (e.g., CMV).

Researchers have proposed that HSCT recipients wear surgical mask and gloves when exiting their hospital rooms before engraftment (CIII). All HSCT recipients who are immunocompromised (phases I–III of immune system recovery) and candidates undergoing conditioning therapy should minimize the time spent in crowded areas of the hospital (e.g., waiting areas and elevators) (BIII) to minimize potential exposure to persons with CRV infections.

Hand Hygiene

Hand washing is the single-most critical and effective procedure for preventing nosocomial infection (*62*). All persons, but particularly HCWs, should wash their hands before entering and after leaving the rooms of HSCT recipients and candidates undergoing conditioning therapy (*62,249*) or before and after any direct contact with patients regardless of whether they were soiled from the patient, environment, or objects (AI). HSCT recipients should be encouraged to practice safe hand hygiene (e.g., washing hands before eating, after using the toilet, and before and after touching a wound) (BIII). Hand washing should be done with an antimicrobial soap and water (AIII); alternatively, use of hygienic hand rubs is another acceptable means of maintaining hand hygiene (*250,251*). If gloves are worn, HCWs should put them on in the patient's room after hand washing and then discard them in the same patient's room before washing hands again after exiting the room. When worn, gloves should always be changed between patients or when soiled before touching a clean area (e.g., change gloves after touching the perineum and before going to a "clean" area) (AIII). Appropriate gloves should be used by all persons when handling potentially contaminated biological materials (AII). Items worn on the hands and fingers (e.g., rings or artificial nails [*248,252*]) and adhesive bandage strips, can create a nidus for pathogenic organisms that is difficult to clean. Thus, HCWs should avoid wearing such items whenever possible (BII).

Equipment

All HSCT center personnel should sterilize or disinfect and maintain equipment and devices using only EPA-registered compounds as directed by established guidelines (*140,180,246,247,253–256*) (AIII). HSCT center personnel should monitor opened and unopened wound-dressing supplies (e.g., adhesive bandages [*257,258*] and surgical and elastic adhesive tape [*259*]) to detect mold contamination and prevent subsequent cutaneous transmission to patients (BII).

Monitoring should consist of discarding all bandages and wound dressings that are out of date, have damaged packaging, or are visually contaminated by construction debris or moisture (BIII). When arm boards are used to provide support for intravenous lines, only sterile dressing materials should be used (*260*), and arm boards should be changed frequently (e.g., daily) (BIII). Additionally, unsterile tongue depressors inserted into a piece of foam tubing should not be used as splints for intravenous and arterial catheter sites because these have been associated with an outbreak of fatal invasive nosocomial *Rhizopus microsporus* among preterm (i.e., very low-birth–weight) infants (*261*) (DII). HSCT centers should not install carpeting in hallways outside (DII) or in patient rooms (DIII) because contaminated carpeting has been associated with outbreaks of aspergillosis among HSCT recipients (*262,263*).

Plants, Play Areas, and Toys

Although to date, exposure to plants and flowers has not been conclusively reported to cause fungal infections among HSCT recipients, most researchers strongly recommend that plants and dried or fresh flowers should not be allowed in the rooms of hospitalized HSCT candidates undergoing conditioning therapy and HSCT recipients (phases I–III of immune system recovery) because *Aspergillus* species have been isolated from the soil of potted ornamental plants (e.g., cacti), the surface of dried flower arrangements, and fresh flowers (*140,174,178,264*) (BIII).

Play areas for pediatric HSCT recipients and candidates undergoing conditioning therapy should be cleaned and disinfected ≥1 times/week and as needed (BIII). Only toys, games, and videos that can be kept clean and disinfected should be allowed in the HSCT center (BIII). HSCT centers should follow published recommendations for washing and disinfecting toys (*265*) (BIII). All HSCT center toys, games, and videos should be routinely and thoroughly washed or wiped down when brought into the HSCT center and thereafter ≥1 times/week and as needed by using a nontoxic FDA- or EPA-registered disinfectant (*246,247,265*) followed by a water rinse (BIII). Cloth or plush toys should be washed in a hot cycle of a washing machine or dry-cleaned ≥1 times/week and as needed (BIII). Alternatively, machine washing in a cold cycle is acceptable if laundry chemicals for cold water washing are used in proper concentration (*265*). Hard plastic toys should be scrubbed with warm soapy water using a brush to clean crevices, rinsed in clean water, immersed in a mild bleach solution, which should be made fresh daily, for 10–20 minutes, rinsed again, and allowed to air dry (*246*). Alternatively, hard plastic toys can be washed in a dishwasher or hot cycle of a washing machine (BIII). Broviac dolls* should be disassembled upon completion of play and washed with a nontoxic FDA- or EPA-registered disinfectant (*246,247*), rinsed with tap water, and allowed to air dry before other children are allowed to play with them (BIII). Toys that cannot be washed, disinfected, or dry-cleaned after use should be avoided (BIII). Infants, toddlers, and children who put toys in their mouths should not share toys (*265*) (DIII). For children in isolation, researchers recommend the following:

- Disposable play items should be offered whenever possible (BIII).
- Before returning a washable toy used in an isolation room to the pediatric play room for use by another child, it should be cleaned again as previously described (BIII).

*Broviac dolls are used to demonstrate medical procedures (e.g., insertion of catheters) to children to lessen their fears.

- When a child is taken out of isolation, toys, games, and videos used during the period of isolation and that might serve as fomites for infection should be thoroughly disinfected with a nontoxic FDA- or EPA-registered disinfectant (*246,247,265*) (BIII). After use in isolation rooms, cloth or plush toys should be placed in a plastic bag and separated from unused toys. All cloth or plush toys used in isolation rooms should be washed in a washing machine or dry-cleaned before being used in a nonisolation room (BIII). Toys that cannot be disinfected or dry-cleaned after use in an isolation room should be discarded (BIII).

Water-retaining bath toys have been associated with an outbreak of *Pseudomonas aeruginosa* in a pediatric oncology ward (*266*); therefore, these toys should not be used by immunocompromised HSCT recipients and candidates (DII). Occupational and physical therapy items should be cleaned and disinfected as previously described (BIII). Soil-based materials (e.g., clay or potting soil) should be avoided (BIII).

HCWs

HSCT center personnel should have a written comprehensive policy regarding their immunizations and vaccinations, and that policy should meet current CDC, Advisory Committee on Immunization Practices, and Healthcare Infection Control Practices Advisory Committee recommendations (*267*) (BIII). Immunizations are needed to prevent transmission of vaccine-preventable diseases to HSCT recipients and candidates undergoing conditioning therapy. All HCWs with diseases transmissible by air, droplet, and direct contact (e.g., VZV, infectious gastroenteritis, HSV lesions of lips or fingers, and URIs) should be restricted from patient contact and temporarily reassigned to other duties (AI). HSCT center personnel should follow published recommendations regarding the duration of work restrictions for HCWs with infectious diseases (*268,269*) (BIII). HSCT center HCWs with bloodborne viruses (e.g., HIV or hepatitis B or C viruses) should not be restricted from patient contact (DIII) as long as they do not perform procedures that pose a high risk for injury that could result in patient exposure to the HCW's blood or body fluids. Work exclusion policies should be designed to encourage HCWs to report their illnesses or exposures (AII).

HSCT Center Visitors

Hospitals should have written policies for screening HSCT center visitors, particularly children, for potentially infectious conditions. Such screening should be performed by clinically trained HCWs (BII). Visitors who might have communicable infectious diseases (e.g., URIs, flu-like illnesses, recent exposure to communicable diseases, an active shingles rash whether covered or not, a VZV-like rash within 6 weeks of receiving a live-attenuated VZV vaccine, or a history of receiving an oral polio vaccine within the previous 3–6 weeks) should not be allowed in the HSCT center or allowed to have direct contact with HSCT recipients or candidates undergoing conditioning therapy (AII). No absolute minimum age requirement for HSCT center visitors exists; however, all visitors must be able to understand and follow appropriate hand washing and isolation precautions (AIII). The number of HSCT center visitors at any one time should be restricted to a number that permits the nursing staff to perform appropriate screening for contagious diseases and adequate instruction and supervision of hand washing, glove and mask use, and biosafety precautions (BIII).

Patient Skin and Oral Care

To optimize skin care, HSCT recipients should take daily showers or baths during and after transplantation (BIII), using a mild soap (BIII). Skin care during neutropenia should also include daily inspection of skin sites likely to be portals of infection (e.g., the perineum and intravascular access sites) (BIII). HSCT recipients and candidates undergoing conditioning therapy should maintain good perineal hygiene to minimize loss of skin integrity and risk for infection (BIII). To facilitate this precaution, HSCT center personnel should develop protocols for patient perineal care, including recommendations for gentle but thorough perineal cleaning after each bowel movement and thorough drying of the perineum after each urination (BIII). Females should always wipe the perineum from front to back after using the toilet to prevent fecal contamination of the urethra and urinary tract infections (AIII). Moreover, to prevent vaginal irritation, menstruating immunocompromised HSCT recipients should not use tampons (DIII) to avoid the risk for cervical and vaginal abrasions. Additionally, the use of rectal thermometers, enemas, suppositories, and rectal exams are contraindicated among HSCT recipients to avoid skin or mucosal breakdown (DIII).

All HSCT candidates and their caregivers should be educated regarding the importance of maintaining good oral and dental hygiene for at least the first year after HSCT to reduce the risk for oral and dental infections (AIII). For example, HSCT candidates should be informed that establishment of the best possible periodontal health before HSCT is a substantial step in avoiding short- and long-term oral infections and that maintenance of safe oral hygiene after HSCT can minimize the severity of infections and facilitate healing of mucositis, particularly before engraftment (BIII).

All HSCT candidates should receive a dental evaluation and relevant treatment before conditioning therapy begins (*270,271*) (AIII). Likely sources of dental infection should be vigorously eliminated (*271*) (AIII). For example, teeth with moderate to severe caries should be restored; ill-fitting dental prostheses should be repaired; and teeth compromised by moderate to severe periodontal disease should be extracted (*271*). Ideally, 10–14 days should elapse between the completion of tissue-invasive oral procedures and onset of conditioning therapy to allow for adequate healing and monitoring for postsurgical complications (AIII).

HSCT recipients with mucositis and HSCT candidates undergoing conditioning therapy should maintain safe oral hygiene by performing oral rinses 4–6 times/day with sterile water, normal saline, or sodium bicarbonate solutions (*270*) (AIII). HSCT recipients and candidates should brush their teeth ≥2 times/day with a soft regular toothbrush (*270*) (BIII). If the recipient cannot tolerate these brushings, use of an ultrasoft toothbrush or toothette (i.e., foam swab on a stick), can be used (CIII), but physicians should be aware that using the latter products are less desirable than using soft regular or ultrasoft toothbrushes because the toothettes remove less dental debris (*270*). Using toothpaste is optional, depending on the recipient's tolerance (*270*) (CIII). HSCT recipients and candidates undergoing conditioning therapy who are skilled at dental flossing should floss daily if this can be done without trauma (BIII). Routine dental supervision is advised to monitor and guide the patient's maintenance of oral and dental hygiene (BIII). To decrease the risk for mechanical trauma and infection of oral mucosa, fixed orthodontic appliances and space maintainers should not be worn from the start of conditioning therapy until preengraftment mucositis resolves, and these devices should not be worn during any subsequent periods of mucositis (*270*) (DIII). Dental and transplant teams and

the patient's community dentist should coordinate removal of these appliances and long-term rehabilitation of any oral lesions (BIII). However, patients who normally wear removable dental prostheses might be able to wear them during conditioning therapy before HSCT and during mucositis after HSCT, depending on the degree of tissue integrity at the denture-bearing sites and the ability of the patient to maintain denture hygiene on a daily basis (CIII).

Preventing Bacterial Intravascular Catheter-Related Infections

HSCT center personnel are advised to implement published guidelines for preventing intravascular device-related infections (*33*) (AIII). Contact with tap water at the central venous catheter site should be avoided (BIII). For long-term central venous access among children, HSCT physicians can use a totally implantable device among children aged <4 years if the anticipated duration of vascular access is >30 days (CII). However, such a device among children aged <4 years is not generally used as the actual HSCT infusion site because a) problems with skin fragility contraindicate repeated punctures over the port site and b) the port device might have an insufficient number of lumens for optimal patient management immediately after HSCT.

To prevent bloodstream infections associated with needleless intravenous access devices, HSCT recipients should a) cover and protect the catheter tip or end cap during bathing or showering to protect it from tap water contamination, b) change the device in accordance with manufacturers' recommendations, if available, and c) have a caregiver perform intravenous infusions whenever possible (*272,273*) (BII). Also, HSCT recipients and their caregivers should be educated regarding proper care of needleless intravenous access devices (*272*) (BII). No recommendation regarding the use of antibiotic-impregnated central venous catheters among HSCT recipients can be made because of lack of data.

Control of Specific Nosocomial Infections

Recommendations Regarding Legionella *Species*

HSCT physicians should always include Legionnaires' disease (LD) in the differential diagnosis of pneumonia among HSCT recipients (*140*) (AIII). Appropriate tests to confirm LD include a) culturing sputum, BAL, and tissue specimens; b) testing BAL specimens for *Legionellae* by direct fluorescent antibody; and c) testing for *Legionella pneumophila* serogroup 1 antigen in urine. The incubation period for LD is usually 2–10 days; thus, laboratory-confirmed legionellosis that occurs in a patient who has been hospitalized continuously for ≥10 days before the onset of illness is regarded as a definite case of nosocomial LD, and a laboratory-confirmed infection that occurs 2–9 days after hospital admission is a possible case of nosocomial LD (*140*). When a case of laboratory-confirmed nosocomial LD (*274,275*) is identified in a person who was in the inpatient HSCT center during all or part of the 2–10 days before illness onset, or if two or more cases of laboratory-confirmed LD occur among patients who had visited an outpatient HSCT center, hospital personnel should

- report the case(s) to the local or state health department if the disease is reportable in that state or if assistance is needed (*140*) (AIII); and

- in consultation with the hospital infection control team, conduct a thorough epidemiologic and environmental investigation to determine the likely environmental source(s) of *Legionella* species (e.g., showers, tap water faucets, cooling towers, and hot water tanks) (*274,276*) (AI).

The source of *Legionella* infection should be identified and decontaminated or removed (AIII). Extensive hospital investigations of an isolated case of possible nosocomial LD might not be indicated if the patient has had limited contact with the inpatient center during most of the incubation period (CIII). Because HSCT recipients are at much higher risk for disease and death from legionellosis compared with other hospitalized persons (*274*), periodic routine culturing for *Legionellae* in water samples from the center's potable water supply could be regarded as part of an overall strategy for preventing LD in HSCT centers (CIII). However, the optimal methodology (i.e., frequency or number of sites) for environmental surveillance cultures in HSCT centers has not been determined, and the cost-effectiveness of this strategy has not been evaluated. Because HSCT recipients are at high risk for LD and no data were found to determine a safe concentration of *Legionellae* organisms in potable water, the goal, if environmental surveillance for *Legionellae* is undertaken, should be to maintain water systems with no detectable organisms (AIII). Physicians should suspect legionellosis among HSCT recipients with nosocomial pneumonia even when environmental surveillance cultures do not yield *Legionellae* (AIII). If *Legionella* species are detected in the water supplying an HSCT center, the following should be done until *Legionella* species are no longer detected by culture:

- The water supply should be decontaminated (*140*) (AII).
- HSCT recipients should be given sponge baths with water that is not contaminated with *Legionella* species (e.g., not with the HSCT center's *Legionella* species-contaminated potable water system) (BIII).
- Patients should not take showers in LD-contaminated water (DIII).
- Water from faucets containing LD-contaminated water should not be used in patient rooms or the HSCT center and outpatient clinic to avoid creating infectious aerosols (CIII).
- HSCT recipients should be given sterile water instead of tap water for drinking, brushing teeth, or flushing nasogastric tubes during Legionellosis outbreaks (BIII).

HSCT center personnel should use only sterile water (i.e., not distilled unsterile water) for rinsing nebulization devices and other semicritical respiratory-care equipment after cleaning or disinfecting and for filling reservoirs of nebulization devices (*140*) (BII). HSCT centers should not use large-volume room air humidifiers that create aerosols (e.g., by Venturi principle, ultrasound, or spinning disk) and, thus, are actually nebulizers (*140*) (DI) unless these humidifier or nebulizers are sterilized or subjected to daily high-level disinfection and filled with sterile water only (*140*) (CIII).

When a new hospital with an HSCT center is constructed, the cooling towers should be placed so that the tower drift is directed away from the hospital's air-intake system, and the cooling towers should be designed so that the volume of aerosol drift is minimized (*140*) (BII). For operational hospital cooling towers, hospitals should

- install drift eliminators,

- regularly use an effective biocide,
- maintain cooling towers according to the manufacturer's recommendations, and
- keep adequate maintenance records (*140*) (BII).

HSCT physicians are encouraged to consult published recommendations regarding preventing nosocomial Legionellosis (*140,277*) (BIII). No data were found to determine whether drinking tap water poses a risk for *Legionella* exposure among HSCT recipients in the absence of an outbreak.

Recommendations Regarding Methicillin-Resistant Sta. aureus

HSCT center HCWs should follow basic infection control practices (e.g., hand washing between patients and use of barrier precautions, including wearing gloves whenever entering the methicillin-resistant *Sta. aureus* [MRSA] infected or colonized patient's room); these practices are essential for MRSA control (*62*) (AII). If MRSA is a substantial problem in the HSCT center and evidence exists of ongoing MRSA transmission, MRSA infected or colonized patients should be treated as a cohort (e.g., cared for exclusively by a limited number of HCWs) (BIII). HSCT transplant recipients with recurrent *Sta. aureus* infections should undergo extensive evaluation for persistent colonization, including cultures of nares, groin, axilla, and ostomy sites (e.g., tracheostomy or gastrointestinal tube) (BIII). For patients with recurrent MRSA infection, elimination of the carrier state should be attempted by applying a 2% mupirocin calcium ointment to the nares (BIII), although this strategy has been only marginally effective in certain institutions (*278*) (Appendix). High-level mupirocin-resistant MRSA has been reported in Europe, the Middle East, and South America (*279–283*) but is uncommon in the United States. As with any antibiotic, incorrect or overuse of mupirocin can result in mupirocin-resistant *Staphylococci*; therefore, mupirocin use should be reserved for infection control strategies only (*279,280*). For patients who fail mupirocin, physicians have used bacitracin, TMP-SMZ, or rifampin administered with another antibiotic, but no standardized protocol using these drugs for this indication has been evaluated and no recommendations can be made because of lack of data. Selection of a systemic antibiotic should be guided by susceptibility patterns.

Intravascular cannulas or other implantable devices that are infected or colonized with MRSA should be removed (AIII). Patients with MRSA should be placed under contact precautions until all antibiotics are discontinued and until three consecutive cultures, taken ≥1 weeks apart, are negative (*62*) (BIII). Screening cultures for MRSA include the anterior nares, any body site previously positive for MRSA, and any wounds or surgical sites.

Recommendations Regarding Staphylococcus *Species with Reduced Susceptibility to Vancomycin*

All HSCT centers should have sufficient laboratory capability to identify all *Staphylococci* isolates and their susceptibility patterns to antibiotics, including vancomycin (*284,285*) (AIII). Additionally, all HSCT center personnel should conduct routine surveillance for the emergence of *Staphylococcus* species strains with reduced susceptibility to vancomycin (*285,286*) (AIII). Reduced susceptibility should be considered for all *Sta. aureus* strains that have a vancomycin MIC of ≥4 µg/mL and all coagulase-negative

Staphylococci that have a vancomycin MIC of ≥8 µg/mL. If repeat testing of the organism in pure culture confirms the genus, species, and elevated vancomycin MICs, the following steps should be taken (*287*):

- The laboratory should immediately contact hospital infection control personnel, the patient's clinical center, and the patient's attending physician, as well as the local or state health department, and CDC's Hospital Infections Program Help Desk ([404] 639-6106 or [800] 893-0485) (*284,285,287,288*) (AIII).
- The HSCT center's infection control personnel, in collaboration with appropriate authorities (i.e., state and local health departments and CDC) should promptly initiate an epidemiologic and laboratory investigation (*287,288*) (AIII) and follow published guidelines for the control of such species (*285,287,288*) (BIII).
- Medical and nursing staff should
  - — institute contact precautions (e.g., wearing of gown and gloves, using antibacterial soap for hand washing, and wearing masks when contamination of the HCW with secretions is likely) as recommended for multidrug-resistant organisms (*62,284,287*);
  - — minimize the number of persons with access to colonized or infected patients (*287*); and
  - — treat as a cohort colonized or infected patients (e.g., care for them exclusively with a limited number of HCWs) (*286,287*) (AIII).
- If a patient in an HSCT center is colonized or infected with *Staphylococci* that have reduced susceptibility to vancomycin, the infection control personnel should follow published guidelines for the control of such species (*285,287,288*) (BIII).

Avoiding overuse and misuse of antibiotics will decrease the emergence of *Staphylococcus* species with reduced susceptibility to vancomycin (*286,287*). Therefore, medical and ancillary staff members who are responsible for monitoring antimicrobial use patterns in the facility should routinely review vancomycin-use patterns (*284,285,287*) (AIII). Additionally, HSCT center personnel should institute prudent use of all antibiotics, particularly vancomycin, to prevent the emergence of *Staphylococcus* with reduced susceptibility to vancomycin (*284,285,287–289*) (AII). Intravascular cannulas or other implantable devices that are infected or colonized with *Staphylococcus* species strains with reduced susceptibility to vancomycin should be removed (AIII).

Recommendations Regarding VRE

Use of intravenous vancomycin is associated with VRE emergence. Vancomycin and all other antibiotics, particularly antianaerobic agents (e.g., metronidazole and third-generation cephalosporins) must be used judiciously (*284,290–292*) (AII). Oral vancomycin use can be limited by treating recurrences of *Cl. difficile* diarrhea with oral metronidazole instead of vancomycin (BIII). Physicians have placed patients with a history of VRE or VRE colonization into continuous isolation during clinic visits and hospitalizations; however, this practice is controversial because certain non-HSCT recipients might clear VRE from their stools. No recommendation regarding use of continuous

isolation among HSCT recipients can be made because of lack of data. To control VRE exposure, strict adherence to the following standard infection control measures is necessary (*292*) (AI):

- Wash hands with antibacterial soap before entering and after leaving HSCT recipients' rooms, particularly those who have VRE colonization or infection; alternatively, wash hands with a waterless antiseptic agent (e.g., an alcohol-based rinse or gel) (*250*).
- Whenever possible, treat as a cohort patients who are known to be colonized or infected with VRE (*290*).
- Disinfect patient rooms and equipment (*291,293*), including surfaces of the hospital ward environment (e.g., floors, walls, bed frames, doors, bathroom surfaces) with an FDA- or EPA-registered disinfectant (*246,247*). A nontoxic disinfectant should be used for pediatric areas (BIII).
- Place patients with VRE under contact precautions until all antibiotics are discontinued (CIII) and repeated cultures are negative (*62*) (BIII). HCWs should always wear gloves when in the VRE patient or carrier's room and discard gloves in the patient's room before exiting.

No evidence exists that treating VRE carriers is beneficial; therefore, chronic antibiotic treatment of carriers is not recommended (DIII). HSCT recipients and candidates should be screened for VRE colonization at the time of interfacility transfer to allow for immediate institution of appropriate infection control practices and to minimize transmission of VRE between and within facilities (*294*) (BII). However, the role of outpatient surveillance in VRE control is unknown; such surveillance is costly and should not be undertaken in nonoutbreak settings (DIII). A history of having resolved VRE bacteremia or being a VRE carrier are not contraindications to HSCT (BIII).

Recommendations Regarding Cl. difficile

HSCT physicians should follow published recommendations for preventing and controlling *Cl. difficile* disease, including minimizing the duration of antibiotic therapy and number of antibiotics used for any indication (*295,296*) (AIII). All patients with *Cl. difficile* disease should be placed under contact precautions for the duration of illness (*62*) (AII). All HCWs who anticipate contact with a *Cl. difficile*-infected patient or the patient's environment or possessions should put on gloves before entering the patient's room (*62,295–298*) and before handling the patient's secretions and excretions (AI). During *Cl. difficile* outbreaks, HSCT center personnel should restrict use of antibiotics (e.g., clindamycin) (*299*) (BII). To prevent transmission of *Cl. difficile* to patients during nosocomial *Cl. difficile* outbreaks, HSCT center HCWs should a) use disposable rectal thermometers or tympanic thermometers; b) disinfect gastrointestinal endoscopes with 2% glutaraldehyde immersion for 10 minutes or use an equivalent disinfectant strategy (*255,256*); and c) perform surface sterilization of the hospital ward environment (e.g., floors, walls, bed frames, doors, bathroom surfaces) with an FDA- or EPA-registered sterilant (e.g., phosphate-buffered sodium hypochlorite solution [1,660 ppm available chloride]; unbuffered hypochlorite solution [500 ppm available chloride]; 0.04% formaldehyde and 0.03% glutaraldehyde [*255,295,300*]; or ethylene oxide [*247,296*]) (BII). Additionally, physicians should treat patients with *Cl. difficile* disease with antibiotics as recommended in published reports (*62,295*) (BII).

Certain researchers also recommend antibiotic treatment of *Cl. difficile* carriers (*301*). However, other researchers have reported that treatment of asymptomatic *Cl. difficile* carriers with metronidazole is not effective and that treatment with vancomycin is only effective temporarily (i.e., <2 months after treatment) (*302*). Consequently, no recommendation regarding treatment of asymptomatic *Cl. difficile* carriers can be made. Similarly, although symptomatic *Cl. difficile* disease recurrence or relapse occurs among 7%–20% of patients (*295*), data are insufficient to make a recommendation for preventing multiple *Cl. difficile* relapses.

The following practices are not recommended for *Cl. difficile* control:

- routine stool surveillance cultures for *Cl. difficile* for asymptomatic patients or HCWs, even during outbreaks (DIII);
- culturing HCWs' hands for *Cl. difficile* (DIII); or
- treating patients presumptively for *Cl. difficile* disease pending toxin results (DIII), unless the patient is very sick with a compatible syndrome or the hospital has a high prevalence of *Cl. difficile* (CIII).

Prophylactic use of lyophilized *Saccharomyces boulardii* to reduce diarrhea among antibiotic recipients is not recommended because this therapy is not associated with a substantial reduction in diarrhea associated with *Cl. difficile* disease (*303*) and has been associated with *Saccharomyces boulardii* fungemia (*304*) (DII).

Recommendations Regarding CRV Infections

Physicians should institute appropriate precautions and infection control measures for preventing nosocomial pneumonia among hospitalized HSCT recipients and candidates undergoing conditioning therapy, particularly during community or nosocomial CRV outbreaks (*140*) (AIII). Patients with URI or LRI symptoms should be placed under a) contact precautions for most viral respiratory infections including varicella; b) droplet precautions for influenza or adenovirus; or c) airborne precautions for measles or varicella to avoid transmitting infection to other HSCT candidates and recipients as well as to HCWs and visitors (BIII). Identifying HSCT recipients with RSV infection and placing them under contact precautions immediately (AIII) to prevent nosocomial transmission is critical. When suctioning the respiratory tract of patients with URI or LRI symptoms, HCWs should wear gowns, surgical masks, and eye protection to avoid contamination from the patient's respiratory secretions. All protective clothing (e.g., gown, gloves, surgical mask, and eye protection) should be put on when entering a patient's room and discarded in the same room before exiting; protective clothing should always be changed between patient rooms (*140*) (AIII). When caring for an HSCT recipient or candidate undergoing conditioning therapy with URI or LRI, HCWs and visitors should change gloves and wash hands a) after contact with a patient; b) after handling respiratory secretions or objects contaminated with secretions from one patient and before contact with another patient, object, or environmental surface; and c) between contacts with a contaminated body site and the respiratory tract of or respiratory device used on the same patient (*140*) (AII). This practice is critical because most respiratory infections are usually transmitted by contact, particularly by hand to nose and eye. Therefore just wearing a mask, without appropriate hand washing, glove-wearing, or use of eye protection is insufficient to prevent transmission of CRV infections.

Researchers have proposed that HSCT recipients or candidates undergoing conditioning therapy be placed under contact precautions during nosocomial outbreaks (*131*) (CIII). Even when no nosocomial or community outbreak of CRV infections exists, all persons who enter the HSCT center should be screened daily for URI symptoms, including visitors and HCWs (BIII). Researchers also describe systems where HCWs provide daily verification (e.g., using sign-in sheets) that they are free of URI symptoms before being allowed to provide HSCT patient care. HCWs and visitors with URI symptoms should be restricted from contact with HSCT recipients and candidates undergoing conditioning therapy to minimize the risk for CRV transmission (*131*) (AIII). All HCWs with URI symptoms should be restricted from patient contact and reassigned to nonpatient care duties until the HCW's symptoms resolve (BIII). Visitors with URI symptoms should be asked to defer their visit to the HSCT center (*131*) until their URI symptoms resolve (BIII).

Respiratory secretions of any hospitalized HSCT candidate or recipient with signs or symptoms of CRV infection should be tested promptly by viral culture and rapid diagnostic tests for CRV (BIII). Appropriate samples include nasopharyngeal washes, swabs, aspirates, throat swabs, and BAL fluid. This practice is critical because preemptive treatment of certain CRVs (e.g., influenza and RSV) (*133*) might prevent severe disease and death among HSCT recipients. Viral shedding among HSCT recipients with CRV infection has been reported to last ≤4 months for influenza (*143*), ≤2 years for adenovirus (*305,306*), and ≤22 days for RSV (*136*); however, RSV viral shedding has been reported to last 112 days in a child with severe combined immunodeficiency (*307*). Therefore, to prevent nosocomial transmission of CRV (*136*), HSCT center HCWs should recognize that prolonged CRV shedding can occur when determining the duration of appropriate precautions for CRV-infected HSCT recipients or candidates undergoing conditioning therapy (CIII). HSCT centers should use serial testing by using cultures from nasopharyngeal swabs, throat swabs or aspirates, or rapid antigen tests to help determine whether patients have stopped shedding influenza virus (BIII). Researchers have proposed that HSCT physicians conduct routine CRV surveillance among HSCT recipients to detect outbreaks and implement infection control measures as early as possible (CIII). During RSV season, HSCT recipients and candidates with signs or symptoms should be tested for RSV infection (i.e., the presence of RSV antigen in respiratory secretions tested by enzyme-linked immunosorbent assay and viral culture) starting with admission to the HSCT center. All patients who are RSV-antigen positive should be treated as a cohort during nosocomial RSV outbreaks because this practice reduces nosocomial RSV transmission (*130,131*) (BII). Symptomatic HCWs should be excluded from patient contact until symptoms resolve. HCWs and visitors with infectious conjunctivitis should be restricted from direct patient contact until the drainage resolves (i.e., usually, 5–7 days for adenovirus) and the ophthalmology consultant concurs that the infection and inflammation have resolved (*268*) (AII) to avoid possible transmission of adenovirus to HSCT recipients.

Preventing CRV exposure among HSCT recipients after hospital discharge is more challenging because of high CRV prevalence. Preventive measures should be individualized in accordance with the immunologic status and tolerance of the patient. In outpatient waiting rooms, patients with CRV infections should be separated to the extent possible from other patients (BIII).

Recommendations Regarding TB

HSCT candidates should be screened for TB by careful medical history and chart review to ascertain any history of prior TB exposure (AIII) because immunocompromised persons have higher risk for progression from latent TB infection to active disease (*244*). Also, physicians can administer a tuberculin skin test (TST) using the Mantoux method with five tuberculin units of purified protein derivative (CIII); but because of a patient's immunocompromise, this test might not be reliable. If a TST is administered, either the Tubersol® or Aplisol® formulation of purified protein derivative can be used (*244,308*). Persons with a recently positive TST or a history of a positive TST and no prior preventive therapy should be administered a chest radiograph and evaluated for active TB (*309*) (AI). For immunocompromised persons, a positive TST is defined as ≥5 mm of induration (*309,310*) because of their decreased ability to mount a delayed hypersensitivity response (CIII). Because immunosuppressive therapy decreases the sensitivity of the TST, HSCT physicians should not rely solely on the TST to determine whether latent TB infection is present and whether preventive therapy should be administered to HSCT recipients or candidates (DIII). Instead, a full 9-month course of isonicotinic acid hydrazide preventive therapy should be administered to immunocompromised HSCT recipients or candidates who have been substantially exposed to someone with active, infectious (i.e., sputum-smear positive) pulmonary or laryngeal TB, regardless of the HSCT recipient's or candidate's TST status (*309*) (BIII). A full 9-month course of isonicotinic acid hydrazide preventive therapy should also be administered to HSCT recipients or candidates with a positive TST who were not previously treated and have no evidence of active TB disease (*309*) (AIII) (Appendix). Routine anergy screening might not be reliable among HSCT recipients and candidates undergoing conditioning therapy and, therefore, is not recommended (DIII). An HSCT should not be canceled or delayed because of a positive TST (DIII).

Use of a 2-month course of a daily pyrazinamide/rifampin (PZA/RIF) regimen has been recommended as an alternate preventive therapy for persons with TB (*309*). However, limited data were found regarding safety and efficacy of this regimen among non-HIV–infected persons. Furthermore, rifampin has substantial drug interactions with certain medications, including cyclosporine, tacrolimus (FK506), corticosteroids, fluconazole, and pain medications. Therefore, routine use of the 2-month PZA/RIF prophylactic regimen among HSCT recipients is not recommended (DIII). However, this regimen can be used for HSCT candidates who are not at risk for serious rifampin drug interactions and whose HSCT is not scheduled until ≥2 weeks after completion of the 2-month PZA/RIF course (CIII). This delay will diminish the possibility of adverse effects of rifampin on drugs used for routine HSCT OI prophylaxis (e.g., fluconazole) (*311*). An HSCT candidate or recipient who has been exposed to an active case of extrapulmonary, and therefore, noninfectious TB does not require preventive therapy (DIII).

HSCT center personnel should follow guidelines regarding the control of TB in healthcare facilities (*244,245*), including instituting airborne precautions and negative-pressure rooms for patients with suspected or confirmed pulmonary or laryngeal TB (*62,244*) (AII). HCWs should wear N95 respirators, even in isolation rooms, to protect themselves from possible TB transmission from patients with active pulmonary or laryngeal TB, particularly during cough-inducing procedures (*62,244,245,312*) (AIII). To be maximally effective, respirators (e.g., N95) must be fit-tested, and all respirator users

must be trained to use them correctly (*243*) (AIII). Unless they become soiled or damaged, changing N95 respirators between patient rooms is not necessary (DIII). Bacillus of Calmette and Guérin vaccination is contraindicated among HSCT candidates and recipients because it might cause disseminated or fatal disease among immunocompromised persons (*313,314*) (EII). No role has been identified for chronic suppressive therapy or follow-up surveillance cultures among HSCT recipients who have a history of successfully treated TB (DIII).

Infection Control Surveillance

HSCT center personnel are advised to follow standard guidelines for surveillance of antimicrobial use and nosocomial pathogens and their susceptibility patterns (*315*) (BIII). HSCT center personnel should not perform routine fungal or bacterial cultures of asymptomatic HSCT recipients (*166,167*) (DII). In the absence of epidemiologic clusters of infections, HSCT center personnel should not perform routine periodic bacterial surveillance cultures of the HSCT center environment or of equipment or devices used for respiratory therapy, pulmonary-function testing, or delivery of inhalation anesthesia (*140*) (DIII). Researchers recommend that hospitals perform routine sampling of air, ceiling tiles, ventilation ducts, and filters to test for molds, particularly when construction or renovation occurs near or around the rooms of immunocompromised patients (*167,174*) or when clinical surveillance demonstrates a possible increase in mold (i.e., aspergillosis) cases (CIII). Strategies that might decrease fungal spores in the ventilation system include eliminating access of birds (i.e., primarily pigeons) to air-intake systems, removing bird droppings from the air-intake ducts, and eliminating moss from the hospital roof (*174*). Furthermore, in the absence of a nosocomial fungal outbreak, HSCT centers need not perform routine fungal cultures of devices and dust in the rooms of HSCT recipients and candidates undergoing conditioning therapy (DIII). HSCT center personnel should routinely perform surveillance for the number of aspergillosis cases occurring among HSCT recipients, particularly during hospital construction or renovation (BIII). A two-fold or greater increase in the attack rate of aspergillosis during any 6-month period indicates that the HSCT center environment should be evaluated for breaks in infection control techniques and procedures and that the ventilation system should be investigated carefully (*174*) (BIII).

STRATEGIES FOR SAFE LIVING AFTER HSCT — PREVENTING EXPOSURE AND DISEASE

Avoiding Environmental Exposures

HSCT recipients and candidates undergoing conditioning therapy, particularly allogeneic recipients, and parents of pediatric HSCT recipients and candidates should be educated regarding strategies to avoid environmental exposures to opportunistic pathogens (AIII).

Preventing Infections Transmitted by Direct Contact

HSCT recipients and candidates should wash their hands thoroughly (i.e., with soap and water) and often. For example, hands should be washed

- before eating or preparing food;
- after changing diapers;
- after gardening or touching plants or dirt;
- after touching pets or animals;
- after touching secretions or excretions or items that might have had contact with human or animal stool (e.g., clothing, bedding, toilets, or bedpans);
- after going outdoors; and
- before and after touching wounds (*249*) (AIII).

Conscientious hand washing is critical during the first 6 months after HSCT and during other periods of substantial immunosuppression (e.g., GVHD, systemic steroid use, or relapse of the underlying disease for which the transplant was performed) (AIII). Pediatric HSCT recipients and candidates should be supervised by adults during hand washing to ensure thorough cleaning (*316*) (BIII). Hand washing should be performed with an antimicrobial soap and water (AIII); alternatively, use of hygienic hand rubs is an acceptable means of maintaining hand hygiene (*250,251*). HSCT recipients who visit or live on farms should follow published recommendations for preventing cryptosporidiosis (*5,316,317–319*) (BIII).

Preventing Respiratory Infections

To prevent respiratory infections after hospital discharge, HSCT recipients should observe the following precautions:

- Frequent and thorough hand washing is critical (BIII), but HSCT recipients should also avoid touching their mucus membranes, unless they have washed their hands first, to avoid inoculating themselves with CRV.
- HSCT recipients should avoid close contact with persons with respiratory illnesses (BIII). When close contact is unavoidable, those persons with respiratory illnesses should be encouraged to wash their hands frequently and to wear surgical masks or, at a minimum, smother their sneezes and coughs in disposable tissues. Alternatively, the HSCT recipient can wear a surgical mask (CIII).
- HSCT recipients should avoid crowded areas (e.g., shopping malls or public elevators) where close contact with persons with respiratory illnesses is likely (BIII).
- HSCT candidates or recipients should be advised that certain activities and occupations (e.g., work in health-care settings, prisons, jails, or homeless shelters) can increase their risk for TB exposure (BIII). In deciding whether a patient should continue activities in these settings, physicians should evaluate the patient's specific duties, the precautions used to prevent TB exposure in the workplace, and the prevalence of TB in the community. The decision to continue or terminate such activities should be made jointly between patient and physician (BIII). HSCT recipients should avoid exposure to persons with active tuberculosis, particularly during the first 6 months after HSCT and during other periods of substantial immunosuppression (e.g., GVHD, systemic steroid use, or relapse of the underlying disease for which the transplant was performed) (BIII).

Researchers report that allogeneic recipients should avoid construction or excavation sites or other dust-laden environments for the first 6 months after HSCT and during other periods of substantial immunosuppression (e.g., GVHD, systemic steroid use, or relapse of the underlying disease for which the transplant was performed) to avoid exposures to molds (CIII). Researchers also report that outpatient HSCT recipients should be advised of travel routes to the HSCT center that will avoid or minimize exposure to construction sites (CIII).

Coccidioidomycosis is uncommon after allogeneic HSCT; however, researchers report that HSCT recipients traveling to or residing in coccidioidomycosis-endemic areas (e.g., the American southwest, Mexico, and Central and South America) should avoid or minimize exposure to disturbed soil, including construction or excavation sites, areas with recent earthquakes, farms, or other rural areas (CIII). Histoplasmosis (*Histoplasma capsulatum*) after allogeneic HSCT is also rare; however, researchers report that HSCT recipients in histoplasmosis-endemic areas should avoid exposure to chicken coops and other bird-roosting sites and caves for the first 6 months after HSCT and during periods of substantial immunosuppression (e.g., GVHD, systemic steroid use, or relapse of the underlying disease for which the transplant was performed) (CIII).

Smoking tobacco and exposure to environmental tobacco smoke are risk factors for bacterial and CRV infections among healthy adults and children (*320–325*); consequently, logic dictates that physicians advise HSCT recipients not to smoke and to avoid exposure to environmental tobacco smoke (CIII). However, no data were found that specifically assess whether smoking or environmental smoke exposure are risk factors for OIs among HSCT recipients. Researchers have reported that marijuana smoking might be associated with generation of invasive pulmonary aspergillosis among immunocompromised persons, including HSCT recipients (*326–329*). Therefore, HSCT recipients should refrain from smoking marijuana to avoid *Aspergillus* species exposure (*326,330–334*) (BIII).

Preventing Infections Transmitted Through Direct Contact and Respiratory Transmission

Researchers have proposed that immunocompromised HSCT recipients and candidates who are undergoing conditioning therapy avoid gardening or direct contact with soil, plants, or their aerosols to reduce exposure to potential pathogens (e.g., *To. gondii*, *Hi. capsulatum*, *Cryptococcus neoformans*, *Nocardia* species, and *Aspergillus* species) (CIII). HSCT recipients, particularly allogeneic recipients, could wear gloves while gardening or touching plants or soil (*335*) (CIII), and they should avoid creating plant or soil aerosols (BIII). Additionally, they should always wash their hands afterwards (*335*) and care for skin abrasions or cuts sustained during soil or plant contact (AIII).

Persons whose occupations involve animal contact (e.g., veterinarians, pet store employees, farmers, or slaughterhouse workers) could be at increased risk for toxoplasmosis and other zoonotic diseases. Although data are insufficient to justify a general recommendation against HSCT recipients working in such settings, these exposures should be avoided during the first 6 months after HSCT and during other periods of substantial immunosuppression (e.g., GVHD, systemic steroid use, or relapse of the underlying disease for which the transplant was performed) (BIII).

Safe Sex

Sexually active HSCT recipients should avoid sexual practices that could result in oral exposure to feces (*5,316*) (AIII). Sexually active patients who are not in long-term

monogamous relationships should always use latex condoms during sexual contact to reduce their risk for exposure to CMV, HSV, HIV, hepatitis B and C, and other sexually transmitted pathogens (AII). However, even long-time monogamous partners can be discordant for these infections. Therefore, during periods of immunocompromise, sexually active HSCT recipients in such relationships should consider using latex condoms during sexual contact to reduce the risk for exposure to these sexually transmitted infections (CIII).

Pet Safety

Preventing Pet-Transmitted Zoonotic Infections

HSCT physicians should advise recipients and candidates undergoing conditioning therapy of the potential infection risks posed by pet ownership; however, they should not routinely advise HSCT recipients to part with their pets, with limited exceptions. Generally, immunocompromised HSCT recipients and candidates undergoing conditioning therapy should minimize direct contact with animals (*336,337*), particularly those animals that are ill (e.g., with diarrhea) (*335*) (BIII). Immunocompromised persons who choose to own pets should be more vigilant regarding maintenance of their pet's health than immunocompetent pet owners (BIII). This recommendation means seeking veterinary care for their pet early in the pet's illness to minimize the possible transmission of the pet's illness to the owner (*335*) (BIII). Feeding pets only high-quality commercial pet foods reduces the possibility of illness caused by spoiled or contaminated foods, thus reducing the possibility of transmitting illness from the pet to the HSCT recipient. If eggs, poultry, or meat products are given to the pet as supplements, they should be well-cooked. Any dairy products given to pets should be pasteurized (*335*) (BIII). Pets should be prevented from drinking toilet bowl water and from having access to garbage; pets should not scavenge, hunt, or eat other animals' feces (*335*) (BIII).

If HSCT recipients have contact with pets or animals, they should wash their hands after handling them (particularly before eating) and after cleaning cages; HSCT recipients should avoid contact with animal feces to reduce the risk for toxoplasmosis, cryptosporidiosis, salmonellosis, and campylobacteriosis (*335*) (BIII). Adults should supervise hand washing of pediatric HSCT recipients (BIII). Immunocompromised HSCT recipients and candidates should not clean pet litter boxes or cages or dispose of animal waste (DIII). If this cannot be avoided, patients should wear disposable gloves during such activities and wash their hands thoroughly afterwards (BIII). Immunocompromised HSCT recipients and candidates should avoid adopting ill or juvenile pets (e.g., aged <6 months for cats) (*335*) and any stray animals (*5,316*) (BIII). Any pet that experiences diarrhea should be checked by a veterinarian for infection with *Cryptosporidium* (*5,316*), *Giardia* species (*335*), *Salmonella* , and *Campylobacter* (*5,335,337*) (BIII).

Immunocompromised HSCT recipients and candidates should not have contact with reptiles (e.g., snakes, lizards, turtles, or iguanas) (DII) to reduce their risk for acquiring salmonellosis (*335,338–341*). Additionally, patients should be informed that salmonellosis can occur from fomite contact alone (*342*). Therefore, HSCT recipients and candidates should avoid contact with a reptile, its food, or anything that it has touched, and if such contact occurs, recipients and candidates should wash their hands thoroughly afterwards (AIII). Immunocompromised HSCT recipients and candidates should avoid contact with ducklings and chicks because of the risk for acquiring *Salmonella* or

Campylobacter species infections (*338,343*) (BIII). Immunocompromised HSCT recipients and candidates should avoid contact with exotic pets (e.g., nonhuman primates) (BIII). Bird cage linings should be cleaned regularly (e.g., daily) (*337*). All persons, but particularly immunocompromised HSCT candidates and recipients, should wear gloves whenever handling items contaminated with bird droppings (*337*) (BIII) because droppings can be a source of *Cryptococcus neoformans*, *Mycobacterium avium*, or *Hi. capsulatum*. However, routine screening of healthy birds for these diseases is not recommended (*335*) (DIII). To minimize potential exposure to *Mycobacterium marinum*, immunocompromised HSCT recipients and candidates should not clean fish tanks (DIII). If this task cannot be avoided, patients should wear disposable gloves during such activities and wash their hands thoroughly afterwards (*335,337*) (BIII).

Preventing Toxoplasmosis

The majority of toxoplasmosis cases in the United States is acquired through eating undercooked meat (*335,337*). However, all HSCT recipients and candidates, particularly those who are *To. gondii* seronegative, should be informed of the risks for contracting toxoplasmosis from cat feces (BIII), but need not be advised to give away their cats (DII). For households with cats, litter boxes should not be placed in kitchens, dining rooms, or other areas where food preparation and eating occur (*335*). Additionally, litter boxes should be cleaned daily by someone other than the HSCT recipient during the first 6 months after HSCT and during periods of substantial immunosuppression (e.g., GVHD, steroid use, or relapse of the underlying disease for which the transplant was performed) to reduce the risk for transmitting toxoplasmosis to the HSCT recipient (BIII). Daily litter box changes will minimize the risk for fecal transmission of *To. gondii* oocysts, because fecal oocysts require ≥2 days of incubation to become infectious. If HSCT recipients perform this task during the first 6 months after HSCT and during subsequent periods of substantial immunocompromise (e.g., during GVHD, systemic steroid use, or relapse of the underlying neoplastic disease for which the transplant was performed), they should wear disposable gloves (*335*). Gloves should be discarded after a single use (BIII). Soiled, dried litter should be disposed of carefully to prevent aerosolizing the *To. gondii* oocysts (BIII). Cat feces (but not litter) can be flushed down the toilet (BIII). Also, persons who clean cat litter, particularly HSCT recipients, should wash their hands thoroughly with soap and water afterwards to reduce their risk for acquiring toxoplasmosis (BIII).

HSCT recipients and candidates with cats should keep their cats inside (BIII) and should not adopt or handle stray cats (DIII). Cats should be fed only canned or dried commercial food or well-cooked table food, not raw or undercooked meats, to eliminate the possibility of causing an illness that could be transmitted from the cat to the HSCT recipient (BIII). Pet cats of HSCT recipients do not need to be tested for toxoplasmosis (EII). Playground sandboxes should be kept covered when not in use to prevent cats from soiling them (BIII). HSCT recipients and candidates undergoing conditioning therapy should avoid drinking raw goat's milk to decrease the risk for acquiring toxoplasmosis (BIII).

Water and Other Beverage Safety

Although limited data were found regarding the risks for and epidemiology of *Cryptosporidium* disease among HSCT recipients, HSCT recipients are prudent to avoid possible exposures to *Cryptosporidium* (BIII) because it has been reported to cause

severe, chronic diarrhea, malnutrition, and death among other immunocompromised persons (*5,318,319*). HSCT recipients should avoid walking, wading, swimming, or playing in recreational water (e.g., ponds or lakes) that is likely to be contaminated with *Cryptosporidium*, *Es. coli* O157:H7 (*344–346*), sewage, or animal or human waste (BII). HSCT recipients should also avoid swallowing such water (e.g., while swimming) (*5,344,346*) as well as any water taken directly from rivers and lakes (*5,316*) (AIII).

HSCT recipients should not use well water from private wells or from public wells in communities with limited populations (DIII) because tests for microbial contamination are performed too infrequently (e.g., in certain locations, tests are performed ≤1 times/month) to detect sporadic bacterial contamination. However, drinking well water from municipal wells serving highly populated areas is regarded as safe from bacterial contamination because the water is tested ≥2 times/day for bacterial contamination. If HSCT recipients consume tap water, they should routinely monitor mass media (e.g., radio, television, or newspapers) in their area to immediately implement any boil-water advisories that might be issued for immunocompromised persons by state or local governments (BIII). A boil-water advisory means that all tap water should be boiled for ≥1 minutes before it is consumed. Tap water might not be completely free of *Cryptosporidium*. To eliminate the risk for *Cryptosporidium* exposure from tap water, HSCT recipients can boil tap water for ≥1 minutes before consuming it (e.g., drinking or brushing teeth) (*5*) (CIII). Alternately, they can use certain types of water filters (*316*) or a home distiller (*317*) to reduce their risk for *Cryptosporidium* (*5*) and other waterborne pathogens (CIII). If a home water filter* is used, it should be capable of removing particles ≥1 µm in diameter, or filter by reverse osmosis. However, the majority of these filters are not capable of removing smaller microbes (e.g., bacteria or viruses), and therefore, should only be used on properly treated municipal water. Further, the majority of these devices would not be appropriate for use on an unchlorinated private well to control viral or bacterial pathogens. Bottled water can be consumed if it has been processed to remove *Cryptosporidium* by one of three processes — reverse osmosis, distillation, or 1-µm particulate absolute filtration. To confirm that a specific bottled water has undergone one of these processes, HSCT recipients should contact the bottler directly.†

Patients can take other precautions in the absence of boil-water advisories to further reduce their risk for cryptosporidiosis. These extra precautions include avoiding fountain beverages and ice made from tap water at restaurants, bars, and theaters (*5*), fruit drinks made from frozen concentrate mixed with tap water, and iced tea or coffee made with tap water (*317*). Drinks that are likely to be *Cryptosporidium* safe for HSCT recipients include nationally distributed brands of bottled or canned carbonated soft drinks and beers (*5*); commercially packaged noncarbonated drinks that contain fruit juice; fruit juices that do not require refrigeration until after opening (e.g., those that are stored unrefrigerated on grocery shelves) (*5*); canned or bottled soda, seltzer or fruit drinks; steaming hot (≥175 F) tea or coffee (*317*); juices labeled as pasteurized; and nationally distributed brands of frozen fruit juice concentrate that are reconstituted with water from

*For a list of filters certified under NSF Standard 053 for cyst (i.e., *Cryptosporidium*) removal, contact the NSF International consumer line at (800) 673-8010 or <http://www.nsf.org/notice/crypto.html>.

† The International Bottled Water Association can be contacted at (703) 683-5213 from 9 a.m. to 5 p.m. EST or anytime at their Internet site (<http://www.bottledwater.org>) to obtain contact information regarding water bottlers.

a safe source (*5*). HSCT recipients should not drink unpasteurized milk or fruit or vegetable juices (e.g., apple cider or orange juice) to avoid infection with *Brucella* species, *Es. coli* O157:H7, *Salmonella* species, *Cryptosporidium*, and others (*319,347–351*) (DII).

Food Safety

HSCT candidates and household or family members who prepare food for them after HSCT should review food safety practices that are appropriate for all persons (*352*) (AIII), and food preparers should be educated regarding additional food safety practices appropriate for HSCT recipients. This review and education should be done before the conditioning regimen (i.e., chemotherapy and radiation) begins (BIII). Adherence to these guidelines will decrease the risk for foodborne disease among HSCT recipients.

Food Safety Practices Appropriate for All Persons

Raw poultry, meats, fish, and seafood should be handled on separate surfaces (e.g., cutting board or counter top) from other food items. Food preparers should always use separate cutting boards (i.e., one for poultry and other meats and one for vegetables and remaining cutting or carving tasks) (AIII), or the board(s) should be washed with warm water and soap between cutting different food items (AIII). To prevent foodborne illnesses caused by *Campylobacter jejuni* and *Salmonella enteritidis*, which can cause severe and invasive infections among immunocompromised persons (*353,354*), uncooked meats should not come in contact with other foods (BIII).

After preparing raw poultry, meats, fish, and seafood and before preparing other foods, food handlers should wash their hands thoroughly in warm, soapy water. Any cutting boards, counters, knives, and other utensils used should be washed thoroughly in warm, soapy water also (AIII). Food preparers should keep shelves, counter tops, refrigerators, freezers, utensils, sponges, towels, and other kitchen items clean (AIII). All fresh produce should be washed thoroughly under running water before serving (*355*) (AIII). Persons preparing food should follow published U.S. Department of Agriculture recommendations regarding safe food thawing (*356*) (BIII).

Persons cooking food for HSCT recipients should follow established guidelines for monitoring internal cooking temperatures for meats (*357*) (AII). The only method for determining whether the meat has been adequately cooked is to measure its internal temperature with a thermometer because the color of the meat after cooking does not reliably reflect the internal temperature. Different kinds of meat should be cooked to varying internal temperatures, all ≥150 F (AII). Specifically, the U.S. Department of Agriculture recommends that poultry be cooked to an internal temperature of 180 F; other meats and egg-containing casseroles and souffles should be cooked to an internal temperature of ≥160 F. Cold foods should be stored at <40 F; hot foods should be kept at >140 F (BIII). Food preparers should

- wash their hands before and after handling leftovers (AIII);
- use clean utensils and food-preparation surfaces (AIII);
- divide leftovers into small units and store in shallow containers for quick cooling (AII);
- refrigerate leftovers within 2 hours of cooking (AII).
- discard leftovers that were kept at room temperature for >2 hours (AIII);

- reheat leftovers or heat partially cooked foods to ≥165 F throughout before serving (AII);
- bring leftover soups, sauces, and gravies to a rolling boil before serving (AIII); and
- follow published guidelines for cold storage of food (*352*) (AII).

Additional Food Safety Practices Appropriate for HSCT Recipients

HSCT recipients' diets should be restricted to decrease the risk for exposure to foodborne infections from bacteria, yeasts, molds, viruses, and parasites (BIII). Currently, a low microbial diet is recommended for HSCT recipients (*358,359*) (BIII). This diet should be continued for 3 months after HSCT for autologous recipients. Allogeneic recipients should remain on the diet until all immunosuppressive drugs (e.g., cyclosporine, steroids, and tacrolimus) are discontinued. However, the HSCT physician should have final responsibility for determining when the diet can be discontinued safely. Only one study has reported that dietary changes (e.g., consuming yogurt) have decreased the risk for mycotic infections (e.g., candidal vaginitis) (*360*) (Table 3). HSCT recipients should not eat any raw or undercooked meat, including beef, poultry, pork, lamb, venison or other wild game, or combination dishes containing raw or undercooked meats or sweetbreads from these animals (e.g., sausages or casseroles) (AII). Also, HSCT recipients should not consume raw or undercooked eggs or foods that might contain them (e.g., certain preparations of hollandaise sauce, Caesar and other salad dressings, homemade mayonnaise, and homemade eggnog) because of the risk for infection with *Salmonella enteritidis* (*354*) (AII). HSCT recipients should not consume raw or undercooked seafood (e.g., oysters or clams) to prevent exposure to *Vibrio* species, viral gastroenteritis, and *Cryptosporidium parvum* (*361–364*) (AII).

HSCT recipients and candidates should only consume meat that is well-done when they or their caretakers do not have direct control over food preparation (e.g., when eating in a restaurant) (AI). To date, no evidence exists in the United States that eating food at a fast food restaurant is riskier than eating at a conventional sit-down restaurant. Generally, HSCT candidates undergoing conditioning therapy and HSCT recipients with neutropenia (i.e., ANC < 1,000/ml^3), GVHD, or immunosuppression should avoid exposures to naturopathic medicines that might contain molds (*365*) (DIII). HSCT recipients wishing to take naturopathic medications are advised to use them only as prescribed by a licensed naturopathic physician working in consultation with the recipient's transplant and infectious disease physicians (CIII).

Travel Safety

Travel to developing countries can pose substantial risks for exposure to opportunistic pathogens for HSCT recipients, particularly allogeneic recipients chronically immunosuppressed. HSCT recipients should not plan travel to developing countries without consulting their physicians (AIII), and travel should not occur until the period of severe immunosuppression has resolved. Generally, allogeneic recipients should not plan travel to developing countries for 6–12 months after HSCT, particularly if GVHD has occurred. Autologous recipients can travel to developing countries 3–6 months after HSCT if their physicians agree.

HSCT recipients should be informed regarding strategies to minimize the risk for acquiring foodborne and waterborne infections while traveling. They should obtain updated, detailed health information for international travelers from health organizations (*366,367*) (AIII). Generally, while traveling in developing countries, HSCT recipients should avoid consuming the following (BIII):

- raw fruits and vegetables,
- tap water or any potentially untreated or contaminated water,
- ice made from tap water or any potentially contaminated water,
- unpasteurized milk or any unpasteurized dairy products,
- fresh fruit juices,
- food and drinks from street vendors, and
- raw or undercooked eggs.

Steaming hot foods, fruits peeled by oneself, bottled and canned processed drinks, and hot coffee or tea are probably safe (*367,368*). Travelers should plan for treating their drinking water while in developing countries. If bottled water is not available, boiling is the best method of making water safe. However, if boiling water is not feasible, the traveler should carry supplies for disinfecting water (e.g., commercially available iodine disinfection tablets or a portable water filter) (*366,368*).

Antimicrobial prophylaxis for traveler's diarrhea is not recommended routinely for HSCT recipients traveling to developing countries (DIII) because traveler's diarrhea is not known to be more frequent or more severe among immunocompromised hosts. However, HSCT physicians who wish to provide prophylaxis to HSCT recipients who are traveling can prescribe a fluoroquinolone (e.g., ciprofloxacin hydrochloride) or TMP-SMZ (CIII), although resistance to TMP-SMZ is now common and resistance to fluoroquinolones is increasing in tropical areas (Appendix). Researchers recommend using bismuth subsalicylate to prevent traveler's diarrhea among adults (*366*). However, no data were found regarding safety and efficacy among HSCT recipients, and salicylates are not recommended for use among persons aged <18 years because salicylates are associated with Reye's syndrome (*369*).

HSCT recipients' immunization status should be assessed and their vaccinations updated as needed before travel (*366*). Influenza chemoprophylaxis with rimantadine or amantadine can be used for immunocompromised HSCT recipients who are traveling outside the continental United States and who could be exposed to influenza A (CIII).

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 (*66,370–373*) 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 (*66*); therefore, HSCT recipients should be routinely revaccinated after HSCT so that they can experience immunity to the same vaccine-preventable diseases as others (Table 4).

HSCT center personnel have developed vaccination schedules for HSCT recipients (*374*). One study determined that HSCT center personnel used 3–11 different vaccination schedules per vaccine (*374*); 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 4). 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 5–8).

HEMATOPOIETIC STEM CELL SAFETY

With allogeneic HSCT, the life of the recipient might depend on the timely selection of an acceptable HLA-matched donor. Only a limited number of HLA-matched donors might be identified; hence, the transplant physician often has to accept a higher risk for transmission of an infectious agent through HSCT than would be permitted for routine blood transfusion. This section provides strategies for the HSCT physician to minimize transmission of infectious diseases, whenever possible, from donors to recipients.*† Whether to select a donor who is at risk for or who has an infectious disease transmissible by HSCT, should be determined on a case-by-case basis (AIII) and is the final responsibility of the HSCT physician (AIII). If the only possible donor is at risk for or known to be infected with a bloodborne pathogen and the patient is likely to succumb rapidly from his or her disease if an HSCT is not received, the physician must carefully weigh the risks and benefits of using potentially infected donor cells. No person should be denied a potentially life-saving HSCT procedure solely on the basis of the risk for an infectious disease. However, HSCT physicians should avoid transplanting any infected or infectious donor hematopoietic stem cell product unless no other stem cell product can be obtained and

*The U.S. Public Health Service is reexamining the current donor deferral recommendations regarding risk behaviors for donors of organs, cells, tissues, xenotransplantation, and reproductive cells and tissue, including semen, and revisions to these guidelines could become necessary as the research evolves.

† Guidelines for screening UCB donors and their mothers are evolving and will not be addressed in this document.

the risk for death from not undergoing transplantation is deemed to be greater than the risk for morbidity or death from the infection that could potentially be transmitted (DII). If such a product is selected for use, it should be done on a case-by-case basis (*375*) and the following should be noted in the recipient's chart:

- knowledge and authorization of the recipient's HSCT physician regarding the potential for transmission of an infectious agent during HSCT, and
- advance informed consent from the recipient or recipient's legal guardian acknowledging the possible transmission of an infectious agent during the transplantation (AIII).

Subsequently, the HSCT physician should include the infectious agent in the differential diagnosis of any illness that the HSCT recipient experiences so that the infection, if transmitted, can be diagnosed early and treated preemptively, if possible. Infectious products (except those in which CMV seropositivity is the only evidence of infectiousness) should be labeled as being a biohazard or as untested for biohazards, as applicable. Tissue intended for autologous use should be labeled "For Autologous Use Only — Use Only for (Patient's Name)."

Preventing Transmission of Infections from HSCT Donors to Recipients

All prospective HSCT donors should be evaluated through a physical history and examination to determine their general state of health and whether they pose a risk for transmitting infectious diseases to the recipient (*376*). To detect transmissible infections, all HSCT donor collection site personnel should follow up-to-date published guidelines and standards for donor screening (e.g., medical history), physical exam, and serologic testing (*377–383*) (AIII). Initial donor screening and physical exam should be performed ≤8 weeks before the planned donation (BIII). Donor serologic testing should be done ≤30 days before donation to detect potentially transmissible infections (BII); additionally, researchers recommend that donors be retested ≤7 days before collection. If testing is done >7 days before donation, donor screening should be repeated to ensure that no new risk behaviors have occurred during the interval between the original screening and the time of donation (BIII). This practice is critical because if new behavioral risk factors have occurred, the potential donor might need to be deferred. Screening and testing should be done on all allogeneic or syngeneic donors (AIII). Screening and testing of autologous donors is recommended to ensure the safety of laboratory personnel and to prevent cross contamination (BIII). If autologous donors are not tested, their autologous units should be specially labeled and handled as if potentially infected (BIII). For donors screened in the United States, FDA-licensed or -approved tests should be used in accordance with the manufacturers' instructions (AIII), and the donor samples should be tested in laboratories certified by the Clinical Laboratory Improvement Amendments of 1988 (AIII).

All HSCT donors should be in good general health (*376*) (BIII). Acute or chronic illness in the prospective donor should be investigated to determine the etiology. Generally, persons who are ill should not be HSCT donors (DIII). A flu-like illness in a prospective donor at the time of evaluation or between the time of evaluation and donation should prompt evaluation of and serologic testing for infections that might pose a risk to the

recipient (e.g., EBV, CMV, *To. gondii*) (BIII). Persons with a positive serum EBV-viral capsid antigen IgM but negative serum EBV-viral capsid antigen IgG should not serve as donors for allogeneic T-cell–depleted HSCT, particularly for unrelated or mismatched transplants, until their serum EBV-viral capsid antigen IgG becomes positive (DIII). Persons with acute toxoplasmosis should not donate until the acute illness has resolved (DII); however, physicians should be aware that persons who are asymptomatically seropositive for *To. gondii* might transmit this infection through HSCT (*218*).

Prospective donors with symptoms of active TB should be evaluated for that disease (*383*) (BIII). Prospective donors with active TB should not donate (EIII) until the TB is well-controlled (e.g., no longer contagious as determined by the donor's primary physician) after appropriate medical therapy. However, no known risk exists from transplanting marrow from an untreated, tuberculin-positive donor who has no evidence of active disease. Screening potential donors for TB with Mantoux skin tests (DIII) is not necessary. Prospective HSCT donors who reside in or have traveled to areas endemic for rickettsia or other tickborne pathogens and who are suspected of having an acute tickborne infection should be temporarily deferred as donors until infection with these pathogens is excluded (DIII). Relevant pathogens include *Rickettsia rickettsii*, *Babesia microti* and other *Babesia* species, *Coxiella burnetii*, and the Colorado tick fever virus, which are the etiologic agents of Rocky Mountain spotted fever, babesiosis, Q fever, and Colorado tick fever, respectively; these pathogens have been reported to be transmitted by blood transfusion (*384–388*). Researchers recommend deferral for a past history of Q fever or babesiosis because these infections can be chronic and the babesiosis parasite might persist despite appropriate therapy (*389*) (CIII). Additionally, researchers have recommended deferring persons with acute human ehrlichiosis (e.g., human active human granulocytic ehrlichiosis [*390*], human monocytic ehrlichiosis, as well as any infections from *Ehrlichia ewingii*) from HSCT donation (CIII).

The medical history of the prospective HSCT donor should include the following:

- History of vaccinations (*377*) during the 4 weeks before donation (AII). If the potential donor is unsure of vaccinations received, his or her records should be reviewed. HSCT donation should be deferred for 4 weeks after the donor receives any live-attenuated vaccine (e.g., rubeola [measles], mumps, rubella [German measles], oral polio, varicella, yellow fever, and oral typhoid vaccines) (EIII). This deferral will avoid the possibility of infusing a live infectious agent into an HSCT recipient. HSCT donation need not be deferred for persons who have recently received toxoid or killed (i.e., inactivated), recombinant viral, bacterial, or rickettsial vaccines as long as the donor is asymptomatic and afebrile (*389*) (BIII). Such vaccines include tetanus toxoid, diphtheria toxoid, hepatitis A and B, cholera, influenza (i.e., killed intramuscular vaccine), meningococcal, paratyphoid, pertussis, plague, polio (i.e., inactivated polio vaccine), rabies, typhoid (i.e., inactivated intramuscular vaccine), or typhus vaccines (*389*).

- Travel history (BIII) to determine whether the donor has ever resided in or traveled to countries with endemic diseases that might be transmitted through HSCT (e.g., malaria). Permanent residents of nonendemic countries who have traveled to an area that CDC regards as endemic for malaria can be accepted as HSCT donors if 1 year has elapsed since the donor's departure from the endemic area and if the donor has been free of malaria symptoms, regardless of whether he or she received antimalarial chemoprophylaxis. Because cases of

HSCT-transmitted malaria have been reported (*391,392*), persons who have had malaria and received appropriate treatment should be deferred from HSCT donation for 3 years after becoming asymptomatic. Immigrants, refugees, citizens, or residents for ≥5 years of endemic countries can be accepted as HSCT donors if 3 years have elapsed since they departed the malarious area and if they have been free of malaria symptoms.

- History of Chagas' disease and leishmaniasis. Persons with active Chagas' disease or leishmaniasis should not serve as HSCT donors (DIII) because these diseases can be transmitted by transfusion (*227,229,231,393–395*). Researchers also recommend deferral of HSCT donation if a past history exists of either of these diseases because the parasite can persist despite therapy (*227–229,231, 389,393–395*) (CIII).

- History of any deferral from plasma or blood donation. The reason for such a deferral (*376*) and whether it was based on a reported infectious disease or behavioral or other risk factor should be investigated (BIII).

- History of viral hepatitis. A person with a history of viral hepatitis after his or her eleventh birthday should be excluded from HSCT donation (BIII).

- History of blood product transfusion, solid organ transplantation, or transplantation of tissue within the last 12 months (BIII). Such persons should be excluded from HSCT donation (DIII). Xenotransplant product recipients and their close contacts should be indefinitely deferred from donating any blood products, including hematopoietic stem cells, whole blood, or other blood components including plasma, leukocytes, and tissues (*396*) (AIII). Close contacts to be deferred from donations include persons who have engaged repeatedly in activities that could result in an intimate exchange of body fluids with a xenotransplantation product recipient. Such close contacts could include sexual partners, household members who share razors or toothbrushes, and HCWs or laboratory personnel with repeated percutaneous, mucosal, or other direct exposures.

- History of risk factors for classic Creutzfeldt-Jakob disease (CJD), including any blood relative with Creutzfeldt-Jakob disease, receipt of a human pituitary-derived growth hormone or receipt of a corneal or dura mater graft (*383,397–399*) (BIII). Potential HSCT donors should also be screened for new variant Creutzfeldt-Jakob Disease (nvCJD) risk factors, including a history of cumulative travel or residence in the United Kingdom for ≥6 months during 1980–1996 or receipt of injectable bovine insulin since 1980, unless the product was not manufactured since 1980 from cattle in the United Kingdom (*398*) (BIII). The clinical latency period for iatrogenic, classic CJD can be >30 years (*398*), and transmission of classic CJD by blood products is highly unlikely (*398*). Although no classic or nvCJD has ever been reported among HSCT recipients, persons with a history of classic or nvCJD risk factors should be excluded from donation for unrelated HSCT (DIII) if a choice exists between two otherwise equally suitable donors. The risk for transmitting classic or nvCJD from an HSCT donor to a recipient is unknown, but researchers believe that persons with nvCJD risk

factors could be at higher risk for transmitting nvCJD to HSCT recipients than persons with classic CJD risk factors.

- Past medical history that indicates the donor has clinical evidence of or is at high risk for acquiring a bloodborne infection (e.g., HIV-1 or -2, human T-lymphotropic virus [HTLV]-I or -II, hepatitis C, or hepatitis B) (*381,383*), including
  - — men who have had sex with another man during the preceding 5 years (*381,383*) (BIII);
  - — persons who report nonmedical intravenous, intramuscular, or subcutaneous injection of drugs during the preceding 5 years (*381*) (BIII);
  - — persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates (*381*) (BIII);
  - — persons who have engaged in sex in exchange for money or drugs during the preceding 5 years (*381*) (BIII);
  - — persons who have had sex during the preceding 12 months with any person described previously (*381*) or with a person known or suspected to have HIV (*381*) or hepatitis B infections (BIII);
  - — persons who have been exposed during the preceding 12 months to known or suspected HIV, hepatitis B- or C-infected blood through percutaneous inoculation or through contact with an open wound, nonintact skin, or mucous membrane (*381*) (BIII);
  - — inmates of correctional systems (*379–381*) and persons who have been incarcerated for >72 consecutive hours during the previous 12 months (BIII);
  - — persons who have had or have been treated for syphilis or gonorrhea during the preceding 12 months (*376,379,380*) (BIII); and
  - — persons who within 12 months have undergone tattooing, acupuncture, ear or body piercing (*380,400,401*) in which shared instruments are known to have been used (BIII) or other nonsterile conditions existed.

Persons reporting any of these past medical histories should be excluded from donation (DIII).

The following serologic tests should be performed for each prospective donor:

- HIV-1 antigen, anti-HIV-1 and -2, anti-HTLV-I and -II, hepatitis B surface antigen, total antihepatitis B core antigen, antihepatitis C, anti-CMV, and a serologic test for syphilis (*376,379,380,383*) (AIII). Potential donors who have repeatedly reactive screening tests for HIV-1 antigen, anti-HIV-1 or -2, anti-HTLV-I or -II, antihepatitis C, hepatitis B surface antigen, or antihepatitis B core antigen should be excluded as HSCT donors (*381*) (EII). Persons who refuse infectious disease testing should also be excluded as HSCT donors (*381*) (EIII).
- Investigational nucleic acid tests to detect hepatitis C virus RNA and HIV RNA are currently being used in the United States to screen blood donors and could be

used for screening HSCT donors. If nucleic acid tests are approved by FDA, these tests should be incorporated into routine screening regimens for HSCT donors. When nucleic acid testing is done for HIV and hepatitis C investigationally, a positive result should exclude the potential donor.

All infectious disease testing and results should be reported to the HSCT physician before the candidate's conditioning regimen begins (*381*) (AIII). Bone marrow should be collected using sterile technique in a medically acceptable setting and according to standard operating procedures (AIII).

HSCT transplant center personnel should keep accurate records of all HSCT received and the disposition of each sample obtained (*381*). These tracking records must be separate from patients' medical records (e.g., in a log book) so that this information is easily obtainable. Recorded information should include the donor identification number, name of procurement of distribution center supplying the HSCT, recipient-identifying information, name of recipient's physician, and dates of a) receipt by the HSCT center and b) either transplantation to the recipient or further distribution (*381*) (AIII). All centers for donation, transplantation, or collection of hematopoietic stem cells should keep records of donor screening and testing, and HSCT harvesting, processing, testing, cryopreservation, storage, and infusion or disposal of each aliquot of donated hematopoietic progenitor cells for ≥10 years after the date of implantation, transplantation, infusion, or transfer of the product (*378*) (AIII). However, if that date is not known, records should be retained ≥10 years after the product's distribution, disposition, or expiration, whichever is latest.

Pediatric Donors

Children aged >18 months who are born to mothers with or at risk for HIV infection, who have not been breast-fed during the past 12 months, and whose HIV antibody tests, physical examination, and medical records do not indicate evidence of HIV infection can be accepted as donors (*381*) (BIII). Children aged <18 months who are born to mothers with or at risk for HIV infection and who have not been breast-fed by an HIV-infected woman during the past 12 months can be accepted as donors only if HIV infection has been excluded according to established criteria (*402*) (BIII). Children who have been breast-fed by an HIV-infected woman during the past 12 months should be excluded as stem cell donors regardless of HIV infection status (AIII). The mother and, if possible, the father of all pediatric stem-cell donors who are at risk for perinatal transmission of HIV and other bloodborne infections, should be interviewed by a health-care professional competent to elicit information regarding risk factors for possible bloodborne infection in the potential pediatric donor (AIII). Children who meet any of the adult donor exclusion criteria should not become HSCT donors (*381*) (EIII).

Preventing Infection from Extraneous Contamination of Donated Units

Personnel of donation, collection, or transplantation centers, cell-processing laboratories, and courier services should follow current standards for detecting and preventing extrinsic bacterial and fungal contamination of collected stem cell units at the collection

site, during processing and transportation, and at the transplant center (*376*) (AIII). Quality improvement programs and procedure manuals of collection centers, cell-processing laboratories, and transplant programs should include strategies for preventing transplant-associated infections. For example, collection centers should use aseptic techniques when collecting marrow, peripheral blood, and UCB hematopoietic stem cells (*376,378*) (AIII). Whenever possible, closed systems should be used for pooling hematopoietic stem cells during a collection procedure (BIII) because higher rates of microbial contamination seen in marrow harvests versus blood stem cell collections can be caused by use of open collecting systems (*375,403,404*). The highest risk for extraneous microbial contamination of hematopoietic stem cells occurs during extensive manipulation and processing in the laboratory (*404,405*). Potential sources include unprotected hands and laboratory equipment and freezers (*406*), particularly the liquid phases of liquid nitrogen freezers (*407*). Therefore, stem cell processing should be performed according to current standards (*378*) using approved manufacturing practices (AIII). Hematopoietic stem cell units thawed in a water bath should be enclosed in a second bag (i.e., double-bagged technique) to prevent contamination of the ports or caps from unsterile bath water (*407*) (BIII). Additionally, water baths should be cleaned routinely (BIII) and certain researchers have proposed that the bath contain sterile water (*407*) (CIII). Researchers also report sterilizing liquid nitrogen freezers before initial use for hematopoietic stem cell storage (*407*) until fungal and bacterial cultures are negative (CIII).

Cell-processing laboratory personnel should implement programs to detect extrinsic bacterial or fungal contamination of collected stem cell units, ideally before transplantation (AIII). Although repeated cultures are costly (*408*), donated hematopoietic stem cells should be cultured for aerobic bacteria and fungi ≥1 times during initial processing and freezing (BIII). Researchers also have proposed adding anaerobic bacterial cultures and culturing twice, once at the end of processing, and once after thawing just before use (*407*) (CIII). If bacterial culture results are positive, antibiotic-susceptibility tests should be performed (BIII). Results of cultures and antibiotic-susceptibility tests should be provided to the transplant physician before release of a cryopreserved marrow or blood stem cell unit, and as soon as feasible for transplants infused before completion of culture incubation (BIII).

Collection center, cell-processing laboratory, and transplant program personnel should maintain active surveillance of infections among persons who have received hematopoietic stem cells from those facilities to collect data regarding the number of infections after HSCT that might have been caused by exogenous contamination of donor stem cells (BIII) because this type of infection has been reported (*405*).

In Utero or Fetal HSCT

No national standards exist for in utero or fetal HSCT, and the overall risks for transmitting infections to a fetus through HSCT (*409,410*) have not been determined. However, in addition to precautions appropriate for adult recipients, physicians performing in utero or fetal HSCT are advised to evaluate potential donors for evidence of active infectious diseases that could cause serious congenital infections (e.g., rubella, varicella, CMV, syphilis, or *To. gondii*) in the fetus (CIII).

Acknowledgments

The authors gratefully acknowledge the assistance of the following persons in the preparation of this report: Jon S. Abramson, M.D.; Saundra N. Aker, R.D.; George J. Alangaden, M.D.; Ann Arvin, M.D.; Carol Baker, M.D.; Michael Boeckh, M.D.; Brian J. Bolwell, M.D.; John M. Boyce, M.D.; C. Dean Buckner, M.D.; Pranatharthi H. Chandrasekar, M.D.; D.W. Chen, M.D., M.P.H.; Joan Chesney, M.D.; Raymond Chinn, M.D.; Christina Cicogna, M.D.; Dennis Confer, M.D.; Stella M. Davies, M.D., Ph.D.; Alfred DeMaria, Jr., M.D.; David W. Denning, M.B.B.S.; Joseph Fay, M.D.; Stephen Forman, M.D.; Michael Gerber, M.D.; Anne A. Gershon, M.D.; Stuart L. Goldberg, M.D.; Marie Gourdeau, M.D.; Christine J. Hager, Ph.D.; Rebecca Haley, M.D.; Liana Harvath, Ph.D.; Kelly Henning, M.D.; Steve Heyse; Elizabeth Higgs; Kevin High, M.D.; Mary M. Horowitz, M.D.; Craig W.S. Howe, M.D., Ph.D.; David D. Hurd, M.D.; Hakan Kuyu, M.D.; Amelia A. Langston, M.D.; Catherine Laughlin, Ph.D.; Hillard M. Lazarus, M.D.; Joseph H. Laver, M.D.; Helen Leather, Phar.D.; Paul R. McCurdy, M.D.; Carole Miller, M.D.; I. George Miller, M.D.; Per Ljungman, M.D., Ph.D.; Paul R. McCurdy, M.D.; Richard J. O'Reilly, M.D.; Gary Overturf, M.D.; Jan E. Patterson, M.D.; Lauren Patton, D.D.S.; Doug Peterson, D.D.S., Ph.D.; Donna Przepiorka, M.D., Ph.D.; Philip A. Pizzo, M.D.; Charles G. Prober, M.D.; Issam Raad, M.D.; Elizabeth C. Reed, M.D.; Frank Rhame, M.D.; Olle Ringdén, M.D.; Stephen M. Rose, Ph.D.; Scott D. Rowley, M.D.; Pablo Rubinstein, M.D.; Martin Ruta; Joel Ruskin, M.D.; Thomas N. Saari, M.D.; Stephen Schoenbaum, M.D.; Mark Schubert, D.D.S., M.S.D.; Jane D. Siegel, M.D.; Jacqueline Sheridan; Alicia Siston, M.D.; Trudy N. Small, M.D.; Frank O. Smith, M.D.; Ruth Solomon, M.D.; Cladd Stevens, M.D.; Patrick J. Stiff, M.D.; Andrew J. Streifel, M.P.H.; Donna A. Wall, M.D.; Thomas Walsh, M.D.; Phyllis Warkentin, M.D.; Robert A. Weinstein, M.D.; Estella Whimbey, M.D.; Richard Whitley, M.D.; Catherine Wilfert, M.D.; Drew J. Winston, M.D.; Jeffrey Wolf, M.D.; Andrew Yeager, M.D.; John A. Zaia, M.D.; and Carol Zukerman.

Contributions from the following CDC staff are also gratefully acknowledged: Larry J. Anderson, M.D.; Fred Angulo, D.V.M.; Richard Besser, M.D.; Jay C. Butler, M.D.; Donald Campbell; Mary E. Chamberland, M.D.; James Childs, Sc.D.; Nancy J. Cox, Ph.D.; Robert B. Craven, M.D.; Jackie Curlew; Vance J. Dietz, M.D., M.P.H.T.M.; Richard Facklam, Ph.D.; Cindy R. Friedman, M.D.; Keiji Fukuda, M.D., M.P.H.; Rana A. Hajjeh, M.D.; Barbara Herwaldt, M.D., M.P.H.; AnnMarie Jenkins; Dennis D. Juranek, D.V.M., M.Sc.; Paul Kilgore, M.D.; William Kohn, D.D.S.; Jacobus Kool, M.D., D.T.M.H.; John R. Livengood, M.D., M.Phil.; Eric Mast, M.D., M.P.H.; Michael McNeil, M.D., M.P.H.; Robin R. Moseley, M.A.T.; Thomas R. Navin, M.D.; Adelisa Panlilio, M.D., M.P.H.; Monica Parise, M.D.; Michele Pearson, M.D.; Bradford A. Perkins, M.D.; Renee Ridzon, M.D.; Martha Rogers, M.D.; Nancy Rosenstein, M.D.; Charles Rupprecht, Ph.D., V.M.D.; Peter Schantz, Ph.D.; Lawrence B. Schonberger, M.D., M.P.H.; Jane Seward, M.B.B.S., M.P.H.; John A. Stewart, M.D.; Raymond Strikas, M.D.; Robert V. Tauxe, M.D., M.P.H.; Theodore Tsai, M.D.; Rodrigo Villar, M.D.; David Wallace; and Sherilyn Wainwright, D.V.M., M.D.

The contributions of staff from other federal and nongovernmental agencies are also gratefully acknowledged: Agency for Healthcare Research and Quality; Food and Drug Administration; Health Resources and Services Administration; National Institutes of Health; National Cancer Institute; National Heart, Lung, and Blood Institute; National Institute for Allergy and Infectious Diseases; CDC's Advisory Committee on Immunization Practices; American Academy of Pediatrics' Committee on Infectious Diseases; American Association of Blood Banks; Hospital Infection Control Advisory Committee; International Society of Hematotherapy and Graft Engineering; National Marrow Donor Program; Southwest Oncology Group; Foundation for the Accreditation of Hematopoietic Cell Therapy; and Society for Healthcare Epidemiology of America.

References

Introduction

1. Institute of Medicine/Committee on Emerging Microbial Threats to Health. Emerging infections: microbial threats to health in the United States. Lederberg J, Shope RE, and Oaks SC Jr., eds. Washington, DC: National Academy Press, 1992. Available at <http://books.nap.edu/books/0309047412/html/index.html>. Accessed June 28, 2000.
2. CDC. Addressing emerging infectious disease threats: a prevention strategy for the United States. Atlanta, GA: US Department of Health and Human Services, Public Health Service, CDC, 1994. Available at <http://www.cdc.gov/ncidod/publications/eid_plan>. Accessed May 17, 2000.
3. CDC. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: a summary. MMWR 1995;44(No. RR-8):1–34.
4. CDC. 1997 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. MMWR 1997;46(No. RR-12):1–46.
5. CDC. 1999 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. MMWR 1999;48(No. RR-10):1–66.
6. Gross PA, Barrett TL, Dellinger EP, et al. Purpose of quality standards for infectious diseases. Clin Infect Dis 1994;18(3):421.

Background

7. Appelbaum FR. Use of bone marrow and peripheral blood stem cell transplantation in the treatment of cancer. CA Cancer J Clin 1996;46(3):142–64.
8. Kessinger A, Armitage JO. Use of peripheral stem cell support of high-dose chemotherapy. In: DeVita VT Jr., Hellman S, Rosenberg SA, eds. Important advances in oncology 1993. Philadelphia, PA: J.B.Lippincott Co. 1993.
9. 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.
10. Sobocinski KA, Horowitz MM, Rowlings PA, et al. Bone marrow transplantation—1994: a report from the International Bone Marrow Transplant Registry and the North American Autologous Bone Marrow Transplant Registry. J Hematother 1994;3:95–102.
11. Zittoun RA, Mandelli F, Willemze R, et al. Autologous or allogeneic bone marrow transplantation compared with intensive chemotherapy in acute myelogenous leukemia. New Engl J Med 1995;332(4):217–23.
12. Thomas ED, Clift RA, Fefer A, et al. Marrow transplantation for the treatment of chronic myelogenous leukemia. Ann Intern Med 1986;104(2):155–63.
13. Storb R, Longton G, Anasetti C, et al. Changing trends in marrow transplantation for aplastic anemia [Review]. Bone Marrow Transplant 1992;10(suppl 1):45–52.
14. Mackinnon S, Hows JM, Goldman JM, et al. Bone marrow transplantation for chronic myeloid leukemia: the use of histocompatible unrelated volunteer donors. Exp Hematol 1990;18(5):421–5.
15. Kernan NA, Bartsch G, Ash RC, et al. Analysis of 462 transplantations from unrelated donors facilitated by the National Marrow Donor Program. N Engl J Med 1993;328(9):593–602.
16. Nademanee AP, Schmidt GM, Parker P, et al. Outcome of matched unrelated donor bone marrow transplantation in patients with hematologic malignancies using molecular typing for donor selection and graft-versus-host disease prophylaxis regimen of cyclosporine, methotrexate, and prednisone. Blood 1995;86:1228–34.
17. Clift RA, Hansen JA, Thomas ED, et al. Marrow transplantation from donors other than HLA-identical siblings. Transplant 1979;28(3):235–42.
18. Beatty PG, Clift RA, Mickelson EM, et al. Marrow transplantation from related donors other than HLA-identical siblings. N Engl J Med 1985;313(13):765–71.
19. Ferrara JL, Deeg HJ. Graft-versus-host disease [Review]. N Engl J Med 1991;324(10):667–74.

20. Marmont AM, Horowitz MM, Gale RP, et al. T-cell depletion of HLA-identical transplants in leukemia. Blood 1991;78(8):2120–30.
21. Rowlings PA. 1996 summary slides show current use and outcome of blood and marrow transplantation. Autologous Blood & Marrow Transplant Registry—North America: ABMTR Newsletter 1996;3(1):6–12.
22. Rubinstein P, Rosenfield RE, Adamson JW, Stevens CE. Stored placental blood for unrelated bone marrow reconstitution [Review]. Blood 1993;81(7):1679–90.
23. Kurtzberg J, Laughlin M, Graham ML, et al. Placental blood as a source of hematopoietic stem cells for transplantation into unrelated recipients. N Engl J Med 1996;335(3): 157–66.
24. Wagner JE, Rosenthal J, Sweetman R, et al. Successful transplantation of HLA-matched and HLA-mismatched umbilical cord blood from unrelated donors: analysis of engraftment and acute graft-versus-host disease. Blood 1996;88(3):795–802.
25. Meropol NJ, Overmoyer BA, Stadtmauer EA. High-dose chemotherapy with autologous stem cell support for breast cancer. Oncology (Huntingt) 1992;6(12):53–60, 63; discussion, 63–4, 69; published erratum, Oncology (Huntingt) 1993;7(3):105.
26. Sullivan KM, Storek J, Kopecky KJ, et al. Controlled trial of long-term administration of intravenous immunoglobulin to prevent late infection and chronic graft-vs.-host disease after marrow transplantation: clinical outcome and effect on subsequent immune recovery. Biol Blood Marrow Transplant 1996;2(1):44–53.
27. Lazarus HM, Vogelsang GB, Rowe JM. Prevention and treatment of acute graft-versus-host disease: the old and the new; a report from The Eastern Cooperative Oncology Group (ECOG) [Review]. Bone Marrow Transplant 1997;19(6):577–600.
28. 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.
29. Nevill TJ, Shepherd JD, Nantel SH, et al. Stem cell transplant-related mortality (TRM) 1985–1996: the Vancouver experience [Abstract 4426]. Blood 1997;90(10)(suppl 1 [part 2 of 2]):373b.
30. Duell T, van Lint MT, Ljungman P, et al. Health and functional status of long-term survivors of bone marrow transplantation. Ann Intern Med 1997;126(3):184–92.
31. Bush NE, Haberman M, Donaldson G, Sullivan KM. Quality of life of 125 adults surviving 6–18 years after bone marrow transplantation. Soc Sci Med 1995;40(4):479–90.
32. Ochs L, Shu XO, Miller J, et al. Late infections after allogeneic bone marrow transplantation: comparison of incidence in related and unrelated donor transplant recipients. Blood 1995;86(10):3979–86.
33. Pearson ML. Guideline for prevention of intravascular device-related infections. Part I. Intravascular device-related infections: an overview. Am J Infect Control 1996;24:262–93.
34. Paulin T, Ringdén O, Lönnqvist B. Faster immunological recovery after bone marrow transplantation in patients without cytomegalovirus infection. Transplant 1985;39(4): 377–84.
35. Armitage JO. Bone marrow transplantation. N Engl J Med 1994;330(12):827–38.
36. Thomas ED, Storb R, Clift RA, et al. Bone marrow transplantation (second of two parts) [Review]. N Engl J Med 1975;292(17):895–902.
37. Yeager AM, Vogelsang GB, Jones RJ, et al. Induction of cutaneous graft-versus-host disease by administration of cyclosporine to patients undergoing autologous bone marrow transplantation for acute myeloid leukemia. Blood 1992;79(11):3031–5.
38. Rinehart JJ, Balcerzak SP, Sagone AL, LoBuglio AF. Effects of corticosteroids on human monocyte function. J Clin Invest 1974;54(6):1337–43.
39. Atkinson K, Horowitz MM, Gale RP, et al. Consensus among bone marrow transplanters for diagnosis, grading and treatment of chronic graft-versus-host disease. Bone Marrow Transplant 1989;4(3):247–54.

40. Sullivan KM, Agura E, Anasetti C, et al. Chronic graft-versus-host disease and other late complications of bone marrow transplantation. Semin Hematol 1991;28(3):250–9.
41. Witherspoon RP, Storb R, Ochs HD, et al. Recovery of antibody production in human allogeneic marrow graft recipients: influence of time posttransplantation, the presence or absence of chronic graft-versus-host disease, and antithymocyte globulin treatment. Blood 1981;58(2):360–8.
42. Lum LG, Munn NA, Schanfield MS, Storb R. Detection of specific antibody formation to recall antigens after human bone marrow transplantation. Blood 1986;67(3):582–7.
43. Ambrosino DM, Molrine DC. Critical appraisal of immunization strategies for the prevention of infection in the compromised host. Hematol Oncol Clin North Am 1993;7(5):1027–50.
44. Lum LG. Kinetics of immune reconstitution after human marrow transplantation. Blood 1987;69(2):369–80.
45. Shulman HM, Sullivan KM, Weiden PL, et al. Chronic graft-versus-host syndrome in man: a long-term clinicopathologic study of 20 Seattle patients. Am J Med 1980;69(2):204–17.
46. Izutsu KT, Sullivan KM, Schubert MM, et al. Disordered salivary immunoglobulin secretion and sodium transport in human chronic graft-versus-host disease. Transplant 1983;35(5): 441–6.
47. Aucouturier P, Barra A, Intrator L, et al. Long lasting IgG subclass and antibacterial polysaccharide antibody deficiency after allogeneic bone marrow transplantation. Blood 1987;70(3):779–85.
48. Hughes WT, Armstrong D, Bodey GP, et al. 1997 guidelines for the use of antimicrobial agents in neutropenic patients with unexplained fever [Review]. Clin Infect Dis 1997;25(3): 551–73.
49. Pizzo PA, Hathorn JW, Hiemenz J, et al. Randomized trial comparing ceftazidime alone with combination antibiotic therapy in cancer patients with fever and neutropenia. N Engl J Med 1986;315(9):552–8.
50. Amgen, Inc. Filgrastim. In: Physician's desk reference. 54th edition. Montvale, NJ: Medical Economics Company, Inc., 2000:528–33.

Bacterial Infections

51. Cruciani M, Rampazzo R, Malena M, et al. Prophylaxis with fluoroquinolones for bacterial infections in neutropenic patients: a meta-analysis. Clin Infect Dis 1996(4);23:795–805.
52. Murphy M, Brown AE, Sepkowitz KA, et al. Fluoroquinolone prophylaxis for the prevention of bacterial infections in patients with cancer—is it justified [Letter]? Clin Infect Dis 1997;25(2):346–8.
53. Cometta A, Calandra T, Bille J, Glauser MP. *Escherichia coli* resistant to fluoroquinolones in patients with cancer and neutropenia. N Engl J Med 1994;330(17):1240–1.
54. Kirkpatrick BD, Harrington SM, Smith D, et al. Outbreak of vancomycin-dependent *Enterococcus faecium* in a bone marrow transplant unit. Clin Infect Dis 1999;29(5): 1268–73.
55. Vose JM, Armitage JO. Clinical applications of hematopoietic growth factors. J Clin Oncol 1995;13(4):1023–35.
56. Rand KJ, Houck H, Ganju A, Babington RG, Elfenbein GJ. Pharmacokinetics of cytomegalovirus specific IgG antibody following intravenous immunoglobulin in bone marrow transplant patients. Bone Marrow Transplant 1989;4(6):679–83.
57. Bosi A, De Majo E, Guidi S, et al. Kinetics of anti-CMV antibodies after administration of intravenous immunoglobulins to bone marrow transplant recipients. Haematologica 1990;75(2):109–12.
58. Buckley RH, Schiff RI. Use of intravenous immune globulin in immunodeficiency diseases. N Engl J Med 1991;325(2):110–7.
59. Bowden RA, Myers JD. Infection complicating bone marrow transplantation. In: Rubin RH, Young LS, eds. Clinical approach to infection in the compromised host. 3rd edition. New York, NY: Plenum Medical Book Co., 1994:601–28.

60. Sullivan KM, Storek J, Kopecky KJ, et al. Controlled trial of long-term administration of intravenous immunoglobulin to prevent late infection and chronic graft-versus-host disease following marrow transplantation: clinical outcome and effect on subsequent immune recovery. Biol Blood Marrow Transplant 1996;2:44–53.
61. 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.
62. Garner JS. Guideline for isolation precautions in hospitals. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 1996;17(1):53–80; published erratum, Infect Control Hosp Epidemiol 1996;17(4):214.
63. CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1997;46(No. RR-8):1–24.
64. Winston DJ, Schiffman G, Wang DC, et al. Pneumococcal infections after human bone-marrow transplantation. Ann Intern Med 1979;91(6):835–41.
65. Hammarström V, Pauksen K, Azinge J, et al. Pneumococcal immunity and response to immunization with pneumococcal vaccine in bone marrow transplant patients: the influence of graft versus host reaction. Support Care Cancer 1993;1:195–9.
66. Guinan EC, Molrine DC, Antin JH, et al. Polysaccharide conjugate vaccine responses in bone marrow transplant patients. Transplant 1994;57(5):677–84.
67. Schubert MM, Peterson DE, Lloid ME. Oral complications. In: Thomas ED, Blume KG, Forman SJ, eds. Hematopoietic cell transplantation. 2nd ed. Oxford, England: Blackwell Science, Inc., 1999;751–63.
68. Alcaide F, Linares JA, Pallares R, et al. In vitro activities of 22 ß-lactam antibiotics against penicillin-resistant and penicillin-susceptible viridans group *Streptococci* isolated from blood. Antimicrob Agents Chemother 1995;39(10):2243–7.
69. Steiner M, Villablanca J, Kersey J, et al. Viridans streptococcal shock in bone marrow transplant patients. Am J Hematol 1993;42(4):354–8.
70. American Academy of Pediatrics/Committee on Infectious Diseases. *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.
71. 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.
72. Granoff DM, Basden M. *Haemophilus influenzae* infections in Fresno County, California: a prospective study of the effects of age, race, and contact with a case on incidence of disease. J Infect Dis 1980;141(1):40–6.
73. Band JD, Fraser DW, Ajello G. Prevention of *Haemophilus influenzae* type b disease. JAMA 1984;251(18):2381–6.
74. Band JD, Fraser DW, Hightower AW, Broome CV. Prophylaxis of *Haemophilus influenzae* type b disease [Letter]. JAMA 1984;252(23):3249–50.
75. Barra A, Cordonnier C, Prezilosi MP, et al. Immunogenicity of *Haemophilus influenzae* type b conjugate vaccine in allogeneic bone marrow transplant recipients. J Infect Dis 1992;166(5):1021–8.
76. Sable CA, Donowitz GA. Infections in bone marrow transplant recipients. Clin Infect Dis 1994;18(3):273–84; quiz 282–4.
77. Roy V, Ochs L, Weisdorf D. Late infections following allogeneic bone marrow transplantation: suggested strategies for prophylaxis [Review]. Leuk Lymphoma 1997;26(1–2):1–15.

Viral Infections

78. Bowden RA, Slichter SJ, Sayers M, et al. Comparison of filtered leukocyte-reduced and cytomegalovirus (CMV) seronegative blood products for the prevention of transfusion-associated CMV infection after marrow transplantation. Blood 1995;86(9):3598–603.

79. Boeckh M, Gooley TA, Myerson D, Cunningham T, Schoch G, Bowden RA. Cytomegalovirus pp65 antigenemia-guided early treatment with ganciclovir versus ganciclovir at engraftment after allogeneic marrow transplantation: a randomized double blind study. Blood 1996;88(10):4063–71.
80. Boeckh M, Stevens-Ayers T, Bowden R. Cytomegalovirus pp65 antigenemia after autologous marrow and peripheral blood stem cell transplantation. J Infect Dis 1996;174(5):907–12.
81. Boeckh M, Bowden R. Cytomegalovirus infection in marrow transplantation. In: Buckner CD, Clift RA, ed. Technical and biological components of marrow transplantation. Boston, MA: Kluwer Academic Publishers, 1995:97–136.
82. Einsele H, Ehninger G, Hebart H, et al. Polymerase chain reaction monitoring reduces the incidence of cytomegalovirus disease and the duration and side effect of antiviral therapy after bone marrow transplantation. Blood 1995;86(7):2815–20.
83. Mendez JC, Sia IG, Paya CV. Human cytomegalovirus. In: Lennette EH, Smith TF, eds. Laboratory diagnosis of viral infections. 3rd ed., revised and expanded. New York, NY: Marcel Decker, Inc., 1999: 361–72.
84. Goodrich JM, Mori M, Gleaves CA, et al. Early treatment with ganciclovir to prevent cytomegalovirus disease after allogeneic bone marrow transplant. N Engl J Med 1991;325(23):1601–7.
85. Schmidt GM, Horak DA, Niland JC, Duncan SR, Forman SJ, Zaia JA. Randomized controlled trial of prophylactic ganciclovir for cytomegalovirus pulmonary infection in recipients of allogeneic bone marrow transplants. New Engl J Med 1991;324(15):1005–11.
86. Goodrich JM, Bowden RA, Fisher L, Keller C, Schoch G. Meyers JD. Ganciclovir prophylaxis to prevent cytomegalovirus disease after allogeneic marrow transplant. Ann Intern Med 1993;118(3):173–8.
87. Mazzulli T, Drew LW, Yen-Lieberman B, et al. Multicenter comparison of the Digene Hybrid Capture CMV DNA Assay (Version 2.0), the pp65 antigenemia assay, and cell culture for the detection of cytomegalovirus viremia. J Clin Microbiol 1999;37(4):958–63.
88. Gerna G, Baldanti F, Middeldorp JM, et al. Clinical significance of expression of human cytomegalovirus pp67 late transcript in heart, lung, and bone marrow transplant recipients as determined by nucleic acid sequence-based amplification. J Clin Microbiol 1999;37(4):902–11.
89. Singhal S, Mehta J, Powles R, et al. Three weeks of ganciclovir for cytomegalovirus after allogeneic bone marrow transplantation. Bone Marrow Transplant 1995;15(5):777–81.
90. Verdonck LF, Dekker AW, Rozenberg-Arska M, van den Hoek MR. Risk-adapted approach with a short course of ganciclovir to prevent cytomegalovirus (CMV) pneumonia in CMV-seropositive recipients of allogeneic bone marrow transplants. Clin Infect Dis 1997;24(5): 901–7.
91. Zaia J, Gallez-Hawkins GM, Longmate J, et al. Late bacterial and fungal sepsis and mortality after BMT are increased by duration of early ganciclovir preemptive therapy for CMV infection [Abstract 2128]. Blood 1998;92(10)(suppl 1 [part 1 of 2]):518a.
92. Bacigalupo A, Bregante S, Tedone E, et al. Combined foscarnet-ganciclovir treatment for cytomegalovirus infections after allogeneic hematopoietic stem cell transplantation. Transplant 1996;62(3);376–80.
93. Moretti S, Zikos P, Van Lint MT, et al. Foscarnet vs ganciclovir for cytomegalovirus (CMV) antigenemia after allogeneic hematopoietic stem cell transplantation (HSCT): a randomized study. Bone Marrow Transplant 1998;22(2):175–80.
94. Boeckh M, Hoy C, Torok-Storb B. Occult cytomegalovirus infection of marrow stroma. Clin Infect Dis 1998;26(1):209–10.
95. Krause H, Hebart H, Jahn G, Muller CA, Einsele H. Screening for CMV-specific T-cell proliferation to identify patients at risk of developing late onset CMV disease. Bone Marrow Transplant 1997;19(11):1111–16.

96. Gor D, Sabin C, Prentice HG, et al. Longitudinal fluctuations in cytomegalovirus load in bone marrow transplant patients: relationship between peak virus load, donor/recipient serostatus, acute GVHD and CMV disease. Bone Marrow Transplant 1998;21(6):597–605.
97. Zaia JA, Gallez-Hawkins GM, Teftmeier BR, et al. Late cytomegalovirus disease in marrow transplantation is predicted by virus load in plasma. J Infect Dis 1997;176(3):782–5.
98. Ljungman P, Aschan J, Azinge JN, et al. Cytomegalovirus viremia and specific T-helper cell responses as predictors of disease after allogeneic marrow transplantation. Br J Haematol 1993;83(1):118–24.
99. Lazzarotto T, Varani S, Spezzacatena P, et al. Delayed acquisition of high-avidity anti-cytomegalovirus antibody is correlated with prolonged antigenemia in solid organ transplant recipients. J Infect Dis 1998;178(4):1145–9.
100. Boeckh M, Gallez-Hawkins GM, Myerson D, Zaia JA, Bowden RA. Plasma polymerase chain reaction for cytomegalovirus DNA after allogeneic marrow transplantation: comparison with polymerase chain reaction using peripheral blood leukocytes, pp65 antigenemia, and viral culture. Transplant 1997;64(1):108–13.
101. Prentice HG, Gluckman E, Powles RL, et al. Impact of long-term acyclovir on cytomegalovirus infection and survival after allogeneic bone marrow transplantation. Lancet 1994;343(8900):749–53.
102. Boeckh M, Gooley TA, Bowden RA. Effect of high-dose acyclovir on survival in allogeneic marrow transplant recipients who received ganciclovir at engraftment or for cytomegalovirus pp65 antigenemia. J Infect Dis 1998;178(4):1153–7.
103. Boeckh M, Gooley TA, Reusser P, Buckner CD, Bowden RA. Failure of high-dose acyclovir to prevent cytomegalovirus disease after autologous marrow transplantation. J Infect Dis 1995;172(4):939–43.
104. American Public Health Association. Mononucleosis, infectious. In: Chin J, ed. Control of communicable diseases manual. 17th ed. Washington, DC: American Public Health Association, 2000:350–2.
105. Papadopoulos E, Ladanyi M, Emanuel D, et al. Infusions of donor leukocytes to treat Epstein-Barr virus-associated lymphoproliferative disorders after allogeneic bone marrow transplantation. New Engl J Med 1994;330(17):1185–91.
106. Rooney CM, Smith CA, Ng CY, et al. Infusion of cytotoxic T cells for the prevention and treatment of Epstein-Barr virus-induced lymphoma in allogeneic transplant recipients. Blood 1998;92(5):1549–55.
107. Shapiro RS, McClain K, Frizzera G, et al. Epstein-Barr virus associated B cell lymphoproliferative disorders following bone marrow transplantation. Blood 1988;71(5): 1234–43.
108. Zutter MM, Martin PJ, Sale GE, et al. Epstein-Barr virus lymphoproliferation after bone marrow transplantation. Blood 1988;72(2):520–9.
109. Saral R, Burns WH, Laskin OL, Santos GW, Lietman PS. Acyclovir prophylaxis of herpes-simplex-virus infections. N Engl J Med 1981;305(2):63–7.
110. Gluckman E, Lotsberg J, Devergie A, et al. Prophylaxis of herpes infections after bone marrow transplantation by oral acyclovir. Lancet 1983;2(8352):706–8.
111. Wade JC, Newton B, McLaren C, Flournoy N, Keeney RE, Meyers JD. Intravenous acyclovir to treat mucocutaneous herpes simplex virus infection after marrow transplantation: a double-blind trial. Ann Intern Med 1982;96(3):265–9.
112. Wade JC, Newton B, Flournoy N, Meyers JD. Oral acyclovir for prevention of herpes simplex reactivation after marrow transplantation. Ann Intern Med 1984;100(6):823–8.
113. Johnson JR, Egaas S, Gleaves CA, Hackman R, Bowden RA. Hepatitis due to herpes simplex virus in marrow-transplant recipients. Clin Infect Dis 1992;14(1):38–45.
114. Crumpacker CS. Ganciclovir [Review]. New Engl J Med 1996;335(10):721–9.
115. Chulay JD, Bell AR, Miller GB, and the International Valaciclovir HSV Study Group. Long-term safety of valaciclovir for suppression of herpes simplex virus infections [Abstract 105]. In: Infectious Diseases Society of America (IDSA) Program and Abstracts, 34th annual meeting, September 18–20, 1996, New Orleans, Louisiana;55.

116. Han CS, Miller W, Haake R, Weisdorf D. Varicella zoster infection after bone marrow transplantation: incidence, risk factors, and complications. Bone Marrow Transplant 1994;13(3):277–83.
117. Lawrence R, Gershon AA, Holzman R, Steinberg SP. Risk of zoster after varicella vaccination in children with leukemia. New Engl J Med 1988;318(9):543–8.
118. Locksley RM, Fluornoy N, Sullivan KM, Meyers JD. Infection with varicella-zoster virus after marrow transplantation. J Infect Dis 1985;152(6):1172–81.
119. Schuchter LM, Wingard J, Piantadose S, Burns WH, Santos GW, Saral R. Herpes zoster infection after autologous bone marrow transplantation. Blood 1989;74(4):1424–27.
120. CDC. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1996;45(No. RR-11):1–36.
121. CDC. Prevention of varicella: updated recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1999;48(No. RR-06):1–5.
122. Wacker P, Hartmann O, Benhamou E, Salloum E, Lamerle J. Varicella-zoster virus infections after autologous bone marrow transplantation in children. Bone Marrow Transplant 1989;4(2):191–4.
123. Josephson A, Gombert ME. Airborne transmission of nosocomial varicella from localized zoster. J Infect Dis 1988;158(1):238–41.
124. Sempere A, Sanz GF, Senent L, et al. Long-term acyclovir prophylaxis for prevention of varicella zoster virus infection after autologous bone stem cell transplantation in patients with acute leukemia. Bone Marrow Transplant 1992;10(6):495–8.
125. Selby PJ, Powles RL, Easton D, et al. Prophylactic role of intravenous and long-term oral acyclovir after allogeneic bone marrow transplantation. Br J Cancer 1989;59(3):434–8.
126. Ljungman P, Wilczek H, Gahrton G, et al. Long-term acyclovir prophylaxis in bone marrow transplant recipients and lymphocyte proliferation to herpes antigens in vitro. Bone Marrow Transplant 1986;1(2):185–92.
127. Cirrelli R, Herne K, McCrary M, Lee P, Tyrine, SK. Famciclovir: review of clinical efficacy and safety [Review]. Antiviral Res 1996;29(2–3):141–51.
128. Cat LK, Yamauchi NK. Varicella vaccine in immunocompromised patients [Review]. Annuals of Pharmacology 1996;30(2):181–4.
129. Redman RL, Nader S, Zerboni L, et al. Early reconstitution of immunity and decreased severity of herpes zoster in bone marrow transplant recipients immunized with inactivated varicella vaccine. J Infect Dis 1997;176(3):578–85.
130. Garcia R, Raad I, Abi-Said D, et al. Nosocomial respiratory syncytial virus infections: prevention and control in bone marrow transplant patients. Infect Control Hosp Epidemiol 1997;18(6):412–6.
131. Raad I, Abbas J, Whimbey E. Infection control of nosocomial respiratory viral disease in the immunocompromised host. Am J Med 1997;102(3A):48–52.
132. Sable CA, Hayden FG. Orthomyxoviral and paramyxoviral infections in transplant patients [Review]. Infect Dis Clin North Am 1995;9(4):987–1003.
133. Whimbey E, Champlin R, Couch RB, et al. Community respiratory virus infections among hospitalized adult bone marrow transplant recipients. Clin Infect Dis 1996;22(5):778–82.
134. Whimbey E, Englund JA, Couch RB. Community respiratory virus infections in immunocompromised patients with cancer. Am J Med 1997;102(3A):10–8.
135. Bowden RA. Respiratory virus infections in bone marrow transplant: the Fred Hutchinson Cancer Research Center experience. Am J Med 1997;102(3A):27–30.
136. Harrington RD, Hooton RD, Hackman RC, et al. Outbreak of respiratory syncytial virus in a bone marrow transplant center. J Infect Dis 1992;165(6):987–93.
137. Whimbey E, Champlin R, Englund JA, et al. Combination therapy with aerosolized ribavirin and intravenous immunoglobulin for respiratory syncytial virus disease in adult bone marrow transplant recipients. Bone Marrow Transplant 1995;16(3):393–9.
138. Folz RJ, Elkordy MA. Coronavirus pneumonia following autologous bone marrow transplantation for breast cancer. Chest 1999;115(3):901–5.

139. Whimbey E, Elting LS, Couch RB, et al. Influenza A virus infection among hospitalized adult bone marrow transplant recipients. Bone Marrow Transplant 1994;13(4):437–40.
140. CDC. Guideline for prevention of nosocomial pneumonia. Respiratory Care 1994;39(12): 1191–236.
141. CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2000;49(No. RR-3):1–38.
142. Engelhard D, Nagler A, Hardan I, et al. Antibody response to a two-dose regimen of influenza vaccine in allogeneic T cell-depleted and autologous BMT recipients. Bone Marrow Transplant 1993;11(1):1–5.
143. Hayden FG. Prevention and treatment of influenza in immunocompromised patients. Am J Med 1997;102(3A):55–60.
144. 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.
145. 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.
146. 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.
147. CDC. Neuraminidase inhibitors for treatment of influenza A and B infections. MMWR 1999;48(No. RR-14):1–10.
148. Englund JA, Champlin RE, Wyde PR, et al. Common emergence of amantadine- and rimantadine-resistant influenza A viruses in symptomatic immunocompromised adults. Clin Infect Dis 1998;26(6):1418–24.
149. Klimov AI, Rocha E, Hayden FG, et al. Prolonged shedding of amantadine-resistant influenzae A viruses by immunodeficient patients: detection by polymerase chain reaction-restriction analysis. J Infect Dis 1995;172(5):1352–55.
150. Knight V, Gilbert BE. Ribavirin aerosol treatment of influenza [Review]. Infect Dis Clin North Am 1987;1(2):441–57.
151. Hayden FG, Sabie CA, Connor JD, Lane J. Intravenous ribavirin by constant infusion for serious influenza and parainfluenza virus infection. Antiviral Therapy 1996;1:51–6.
152. Hayden FG, Treanor JJ, Betts RF, Lobo M, Esinhart JD, Hussey EK. Safety and efficacy of the neuraminidase inhibitor GG167 in experimental human influenza. JAMA 1996;275(4): 295–9.
153. Hayden FG. Combination antiviral therapy for respiratory virus infections. Antiviral Res 1996;29(1):45–8.
154. Martin MA, Bock MJ, Pfaller MA, Wenzel RP. Respiratory syncytial virus infections in adult bone marrow transplant recipients [Letter]. Lancet 1988;1(8599):1396–7.
155. Hertz MI, Englund JA, Snover D, Bitterman PB, McGlave PB. Respiratory syncytial virus-induced acute lung injury in adult patients with bone marrow transplants: a clinical approach and review of the literature [Review]. Medicine 1989;68(5):269–81.
156. Win N, Mitchell D, Pugh S, Russell NH. Successful therapy with ribavirin of late onset respiratory syncytial virus pneumonitis complicating allogeneic bone transplantation. Clin Lab Haematol 1992;14(1):29–32.
157. DeVincenzo JP, Leombuno D, Soiffer RJ, Siber GR. Immunotherapy of respiratory syncytial virus pneumonia following bone marrow transplantation. Bone Marrow Transplant 1996;17(6):1051–6.
158. Boeckh M, Bowden RA, Berrey MM, et al. Phase I evaluation of a RSV-specific humanized monoclonal antibody (MEDI-493) after hematopoietic stem cell transplantation (HSCT) [Abstract MN-20]. 38th Interscience Conference on Antimicrobial Agents and Chemotherapy, September 24–27, 1998, San Diego, CA;593.

159. Flomenberg P, Babbitt J, Drobyski WR, et al. Increasing incidence of adenovirus disease in bone marrow transplant recipients. J Infect Dis 1994;169(4):775–81.
160. Englund JA, Piedra PA, Whimbey EA. Prevention and treatment of respiratory syncytial virus and parainfluenza viruses in immunocompromised patients. Am J Med 1997;102(3A):61–70.
161. 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.
162. American Academy of Pediatrics. Parainfluenza viral 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, 2000:419–20.
163. American Academy of Pediatrics. Adenovirus 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, 2000:162–3.
164. 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.

Fungal Infections

165. Vose JM, Armitage JO. Clinical applications of hematopoietic growth factors. J Clin Oncol 1995;13(4):1023–35.
166. Riley DK, Pavia AT, Beatty PG, Denton D, Carroll KC. Surveillance cultures in bone marrow transplant recipients: worthwhile or wasteful? Bone Marrow Transplant 1995;15(3): 469–73.
167. Walsh TJ. Role of surveillance cultures in prevention and treatment of fungal infections. National Cancer Institute Monograph No. 9;1990:43–5.
168. Crawford SW. Bone-marrow transplantation and related infections. Semin Respir Infect 1993;8(3):183–90.
169. Goodman JL, Winston DJ, Greenfield RA, et al. Controlled trial of fluconazole to prevent fungal infections in patients undergoing bone marrow transplantation. N Engl J Med 1992;326(13):845–51.
170. Slavin MA, Osborne B, Adams R, et al. Efficacy and safety of fluconazole prophylaxis for fungal infections after marrow transplantation—a prospective, randomized, double-blind study. J Infect Dis 1995;171(6):1545–52.
171. Reed EC. Infectious complications during autotransplantation [Review]. Hematol Oncol Clin North Am 1993;7:717–35.
172. Donowitz G, Harman C. Low dose fluconazole prophylaxis in neutropenia [Abstract 024]. 9th International Symposium on Infections in the Immunocompromised Host, Assisi, Italy, June 23–26, 1996.
173. Bjerke JW, Meyers JD, Bowden RA. Hepatosplenic candidiasis—a contraindication to marrow transplantation? Blood 1994;84(8):2811–4.
174. Walsh TJ, Dixon DM. Nosocomial aspergillosis: environmental microbiology, hospital epidemiology, diagnosis and treatment. Eur J Epidemiol 1989;5(2):131–42.
175. Weems JJ Jr, Davis BJ, Tablan OC, Kaufman L, Martone WJ. Construction activity: an independent risk factor for invasive aspergillosis and zygomycosis in patients with hematologic malignancy. Infect Control 1987;8(2):71–5.
176. Krasinski K, Holzman RS, Hanna B, Greco MA, Graff M, Bhogal M. Nosocomial fungal infection during hospital renovation. Infection Control 1985;6(7):278–82.
177. Thio CL, Smith D, Merz WG, et al. Refinements of environmental assessment during an outbreak investigation of invasive aspergillosis in a leukemia and bone marrow transplant unit. Infect Control Hosp Epidemiol 2000;21(1):18–23.
178. Rhame FS, Streifel AJ, Kersey JH Jr, McGlave PB. Extrinsic risk factors for pneumonia in the patient at high risk of infection [Review]. Am J Med 1984;76(5A):42–52.

179. Opal SM, Asp AA, Cannady, PB Jr, Morse PL, Burton LJ, Hammer PG 2nd. Efficacy of infection control measures during a nosocomial outbreak of disseminated aspergillosis associated with hospital construction. J Infect Dis 1986;153(3):634–7.
180. American Institute of Architects Academy of Architecture for Health, with assistance from the US Department of Health and Human Services. Guidelines for design and construction of hospital and medical facilities. Washington, DC: American Institute of Architects Press, 1996–67:58.
181. Bowden RA, Cays M, Gooley T, Mamelok RD, van Burik JA. Phase I study of amphotericin B colloidal dispersion for the treatment of invasive fungal infections after marrow transplant. J Infect Dis 1996;173(5):1208–15.
182. Kruger W, Stockschlader M, Russman B, et al. Experience with liposomal amphotericin-B in 60 patients undergoing high-dose therapy and bone marrow or peripheral blood stem cell transplantation. Br J Haematol 1995;91(3):684–90.
183. Ringdén O, Tollemar J, Dahllof G, Tyden G. High cure rate of invasive fungal infections in immunocompromised children using AmBisome. Transplant Proc 1994;26(1):175–7.
184. Andstrom EE, Ringdén O, Remberger M, Svahn BM, Tollemar J. Safety and efficacy of liposomal amphotericin B in allogeneic bone marrow transplant recipients. Mycoses 1996;39(5–6):185–93.
185. O'Donnell MR, Schmidt GM, Tegtmeier BR, et al. Prediction of systemic fungal infection in allogeneic marrow recipients: impact of amphotericin prophylaxis in high-risk patients. J Clin Oncol 1994;12(4):827–34.
186. Rousey SR, Russler S, Gottlieb M, Ash RC. Low-dose amphotericin B prophylaxis against invasive *Aspergillus* infections in allogeneic marrow transplantation. Am J Med 1991;91(5):484–92.
187. Perfect JR, Klotman ME, Gilbert CC, et al. Prophylactic intravenous amphotericin B in neutropenic autologous bone marrow transplant recipients. J Infect Dis 1992;165(5): 891–7.
188. Wade JC. Chapter 5: epidemiology of *Candida* infections. In: Bodey GP, ed. Candidiasis: pathogenesis, diagnosis and treatment. New York, NY: Raven Press, Ltd., 1993:85–107.
189. Tollemar J, Ringdén O, Andersson S, et al. Prophylactic use of liposomal amphotericin B (AmBisome) against fungal infections: a randomized trial in bone marrow transplant recipients. Transplant Proc 1993;25(1 part 2):1495–7.
190. Conneally E, Cafferkey MT, Daly PA, Keane CT, McCann SR. Nebulized amphotericin B as prophylaxis against invasive aspergillosis in granulocytopenic patients. Bone Marrow Transplant 1990;5(6):403–6.
191. Cleary JD, Taylor JW, Chapman SW. Itraconazole in antifungal therapy. Ann of Pharmacother 1992;26(4):502–9.
192. Jennings TS, Hardin TC. Treatment of aspergillosis with itraconazole [Review]. Annals of Pharmacother 1993;27(10):1206–11.
193. Poirier JM, Berlioz F, Isnard F, Chrymol G. Marked intra- and inter-patient variability of itraconazole steady state plasma concentrations. Thérapie 1996;51(2):163–7.
194. Prentice AG, Warnock DW, Johnson SA, Phillips MJ, Oliver DA. Multiple dose pharmacokinetics of an oral solution of itraconazole in autologous bone marrow transplant recipients. J Antimicrob Chemother 1994;34(2):247–52.
195. Tam JY, Hamed KA, Blume K, Prober CG. Use of itraconazole in treatment of prevention of invasive aspergillosis in bone marrow transplant recipients [Abstract 813]. 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), New Orleans, LA, 1993;268.
196. Ortho Biotech, Inc. Itraconazole. In: Physician's desk reference (PDR), Montvale, NJ: Medical Economics Company, 2000:2131–4.
197. Denning DW. Invasive aspergillosis [Review]. Clin Infect Dis 1998;26(4):781–803; quiz 804–5.

198. McWhinney PHM, Kibbler CC, Hamon MD, et al. Progress in the diagnosis and management of aspergillosis in bone marrow transplantation: 13 years' experience. Clin Infect Dis 1993;17(3):397–404.
199. Lupinetti FM, Behrendt DM, Giller RH, Trigg ME, de Alarcon P. Pulmonary resection for fungal infection in children undergoing bone marrow transplantation. J Thorac Cardiovasc Surg 1992;104(3):684–7.
200. Richard C, Romon I, Baro J, et al. Invasive pulmonary aspergillosis prior to BMT in acute leukemia patients does not predict a poor outcome. Bone Marrow Transplant 1993;12(3):237–41.

Protozoal and Helminthic Infections

201. Brazinsky JH, Phillips JE. Pneumocystis pneumonia transmission between patients with lymphoma. JAMA 1969;209(10):1527.
202. Chave JP, David S, Wauters JP, Van Meller G, Francioli P. Transmission of *Pneumocystic carinii* from AIDS patients to other immunosuppressed patients: a cluster of *Pneumocystis carinii* pneumonia in renal transplant patients. AIDS 1991;5(8):927–32.
203. Goesch TR, Götz G, Stellbrinck KH, Albrecht H. Weh HJ, Hossfeld DK. Possible transfer of *Pneumocystis carinii* between immunodeficient patients [Letter]. Lancet 1990;336(8715): 627.
204. Bensousan T, Garo B, Islam S, Bourbigot B, Cledes J, Garre M. Possible transfer of *Pneumocystic carinii* between kidney transplant recipients [Letter]. Lancet 1990;336(8722):1066–7.
205. Ruskin J, Remington JS. Compromised host and infection. I: *Pneumocystic carinii* pneumonia. JAMA 1967;202(12):1070–4.
206. Watanabe JM, Chinchinian H, Weitz C, McIlvanie SK. *Pneumocystis carinii* pneumonia in a family. JAMA 1965;193(8):685–6.
207. Tuan IZ, Dennison D, Weisdorf DJ. *Pneumocystis carinii* pneumonitis following bone marrow transplantation. Bone Marrow Transplant 1992;10(3):267–72.
208. Maltezou HC, Petropoulos D, Choroszy M, et al. Dapsone for *Pneumocystic carinii* prophylaxis in children undergoing bone marrow transplantation [Review]. Bone Marrow Transplant 1997;20(10):879–81.
209. Link H, Vöhringer H-F, Wingen F, Bragas B, Schwardt A, Ehninger G. Pentamidine aerosol prophylaxis of *Pneumocystis carinii* pneumonia after BMT. Bone Marrow Transplant 1993;11(5):403–6.
210. Chan C, Montaner J, Lefebvre EA, et al. Atovaquone suspension compared with aerosolized pentamidine for prevention of *Pneumocystis carinii* pneumonia in human immunodeficiency virus-infected subjects intolerant of trimethoprim or sulfonamides. J Infect Dis 1999;180(2):369–76.
211. Nunn PP, Allistone JC. Resistance to trimethoprim-sulfamethoxazole in the treatment of *Pneumocystis carinii* pneumonia: implication of folinic acid. Chest 1984;86(1):149–50.
212. Safrin S, Lee BL, Sande MA. Adjunctive folinic acid with trimethoprim-sulfamethoxazole for *Pneumocystic carinii* pneumonia in AIDS patients is associated with an increased risk of therapeutic failure and death. J Infect Dis 1994;170(4):912–7.
213. Martino R, Martínez, Brunet S, Sureda A. Successful bone marrow transplantation in patients with recent *Pneumocystis carinii* pneumonia: report of two cases [Letter]. Bone Marrow Transplant 1995;16(3):491.
214. Castagnola E, Dini G, Lanino E, et al. Low CD4 lymphocyte count in a patient with *P. carinii* pneumonia after autologous bone marrow transplantation. Bone Marrow Transplant 1995;15(16):977–8.
215. Derouin F, Devergie A, Auber P, et al. Toxoplasmosis in bone marrow transplant recipients: report of seven cases and review [Review]. Clin Infect Dis 1992;15(2):267–70.
216. Koneru B, Anaissie E, Tricot G, et al. High incidence of and mortality from *Toxoplasma gondii* infections in T-cell depleted allogeneic bone marrow transplant recipients

[Abstract 987]. 39th Annual American Society of Hematology Meeting, San Diego, CA, December 5–9, 1997;224A.
217. Siegel SE, Lunde MN, Gelderman AH, et al. Transmission of toxoplasmosis by leukocyte transfusion. Blood 1971;37(4):388–94.
218. Slavin MA, Meyers JD, Remington JS, Hackman RC. *Toxoplasma gondii* infection in marrow transplant recipients: a 20 year experience. Bone Marrow Transplant 1994;13(5): 549–57.
219. Jurges E, Young Y, Eltumi M, et al. Transmission of toxoplasmosis by bone marrow transplant associated with Campath-1G. Bone Marrow Transplant 1992;9(1):65–6.
220. Chandrasekar PH, Momin F, Bone Marrow Transplant Team. Disseminated toxoplasmosis in marrow recipients: a report of three cases and a review of the literature. Bone Marrow Transplant 1997;19(7):685–9.
221. Foot ABM, Garin YJF, Ribaud P, Devergie A, Derouin F, Gluckman E. Prophylaxis of toxoplasmosis with pyrimethamine/sulfadoxine (Fansidar) in bone marrow transplant recipients. Bone Marrow Transplant 1994;14(2):241–5.
222. Peacock JE Jr, Greven CM, Cruz JM, Hurd DD. Fansidar: reactivation toxoplasmic retinochoroiditis in patients undergoing bone marrow transplantation: is there a role for chemoprophylaxis [Review]? Bone Marrow Transplant 1995;15(6):983–7.
223. Liu LX, Weller PF. Strongyloidiasis and other intestinal nematode infections [Review]. Infect Dis Clin North Am 1993;7(3):655–82.
224. Conway DJ, Atkins NS, Lillywhite JE, et al. Immunodiagnosis of *Strongyloides stercoralis* infection: a method for increasing the specificity of the indirect ELISA. Trans R Soc Trop Med Hyg 1993;87(2):173–6.
225. Fishman JA. *Pneumocystis carinii* and parasitic infections in the immunocompromised host. In: Rubin RH, Young LS, eds. Clinical approach to infection in the compromised host 3rd edition. New York, NY: Plenum Medical Book Company, 1994;275–334.
226. Fishman JA. *Pneumocystis carinii* and parasitic infections in transplantation. Infect Dis Clin North Am 1995;9(4):1005–44.
227. Leiby DA, Fucci MH, Stumpf RJ. *Trypanosoma cruzi* in a low- to moderate-risk blood donor population: seroprevalence and possible congenital transmission. Transfusion 1999;39(3):310–5.
228. Dictar M, Sinagra A, Verón MT, et al. Recipients and donors of bone marrow transplants suffering from Chagas' disease: management and preemptive therapy of parasitemia. Bone Marrow Transplant 1998;21(4):391–3.
229. Moraes-Souza H, Bordin JO. Strategies for prevention of transfusion-associated Chagas' disease. Transfus Med Rev 1996;10(3):161–70.
230. Altclas J, Sinagra A, Jaimovich G, et al. Reactivation of chronic Chagas' disease following allogeneic bone marrow transplantation and successful pre-emptive therapy with benznidazole. Transplant Infectious Disease 1999;1:135–7.
231. Altclas J, Jaimovich G, Milovic V, Klein F, Feldman L. Chagas' disease after bone marrow transplantation. Bone Marrow Transplant 1996;18(2):447–8.

Hospital Infection Control

232. Streifel AJ. Chapter 80: design and maintenance of hospital ventilation systems and the prevention of airborne nosocomial infections. In: Mayhall CG, ed. Hospital epidemiology and infection control. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins 1999; 1211–21.
233. Streifel AJ, Marshall JW. Parameters for ventilation controlled environments in hospitals. In: Moschandreas DJ, ed. Design, construction, and operation of healthy buildings; solutions to global and regional concerns. Atlanta, GA: American Society of Heating, Refrigerating and Air-Conditioning Engineers Press, 1998;305–9.
234. Barnes RA, Rogers TR. Control of an outbreak of nosocomial aspergillosis by laminar airflow isolation. J Hosp Infect 1989;14(2):89–94.

235. Sheretz FJ, Belani A, Kramer BS, et al. Impact of air filtration on nosocomial *Aspergillus* infections: unique risk to bone marrow transplant recipients. Am J Med 1987;83(4):709–18.
236. Walter EA, Bowden RA. Infection in the bone marrow transplant recipient [Review]. Infect Dis Clin North Am 1995;9(4):823–47.
237. Storb R, Prentice RL, Buckner CD, et al. Graft-versus-host disease and survival in patients with aplastic anemia treated by marrow grafts from HLA-identical siblings. N Engl J Med 1983;308(6):302–7.
238. Streifel AJ. Maintenance and engineering; biomedical engineering; support services and facilities management. In: Association for Professionals in Infection Control and Epidemiology, Inc. Principles and practice. 2nd ed. St. Louis, MO: Mosby, 2000 (in press).
239. Vesley D, Streifel AJ. Chapter 69: environmental services. In: Mayhall CG, ed. Hospital epidemiology and infection control. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins, 1999;1047–53.
240. Carter CD, Barr BA. Infection control issues in construction and renovation. Infect Control Hosp Epidemiol 1997;18(8):587–96.
241. Loo VG, Bertrand C, Dixon C, et al. Control of construction-associated nosocomial aspergillosis in an antiquated hematology unit. Infect Control Hospital Epidemiol 1996;17(6):360–4.
242. Rask DR, Dziekan B, Swincicki WC, et al. Air quality control during renovation in health care facilities. In: Moschandreas DJ, ed. Design, construction, and operation of healthy buildings; solutions to global and regional concerns. Atlanta, GA: American Society of Heating, Refrigerating, and Air-Conditioning Engineers Press, 1998:291–304.
243. CDC. Laboratory performance evaluation of N95 filtering facepiece respirators, 1996. MMWR 1998;47(48):1045–9.
244. CDC. Guidelines for preventing the transmission *Mycobacterium tuberculosis* in health-care facilities, 1994. MMWR 1994;43(No. RR-13):1–132.
245. CDC/National Institute of Occupational Safety and Health. Protect yourself against tuberculosis—a respiratory protection guide for health care workers. Cincinnati, OH: US Department of Health and Human Services, US Public Health Service, CDC, National Institute for Occupational Health and Safety, 1995; DHHS publication no. (NIOSH) 96-102:1–132. Available at <http://www.cdc.gov/niosh>. Accessed May 15, 2000.
246. Rutala WA. APIC guideline for selection and use of disinfectants. Am J Infect Control 1996;24(4):313–42.
247. National Antimicrobial Information Network. List of EPA registered products. Available at <http://ace.orst.edu/info/nain/lists.htm>. Accessed May 15, 2000.
248. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR, Hospital Infection Control Practices Advisory Committee. Guideline for prevention of surgical site infection, 1999. Infect Control Hosp Epidemiol 1999;20(4):247–80 or Am J Infect Control 1999;27(2): 97–134.
249. Garner JS, Favero MS. Guideline for handwashing and hospital environmental control, 1985; supersedes guideline for hospital environmental control published in 1981. Available at <http://www.cdc.gov/ncidod/hip/Guide/handwash.htm>. Accessed May 15, 2000.
250. Rotter ML. Chapter 87: hand washing and hand disinfection. In: Mayhall CG, ed. Hospital epidemiology and infection control. 2nd ed. Baltimore, MD: Lippincott Williams and Wilkins, 1999:1339–55.
251. Larson EL. APIC guideline for handwashing and hand antisepsis in health care settings. Am J Infect Control 1995;23(4):251–69.
252. McNeil SA, Foster CL, Kauffman CA. Effect of hand cleansing with antimicrobial soap gel on microbial colonization of artificial nails (AN) [Abstract 1696]. 39th Interscience Conference on Antimicrobial Agents and Chemotherapy Abstracts, San Francisco, CA, 1999;635.

253. CDC/National Center for Infectious Diseases/Hospital Infections Program. Sterilization or disinfection of medical devices: general principles. Atlanta, GA: US Department of Health and Human Services, CDC, 2000. Available at <http://www.cdc.gov/ncidod/hip/sterile/sterilgp.htm>. Accessed May 15, 2000.
254. Favero MS, Bond WW. Chapter 24: sterilization, disinfection, and antisepsis in the hospital. In: Hauser WJ Jr, Herrmann KL, Isenberg HD, Shadomy HJ, eds. Manual of clinical microbiology. Washington DC: American Society for Microbiology, 1991:183–200.
255. Johnson S, Gerding DN. Chapter 29: *Clostridium difficile*. In: Mayhall CG, ed. Hospital epidemiology and infection control. 2nd ed., Philadelphia, PA: Lippincott Williams & Wilkins, 1999:467–76.
256. Rutala WA, Weber DJ. Disinfection of endoscopes: review of new chemical sterilants used for high-level disinfection. Infect Control and Hospital Epidemiol 1999;20(1):69–75; published erratum, Infect Control Hosp Epidemiol 1999;20(5):302.
257. CDC. Nosocomial outbreak of *Rhizopus* infections associated with Elastoplast® wound dressings—Minnesota. MMWR 1978;27(5):33–4.
258. CDC. Follow-up on *Rhizopus* infections associated with Elastoplast® bandages—United States. MMWR 1978;27(28):243–4.
259. Bryce EA, Walker M, Scharf S, et al. Outbreak of cutaneous aspergillosis in a tertiary-care hospital. Infect Control Hosp Epidemiol 1996;17(3):170–2.
260. McCarty JM, Flam MS, Pullen G, Jones R, Kassel SH. Outbreak of primary cutaneous aspergillosis related to intravenous arm boards. J Pediatr 1986;108(5 Pt 1):721–4.
261. Mitchell SJ, Gray J, Morgan MEI, Hocking MC, Durbin GM. Nosocomial infection with *Rhizopus microsporus* in preterm infants: association with wooden tongue depressors. Lancet 1996;348(9025):441–3.
262. Gerson SL, Parker P, Jacobs MR, Creger R, Lazarus HM. Aspergillosis due to carpet contamination [Letter]. Infect Control Hosp Epidemiol 1994;15(4 Pt 1):221–3.
263. Richet H, McNeil M, Pewters W, et al. *Aspergillus flavus* in a bone marrow transplant unit (BMTU): pseudofungemia traced to hallway carpeting [Abstract F-23]. 89th Annual Meeting of the American Society for Microbiology, New Orleans, Louisiana, May 14–18, 1989:462.
264. Staib F. Ecological and epidemiological aspects of *Aspergilli* pathogenic for man and animal in Berlin (West). Zentrablatt fur Bakteriologie, Mikrobiologie, und Hygiene—Series A 1984;257(2):240–5.
265. CDC. ABCs of safe and healthy child care: an on-line handbook for child care providers. Atlanta, GA: US Department of Health and Human Services, CDC, 2000. Available at <http://www.cdc.gov/ncidod/hip/ABC/abc.htm>. Accessed May 15, 2000.
266. Buttery JP, Alabaster SJ, Heine RG, et al. Multiresistant *Pseudomonas aeruginosa* outbreak in a pediatric oncology ward related to bath toys. Pediatr Infect Dis J 1998;17(6):509–13.
267. 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.
268. Bolyard EA, Tablan OC, Williams WW, et al. Guideline for infection control in health care personnel. Infect Control Hospital Epidemiol 1998;19(6):407–63.
269. Stover BH, Bratcher DF. Varicella-zoster virus: infection, control, and prevention [Review]. Am J Infect Control 1998;26(3):369–83; quiz 382–4.
270. Schubert MM, Peterson DE, Lloid ME. Oral complications. In: Thomas ED, Blume KG, Forman SJ, eds. Hematopoietic cell transplantation. 2nd ed. Oxford, England: Blackwell Science, Inc., 1999;751–63.
271. Wilkes JD. Prevention and treatment of oral mucositis following cancer chemotherapy [Review]. Semin Oncol 1998;25(5):538–51.
272. Toscano CM, Bell M, Zukerman C, et al. Bloodstream infections (BSI) associated with needleless device use, bathing practices and home infusion [Poster abstract P3]. 48th Annual Epidemic Intelligence Service Conference, April 19–23, 1999, Atlanta, GA;47.

273. Do AN, Ray BJ, Banerjee SN, et al. Bloodstream infection associated with needleless device use and the importance of infection-control practices in the home health care setting. J Infect Dis 1999;179(2):442–8.
274. Kool JL, Fiore AE, Kioski CM, et al. More than 10 years of unrecognized nosocomial transmission of Legionnaires' disease among transplant patients. Infect Control Hosp Epidemiol 1998;19(12):898–904.
275. CDC. Sustained transmission of nosocomial Legionnaires' disease—Arizona and Ohio. MMWR 1997;46(19):416–21.
276. Lepine LA, Jernigan DB, Butler JC, et al. Recurrent outbreak of nosocomial Legionnaires' disease detected by urinary antigen testing: evidence for long-term colonization of a hospital plumbing system. Infect Control Hosp Epidemiol 1998;19(12):905–10.
277. Muraca PW, Yu VL, Goetz A. Disinfection of water distribution systems for *Legionella*: a review of application procedures and methodologies [Review]. Infect Control Hosp Epidemiol 1990;11(2):79–88.
278. Harbarth S, Dharan S, Liassine N, Herrault P, Auckenthaler R, Pittet D. Randomized, placebo-controlled, double-blind trial to evaluate the efficacy of mupirocin for eradicating carriage of methicillin-resistant *Staphylococcus aureus*. Antimicrob Agents Chemother 1999;43(6):1412–6.
279. Leski TA, Gniadkowski M, Skoczynska A, Stefaniuk E, Trzcinski K, Hryniewicz W. Outbreak of mupirocin-resistant *Staphylococci* in a hospital in Warsaw, Poland, due to plasmid transmission and clonal spread of several strains. J Clin Microbiol 1999;37(9):2781–8.
280. Schmitz FJ, Lindenlauf E, Hofmann B, et al. Prevalence of low- and high-level mupirocin resistance in *Staphylococci* from 19 European hospitals. J Antimicrob Chemother 1998;42(4):489–95.
281. Irish D, Eltringham I, Teall A, et al. Control of an outbreak of an epidemic methicillin-resistant *Staphylococcus aureus* also resistant to mupirocin. J Hosp Infect 1998;39(1): 19–26.
282. Udo EE, Farook VS, Mokadas EM, Jacob LE, Sanyal SC. Molecular fingerprinting of mupirocin-resistant methicillin-resistant *Staphylococcus aureus* from a burn unit. Int J Infect Dis 1998–99;3(2):82–7.
283. Bastos MC, Mondino PJ, Azevedo ML, Santos KR, Giambiagi-deMarval M. Molecular characterization and transfer among *Staphylococcus* strains of a plasmid conferring high-level resistance to mupirocin. Eur J Clin Microbiol Infect Dis 1999;18(6):393–8.
284. CDC. Recommendations for preventing the spread of vancomycin resistance: recommendations of the Hospital Infection Control Practices Advisory Committee (HICPAC). MMWR 1995;44(No. RR-12):1–13.
285. CDC. Update: *Staphylococcus aureus* with reduced susceptibility to vancomycin—United States, 1997. MMWR 1997;46(35):813–5.
286. Smith TL, Pearson ML, Wilcox KR, et al. Emergence of vancomycin resistance in *Staphylococcus aureus*. N Engl J Med 1999;340(7):493–501.
287. CDC. Interim guidelines for prevention and control of staphylococcal infection associated with reduced susceptibility to vancomycin. MMWR 1997;46(27):626–35.
288. CDC. Reduced susceptibility of *Staphylococcus aureus* to vancomycin—Japan, 1996. MMWR 1997;46(27):624–35.
289. Waldvogel FA. New resistance in *Staphylococcus aureus*. N Engl J Med 1999;340(7): 556–7.
290. Montecalvo MA, Shay DK, Patel P, et al. Bloodstream infections with vancomycin-resistant *Enterococci*. Arch Intern Med 1996;156:1458–62.
291. Hospital Infection Control Practices Advisory Committee (HICPAC). Recommendations for preventing the spread of vancomycin resistance. Infect Control Hosp Epidemiol 1995;16:105–13.

292. Kirkpatrick BD, Harrington SM, Smith D, et al. Outbreak of vancomycin-dependent *Enterococcus faecium* in a bone marrow transplant unit. Clin Infect Dis 1999;29(5):1268–73.
293. Byers KE, Durbin LJ, Simonton BM, Anglim AM, Adel KA, Farr BM. Disinfection of hospital rooms contaminated with vancomycin-resistant *Enterococcus faecium*. Infect Control Hosp Epidemiol 1998;19(4):261–4.
294. Trick WE, Kuehnert MJ, Quirk SB, et al. Regional dissemination of vancomycin-resistant *Enterococci* resulting from interfacility transfer of colonized patients. J Infect Dis 1999;180(2):391–6.
295. Gerding DN, Johnson S, Peterson LR, Mulligan ME, Silva J Jr. *Clostridium difficile*-associated diarrhea and colitis [Review]. Infect Control Hosp Epidemiol 1995;16(8): 459–77.
296. Johnson S, Gerding DN. *Clostridium difficile*-associated diarrhea. Clin Infect Dis 1998;26:1027–36; quiz 1035–6.
297. McFarland LV, Mulligan M, Kwok RY, Stamm WE. Nosocomial acquisition of *Clostridium difficile* infection. N Engl J Med 1989;321(3):204–10.
298. Johnson S, Gerding DN, Olson MM, et al. Prospective, controlled study of vinyl glove use to interrupt *Clostridium difficile* nosocomial transmission. Am J Med 1990;88(2): 137–40.
299. Pear SM, Williamson T, Bettin K, Gerding DN, Galgiami JN. Decrease in nosocomial *Clostridium difficile*-associated diarrhea by restricting clindamycin use. Ann Intern Med 1994;120(4):272–7.
300. Kaatz GW, Gitlin SD, Schaberg DR et al. Acquisition of *Clostridium difficile* from the hospital environment. Am J Epidemiol 1988;127(6):1289–94.
301. Delmee M, Vandercam B, Avesani V, Michaux JL. Epidemiology and prevention of *Clostridium difficile* infections in a leukemia unit. Eur J Clin Microbiol 1987;6(6):623–7.
302. Johnson S, Homann SR, Bettin KM, et al. Treatment of asymptomatic *Clostridium difficile* carriers (fecal excretors) with vancomycin or metronidazole. Ann Intern Med 1992;117(4):297–302.
303. Surawicz CM, Elmer GW, Speelman P, McFarland LV, Chinn J, Van Belle G. Prevention of antibiotic associated diarrhea by *Saccharomyces boulardii*: a prospective study. Gastroenterology 1989;96(4):981–8.
304. Niault M, Thomas F, Prost J, Ansai FH, Kalfon P. Fungemia due to *Saccharomyces* species in a patient treated with enteral *Saccharomyces boulardii*. Clin Infect Dis 1999;28:930.
305. Fox JP, Brandt CD, Wasserman FE, et al. Virus watch program: a continuing surveillance of viral infections in metropolitan New York families. VI: observations of adenovirus infections: virus excretion patterns, antibody response, efficacy of surveillance, patterns of infections, and relation to illness. Am J Epidemiol 1969;89(1):25–50.
306. Hillis WO, Cooper MR, Bang FB. Adenovirus infection in West Bengal. I: persistence of viruses in infants and young children. Indian J Med Res 1973;61(7):980–8.
307. Hall CB, Powell KR, MacDonald DE, et al. Respiratory syncytial virus infection in children with compromised immune function. New Engl J Med 1986;315(2):77–81.
308. Villarino ME, Burman W, Wang YC, et al. Comparable specificity of 2 commercial tuberculin reagents in persons at low risk for tuberculous infection. JAMA 1999;281(2):169–71.
309. American Thoracic Society/CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. Am J Respir Crit Care Med 2000;161(4, part 2):S221–47.
310. American Academy of Pediatrics. Tuberculosis. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics;2000:593–613.
311. CDC. Notice to readers: use of short-course tuberculosis preventive therapy regimens in HIV-seronegative persons. MMWR 1998;47(42):911–2.

312. Fennelly KP. Transmission of tuberculosis during medical procedures [Letter]. Clin Infect Dis 1997;25:1273–5.
313. Talbot EA, Perkins MD, Silva SFM, Frothingham R. Disseminated Bacille Calmette-Guérin disease after vaccination: case report and review. Clin Infect Dis 1997;24(6):1139–46.
314. CDC. Role of BCG 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):13.
315. Gaynes RP, Horan TC. Chapter 85: surveillance of nosocomial infections. In: Mayhall CG, ed. Hospital epidemiology and infection control. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins, 1999:1285–317.

Strategies for Safe Living After HSCT — Prevention of Exposure and Disease

316. CDC/National Center for Infectious Diseases/Working Group on Waterborne Cryptosporidiosis. Cryptosporidium and water: a public health handbook. Atlanta, GA: US Department of Health and Human Services, CDC, 1997. Available at <http://www.cdc.gov/ncidod/diseases/crypto/crypto.pdf>. Accessed May 15, 2000.
317. CDC/National Center for Infectious Diseases. Cryptosporidiosis [Fact sheet]. Atlanta, GA: US Department of Health and Human Services, CDC, 1999. Available at <http://www.cdc.gov/ncidod/dpd/parasites/cryptosporidiosis/factsht_cryptosporidiosis.htm>. Accessed May 15, 2000.
318. American Academy of Pediatrics. Cryptosporidiosis. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics 2000:223–4.
319. American Public Health Association. Cryptosporidiosis. In: Chin J, ed. Control of communicable diseases manual. 17th ed. Washington, DC: American Public Health Association, 2000:134–7.
320. DiFranza JR, Lew RA. Morbidity and mortality in children associated with the use of tobacco products by other people. Pediatrics 1996;97(4):560–8.
321. Cohen S, Tyrrell DA, Russell MA, Jarvis MJ, Smith AP. Smoking, alcohol consumption, and susceptibility to the common cold. Am J Pub Health 1993;83(9):1277–83.
322. Fischer M, Hedberg K, Cardosi P, et al. Tobacco smoke as a risk factor for meningococcal disease. Pediatr Infect Dis J 1997;16:979–83.
323. Lipsky BA, Boyko EJ, Inui TS, Koepsell TD. Risk factors for acquiring pneumococcal infections. Arch Intern Med 1986;146:2179–85.
324. Hall CB, Hall WJ, Gala CL, MaGill FB, Leddy JP. Long-term prospective study in children after respiratory syncytial virus infection. J Pediatr 1984;105(3):358–64.
325. Nuorti JP, Butler JC, Farley MM, et al. Cigarette smoking and invasive pneumococcal disease. New Engl J Med 2000;342(10):681–9.
326. Levitz SM, Diamond RD. Aspergillosis and marijuana [Letter]. Ann Intern Med 1991;115(7):578–9.
327. Marks WH, Florence L, Lieberman J, et al. Successfully treated invasive pulmonary aspergillosis associated with smoking marijuana in a renal transplant recipient [Review]. Transplant 1996;61(12):1771–4.
328. Chusid MJ, Gelfand JA, Nutter C, Fauci AS. Letter: pulmonary aspergillosis, inhalation of contaminated marijuana smoke, chronic granulomatous disease. Ann Intern Med 1975;82(5):682–3.
329. Hamadeh R, Ardehali A, Locksley RM, York MK. Fatal aspergillosis associated with smoking contaminated marijuana in a marrow transplant recipient. Chest 1988;94(2):432–3.
330. Kurup VP, Resnick A, Kagen SL, Cohen SH, Fink JN. Allergenic fungi and actinomycetes in smoking materials and their health implications. Mycopathologia 1983;82(1):61–4.
331. Kagen SL. *Aspergillus*: an inhalable contaminant of marihuana. N Engl J Med 1981;304(8):483–4.

332. Schwartz IS. Marijuana and fungal infection [Letter]. Am J Clin Pathol 1985;84(2):256.
333. Schwartz IS. Non-*Aspergillus* sinusitis and marijuana use [Letter]. Am J Clin Pathol 1992;97(4):601–2.
334. Llamas R, Hart R, Schneider NS. Allergic bronchopulmonary aspergillosis associated with smoking moldy marihuana. Chest 1978;73(6):871–2.
335. Angulo FJ, Glaser CA, Juranek DD, Lappin MR, Regnery RL. Caring for pets of immunocompromised persons. J Am Vet Med Assoc 1994;205(12):1711–8.
336. Elliott DL, Tolle SW, Goldberg L, Miller JB. Pet-associated illness. New Engl J Med 1985;313(16):985–94.
337. Glaser CA, Angulo FJ, Rooney JA. Animal-associated opportunistic infections among persons infected with the human immunodeficiency virus. Clin Infect Dis 1994;18:14–24.
338. Adams RM. Animals in schools: a zoonosis threat? Pediatr Infect Dis J 1998;17(2):174–6.
339. Dalton C, Hoffman R, Pape J. Iguana-associated salmonellosis in children. Pediatr Infect Dis J 1995;14(4):319–20.
340. CDC. Reptile-associated salmonellosis—selected states, 1996–1998. MMWR 1999;48(44):1009–13.
341. CDC. Errata: Reptile-associated salmonellosis—selected states, 1996–1998. MMWR 1999;48(45):1051.
342. Mermin J, Hoar B, Angulo FJ. Iguanas and *Salmonella marina* infection in children: a reflection of the increasing incidence of reptile-associated salmonellosis in the United States. Pediatr 1997;99(3):399–402.
343. CDC. Salmonellosis associated with chicks and ducklings—Michigan and Missouri, Spring 1999. MMWR 2000;49(14):297–9.
344. CDC. Lake-associated outbreak of *Escherichia coli* O157:H7—Illinois, 1995. MMWR 1996;45(21):437–9.
345. CDC. Outbreak of cryptosporidiosis associated with a water sprinkler foundation—Minnesota, 1997. MMWR 1998;47(40):856–60.
346. Kramer MH, Sorhage FE, Goldstein ST, Dalley E, Wahlquist SP, Herwaldt BL. First reported outbreak in the United States of cryptosporidiosis associated with a recreational lake. Clin Infect Dis 1998;26(1):27–33.
347. al-Eissa YA, Kambal AM, al-Nasser MN, al-Habib SA, al-Fawaz IM, al-Zamil FA. Childhood brucellosis: a study of 102 cases. Pediatr Infect Dis J 1990;9(2):74–9.
348. Keene WE, Hedberg K, Herriott DE, et al. Prolonged outbreak of *Escherichia coli* O157:H7 infections caused by commercially distributed raw milk. J Infect Dis 1997;176(3):815–8.
349. CDC. Outbreak of *Escherichia coli* O157:H7 infections associated with drinking unpasteurized commercial apple juice—British Columbia, California, Colorado, and Washington, October 1996. MMWR 1996;45(44):975.
350. CDC. Outbreaks of *Escherichia coli* O157:H7 infection and cryptosporidiosis associated with drinking unpasteurized apple cider—Connecticut and New York, October 1996. MMWR 1997;46(1):4–8.
351. CDC. Outbreak of *Salmonella* serotype Muenchen infections associated with unpasteurized orange juice—United States and Canada, June 1999. MMWR 1999;48(27):582–5.
352. CDC/National Center for Infectious Diseases. Handle and prepare food safely. Atlanta, GA: US Department of Health and Human Services, CDC, 2000. Available at <http://www.cdc.gov/ncidod/op/food.htm>. Accessed May 15, 2000.
353. CDC. Outbreak of *Campylobacter* enteritis associated with cross-contamination of food—Oklahoma, 1996. MMWR 1998;47(7):129–31.
354. CDC. Outbreaks of *Salmonella* serotype enteritidis infection associated with consumption of raw shell eggs—United States, 1994–1995. MMWR 1996;45(34):737–42.
355. CDC. Foodborne outbreak of cryptosporidiosis—Spokane, Washington, 1997. MMWR 1998;47(27):565–7.

356. US Department of Agriculture/Food Safety and Inspection Service. Big thaw—safe defrosting methods. Washington, DC: US Department of Agriculture, Food Safety and Inspection Service, Consumer Education and Information, 1996;1–2. Available at <http://www.fsis.usda.gov/OA/news/bigthaw.htm>. Accessed May 15, 2000.
357. US Department of Agriculture/Food Safety and Inspection Service. Kitchen thermometers. Washington, DC: US Department of Agriculture Consumer, Food Safety and Inspection Service, Education and Information, 2000 (in press).
358. Moe GL. Chapter 12: low-microbial diets for patients with granulocytopenia. In: Bloch AS, ed. Nutrition management of the cancer patient. Rockville, MD: Aspen Publishing, Inc., 1990:125–34.
359. Aker SN, Lenssen P. Chapter 80: nutritional support of patients with hematologic malignancies. In: Benz EJ Jr, Cohen HJ, Burie B, et al., eds. Hematology: basic principles and practice, 3rd ed. New York, NY: Churchill Livingstone, 2000:1501–14.
360. Hilton E, Isenberg HD, Alperstein P, France K, Borenstein MT. Ingestion of yogurt containing *Lactobacillus acidophilus* as prophylaxis for candidal vaginitis. Ann Intern Med 1992;116(5):353–7.
361. CDC. *Vibrio vulnificus* infections associated with eating raw oysters—Los Angeles, 1996. MMWR 1996;45(29):621–4.
362. CDC. Outbreak of *Vibrio parahaemolyticus* infection associated with eating raw oysters and clams harvested from Long Island Sound—Connecticut, New Jersey, and New York, 1998. MMWR 1999;48(03):48–51.
363. CDC. Viral gastroenteritis associated with eating oysters—Louisiana, December 1996–January 1997. MMWR 1997;46(47):1109–12.
364. Fayer R, Lewis EJ, Trout JM, et al. *Cryptosporidium parvum* in oysters from commercial harvesting sites in Chesapeake Bay. Emerg Infect Dis 1999;5(5):706–10.
365. Oliver MR, van Voorhis WC, Boeckh M, Mattson D, Bowden RA. Hepatic mucormycosis in a bone marrow transplant recipient who ingested naturopathic medicine. Clin Infect Dis 1996;22:521–4.
366. CDC. Health Information for international travel 1999–2000. Atlanta, GA: US Department of Health and Human Services, CDC, 1999. Available at <http://www.cdc.gov/travel/yellowbk99.pdf>. Accessed May 16, 2000.
367. World Health Organization. Guide on safe food for travelers. Geneva, Switzerland: World Health Organization, 1997:1–4. Available at <http://www.who.int/dsa/cat98/trav8.htm>. Accessed May 15, 2000.
368. CDC/National Center for Infectious Diseases. Food and water precautions and traveler's diarrhea prevention. Atlanta, GA: US Department of Health and Human Services, CDC, 2000;1–2. Available at <http://www.cdc.gov/travel/foodwatr.htm>. Accessed May 15, 2000.
369. Belay E, Bresee JS, Holman RC, Khan AS, Shahriari A, Schonberger LB. Reye's syndrome in the United States from 1981 through 1997. New Engl J Med 1999;340(18):1377–82.

HSCT Recipient Vaccinations

370. Pauksen K, Hammarström V, Ljungman P, et al. Immunity to poliovirus and immunization with inactivated poliovirus vaccine after autologous bone marrow transplantation. Clin Infect Dis 1994;18(4):547–52.
371. Pauksen K, Duraj V, Ljungman P, et al. Immunity to and immunization against measles, rubella and mumps in patients after autologous bone marrow transplantation. Bone Marrow Transplant 1992;9(6):427–32.
372. Ljungman P, Wiklund-Hammarsten M, Duraj V, et al. Responses to tetanus toxoid immunization after allogeneic bone marrow transplantation. J Infect Dis 1990;162(2):496–500.
373. Ljungman P, Fridell E, Lonnqvist B, et al. Efficacy and safety of vaccination of marrow transplant recipients with a live attenuated measles, mumps, and rubella vaccine. J Infect Dis 1989;159(4):610–5.

374. Henning KJ, White MH, Sepkowitz KA, Armstrong D. National survey of immunization practices following allogeneic bone marrow transplantation. JAMA 1997;277(14): 1148–51.

Hematopoietic Stem Cell Safety

375. Padley D, Koontz F, Trigg ME, Gingrich R, Strauss RG. Bacterial contamination rates following processing of bone marrow and peripheral blood progenitor cell preparations. Transfusion 1996;36(1):53–6.
376. National Marrow Donor Program.® Standards: effective September 1, 1999. 17th ed. Minneapolis, MN: National Marrow Donor Program, 1999:1–35.
377. Progenitor Cell Standards Task Force. Standards for hematopoietic progenitor cells. Bethesda, MD: American Association of Blood Banks, 1996:1–36.
378. Foundation for the Accreditation of Hematopoietic Cell Therapy. Standards for hematopoietic progenitor cell collection, processing and transplantation. 1st ed.-North America. Omaha, NE: FAHCT Accreditation Office, 1996:1–58.
379. Food and Drug Administration. Memorandum, June 8, 1995: recommendations for the deferral of current and recent inmates of correctional institutions as donors of whole blood, blood components, source leukocytes, and source plasma. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, 1995. Available at <http://www.fda.gov/cber/bldmem/6_8_95.txt>. Accessed May 16, 2000.
380. American Association of Blood Banks. New uniform donor history questionnaire issued [Association bulletin 99-10]. American Association of Blood Banks News 1999;(Nov/Dec):13–21.
381. CDC. Guidelines for preventing transmission of human immunodeficiency virus through transplantation of human tissue and organs. MMWR 1994;43(No. RR-8):1–17.
382. CDC. Public health service inter-agency guidelines for screening donors of blood, plasma, organs, tissues, and semen for evidence of hepatitis B and hepatitis C. MMWR 1991;40(No. RR-4):1–17.
383. Food and Drug Administration. Suitability determination for donors of human cellular and tissue-based products [Proposed rule]. Federal Register 1999;64:52696–723. Available at <http://www.fda.gov/cber/rules/suitdonor.pdf>. Accessed May 16, 2000.
384. Wells GM, Woodward TE, Fiset P, Hornick RB. Rocky Mountain spotted fever caused by blood transfusion. JAMA 1978;239(26):2763–65.
385. Herwaldt BL, Kjemtrup AM, Conrad PA, et al. Transfusion-transmitted babesiosis in Washington State: first reported case caused by a WA1-type parasite. J Infect Dis 1997;175(5):1259–62.
386. Dobroszycki J, Herwaldt BL, Boctor F, et al. Cluster of transfusion-associated babesiosis cases traced to a single asymptomatic donor. JAMA 1999;281(10):927–30.
387. CDC. Q fever—California. MMWR 1977;26(10):86, 91.
388. CDC. Transmission of Colorado tick fever virus by blood transfusion—Montana. MMWR 1975;24:422–7.
389. American Association of Blood Banks. Standards for blood banks and transfusion services. 19th ed. Bethesda, MD: American Association of Blood Banks, 1999:1–98.
390. Klein MB, Miller JS, Nelson CM, Goodman JL. Primary bone marrow progenitors of both granulocytic and monocytic lineages are susceptible to infection with the agent of human granulocytic ehrlichiosis. J Infect Dis 1997;176(5):1405–9.
391. Dharmasena F, Gordon-Smith EC. Transmission of malaria by bone marrow transplantation [Letter]. Transplant 1986;42(2):228.
392. Villeneuve L, Cassaing S, Magnaval JF, et al. *Plasmodium falciparum* infection following allogeneic bone-marrow transplantation. Ann Trop Med Parasitol 1999;93(5):533–5.
393. Leiby DA, Lenes BA, Tibbals MA, Tames-Olmedo MT. Prospective evaluation of a patient with *Trypanosoma cruzi* infection transmitted by transfusion. New Engl J Med 1999; 341(16):1237–9.

394. Leiby DA, Read EJ, Lenes BA, et al. Seroepidemiology of *Trypanosoma cruzi*, etiologic agent of Chagas' disease, in US blood donors. J Infect Dis 1997;176:1047–52.
395. Dodd RY. Transmission of parasites by blood transfusion [Review]. Vox Sang 1998;74(suppl 2):161–3.
396. Food and Drug Administration. Guidance for industry: precautionary measures to reduce the possible risk of transmission of zoonoses by blood and blood products from xenotransplantation products recipients and their contacts—12/23/99 [Draft guidance]. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, 1999;1–11. Available at <http://www.fda.gov/cber/guidelines.htm>. Accessed May 16, 2000.
397. CDC. Creutzfeldt-Jakob disease associated with cadaveric dura mater grafts—Japan, January 1979–May 1996. MMWR 1997;46(45):1066–9.
398. Food and Drug Administration. Guidance for industry: revised precautionary measures to reduce the possible risk of transmission of Creutzfeldt-Jakob Disease (CJD) and new variant Creutzfeldt-Jakob disease (nvCJD) by blood and blood products—11/23/99. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, 1999;1–16. Available at <http://www.fda.gov/cber/guidelines.htm>. Accessed May 16, 2000.
399. Will RG, Alpers MP, Dormont D, Schonberger LB, Tateishi J. Infectious and sporadic prion diseases. In: Prusiner SB, ed. Prion biology and diseases. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press, 1999:465–507.
400. Food and Drug Administration. Memorandum, April 23, 1992: revised recommendations for the prevention of Human Immunodeficiency Virus (HIV) transmission by blood and blood products. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, 1992:1–24. Available at <http://www.fda.gov/cber/memo.htm>. Accessed May 16, 2000.
401. Pugatch D, Mileno M, Rich JD. Possible transmission of human immunodeficiency virus type 1 from body piercing. Clin Infect Dis 1998;26(3):767–8.
402. CDC. 1995 revised guidelines for prophylaxis against *Pneumocystic carinii* pneumonia for children infected with or perinatally exposed to human immunodeficiency virus. MMWR 1995;44(No. RR-4):1–11.
403. Attarian H, Bensinger WI, Buckner CD, McDonald DL, Rowley SD. Microbial contamination of peripheral blood stem cell collections. Bone Marrow Transplant 1996;17(5):699–702.
404. Rowley SD, Davis J, Dick J, et al. Bacterial contamination of bone marrow grafts intended for autologous and allogeneic bone marrow transplantation: incidence and clinical significance. Transfusion 1988;28(2):109–12.
405. Webb IJ, Coral FS, Andersen JW, et al. Sources and sequelae of bacterial contamination of hematopoietic cell components: implications for the safety of hematotherapy and graft engineering. Transfusion 1996;36(9):782–8.
406. Meyers JD, Huff JC, Holmes KK, Thomas ED, Bryan JA. Parenterally transmitted hepatitis A associated with platelet transfusions: epidemiologic study of an outbreak in a marrow transplantation center. Ann Intern Med 1974;81(2):145–51.
407. Fountain D, Ralston M, Higgins N, et al. Liquid nitrogen freezers: a potential source of microbial contamination of hematopoietic stem cell components. Transfusion 1997;37(6):585–91.
408. Nasser RM, Hajjar I, Sandhaus LM, et al. Routine cultures of bone marrow and peripheral stem cell harvests: clinical impact, cost analysis, and review. Clin Infect Dis 1998;27(4): 886–8.
409. Flake AW, Roncarolo MG, Puck JM, et al. Treatment of x-linked severe combined immunodeficiency by in utero transplantation of paternal bone marrow. N Engl J Med 1996;335(24):1806–10.
410. Flake AW, Zanjani ED. In utero hematopoietic stem cell transplantation: a status report. JAMA 1997;278(11):932–7.

TABLE 1. Evidence-based rating system used to determine strength of recommendations

Category	Definition	Recommendation
A	Strong evidence for efficacy and substantial clinical benefit	Strongly recommended
B	Strong or moderate evidence for efficacy, but only limited clinical benefit	Generally recommended
C	Insufficient evidence for efficacy; or efficacy does not outweigh possible adverse consequences (e.g., drug toxicity or interactions) or cost of chemoprophylaxis or alternative approaches	Optional
D	Moderate evidence against efficacy or for adverse outcome	Generally not recommended
E	Strong evidence against efficacy or of adverse outcome	Never recommended

Source: Adapted from CDC. 1999 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. MMWR 1999;48(RR-10):1–66.

TABLE 2. Evidence-based rating system used to determine quality of evidence supporting recommendation

Category	Definition
I	Evidence from at least one well-executed randomized, controlled trial
II	Evidence from at least one well-designed clinical trial without randomization; cohort or case-controlled analytic studies (preferably from more than one center); multiple time-series studies; or dramatic results from uncontrolled experiments
III	Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

Source: Adapted from CDC. 1999 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. MMWR 1999;48(RR-10):1–66.

TABLE 3. Foods that pose a high risk for hematopoietic stem cell transplant (HSCT) recipients and safer substitutions

Foods That Pose a High Risk	Safer Substitutions
Raw and undercooked eggs* and foods containing them (e.g., french toast, omelettes, salad dressings, egg nog, and puddings)	Pasteurized or hard boiled eggs
Unpasteurized dairy products (e.g., milk, cheese, cream, butter, and yogurt)	Pasteurized dairy products
Fresh-squeezed, unpasteurized fruit and vegetable juices	Pasteurized juices
Unpasteurized cheeses or cheeses containing molds	Pasteurized cheeses
Undercooked or raw poultry, meats, fish, and seafood cooked fish, and seafood	Cooked poultry, well-done meats,
Vegetable sprouts (e.g., alfalfa, bean, and other seed sprouts)†	Should be avoided
Raw fruits with a rough texture (e.g., raspberries)§	Should be avoided
Smooth raw fruits	Should be washed under running water, peeled, or cooked
Unwashed raw vegetables¶	Should be washed under running water, peeled, or cooked
Undercooked or raw tofu	Cooked tofu (i.e., cut into ≤1-inch cubes and boiled for ≥5 minutes in water or broth before eating or using in recipes)
Raw or unpasteurized honey	Should be avoided
Deli meats, hot dogs, and processed meats**	Should be avoided unless further cooked
Raw, uncooked grain products	Cooked grain products including bread, cooked, and ready-to-eat cold cereal, pretzels, popcorn, potato chips, corn chips, tortilla chips, cooked pasta, and rice
Maté tea††	Should be avoided
All moldy and outdated food products	Should be avoided
Unpasteurized beer (e.g., home-brewed and certain microbrewery beer)	Pasteurized beer (i.e., retail bottled or canned, or draft beer that has been pasteurized after fermentation)
Raw, uncooked brewers yeast	Should be avoided; HSCT recipients should avoid any contact with raw yeast (e.g., they should not make bread products themselves)
Unroasted raw nuts	Cooked nuts
Roasted nuts in the shell	Canned or bottled roasted nuts or nuts in baked products

* **Source:** CDC. Outbreaks of *Salmonella* serotype enteritidis infection associated with consumption of raw shell eggs—United States, 1994–1995. MMWR 1996; 45(34):737–42.

† **Source:** Taormina PJ, Beuchat LR, Slutsker L. Infections associated with eating seed sprouts: an international concern. Emerg Infect Dis 1999;5(5):626–34.

§ **Source:** Herwaldt BL, Ackers ML. Outbreak in 1996 of cyclosporiasis associated with imported raspberries. New Engl J Med 1997;336(22):1548–56.

¶ **Source:** CDC. Foodborne outbreak of cryptosporidiosis—Spokane, Washington, 1997. MMWR 1998;47(27):565–7.

** **Source:** CDC. Update: multistate outbreak of listeriosis—United States, 1998–1999. MMWR 1999;47(51):1117–8.

†† **Source:** Kusminsky G, Dictar M, Arduino S, Zylberman M, Sanchez Avalos JC. Do not drink Maté: an additional source of infection in South American neutropenic patients. Bone Marrow Transplant 1996;17(1):127.

TABLE 4. 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 4. (*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 4. (*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 5. 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 5. (*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 6. 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 6. (*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 7. 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 7. (*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).

TABLE 8. Vaccine information

Vaccine or toxoid	Trade name	Manufacturer/ telephone number	Storage recommendation
Diphtheria toxoid-tetanus toxoid-pertussis vaccine	Tripedia®	Aventis Pasteur, Inc. (800) Vaccine	Store at 2–8 C (36–46 F); do not freeze
	Infanrix®	SmithKline Beecham (800) 877-1158	
	Acel-Imune®	Wyeth-Lederle (800) 572-8221	
	Certiva®	North American Vaccine (888) 628-2829	
Diphtheria toxoid-tetanus toxoid-pertussis vaccine–*Haemophilus influenzae* type b	Tetramune®	Wyeth-Lederle (800) 572-8221	Store at 2–8 C (36–46 F); do not freeze
	DTP/ACTHib®	Aventis Pasteur, Inc. (800) Vaccine	
	TriHibit®		
Tetanus-diphtheria toxoid (adult) and Diphtheria-tetanus toxoid (pediatric)	Generic	Aventis Pasteur, Inc. (800) Vaccine Wyeth-Lederle (800) 572-8221	Store at 2–8 C (36–46 F); do not freeze
Haemophilus influenzae type b	ACTHib®	Aventis Pasteur, Inc. (800) Vaccine	Store at 2–8 C (36–46 F); do not freeze
	HibTiter®	Wyeth-Lederle (800) 572-8221	
	PedvaxHIB®	Merck Human Health Division (800) MerckRX (ordering) (800) NSCmerc (questions)	
	OmniHIB®	SmithKline Beecham (800) 877-1158	
Haemophilus influenzae type b-Hepatitis B	COMVAX®	Merck Human Health Division (800) MerckRX (ordering) (800) NSCmerc (questions)	Store at 2–8 C (36–46 F); do not freeze
Inactivated polio vaccine	IPOL®	Aventis Pasteur, Inc. (800) Vaccine	
Measles-mumps-rubella Measles-rubella Mumps-rubella Measles Mumps Rubella	M-M-R II® M-R-Vax II® Biavax II® Attenuvax® Mumpsvax® Meruvax II®	Merck Human Health Division (800) MerckRX (ordering) (800) NSCmerc (questions)	Store at 2–8 C (36–46 F); freezing is permissible
Varicella	Varivax®		Maintain in a frozen state of –15 C (5 F) or colder
Hepatitis A	Vaqta® Havix®	SmithKline Beecham (800) 877-1158	Store at 2–8 C (36–46 F); do not freeze
Hepatitis B	Engerix-B® Recombivax B®	Merck Human Health Division (800) MerckRX (ordering) (800) NSCmerc (questions)	Store at 2–8 C (36–46 F); do not freeze
Influenza	Fluzone®	Aventis Pasteur, Inc. (800) Vaccine	Store at 2–8 C (36–46 F); do not freeze
	Fluvirin®	Celltech Medeva Pharmaceutical (800) 234-5535	
	Flu-Shield®	Wyeth-Ayerst Laboratories (800) 358-7443	
	Fluogen®	Monarch Pharmaceuticals (888) 358-6436	
Japanese encephalitis	JE-VAX	Research Foundation for Microbial Diseases of Osaka University, Japan; Distributed by Aventis Pasteur, Inc. (800) Vaccine SmithKline Beecham	Store at 2–8 C (36–46 F); do not freeze

TABLE 8. (*Continued*) Vaccine information

Vaccine or toxoid	Trade name	Manufacturer/ telephone number	Storage recommendation
Lyme disease	LYMErix™	(800) 877-1158	Store at 2–8 C 36–46 F); do not freeze
Pneumococcal 23-valent	Pru-Immune-23®	Wyeth-Lederle (800) 572-8221	Store at 2–8 C (36–46 F); do not freeze
	Pneumovax 23®	Merck Human Health Division (800) MerckRX (ordering) (800) NSCmerc (questions)	
Meningococcal	Menomune-A/C/Y/W-135®	Aventis Pasteur, Inc. (800) Vaccine	Store at 2–8 C (36–46 F); do not freeze
Rabies	Generic	BioPort Corporation (517) 327-1500; distributed by SmithKline Beecham (800) 877-1158	Store at 2–8 C (36–46 F); do not freeze
	Imovax Rabies® and Imovax Rabies ID®	Aventis Pasteur, Inc. (800) Vaccine	
	RabAvert™	Chiron Corporation (800) 244-7668	
Typhoid	Typhoid Vaccine U.S. P.	Wyeth-Lederle (800) 572-8221	
Typhoid Vi polysaccharide	Typhim Vi™	Aventis Pasteur, Inc. (800) Vaccine	

Notes: Persons needing additional vaccine information or CDC's Advisory Committee on Immunization Practices guidelines can contact the CDC Immunization Hotline at (800) CDC-SHOT ([800] 232-7468) or at <http:// www.cdc.gov/nip>. 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 at (800) 822-7967.

Appendix

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

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

Pathogen: Cytomegalovirus

Indication	First choice	Alternatives
Universal prophylaxis for cytomegalovirus disease among all allogeneic adult or adolescent HSCT recipients at risk throughout phase II (i.e., from engraftment to day 100 after HSCT)	Ganciclovir, 5 mg/kg/dose intravenously every 12 hours for 5–7 days, followed by 5–6 mg/kg intravenously daily for 5 days/week from engraftment until day 100 after HSCT (AI)	Foscarnet, 60 mg/kg intravenously every 12 hours for 7 days, followed by 90–120 mg/kg intravenously daily until day 100 after HSCT (CIII)
Or preemptive cytomegalovirus treatment administered <100 days after HSCT to all allogeneic adult or adolescent HSCT recipients at risk: Start ganciclovir when the patient experiences any level of cytomegalovirus antigenemia or viremia or has ≥2 consecutively positive cytomegalovirus-DNA polymerase chain reaction tests	Ganciclovir, 5 mg/kg/dose intravenously every 12 hours for 7–14 days, followed by 5 mg/kg/day for 5 days/week until day 100 after HSCT or for a minimum of 3 weeks, whichever is longer (AI); or administer ganciclovir for a total of 3–6 weeks; antigen or polymerase chain reaction tests should be negative when ganciclovir is stopped; reinstitute ganciclovir if subsequent weekly cytomegalovirus antigenemia screening tests become positive (BI)	
Preemptive treatment for cytomegalovirus seropositive autologous adult or adolescent HSCT recipients at <100 days after HSCT: Start ganciclovir when antigenemia is ≥5 cells/slide, but CD34+-selected patients should be treated at any level of antigenemia*	Ganciclovir, 5 mg/kg/dose intravenously every 12 hours for 7 days, followed by 5 mg/kg/day intravenously for 5 days/week for 2 weeks (BII)	
Preemptive treatment of allogeneic adult or adolescent HSCT recipients >100 days after HSCT: Start ganciclovir when a) antigenemia is ≥5 cells/slide or b) the patient has had ≥2 consecutively positive viremia or polymerase chain reaction tests (e.g., in a person receiving steroids for graft-versus-host disease or who received ganciclovir or foscarnet at <100 days after HSCT)	Ganciclovir, 5 mg/kg/dose intravenously every 12 hours for 7 days, followed by 5 mg/kg/day intravenously for 5 days/week for 2 weeks (BIII)	

* **Source**: Holmberg LA, Boeckh M, Hooper H, et al. Increased incidence of cytomegalovirus disease after autologous CD34-selected peripheral blood stem cell transplantation [Clinical observations, interventions, and therapeutic trials]. Blood 1999;94(12):4029–35.

Notes: Patients who do not tolerate standard doses of ganciclovir should be administered foscarnet. Ganciclovir and foscarnet doses should be modified for renal impairment. Prehydration is required for foscarnet administration.

Pathogen: Herpes simplex virus

Indication	First choice	Alternatives
Prevention of herpes simplex virus reactivation among seropositive adult or adolescent HSCT recipients: Start acyclovir at the beginning of conditioning therapy and continue until engraftment or until mucositis resolves (i.e., approximately 30 days after HSCT for allogeneic HSCT recipients)	Acyclovir, 200 mg by mouth 3 times/day or 250 mg/m^2/dose infused over 1 hour intravenously every 12 hours (BIII)	Valacyclovir, 500 mg by mouth daily (CIII)

Note: For patients requiring prophylaxis for cytomegalovirus and herpes simplex virus after engraftment, ganciclovir alone provides effective prophylaxis for both pathogens.

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: Bacterial infections, general prophylaxis

Indication	First choice	Alternatives
Prevention of bacterial infections among allogeneic adult or adolescent HSCT recipients with severe hypogammaglobulinemia (i.e., serum immunoglobulin G level < 400 mg/dl) at <100 days after HSCT	Intravenous immunoglobulin, 500 mg/kg/week (CIII)	None

Notes: 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 receive standard immunoglobulin products (**Source**: Siberry GK, Iannone R, eds. Harriet Lane handbook: a manual for pediatric house officers. 15th ed.; St. Louis, MO: Mosby, Inc., 2000:339;739) (DIII). However, researchers have reported that use of immunoglobulin A-depleted immunoglobulin preparations can be used with caution among 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; Stiehm ER. Human intravenous immunoglobulin in primary and secondary antibody deficiencies [Review]. Pediatr Infect Dis J 1997;16[7]:696–707; and American Academy of Pediatrics. Passive immunization. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics;2000:41–53). Researchers also propose checking serum immunoglobulin G levels every 2 weeks among patients receiving intravenous immunoglobulin replacement therapy.

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.

Pathogen: Methicillin-resistant *Staphylococcus aureus*

Indication	First choice	Alternatives
Elimination of methicillin-resistant *Staphylococcus aureus* carrier state among adults or adolescents to prevent this disease among chronic carriers	Mupirocin calcium ointment 2%; use a cotton-tipped applicator or equivalent to apply to nares 2 times/day for 5 days or to wounds daily for 2 weeks	None

Pathogen: *Candida* species

Indication	First choice	Alternatives
Prophylaxis for disease from fluconazole-susceptible *Candida* species among a) allogeneic adult or adolescent HSCT recipients or b) autologous adult or adolescent HSCT recipients with lymphoma or leukemia and who have or will have prolonged neutropenia and mucosal damage from intense conditioning regimens or graft manipulation or who have recently received fludarabine or 2-chlorodeoxyadenosine: Administer prophylaxis from the day of transplantation (i.e., day 0) until engraftment (i.e., approximately 30 days after HSCT) or until 7 days after the absolute neutrophil count > 1,000 cells/mm^3	Fluconazole, 400 mg by mouth or intravenously daily (AI)	None

Pathogen: *Pneumocystis carinii*

Indication	First choice	Alternatives
Prophylaxis for *Pneumocystis carinii* pneumonia among a) all allogeneic adult or adolescent HSCT recipients or b) autologous adult or adolescent HSCT recipients with underlying hematologic malignancies (e.g., lymphoma or leukemia) or for those receiving intense conditioning regimens or graft manipulation or for those who have recently received fludarabine or 2-chlorodeoxyadenosine:* Administer prophylaxis from time of engraftment for ≥6 months after HSCT; continue >6 months after HSCT for the duration of immunosuppression for all persons who a) are receiving immunosuppressive therapy (e.g., prednisone or cyclosporine) or who b) have chronic graft-versus-host disease	Trimethoprim-sulfamethoxazole, 1 double-strength tablet by mouth daily or 1 single-strength tablet by mouth daily or 1 double-strength tablet by mouth 3 times/week (AII); researchers also recommend administering prophylaxis for 1–2 weeks before HSCT (i.e., day –14 to –2) (CIII)	Dapsone, 50 mg by mouth 2 times/day or 100 mg by mouth daily (BIII) or pentamidine, 300 mg every 3–4 weeks by Respirgard II™ nebulizer (CIII)

* **Source**: Tuan IZ, Dennison D, Weisdorf DJ. *Pneumocystis carinii* pneumonitis after bone marrow transplantation. Bone Marrow Transplant 1992;10(3):267–72.

Note: Patients who are receiving sulfadiazine-pyrimethamine for toxoplasmosis therapy are protected against *Pneumocystis carinii* and do not need additional prophylaxis.

Pathogen: *Toxoplasma gondii*

Indication	First choice	Alternatives
Prophylaxis of *Toxoplasma gondii* disease among seropositive allogeneic adult or adolescent HSCT recipients: Start after engraftment and administer as long as patients remain on immunosuppressive therapy (i.e., generally, until 6 months after HSCT)	Trimethoprim-sulfamethoxazole, 1 double-strength tablet by mouth daily or 1 single-strength tablet by mouth daily or 1 double-strength table by mouth 3 times/week (AII)	For those persons who are intolerant of trimethoprim-sulfamethoxazole, the following drugs can be substituted: Clindamycin, 300–450 mg by mouth every 6–8 hours; plus pyrimethamine, 25–75 mg by mouth daily; plus leucovorin, 10–25 mg by mouth 4 times/day (CIII)

Note: Among allogeneic HSCT recipients, clinical toxoplasmosis has occurred despite the use of trimethoprim-sulfamethoxazole for *Pneumocystis carinii* prophylaxis (**Source**: Slavin MA, Meyers JD, Remington JS, Hackman RC. *Toxoplasma gondii* infection in marrow transplant recipients: a 20 year experience. Bone Marrow Transplant 1994;13[5]:549–57).

Pathogen: *Strongyloides* species

Indication	First choice	Alternatives
Prevention of strongyloidiasis hyperinfection among adult or adolescent HSCT candidates whose HSCT screening tests are positive for *Strongyloides* species or who have an unexplained eosinophilia and a travel or residence history suggestive of exposure to *Strongyloides stercoralis*: Administer prophylaxis before HSCT	Ivermectin, 200 µg/kg by mouth daily for 2 consecutive days* (BIII); 1 tablet = 6 mg; doses administered as follows: Body weight (kg) — Oral dose <15 — Not recommended ≥15–24 — ½ tablet 25–35 — 1 tablet 36–50 — 1½ tablets 51–65 — 2 tablets 66–79 — 2½ tablets ≥80 — 200 µg/kg	Albendazole, 400 mg by mouth daily for 3 days or thiabendazole, 25 mg/kg by mouth 2 times/day for 2 days (BIII); maximum dose, 3 g/24 hours

*__Sources__: Liu LX, Weller PF. Strongyloidiasis and other intestinal nematode infections [Review]. Infect Dis Clin North Am 1993;7(3):655–82; and Naquira C, Jimenez G, Guerra JG, et al. Ivermectin for human strongyloidiasis and other intestinal helminths. Am J Trop Med Hyg 1989;40:304–9.

Notes: Among immunocompromised patients, multiple courses at 2-week intervals might be required; however, cure might not be achievable. Safety and efficacy of ivermectin has not been established during pregnancy. Albendazole and thiabendazole are contraindicated during pregnancy.

Pathogen: Traveler's diarrhea

Indication	First choice	Alternatives
Prophylaxis among adult or adolescent HSCT recipients who are immunocompromised and who plan to travel in developing countries	Ciprofloxacin, 500 mg by mouth daily for the duration of stay in developing countries (BIII) or bismuth subsalicylate, 2 oz by mouth 4 times/day or 2 tablets by mouth 4 times/day; can be administered for ≤3 weeks to prevent travelers' diarrhea in adults aged >18 years only	Trimethoprim-sulfamethoxazole, 1 double-strength tablet by mouth daily for the duration of stay in developing country (CIII)

Notes: Use of aspirin-containing products including bismuth subsalicylate is contraindicated in persons aged <18 years unless prescribed by a physician because these products have been associated with Reye's syndrome (**Source**: Belay E, Bresee JS, Holman RC, Khan AS, Shahriari A, Schonberger LB. Reye's syndrome in the United States from 1981 through 1997. New Engl J Med 1999;340[18]:1377–82). Ciprofloxacin, norfloxacin, and ofloxacin are not approved for use among children aged <18 years.

Pathogen: *Mycobacteria tuberculosis*

Indication	First choice	Alternatives
Prevention of *Mycobacteria tuberculosis* among a) highly immunocompromised adult or adolescent HSCT recipients or candidates who have been substantially exposed to someone with active, infectious (e.g., sputum smear positive) pulmonary or laryngeal tuberculosis, regardless of the HSCT recipient's or candidate's tuberculin skin test status, or b) adult or adolescent HSCT recipients or candidates with a positive tuberculin skin test and who were not previously treated and have no evidence of active tuberculosis disease	Isoniazid, 5 mg/kg/day by mouth or intramuscularly for 9 months (i.e., for ≥270 doses);* maximum dose, 300 mg/day, and pyridoxine (vitamin B_6), 25–50 mg by mouth daily for 9 months; administer to nutritionally deficient HSCT recipients and candidates while on isoniazid preventive therapy to reduce the occurrence of isoniazid-induced neuropathy* (BIII)	None

*__Source__: CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. MMWR 1998;47(No. RR-20):1–58.

Notes: A twice-weekly schedule of isoniazid and pyridoxine can be administered (CIII). The twice-weekly isoniazid dose is 15 mg/kg by mouth or intramuscularly (maximum dose, 900 mg). The twice-weekly pyridoxine dose is 50–100 mg by mouth. A 2-month pyrazinamide/rifampin preventive therapy regimen can be used for HSCT candidates who are not at risk for serious rifampin drug interactions and whose HSCT is not scheduled until ≥2 weeks after the 2-month course is completed (**Sources**: CDC. Notice to readers: use of short-course tuberculosis preventive therapy regimens in HIV-seronegative persons. MMWR 1998;47[42]:911–2; and CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. MMWR 1998;47[No. RR-20]:1–58) (CIII). The usual pyrazinamide dose is 15–30 mg/kg/day by mouth or 50–70 mg/kg/dose by mouth 2 times/week (maximum daily pyrazinamide dose, 2.0 gm; maximum twice-weekly dose, 3.5 gm). Rifampin dose is 10 mg/kg/day by mouth or intravenously or 10 mg/kg/dose administered 2 times/week by mouth or intravenously (maximum rifampin dose, 600 mg). Routine use of a 2-month pyrazinamide/rifampin preventive therapy regimen is not recommended after HSCT because of the risk for serious rifampin drug interactions (DIII). Persons who have been exposed to rifampin- and isoniazid-resistant tuberculosis should be placed on preventive therapy regimens that involve ≥2 antituberculosis drugs to which the infecting strain is susceptible, and a tuberculosis specialist should be consulted (**Source**: CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. MMWR 1998;47[No. RR-20]:1–58) (BIII). A tuberculosis specialist should also be consulted for patients who are intolerant to isoniazid (AIII). All intermittent dosing strategies should be administered as directly observed therapy (AIII).

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

Pathogen: Cytomegalovirus

Indication	First choice	Alternatives
Universal prophylaxis for cytomegalovirus disease among all allogeneic pediatric HSCT recipients at risk throughout phase II (i.e., from engraftment to day 100 after HSCT)	Ganciclovir, 5 mg/kg/dose intravenously every 12 hours for 5–7 days, followed by 5 mg/kg/dose intravenously daily for 5 days/week from engraftment until day 100 after HSCT (AI)	Foscarnet, 60 mg/kg intravenously every 12 hours for 14 days, followed by 90–120 mg/kg/day until day 100 after HSCT (CIII)
Or preemptive cytomegalovirus treatment administered <100 days after HSCT to all allogeneic pediatric HSCT recipients at risk: Start ganciclovir when the patient experiences any level of cytomegalovirus antigenemia or viremia or has ≥2 consecutively positive cytomegalovirus-DNA polymerase chain reaction tests	Ganciclovir, 5 mg/kg/dose intravenously every 12 hours for 7–14 days, followed by 5 mg/kg/day for 5 days/week until day 100 after HSCT or for a minimum of 3 weeks, whichever is longer (AI); or administer ganciclovir for a total of 3–6 weeks; antigen or polymerase chain reaction tests should be negative when ganciclovir is stopped; reinstitute ganciclovir if subsequent weekly cytomegalovirus antigenemia screening tests become positive (BI)	
Preemptive treatment for cytomegalovirus seropositive autologous pediatric HSCT recipients at <100 days after HSCT: Start ganciclovir when antigenemia is ≥5 cells/slide, but CD34+-selected patients should be treated at any level of antigenemia*	Ganciclovir, 5 mg/kg/dose intravenously every 12 hours for 7 days, followed by 5 mg/kg/day intravenously for 5 days/week for 2 weeks (BII)	
Preemptive treatment of allogeneic pediatric HSCT recipients >100 days after HSCT: Start ganciclovir when a) antigenemia is ≥5 cells/slide or b) the patient has had ≥2 consecutively positive viremia or polymerase chain reaction tests (e.g., in a person receiving steroids for graft-versus-host disease or who received ganciclovir or foscarnet at <100 days after HSCT)	Ganciclovir, 5 mg/kg/dose intravenously every 12 hours for 7 days, followed by 5 mg/kg/day intravenously for 5 days/week for 2 weeks (BIII)	

* **Source**: Holmberg LA, Boeckh M, Hooper H, et al. Increased incidence of cytomegalovirus disease after autologous CD34-selected peripheral blood stem cell transplantation [Clinical observations, interventions, and therapeutic trials]. Blood 1999;94(12):4029–35.

Notes: Patients who do not tolerate standard doses of ganciclovir should be administered foscarnet. Ganciclovir and foscarnet doses should be modified for renal impairment. Prehydration is required for foscarnet administration.

Pathogen: Herpes simplex virus

Indication	First choice	Alternatives
Prevention of herpes simplex virus reactivation among seropositive pediatric HSCT recipients: Start acyclovir at the beginning of conditioning therapy and continue until engraftment or until mucositis resolves (i.e., approximately 30 days after HSCT for allogeneic HSCT recipients)	Acyclovir, 250 mg/m^2/dose intravenously every 8 hours (BIII) or 125 mg/m^2/dose intravenously every 6 hours (CIII)	Acyclovir 600–1,000 mg/24 hours by mouth, divided in 3–5 doses/day

Note: For patients requiring prophylaxis for cytomegalovirus and herpes simplex virus after engraftment, ganciclovir alone provides effective prophylaxis for both pathogens. Valacyclovir is not approved for use among children.

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 (All); 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: 6–35 mo — Number of doses: 0.25 ml — Type of influenza vaccine: 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: Respiratory syncytial virus

Indication	First choice	Alternatives
Prophylaxis for respiratory syncytial virus (RSV) lower respiratory infection among hypogammaglobulinemic pediatric HSCT recipients	RSV intravenous immunoglobulin can be administered in place of intravenous immunoglobulin during RSV season (i.e., November–April in the United States) for pediatric HSCT recipients who are on routine intravenous immunoglobulin therapy* (e.g., those with hypogammaglobulinemia) (CIII); usual RSV intravenous immunoglobulin dose is 750 mg/kg/month or a 1-mg/1-mg dosing substitution of RSV intravenous immunoglobulin for intravenous immunoglobulin can be used for patients who normally require high intravenous immunoglobulin doses to maintain serum immunoglobulin G > 400 mg/dl; can administer more frequently than monthly as needed to keep serum immunoglobulin G > 400 mg/dl	None
Preemptive treatment of RSV upper respiratory infection or early lower respiratory infection among pediatric HSCT recipients	Aerosolized ribavirin,* 6 g/300 ml sterile water to make a concentration of 20 mg/ml; administer 18 hours/day for 10 days in a tent (CIII); for HSCT recipients with lower respiratory infections who cannot tolerate a tent or who have RSV upper respiratory infection, administer ribavirin as 2 g for 2 hours every 8 hours by face mask for 10 days; use small particle aerosol generator model SPAG-2	

*__Source__: American Academy of Pediatrics. Respiratory syncytial virus. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Disease. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics;2000: 483–7.

__Notes__: RSV intravenous immunoglobulin is contraindicated among patients with immunoglobulin A deficiency or who might have allergic reactions or anaphylaxis when receiving blood products containing immunoglobulin A (DIII). RSV monoclonal antibody is under investigational use among HSCT recipients for treatment with ribavirin but not for prophylaxis.

Pathogen: Bacterial infections, general prophylaxis

Indication	First choice	Alternatives
Prevention of bacterial infections among allogeneic pediatric HSCT recipients with severe hypogammaglobulinemia (i.e., serum immunoglobulin G level < 400 mg/dl) at <100 days after HSCT	Intravenous immunoglobulin 400 mg/kg/month; increase dose or frequency as needed to keep serum immunoglobulin G levels > 400 mg/dl (CIII)	None

Notes: 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 receive standard immunoglobulin products (**Source**: Siberry GK, Iannone R, eds. Harriet Lane handbook: a manual for pediatric house officers. 15th ed.; St. Louis, MO: Mosby, Inc., 2000:339;739) (DIII). 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; Stiehm ER. Human intravenous immunoglobulin in primary and secondary antibody deficiencies [Review]. Pediatr Infect Dis J 1997;16[7]:696–707; American Academy of Pediatrics. Passive immunization. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics;2000:41–53). Researchers also propose checking serum immunoglobulin G levels every 2 weeks for patients receiving intravenous immunoglobulin replacement therapy.

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.

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.

Pathogen: Methicillin-resistant *Staphylococcus aureus*

Indication	First choice	Alternatives
Elimination of methicillin-resistant *Staphylococcus aureus* carrier state among pediatric patients to prevent this disease among chronic carriers	Mupirocin calcium ointment 2%; use a cotton-tipped applicator or equivalent to apply to nares 2 times/day for 5 days or to wounds daily for 2 weeks*	Bacitracin is regarded safe for use among children, and the dose is the same as for mupirocin; however, no standardized protocol has been evaluated

* Safety of mupirocin calcium ointment 2% use among children aged <12 years has not be established.

Pathogen: *Candida* species

Indication	First choice	Alternatives
Prophylaxis for disease from fluconazole-susceptible *Candida* species among a) allogeneic pediatric HSCT recipients or b) autologous pediatric HSCT recipients with lymphoma or leukemia and who have or will have prolonged neutropenia and mucosal damage from intense conditioning regimens or graft manipulation or who have recently received fludarabine or 2-chlorodeoxyadenosine: Administer prophylaxis from the day of transplantation (i.e., day 0) until engraftment (i.e., approximately 30 days after HSCT) or until 7 days after the absolute neutrophil count > 1,000 cells/mm^3	Fluconazole, for children aged 6 months–13 years, administer 3–6 mg/kg/day by mouth or intravenously (AI); maximum dose, 600 mg/day; for children aged >13 years, administer 400 mg by mouth or intravenously daily (AI)	None

Pathogen: *Pneumocystis carinii*

Indication	First choice	Alternatives
Prophylaxis for *Pneumocystis carinii* pneumonia among a) all allogeneic pediatric HSCT recipients or b) autologous pediatric HSCT recipients with underlying hematologic malignancies (e.g., lymphoma or leukemia) or for those receiving intense conditioning regimens or graft manipulation or for those who have recently received fludarabine or 2-chlorodeoxyadenosine:* Administer prophylaxis from time of engraftment for ≥6 months after HSCT; continue >6 months after HSCT for the duration of immunosuppression for all persons who a) are receiving immunosuppressive therapy (e.g., prednisone or cyclosporine) or who b) have chronic graft-versus-host disease	Trimethoprim-sulfamethoxazole, 150 mg trimethoprim/750 mg sulfamethoxazole/m^2/day by mouth in 2 divided doses 3 times/week on consecutive days (AII); or a single dose by mouth 3 times/week on consecutive days; or by mouth in 2 divided doses daily for 7 days; or by mouth in 2 divided doses 3 times/week on alternate days; researchers also report administering prophylaxis for 1–2 weeks before HSCT (i.e., day –14 to –2) (CIII)	Dapsone, for HSCT recipients aged ≥1 months, 2 mg/kg (maximum dose, 100 mg) by mouth daily (BIII); or intravenous pentamidine, 4 mg/kg every 2–4 weeks; or aerosolized pentamidine, for HSCT recipients aged ≤5 years, 9 mg/kg/dose; or for HSCT recipients aged >5 years, 300 mg; should be administered every month by Respirgard II™ nebulizer (CIII)

* **Source**: Tuan IZ, Dennison D, Weisdorf DJ. *Pneumocystis carinii* pneumonitis after bone marrow transplantation. Bone Marrow Transplant 1992;10(3):267–72.

Notes: Trimethoprim-sulfamethoxazole is not recommended for patients aged <2 months because of risk for kernicterus. Patients who are receiving sulfadiazine-pyrimethamine for toxoplasmosis therapy are protected against *Pneumocystis carinii* and do not need additional prophylaxis.

Pathogen: *Toxoplasma gondii*

Indication	First choice	Alternatives
Prophylaxis of *Toxoplasma gondii* disease among seropositive allogeneic pediatric HSCT recipients: Start after engraftment and administer as long as patients remain on immunosuppressive therapy (i.e., generally, until 6 months after HSCT)	Trimethoprim-sulfamethoxazole, 150 mg trimethoprim/750 mg sulfamethoxazole/m^2/day by mouth in 2 divided doses 3 times/week on consecutive days (AII); or a single dose by mouth 3 times/ week on consecutive days; or by mouth in 2 divided doses daily for 7 days; or by mouth in 2 divided doses 3 times/weekly on alternate days	For those persons who are intolerant of trimethoprim-sulfamethoxazole, the following drugs can be substituted: Clindamycin, 20–30 mg/kg/day by mouth, divided in 4 divided doses daily; plus pyrimethamine, 1 mg/ kg by mouth daily; plus leucovorin, 5 mg by mouth every 3 days (CIII)

Note: Trimethoprim-sulfamethoxazole is not recommended for patients aged <2 months because of risk for kernicterus. Among allogeneic HSCT recipients, clinical toxoplasmosis has occurred despite the use of trimethoprim-sulfamethoxazole for *Pneumocystis carinii* prophylaxis (**Source**: Slavin MA, Meyers JD, Remington JS, Hackman RC. *Toxoplasma gondii* infection in marrow transplant recipients: a 20 year experience. Bone Marrow Transplant 1994;13[5]:549–57).

Pathogen: *Strongyloides* species

Indication	First choice	Alternatives
Prevention of strongyloidiasis hyperinfection among pediatric HSCT candidates whose HSCT screening tests are positive for *Strongyloides* species or who have an unexplained eosinophilia and a travel or residence history suggestive of exposure to *Strongyloides stercoralis*: Administer prophylaxis before HSCT	Ivermectin, 200 µg/kg by mouth daily for 2 consecutive days* (BIII); 1 tablet = 6 mg; doses administered as follows: Body weight (kg) — Oral dose <15 — Not recommended ≥15–24 — ½ tablet 25–35 — 1 tablet 36–50 — 1½ tablets 51–65 — 2 tablets 66–79 — 2½ tablets ≥80 — 200 µg/kg	Thiabendazole, 25 mg/kg 2 times daily for 2 days; maximum dose, 3 g/24 hours

* **Sources**: Liu LX, Weller PF. Strongyloidiasis and other intestinal nematode infections [Review]. Infect Dis Clin North Am 1993;7(3):655–82; and Naquira C, Jimenez G, Guerra JG, et al. Ivermectin for human strongyloidiasis and other intestinal helminths. Am J Trop Med Hyg 1989;40:304–9.

Notes: Ivermectin safety among children weighing <15 kg has not been established. Among immunocompromised patients, multiple courses of ivermectin at 2-week intervals might be required; however, cure might not be achievable. Safety and efficacy of ivermectin has not been established during pregnancy. Thiabendazole is contraindicated during pregnancy.

Pathogen: Traveler's diarrhea

Indication	First choice	Alternatives
Prophylaxis among pediatric HSCT recipients who are immunocompromised and who plan to travel in developing countries	Trimethoprim-sulfamethoxazole, 150 mg trimethoprim/750 mg sulfamethoxazole/m^2/day by mouth, divided in 2 doses 3 times/ week on consecutive days (CIII); can be administered for duration of stay in developing country	Trimethoprim-sulfamethoxazole, single dose by mouth 3 times/ week on consecutive days

Notes: Use of aspirin-containing products including bismuth subsalicylate is contraindicated in persons aged <18 years unless prescribed by a physician because these products have been associated with Reye's syndrome (**Source**: Belay E, Bresee JS, Holman RC, Khan AS, Shahriari A, Schonberger LB. Reye's syndrome in the United States from 1981 through 1997. New Engl J Med 1999;340[18]:1377–82). Trimethoprim-sulfamethoxazole is not recommended for patients aged <2 months because of risk for kernicterus. Resistance to trimethoprim-sulfamethoxazole is common in tropical areas. Usual doses of trimethoprim-sulfamethoxazole for *Pneumocystis carinii* pneumonia prophylaxis should provide limited protection against traveler's diarrhea.

Pathogen: *Mycobacteria tuberculosis*

Indication	First choice	Alternatives
Prevention of *Mycobacteria tuberculosis* among a) highly immunocompromised pediatric HSCT recipients or candidates who have been exposed to someone with active, infectious (e.g., sputum smear positive) pulmonary or laryngeal tuberculosis, regardless of the HSCT recipient's or candidate's tuberculin skin test status, or b) pediatric HSCT recipients or candidates with a positive tuberculin skin test and who were not previously treated and have no evidence of active tuberculosis disease	Isoniazid, 10–20 mg/kg/day by mouth or intramuscularly for 9 months (i.e., for ≥270 doses);* maximum dose, 300 mg/day, and pyridoxine (vitamin B_6), 1–2 mg/kg/day by mouth daily for 9 months; dose required might vary by age and condition;† administer to nutritionally deficient HSCT recipients and candidates while on isoniazid preventive therapy to reduce the occurrence of isoniazid-induced neuropathy* (BIII)	None

* **Sources**: American Academy of Pediatrics. Tuberculosis. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics;2000:593–613; CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. MMWR 1998;47(No. RR-20):1–58; and CDC. Notice to readers: use of short-course tuberculosis preventive therapy regimens in HIV-seronegative persons. MMWR 1998;47(42):911–2.

† **Source**: Siberry GK, Iannone R, eds. Harriet Lane handbook: a manual for pediatric house officers. 15th ed.; St. Louis, MO: Mosby, Inc., 2000:834–5.

Notes: A twice-weekly schedule of isoniazid and pyridoxine can be administered (CIII). The twice-weekly isoniazid dose is 20–40 mg/kg by mouth or intramuscularly (maximum dose, 900 mg). A 2-month pyrazinamide/rifampin preventive therapy regimen can be used for HSCT candidates who are not at risk for serious rifampin drug interactions and whose HSCT is not scheduled until ≥2 weeks after the 2-month course is completed. Rifampin dose is 10–20 mg/kg/day by mouth or intravenously or 10–20 mk/kg/dose by mouth or intravenously, administered 2 times/week (maximum pyrazinamide dose, 3.5 g; maximum rifampin dose, 600 mg) (**Sources**: CDC. Notice to readers: use of short-course tuberculosis preventive therapy regimens in HIV-seronegative persons. MMWR 1998;47[42]:911–2; and CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. MMWR 1998;47[No. RR-20]:1–58.) (CIII). The usual pyrazinamide dose is 15–30 mg/kg/day by mouth or 50–70 mg/kg/dose by mouth 2 times/week (maximum) (maximum daily pyrazinamide dose, 2 g). Routine use of a 2-month pyrazinamide/rifampin preventive therapy regimen is not recommended after HSCT because of the risk for serious rifampin drug interactions (DIII). Persons who have been exposed to rifampin- and isoniazid-resistant tuberculosis should be placed on preventive therapy regimens that involve ≥2 antituberculosis drugs to which the infecting strain is susceptible (**Source**: CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. MMWR 1998;47[No. RR-20]:1–58), and a tuberculosis specialist should be consulted (BIII). A tuberculosis specialist should also be consulted for patients who are intolerant to isoniazid (AIII). All intermittent dosing strategies should be administered as directly observed therapy (AIII).

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

MMWR™
MORBIDITY AND MORTALITY
WEEKLY REPORT

October 20, 2000 / Vol. 49 / No. RR-10

Recommendations and Reports

Continuing Education Activity Sponsored by CDC

Guidelines for Preventing Opportunistic Infections Among Hematopoietic Stem Cell Transplant Recipients: Recommendations of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation

EXPIRATION — OCTOBER 20, 2001

You must complete and return the response form electronically or by mail by **October 20, 2001**, to receive continuing education credit. If you answer all of the questions, you will receive an award letter for 4.5 hours Continuing Medical Education (CME) credit, 0.45 hour Continuing Education Units (CEUs), or 5.3 hours Continuing Nursing Education (CNE) credit. If you return the form electronically, you will receive educational credit immediately. If you mail the form, you will receive educational credit in approximately 30 days. No fees are charged for participating in this continuing education activity.

INSTRUCTIONS

By Internet

1. Read this *MMWR* (Vol. 49, RR-10), which contains the correct answers to the questions beginning on the next page.
2. Go to the *MMWR* Continuing Education Internet site at <http://www.cdc.gov/mmwr/cme/conted.html>.
3. Select which exam you want to take and select whether you want to register for CME, CEU, or CNE credit.
4. Fill out and submit the registration form.
5. Select exam questions. To receive continuing education credit, you must answer all of the questions. Questions with more than one correct answer will instruct you to "Indicate all that apply."
6. Submit your answers no later than **October 20, 2001**.
7. Immediately print your Certificate of Completion for your records.

By Mail

1. Read this *MMWR* (Vol. 49, RR-10), which contains the correct answers to the questions beginning on the next page.
2. Complete all registration information on the response form, including your name, mailing address, phone number, and e-mail address, if available.
3. Indicate whether you are registering for CME, CEU, or CNE credit.
4. Select your answers to the questions, and mark the corresponding letters on the response form. To receive continuing education credit, you must answer all of the questions. Questions with more than one correct answer will instruct you to "Indicate all that apply."
5. Sign and date the response form or a photocopy of the form and send no later than **October 20, 2001**, to
   Fax: 404-639-4198
   Mail: MMWR CE Credit
   Office of Scientific and Health Communications
   Epidemiology Program Office, MS C-08
   Centers for Disease Control and Prevention
   1600 Clifton Rd, N.E.
   Atlanta, GA 30333
6. Your Certificate of Completion will be mailed to you within 30 days.

ACCREDITATION

Continuing Medical Education (CME). This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation. CDC is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. CDC designates this educational activity for a maximum of 4.5 hours in category 1 credit towards the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Continuing Education Unit (CEU). CDC has been approved as an authorized provider of continuing education and training programs by the International Association for Continuing Education and Training and awards 0.45 hour Continuing Education Units (CEUs).

Continuing Nursing Education (CNE). This activity for 5.3 contact hours is provided by CDC, which is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation.

Goals and Objectives

This *MMWR* provides guidelines for preventing opportunistic infections (OIs) among hematopoietic stem cell transplant (HSCT) recipients. The goals of these guidelines are to summarize current data regarding preventing opportunistic infections among HSCT recipients and provide evidence-based recommended strategies for preventing these OIs. Upon completion of this educational activity, the reader should be able to identify strategies for a) preventing exposure and disease from bacterial, viral, fungal, protozoa, and helminth infections and b) hospital infection control, safe living, vaccinations, and hematopoietic stem cell safety.

To receive continuing education credit, please answer all of the following questions.

1. What are the three phases of immune system recovery after HSCT?

A. Phase I, –45–21 days; phase II, 30–100 days; and phase III, >100 days.
B. Phase I, 0–21 days; phase II, 30–90 days; and phase III, >90 days.
C. Phase I, 0–30 days; phase II, 30–120 days; and phase III, >120–365 days.
D. Phase I, <30 days; phase II, 30–100 days; and phase III, >100 days.
E. None of the above.

2. Which opportunistic infections commonly occur during phase I?

A. Cytomegalovirus, *Pneumocystis carinii* pneumonia, and aspergillosis.
B. Cytomegalovirus, *Pneumocystis carinii* pneumonia, and varicella-zoster virus.
C. Herpes simplex virus, cytomegalovirus, and *Candida* species.
D. Herpes simplex virus, *Candida* species, and aspergillosis.
E. Herpes simplex virus, aspergillosis, and varicella-zoster virus.

3. HSCT recipients should avoid eating which of the following foods?

A. Raw or undercooked meat.
B. Unpasteurized dairy products.
C. Vegetable sprouts.
D. Soft cheese.
E. All of the above.

4. Which of the following statements is true regarding vaccinations that HSCT recipients should receive?

A. Diphtheria and tetanus toxoids at 12, 14, and 24 months after HSCT.
B. Measles, mumps, rubella vaccinations at 12 and 24 months after HSCT.
C. Pneumococcal vaccinations at 12, 14, and 24 months after HSCT.
D. Varicella-zoster immunoglobulin at 24 months after HSCT.
E. Oral polio vaccine at 12, 14, and 24 months after HSCT.

5. Recommended aspergillosis prophylaxis is . . .

A. Fluconazole, 400 mg by mouth or intravenously daily.
B. Fluconazole, 200 mg by mouth or intravenously daily.
C. Amphotericin B, 1 mg/kg/day intravenously.
D. Itraconazole capsules, 200 mg by mouth daily.
E. None of the above.

6. Which of the following statements is not true regarding use of laminar air flow rooms in HSCT centers?

A. Substantial survival benefit has been reported for all HSCT recipients.
B. Substantial survival benefit has been reported for allogeneic HSCT recipients with aplastic anemia and human lymphocyte antigen-identical sibling donors.
C. Patients are protected from infection during aspergillosis outbreaks related to hospital construction.
D. Use of laminar air flow rooms for HSCT recipients is optional.

7. The number of recommended air exchanges per hour in an HSCT recipient's hospital room is . . .

A. <6.
B. <8.
C. <10.
D. >12.
E. ≥15.

8. Patient rooms in HSCT centers should have negative air pressure when compared with hallways and anterooms.

A. True.
B. False.

9. HSCT recipients should be cared for routinely by using . . .

A. standard precautions.
B. airborne precautions.
C. droplet precautions.
D. contact precautions.
E. all of the above.

10. The single-most critical and effective procedure for preventing nosocomial infection is . . .

A. following isolation precautions.
B. following ventilation precautions.
C. hand washing.
D. environmental disinfection.
E. excluding visitors experiencing illness from the HSCT center.

11. An HSCT recipient can be exposed safely to visitors with . . .

A. an upper respiratory infection.
B. a covered shingles rash.
C. a varicella-zoster virus-like rash occurring ≤4 weeks after the person has received a varicella-zoster virus vaccination.
D. a history of oral polio vaccination within the previous 3–6 weeks.
E. a history of vaccination with inactivated polio vaccine within the previous 3–6 weeks.

12. When constructing cooling towers for a new hospital with an HSCT center, all of the following should be done to prevent legionellosis except . . .

A. installing drift eliminators.
B. regularly using an effective biocide.
C. maintaining the cooling towers according to the manufacturer's directions.
D. locating the cooling towers so that drift is directed towards the hospital's air-intake system.
E. keeping adequate maintenance records.

13. Which of the following animals is a safe pet for HSCT recipients?

A. Reptile.
B. Duckling.
C. Nonhuman primate.
D. Cat aged ≥6 months.
E. Stray dog.

In questions 14–17, match the recommended prophylaxis drug with the pathogen it protects against.

14. Acyclovir.
15. Foscarnet.
16. Dapsone.
17. Fluconazole.

A. *Candida* species.
B. *Aspergillus* species.
C. Herpes simplex virus.
D. Cytomegalovirus.
E. *Pneumocystis carinii*.

Correct answers for questions 1–17.

1. D; 2. D; 3. E; 4. A; 5. E; 6. A; 7. D; 8. B; 9. A; 10. C; 11. E; 12. D; 13. D; 14. C; 15. D; 16. E; 17. A.

18. Indicate your work setting.

A. State/local health department.
B. Other public health setting.
C. Hospital clinic/private practice.
D. Managed care organization.
E. Academic institution.
F. Other.

19. Which best describes your professional activities?

A. Patient care — emergency/urgent care department.
B. Patient care — inpatient.
C. Patient care — primary-care clinic or office.
D. Laboratory/pharmacy.
E. Public health.
F. Other.

20. I plan to use these recommendations as the basis for . . . (*Indicate all that apply.*)

A. health education materials.
B. insurance reimbursement policies.
C. local practice guidelines.
D. public policy.
E. other.

21. Each month, approximately how many patients do you see?

A. None.
B. 1–5.
C. 6–20.
D. 21–50.
E. 51–100.
F. >100.

22. How much time did you spend reading this report and completing the exam?

A. 2–2.5 hours.
B. More than 2.5 hours but fewer than 3 hours.
C. 3–3.5 hours.
D. More than 3.5 hours but fewer than 4 hours.
E. More than 4.5 hours.

23. After reading this report, I am confident I can identify strategies for preventing exposure and disease from bacterial infections among HSCT recipients.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

24. After reading this report, I am confident I can identify strategies for preventing exposure and disease from viral infections among HSCT recipients.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

25. After reading this report, I am confident I can identify strategies for preventing exposure and disease from fungal infections among HSCT recipients.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

26. After reading this report, I am confident I can identify strategies for preventing exposure and disease from protozoa infections among HSCT recipients.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

27. After reading this report, I am confident I can identify strategies for preventing exposure and disease from helminth infections among HSCT recipients.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

28. After reading this report, I am confident I can identify strategies for hospital infection control for HSCT recipients.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

29. After reading this report, I am confident I can identify strategies for safe living for HSCT recipients.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

30. After reading this report, I am confident I can identify strategies for vaccinations for HSCT recipients.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

31. After reading this report, I am confident I can identify strategies for hematopoietic stem cell safety for HSCT recipients.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

32. The objectives are relevant to the goal of this report.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

33. The figure, tables, and appendix are useful.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

34. Overall, the presentation of the report enhanced my ability to understand the material.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

35. These recommendations will affect my practice.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

Detach or Photocopy

MMWR Response Form for Continuing Education Credit
October 20, 2000/Vol. 49/No. RR-10

Guidelines for Preventing Opportunistic Infections Among Hematopoietic Stem Cell Transplant Recipients: Recommendations of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation

To receive continuing education credit, you must

1. ***provide your contact information;***
2. ***indicate your choice of CME, CEU, or CNE credit;***
3. ***answer <u>all</u> of the test questions;***
4. ***sign and date this form or a photocopy;***
5. ***submit your answer form by October 20, 2001.***

Failure to complete these items can result in a delay or rejection of your application for continuing education credit.

Last Name *First Name*

Street/Address or P.O. Box

Apartment or Suite

City *State* *Zip Code*

<u>Check One</u>

☐ *CME Credit*

☐ *CEU Credit*

☐ *CNE Credit*

Fill in the appropriate blocks to indicate your answers. Remember, you must answer <u>all</u> of the questions to receive continuing education credit!

1. [ ] A [ ] B [ ] C [ ] D [ ] E
2. [ ] A [ ] B [ ] C [ ] D [ ] E
3. [ ] A [ ] B [ ] C [ ] D [ ] E
4. [ ] A [ ] B [ ] C [ ] D [ ] E
5. [ ] A [ ] B [ ] C [ ] D [ ] E
6. [ ] A [ ] B [ ] C [ ] D
7. [ ] A [ ] B [ ] C [ ] D [ ] E
8. [ ] A [ ] B
9. [ ] A [ ] B [ ] C [ ] D [ ] E
10. [ ] A [ ] B [ ] C [ ] D [ ] E
11. [ ] A [ ] B [ ] C [ ] D [ ] E
12. [ ] A [ ] B [ ] C [ ] D [ ] E
13. [ ] A [ ] B [ ] C [ ] D [ ] E
14. [ ] A [ ] B [ ] C [ ] D [ ] E
15. [ ] A [ ] B [ ] C [ ] D [ ] E
16. [ ] A [ ] B [ ] C [ ] D [ ] E
17. [ ] A [ ] B [ ] C [ ] D [ ] E
18. [ ] A [ ] B [ ] C [ ] D [ ] E [ ] F
19. [ ] A [ ] B [ ] C [ ] D [ ] E [ ] F
20. [ ] A [ ] B [ ] C [ ] D [ ] E
21. [ ] A [ ] B [ ] C [ ] D [ ] E [ ] F
22. [ ] A [ ] B [ ] C [ ] D [ ] E
23. [ ] A [ ] B [ ] C [ ] D [ ] E
24. [ ] A [ ] B [ ] C [ ] D [ ] E
25. [ ] A [ ] B [ ] C [ ] D [ ] E
26. [ ] A [ ] B [ ] C [ ] D [ ] E
27. [ ] A [ ] B [ ] C [ ] D [ ] E
28. [ ] A [ ] B [ ] C [ ] D [ ] E
29. [ ] A [ ] B [ ] C [ ] D [ ] E
30. [ ] A [ ] B [ ] C [ ] D [ ] E
31. [ ] A [ ] B [ ] C [ ] D [ ] E
32. [ ] A [ ] B [ ] C [ ] D [ ] E
33. [ ] A [ ] B [ ] C [ ] D [ ] E
34. [ ] A [ ] B [ ] C [ ] D [ ] E
35. [ ] A [ ] B [ ] C [ ] D [ ] E

Signature ***Date I Completed Exam***

In this report, Clare A. Dykewicz, M.D., M.P.H., and Harold W. Jaffe, M.D., have included a discussion regarding products that are not labeled for use or are still investigational.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

References to non-CDC sites on the Internet are provided as a service to *MMWR* readers and do not constitute or imply endorsement of these organizations or their programs by CDC or the U.S. Department of Health and Human Services. CDC is not responsible for the content of pages found at these sites.

MMWR

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format and on a paid subscription basis for paper copy. To receive an electronic copy on Friday of each week, send an e-mail message to *listserv@listserv.cdc.gov*. The body content should read *SUBscribe mmwr-toc*. Electronic copy also is available from CDC's World-Wide Web server at *http://www.cdc.gov/mmwr* or from CDC's file transfer protocol server at *ftp://ftp.cdc.gov/pub/Publications/mmwr/*. To subscribe for paper copy, contact Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402; telephone (202) 512-1800.

Data in the weekly *MMWR* are provisional, based on weekly reports to CDC by state health departments. The reporting week concludes at close of business on Friday; compiled data on a national basis are officially released to the public on the following Friday. Address inquiries about the *MMWR* Series, including material to be considered for publication, to: Editor, *MMWR* Series, Mailstop C-08, CDC, 1600 Clifton Rd., N.E., Atlanta, GA 30333; telephone (888) 232-3228.

☆U.S. Government Printing Office: 2000-533-206/28042 Region IV