



## Complete Summary

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### GUIDELINE TITLE

Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients.

### BIBLIOGRAPHIC SOURCE(S)

Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. *Biol Blood Marrow Transplant* 2000;6(6a):659-713; 715; 717-27; quiz 729-33. [410 references]

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 Recomm Rep* 2000 Oct 20;49(RR-10):1-125. [410 references] [PubMed](#)

## COMPLETE SUMMARY CONTENT

SCOPE  
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IMPLEMENTATION OF THE GUIDELINE  
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT  
CATEGORIES  
IDENTIFYING INFORMATION AND AVAILABILITY

## SCOPE

### DISEASE/CONDITION(S)

Opportunistic infections, including:

- Bacterial infections (*Streptococcus pneumoniae*, *Streptococci viridans*, *Haemophilus influenzae* type b)
- Viral infections (Cytomegalovirus, Epstein-Barr virus [EBV], herpes simplex virus [HSV], varicella-zoster virus [VZV], and community-acquired respiratory virus [CRV] infections [e.g., influenza, respiratory syncytial virus (RSV), parainfluenza virus, and adenovirus])
- Fungal infections (yeast and mold infections)
- Protozoal and helminth infections (*Pneumocystis carinii* pneumonia [PCP], *Toxoplasma gondii*, *Strongyloides stercoralis*, *Trypanosoma cruzi*)

### GUIDELINE CATEGORY

Prevention

#### CLINICAL SPECIALTY

Family Practice  
Hematology  
Infectious Diseases  
Internal Medicine  
Oncology  
Pathology  
Pediatrics  
Preventive Medicine

#### INTENDED USERS

Advanced Practice Nurses  
Allied Health Personnel  
Clinical Laboratory Personnel  
Hospitals  
Nurses  
Patients  
Physician Assistants  
Physicians  
Public Health Departments

#### GUIDELINE OBJECTIVE(S)

To summarize current data and provide evidence-based recommendations regarding preventing opportunistic infections among hematopoietic stem cell transplant recipients

#### TARGET POPULATION

Adult and pediatric hematopoietic stem cell transplant recipients, including recipients 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).

#### INTERVENTIONS AND PRACTICES CONSIDERED

Prevention

1. Strategies for preventing exposure to opportunistic infections, including:
  - Appropriate hand-washing practices by hematopoietic stem cell transplant patients, their close contacts, and healthcare workers
  - Avoiding the sharing of cups, glasses, and eating utensils used by hematopoietic stem cell transplant recipients with other individuals
  - Avoiding contact with potentially infected respiratory secretions and saliva

- Rifampin prophylaxis for individuals in contact with both hematopoietic stem cell transplant patients and individuals with Haemophilus influenzae type b
  - Testing of hematopoietic stem cell transplant donors for the presence of serum anti-cytomegalovirus, serum anti-herpes simplex virus and serum anti-varicella-zoster virus immunoglobulin G antibodies before transplantation to determine the risk for infection and/or reactivation after transplantation
  - Testing of hematopoietic stem cell transplant donors for Toxoplasma gondii antibodies and anti Trypanosoma cruzi serum antibodies
  - Use of latex condoms during sexual contact to reduce the risk of exposure to sexually transmitted pathogens
  - Use of gloves by healthcare workers handling blood products
  - Avoiding contact with certain areas/foods that might increase a patient's risk for fungal exposure
  - Avoiding contact with outhouses or cutaneous contact with soil or other surfaces that might be contaminated with human feces
  - Avoiding exposure to persons with protozoal and helminthic infections
2. Disease-specific prophylaxis or preemptive treatment to prevent the first episode of disease, and/or disease recurrence, including:
    - acyclovir
    - aerosolized ribavirin
    - albendazole
    - amantadine
    - bacitracin
    - bismuth subsalicylate
    - 2% mupirocin calcium ointment
    - ciprofloxacin
    - clindamycin
    - dapsone
    - fluconazole
    - foscarnet
    - ganciclovir
    - intravenous immunoglobulin
    - ivermectin
    - isoniazid
    - leucovorin
    - pentamidine
    - pyridoxine
    - pyrimethamine
    - respiratory syncytial virus intravenous immunoglobulin
    - rifampin
    - rimantadine
    - thiabendazole
    - trimethoprim-sulfamethasoxole
    - valacyclovir
    - varicella-zoster immunoglobulin
  3. Vaccinations for hematopoietic stem cell transplant donors, recipients, their close contacts and health-care workers, including: diphtheria, tetanus, pertussis; Haemophilus influenzae type b conjugate; hepatitis B; 23-valent pneumococcal polysaccharide; influenza; inactivated polio; measles-mumps-rubella
  4. Hospital infection control policies and practices, including:

- Room ventilation
  - Construction, renovation, and building cleaning
  - Isolation and barrier precautions
  - Hand hygiene
  - Equipment maintenance (sterilization and disinfection practices)
  - Exposure to plants, communal play areas, and toys
  - Policies for screening hematopoietic stem cell transplant center visitors
  - Patient skin and oral care
  - Preventing bacterial intravascular catheter-related infections
  - Control of specific nosocomial infections: Legionella; methicillin-resistant Staphylococcus aureus; Staphylococcus species with reduced susceptibility to vancomycin; vancomycin-resistant Enterococcus; Clostridium difficile; community-acquired respiratory virus; Mycobacteria tuberculosis
  - Infection control surveillance
5. Strategies for safe living after hematopoietic stem cell transplant, including frequent and thorough handwashing
6. Hematopoietic stem cell safety, including:
- Practices for preventing the transmission of infections from hematopoietic stem cell transplant donors to recipients, including medical history, travel history, serological testing, and investigational nucleic acid tests
  - Pediatric donors
  - Practices for preventing infection from extraneous contamination of donated units
  - In utero or fetal hematopoietic stem cell transplant

## MAJOR OUTCOMES CONSIDERED

Number and severity of opportunistic infections among hematopoietic stem cell transplant recipients.

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

### NUMBER OF SOURCE DOCUMENTS

Not stated

### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

## RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Evidence-based rating system used to determine quality of evidence supporting recommendations

- 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; or dramatic results from uncontrolled experiments.
- III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.

## METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Evidence-based rating system used to determine strength of recommendations

- 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. (Optional)
- D. Moderate evidence against efficacy or for adverse outcome. (Generally not recommended)
- E. Strong evidence against efficacy or for adverse outcome. (Never recommended)

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

External Peer Review  
Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

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.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Please note: June 6, 2003 [Guidelines for Environmental Infection Control in Health-Care Facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee \(HICPAC\)](#), published by the Centers for Disease Control and Prevention (CDC) supplements and updates the section of this guideline titled "Hospital Infection Control".

Definitions of the levels of evidence (I-III) and grades of recommendation (A-E) are repeated at the end of the Major Recommendations field.

#### Bacterial Infections

##### General Recommendations

##### Preventing Exposure

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

##### Preventing Disease

Preventing Early Disease (0 to 100 Days After Hematopoietic Stem Cell Transplant). Routine gut decontamination is not recommended for hematopoietic stem cell transplant candidates (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 hematopoietic stem cell transplant, infection-related fatality rates are not reduced. If physicians choose to use prophylactic antibiotics among asymptomatic, afebrile, neutropenic recipients, they should routinely review hospital and hematopoietic stem cell transplant center antibiotic-susceptibility profiles, particularly when using a single antibiotic for antibacterial prophylaxis (BIII). The emergence of fluoroquinolone-resistant coagulase-negative Staphylococci and Escherichia coli, vancomycin-intermediate Staphylococcus aureus and vancomycin-resistant Enterococcus are increasing concerns.

Vancomycin should not be used as an agent for routine bacterial prophylaxis (DIII). Growth factors (e.g., granulocyte-macrophage colony-stimulating factor and granulocyte colony-stimulating factor) shorten the duration of neutropenia after hematopoietic stem cell transplant; however, no data were found that indicate whether growth factors effectively reduce the attack rate of invasive bacterial disease.

Physicians should not routinely administer intravenous immunoglobulin products to hematopoietic stem cell transplant recipients for bacterial infection prophylaxis (DII), although intravenous immunoglobulin has been recommended for use in producing immune system modulation for graft-versus-host disease prevention. Researchers have recommended routine intravenous immunoglobulin use to prevent bacterial infections among the approximately 20% to 25% of hematopoietic stem cell transplant recipients with unrelated marrow grafts who experience severe hypogammaglobulinemia (e.g., immunoglobulin G <400 mg/dl) within the first 100 days after transplant (CIII). For example, recipients who are hypogammaglobulinemic might receive prophylactic intravenous immunoglobulin to prevent bacterial sinopulmonary infections (e.g., from *Streptococcus pneumoniae*) (CIII). For hypogammaglobulinemic allogeneic recipients, physicians can use a higher and more frequent dose of intravenous immunoglobulin than is standard for non-hematopoietic stem cell transplant recipients because the intravenous immunoglobulin half-life among hematopoietic stem cell transplant recipients (generally 1 to 10 days) is much shorter than the half-life among healthy adults (generally 18 to 23 days). Additionally, infections might accelerate immunoglobulin G catabolism; therefore, the intravenous immunoglobulin dose for a hypogammaglobulinemic recipient should be individualized to maintain trough serum immunoglobulin G concentrations >400 to 500 mg/dl (BII). Consequently, physicians should monitor trough serum immunoglobulin G concentrations among these patients approximately every 2 weeks and adjust intravenous immunoglobulin doses as needed (BIII) (see Appendix in the original guideline document).

Preventing Late Disease (>100 Days After Hematopoietic Stem Cell Transplant). Antibiotic prophylaxis is recommended for preventing infection with encapsulated organisms (e.g., *Streptococcus pneumoniae*, *Haemophilus influenzae*, or *Neisseria meningitidis*) among allogeneic recipients with chronic graft-versus-host disease for as long as active chronic graft-versus-host disease treatment is administered (BIII). Antibiotic selection should be guided by local antibiotic resistance patterns. In the absence of severe demonstrable hypogammaglobulinemia (e.g., immunoglobulin G levels <400 mg/dl, which might be associated with recurrent sinopulmonary infections), routine monthly intravenous immunoglobulin administration to hematopoietic stem cell transplant recipients >90 days after hematopoietic stem cell transplant is not recommended (DI) as a means of preventing bacterial infections.

Other Disease Prevention Recommendations. Routine use of intravenous immunoglobulin among autologous recipients is not recommended (DII). Recommendations for preventing bacterial infections are the same among pediatric or adult hematopoietic stem cell transplant recipients.

Recommendations Regarding *Streptococcus pneumoniae*

## Preventing Exposure

Appropriate care precautions should be taken with hospitalized patients infected with *Streptococcus pneumoniae* (BIII) to prevent exposure among hematopoietic stem cell transplant recipients.

## Preventing Disease

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

Antibiotic prophylaxis is recommended for preventing infection with encapsulated organisms (e.g., *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis*) among allogeneic recipients with chronic graft-versus-host disease for as long as active chronic graft-versus-host disease treatment is administered (BIII). Trimethoprim-sulfamethasazole (TMP-SMZ) administered for *Pneumocystis carinii* pneumonia prophylaxis will also provide protection against pneumococcal infections. However, no data were found to support using trimethoprim-sulfamethasazole prophylaxis among hematopoietic stem cell transplant recipients solely for the purpose of preventing *Streptococcus pneumoniae* disease. Certain strains of *Streptococcus pneumoniae* are resistant to trimethoprim-sulfamethasazole and penicillin. Recommendations for preventing pneumococcal infections are the same for allogeneic or autologous recipients.

As with adults, pediatric hematopoietic stem cell transplant recipients aged  $\geq 2$  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 hematopoietic stem cell transplant 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 hematopoietic stem cell transplant candidates to assess their state

of oral health and to perform any needed dental procedures to decrease the risk for oral infections after transplant (AIII).

Generally, hematopoietic stem cell transplant 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. However, when *Streptococci viridans* infections among hematopoietic stem cell transplant 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).

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

## Recommendations Regarding *Haemophilus influenzae* type b

### Preventing Exposure

Adults with *Haemophilus influenzae* type b (Hib) pneumonia require standard precautions to prevent exposing the hematopoietic stem cell transplant recipient to *Haemophilus influenzae* type b. Adults and children who are in contact with the hematopoietic stem cell transplant recipient and who have known or suspected invasive *Haemophilus influenzae* type b 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 *Haemophilus influenzae* type b disease and who also have contact with hematopoietic stem cell transplant recipients should be administered rifampin prophylaxis according to published recommendations; prophylaxis for household contacts of a patient with *Haemophilus influenzae* type b disease are necessary if all contacts aged <4 years are not fully vaccinated (BIII) (see Appendix in original guideline document). This recommendation is critical because the risk for invasive *Haemophilus influenzae* type b disease among unvaccinated household contacts aged <4 years is increased, and rifampin can be effective in eliminating *Haemophilus influenzae* type b carriage and preventing invasive *Haemophilus influenzae* type b disease. Pediatric household contacts should be up-to-date with *Haemophilus influenzae* type b vaccinations to prevent possible *Haemophilus influenzae* type b exposure to the hematopoietic stem cell transplant recipient (AII).

### Preventing Disease

Although no data regarding vaccine efficacy among hematopoietic stem cell transplant recipients were found, Haemophilus influenzae type b conjugate vaccine should be administered to hematopoietic stem cell transplant recipients at 12, 14, and 24 months after hematopoietic stem cell transplant (BII). This vaccine is recommended because the majority of hematopoietic stem cell transplant recipients have low levels of Haemophilus influenzae type b capsular polysaccharide antibodies  $\geq 4$  months after hematopoietic stem cell transplant, and allogeneic recipients with chronic graft-versus-host disease are at increased risk for infection from encapsulated organisms (e.g., Haemophilus influenzae type b). Hematopoietic stem cell transplant recipients who are exposed to persons with Haemophilus influenzae type b disease should be offered rifampin prophylaxis according to published recommendations (BIII) (available in the Appendix of the original guideline).

Antibiotic prophylaxis is recommended for preventing infection with encapsulated organisms (e.g., Streptococcus pneumoniae, Haemophilus influenzae, or Neisseria meningitidis) among allogeneic recipients with chronic graft-versus-host disease for as long as active chronic graft-versus-host disease treatment is administered (BIII). Antibiotic selection should be guided by local antibiotic-resistance patterns. Recommendations for preventing Haemophilus influenzae type b infections are the same for allogeneic or autologous recipients. Recommendations for preventing Haemophilus influenzae type b disease are the same for pediatric or adult hematopoietic stem cell transplant recipients, except that any child infected with Haemophilus influenzae type b pneumonia requires standard precautions with droplet precautions added for the first 24 hours after beginning appropriate antibiotic therapy (BIII). Appropriate pediatric doses should be administered for Haemophilus influenzae type b conjugate vaccine and for rifampin prophylaxis (see Appendix in original guideline document).

## Viral Infections

### Recommendations Regarding Cytomegalovirus

#### Preventing Exposure

Hematopoietic stem cell transplant candidates should be tested for the presence of serum anti-cytomegalovirus immunoglobulin G antibodies before transplantation to determine their risk for primary cytomegalovirus infection and reactivation after hematopoietic stem cell transplant (AIII). Only U.S. Food and Drug Administration (FDA) licensed or approved tests should be used. Hematopoietic stem cell transplant recipients and candidates should avoid sharing cups, glasses, and eating utensils with others, including family members, to decrease the risk for cytomegalovirus 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 cytomegalovirus and other sexually transmitted pathogens (AII). However, even long-time monogamous pairs can be discordant for cytomegalovirus infections. Therefore, during periods of immunocompromise, sexually active hematopoietic stem cell transplant recipients in monogamous relationships should ask partners to be tested for serum cytomegalovirus immunoglobulin G antibody, and discordant couples should use latex condoms

during sexual contact to reduce the risk for exposure to this sexually transmitted opportunistic infection (CIII).

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

All health-care workers should wear gloves when handling blood products or other potentially contaminated biologic materials (AII) to prevent transmission of cytomegalovirus to hematopoietic stem cell transplant recipients. Hematopoietic stem cell transplant patients who are known to excrete cytomegalovirus should be placed under standard precautions for the duration of cytomegalovirus excretion to avoid possible transmission to cytomegalovirus-seronegative hematopoietic stem cell transplant recipients and candidates (AIII). Physicians are cautioned that cytomegalovirus excretion can be episodic or prolonged.

#### Preventing Disease and Disease Recurrence

Hematopoietic stem cell transplant recipients at risk for cytomegalovirus disease after hematopoietic stem cell transplant (i.e., all cytomegalovirus-seropositive hematopoietic stem cell transplant recipients, and all cytomegalovirus-seronegative recipients with a cytomegalovirus-seropositive donor) should be placed on a cytomegalovirus disease prevention program from the time of engraftment until 100 days after hematopoietic stem cell transplant (i.e., phase II) (AI). Physicians should use either prophylaxis or preemptive treatment with ganciclovir for allogeneic recipients (AI). In selecting a cytomegalovirus 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 cytomegalovirus (i.e.,  $<100$  days after hematopoietic stem cell transplant) for allogeneic recipients involves administering ganciclovir prophylaxis to all allogeneic recipients at risk throughout phase II (i.e., from engraftment to 100 days after hematopoietic stem cell transplant). The induction course is usually started at engraftment (AI), although physicians can add a brief prophylactic course during hematopoietic stem cell transplant preconditioning (CIII) (see Appendix in the original guideline document).

Preemptive strategy against early cytomegalovirus (i.e.,  $<100$  days after hematopoietic stem cell transplant) for allogeneic recipients is preferred over prophylaxis for cytomegalovirus-seronegative hematopoietic stem cell transplant recipients of seropositive donor cells (i.e., D-positive or R-negative) because of the low attack rate of active cytomegalovirus infection if screened or filtered blood

product support is used (BII). Preemptive strategy restricts ganciclovir use for those patients who have evidence of cytomegalovirus infection after hematopoietic stem cell transplant. It requires the use of sensitive and specific laboratory tests to rapidly diagnose cytomegalovirus infection after hematopoietic stem cell transplant and to enable immediate administration of ganciclovir after cytomegalovirus infection has been detected. Allogeneic recipients at risk should be screened  $\geq 1$  times/week from 10 days to 100 days after hematopoietic stem cell transplant (i.e., phase II) for the presence of cytomegalovirus viremia or antigenemia (AIII).

Hematopoietic stem cell transplant physicians should select one of two diagnostic tests to determine the need for preemptive treatment. Currently, the detection of cytomegalovirus pp65 antigen in leukocytes (antigenemia) is preferred for screening for preemptive treatment because it is more rapid and sensitive than culture and has good positive predictive value. Direct detection of cytomegalovirus-DNA (deoxyribonucleic acid) by polymerase chain reaction (PCR) is very sensitive but has a low positive predictive value. Although cytomegalovirus-DNA polymerase chain reaction is less sensitive than whole blood or leukocyte polymerase chain reaction, plasma cytomegalovirus-DNA polymerase chain reaction is useful during neutropenia, when the number of leukocytes/slide is too low to allow cytomegalovirus pp65 antigenemia testing.

Virus culture of urine, saliva, blood, or bronchoalveolar washings by rapid shell-vial culture or routine culture can be used; however, viral culture techniques are less sensitive than cytomegalovirus-DNA polymerase chain reaction or cytomegalovirus pp65 antigenemia tests. Also, rapid shell-viral cultures require  $\geq 48$  hours and routine viral cultures can require weeks to obtain final results. Thus, viral culture techniques are less satisfactory than polymerase chain reaction or antigenemia tests. Hematopoietic stem cell transplant centers without access to polymerase chain reaction or antigenemia tests should use prophylaxis rather than preemptive therapy for cytomegalovirus disease prevention (BII). Physicians do use other diagnostic tests (e.g., hybrid capture cytomegalovirus-DNA assay, Version 2.0 or cytomegalovirus pp67 viral RNA [ribonucleic acid] detection); however, limited data were found regarding use among hematopoietic stem cell transplant recipients, and therefore, no recommendation for use can be made.

Allogeneic recipients  $\leq 100$  days after hematopoietic stem cell transplant (i.e., during phase II) should begin preemptive treatment with ganciclovir if cytomegalovirus viremia or any antigenemia is detected or if the recipient has  $\geq 2$  consecutively positive cytomegalovirus-DNA polymerase chain reaction tests (BIII). After preemptive treatment has been started, maintenance ganciclovir is usually continued until 100 days after hematopoietic stem cell transplant or for a minimum of 3 weeks, whichever is longer (AI) (see Appendix in original guideline document). Antigen or polymerase chain reaction tests should be negative when ganciclovir is stopped. Studies report that a shorter course of ganciclovir (e.g., for 3 weeks or until negative polymerase chain reaction or antigenemia occurs) might provide adequate cytomegalovirus prevention with less toxicity, but routine weekly screening by pp65 antigen or polymerase chain reaction test is necessary after stopping ganciclovir because cytomegalovirus reactivation can occur (BIII).

Presently, only the intravenous formulation of ganciclovir has been approved for use in cytomegalovirus prophylactic or preemptive strategies (BIII). No

recommendation for oral ganciclovir use among hematopoietic stem cell transplant 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 cytomegalovirus prevention, but no recommendation can be made regarding this strategy because of limited data. Patients who are ganciclovir-intolerant should be administered foscarnet instead (BII) (see the Appendix in the original guideline document). Hematopoietic stem cell transplant recipients receiving ganciclovir should have absolute neutrophil counts checked  $\geq 2$  times/week (BIII). Researchers report managing ganciclovir-associated neutropenia by adding granulocyte colony-stimulating factor or temporarily stopping ganciclovir for  $\geq 2$  days if the patient's absolute neutrophil count is  $< 1,000$  (CIII). Ganciclovir can be restarted when the patient's absolute neutrophil count is  $\geq 1,000$  for 2 consecutive days. Alternatively, researchers report substituting foscarnet for ganciclovir if a) the hematopoietic stem cell transplant recipient is still cytomegalovirus viremic or antigenemic or b) the absolute neutrophil count remains  $< 1,000$  for  $> 5$  days after ganciclovir has been stopped (CIII) (see the Appendix in the original guideline document). 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 hematopoietic stem cell transplant recipients at  $> 100$  days after hematopoietic stem cell transplant (i.e., during phase III). However, persons with high risk for late cytomegalovirus disease should be screened biweekly for evidence of cytomegalovirus reactivation as long as substantial immunocompromise persists (BIII). Risk factors for late cytomegalovirus disease include allogeneic hematopoietic stem cell transplant accompanied by chronic graft-versus-host disease, steroid use, low CD4 counts, delay in high avidity anti-cytomegalovirus antibody, and recipients of matched unrelated or T cell-depleted hematopoietic stem cell transplants who are at high risk. If cytomegalovirus is still detectable by routine screening  $\geq 100$  days after hematopoietic stem cell transplant, ganciclovir should be continued until cytomegalovirus is no longer detectable (AI). If low-grade cytomegalovirus antigenemia ( $< 5$  positive cells/slide) is detected on routine screening, the antigenemia test should be repeated in 3 days (BIII). If cytomegalovirus antigenemia indicates  $\geq 5$  cells/slide, polymerase chain reaction is positive, or the shell-vial culture detects cytomegalovirus viremia, a 3-week course of preemptive ganciclovir treatment should be administered (BIII) (see the Appendix in the original guideline document). Ganciclovir should also be started if the patient has had  $\geq 2$  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 hematopoietic stem cell transplant). Current investigational strategies for preventing late cytomegalovirus disease include the use of targeted prophylaxis with antiviral drugs and cellular immunotherapy for those with deficient or absent cytomegalovirus-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 cytomegalovirus should be suspected. If cytomegalovirus viremia recurs during continuous treatment with ganciclovir, researchers report restarting ganciclovir induction or stopping ganciclovir and starting foscarnet (CIII). Limited data were

found regarding the use of foscarnet among hematopoietic stem cell transplant recipients for either cytomegalovirus prophylaxis or preemptive therapy.

Infusion of donor-derived cytomegalovirus-specific clones of CD8+ T-cells into the transplant recipient is being evaluated under Food and Drug Administration 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 cytomegalovirus disease, its utility is limited in a setting where more potent anti-cytomegalovirus agents (e.g., ganciclovir) are used. Acyclovir is not effective in preventing cytomegalovirus disease after autologous hematopoietic stem cell transplant and is, therefore, not recommended for cytomegalovirus preemptive therapy (DII). Consequently, valacyclovir, although under study for use among hematopoietic stem cell transplant recipients, is presumed to be less effective than ganciclovir against cytomegalovirus and is currently not recommended for cytomegalovirus disease prevention (DII).

Although hematopoietic stem cell transplant physicians continue to use intravenous immunoglobulin for immune system modulation, intravenous immunoglobulin is not recommended for cytomegalovirus disease prophylaxis among hematopoietic stem cell transplant recipients (DI). Cidofovir, a nucleoside analog, is approved by Food and Drug Administration for the treatment of AIDS-associated cytomegalovirus retinitis. The drug's major disadvantage is nephrotoxicity. Cidofovir is currently in Food and Drug Administration phase 1 trial for use among hematopoietic stem cell transplant recipients; therefore, recommendations for its use cannot be made.

Use of cytomegalovirus-negative or leukocyte-reduced blood products is not routinely required for all autologous recipients because most have a substantially lower risk for cytomegalovirus disease. However, cytomegalovirus-negative or leukocyte-reduced blood products can be used for cytomegalovirus-seronegative autologous recipients (CIII). Researchers report that cytomegalovirus-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 hematopoietic stem cell transplant for cytomegalovirus reactivation, preferably with quantitative cytomegalovirus pp65 antigen or quantitative polymerase chain reaction (BII).

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

Recommendations Regarding Epstein-Barr Virus (EBV)

## Preventing Exposure

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

## Preventing Disease

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

## Recommendations Regarding Herpes Simplex Virus (HSV)

### Preventing Exposure

Hematopoietic stem cell transplant candidates should be tested for serum anti-herpes simplex virus immunoglobulin G before transplant (AIII); however, type-specific anti-herpes simplex virus immunoglobulin G serology testing is not necessary. Only Food and Drug Administration-licensed or -approved tests should be used. All hematopoietic stem cell transplant candidates, particularly those who are herpes simplex virus-seronegative, should be informed of the importance of avoiding herpes simplex virus infection while immunocompromised and should be advised of behaviors that will decrease the likelihood of herpes simplex virus exposure (AII). Hematopoietic stem cell transplant 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 herpes simplex virus as well as other sexually transmitted pathogens (AII). However, even long-time monogamous pairs can be discordant for herpes simplex virus infections. Therefore, during periods of immunocompromise, sexually active hematopoietic stem cell transplant recipients in such relationships should ask partners to be tested for serum herpes simplex virus immunoglobulin G 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 opportunistic infection (CIII). Any person with disseminated, primary, or severe mucocutaneous herpes simplex virus disease should be placed under contact precautions for the duration of the illness (AI) to prevent transmission of herpes simplex virus to hematopoietic stem cell transplant recipients.

### Preventing Disease and Disease Recurrence

Acyclovir. Acyclovir prophylaxis should be offered to all herpes simplex virus-seropositive allogeneic recipients to prevent herpes simplex virus reactivation during the early post transplant period (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 hematopoietic stem cell transplant (BIII) (see the Appendix in the original guideline document). Without supportive data from controlled studies, routine use of antiviral prophylaxis for >30 days after hematopoietic stem cell transplant to prevent herpes simplex virus is not recommended (DIII). Routine acyclovir prophylaxis is not indicated for herpes simplex virus-seronegative hematopoietic stem cell transplant recipients, even if the donors are herpes simplex virus-seropositive (DIII). Researchers have proposed administration of ganciclovir prophylaxis alone to hematopoietic stem cell transplant recipients who required simultaneous prophylaxis for cytomegalovirus and herpes simplex virus after hematopoietic stem cell transplant (CIII) because ganciclovir has in vitro activity against cytomegalovirus and herpes simplex virus 1 and 2, although ganciclovir has not been approved for use against herpes simplex virus.

Valacyclovir. Researchers have reported valacyclovir use for preventing herpes simplex virus among hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipients. Controlled trial data among hematopoietic stem cell transplant recipients are limited, and the Food and Drug Administration 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) (see the Appendix in the original guideline document).

Foscarnet. Because of its substantial renal and infusion-related toxicity, foscarnet is not recommended for routine herpes simplex virus prophylaxis among hematopoietic stem cell transplant recipients (DIII).

Famciclovir. Presently, data regarding safety and efficacy of famciclovir among hematopoietic stem cell transplant recipients are limited; therefore, no recommendations for herpes simplex virus prophylaxis with famciclovir can be made.

#### Other Recommendations

Herpes simplex virus prophylaxis lasting >30 days after hematopoietic stem cell transplant might be considered for persons with frequent recurrent herpes simplex virus (CIII) (see the Appendix in the original guideline document). Acyclovir can be used during phase I for administration to herpes simplex virus-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 (see the Appendix in the original guideline document), but no published data were found regarding valacyclovir safety and efficacy among children.

#### Recommendations Regarding Varicella-Zoster Virus (VZV)

##### Preventing Exposure

Hematopoietic stem cell transplant candidates should be tested for the presence of serum anti-varicella-zoster virus immunoglobulin G 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 varicella-zoster virus than a low positive titer alone. All hematopoietic stem cell transplant candidates and recipients, particularly those who are varicella-zoster virus-seronegative, should be informed of the potential seriousness of varicella-zoster virus disease among immunocompromised persons and advised of strategies to decrease their risk for varicella-zoster virus exposure (AII).

Although researchers report that the majority of varicella-zoster virus disease after hematopoietic stem cell transplant is caused by reactivation of endogenous varicella-zoster virus, hematopoietic stem cell transplant candidates and recipients who are varicella-zoster virus-seronegative, or varicella-zoster virus-seropositive and immunocompromised, should avoid exposure to persons with active varicella-zoster virus infections (AII). Health-care workers, family members, household contacts, and visitors who are healthy and do not have a reported history of varicella infection or who are varicella-zoster virus-seronegative should receive varicella-zoster virus vaccination before being allowed to visit or have direct contact with an hematopoietic stem cell transplant recipient (AIII). Ideally, varicella-zoster virus-susceptible family members, household contacts, and potential visitors of immunocompromised hematopoietic stem cell transplant recipients should be vaccinated as soon as the decision is made to perform hematopoietic stem cell transplant. The vaccination dose or doses should be completed  $\geq 4$  weeks before the conditioning regimen begins or  $\geq 6$  weeks (42 days) before the hematopoietic stem cell transplant is performed (BIII).

Hematopoietic stem cell transplant recipients and candidates undergoing conditioning therapy should avoid contact with any varicella-zoster virus vaccine recipient who experiences a rash after vaccination (BIII). When this rash occurs, it usually appears 14-21 days after varicella-zoster virus vaccination (median: 22 days; range: 5-35 days). However, to date, no serious disease has been reported among immunocompromised patients from transmission of varicella-zoster virus vaccine virus, and the varicella-zoster virus vaccine strain is susceptible to acyclovir.

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

### Preventing Disease

**Varicella-Zoster Immunoglobulin.** Varicella-zoster virus-seronegative hematopoietic stem cell transplant recipients should be administered varicella-zoster immunoglobulin as soon as possible but ideally within 96 hours after close or household contact with a person having either chickenpox or shingles if the

hematopoietic stem cell transplant recipient is not immunocompetent (i.e., allogeneic patient <24 months after hematopoietic stem cell transplant, ≥24 months after hematopoietic stem cell transplant and on immunosuppressive therapy, or having chronic graft-versus-host disease) (AII). Researchers report varicella-zoster immunoglobulin administration for varicella-zoster virus exposure as described for hematopoietic stem cell transplant recipients who were varicella-zoster virus-seropositive before hematopoietic stem cell transplant (CIII).

Because of the high morbidity of varicella-zoster virus-associated disease among severely immunocompromised hematopoietic stem cell transplant recipients and until further data are published, hematopoietic stem cell transplant physicians should administer varicella-zoster immunoglobulin to all varicella-zoster virus-seronegative hematopoietic stem cell transplant recipients or candidates undergoing conditioning therapy who are exposed to a varicella-zoster virus vaccinee having a varicella-like rash (BIII). Researchers also report varicella-zoster immunoglobulin administration for this situation for varicella-zoster virus-seropositive hematopoietic stem cell transplant 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 varicella-zoster virus has been rarely transmitted by varicella-zoster virus vaccinees with vesicular rashes postvaccination.

If varicella-zoster virus-seronegative hematopoietic stem cell transplant recipients or candidates undergoing conditioning therapy are closely exposed to varicella >3 weeks after receiving varicella-zoster immunoglobulin, they should be administered another dose of varicella-zoster immunoglobulin (BIII). Researchers also recommend varicella-zoster immunoglobulin administration for this condition for varicella-zoster virus-seropositive hematopoietic stem cell transplant recipients and candidates undergoing conditioning therapy (CIII).

**Antiviral Drugs.** Any hematopoietic stem cell transplant recipient or candidate undergoing conditioning therapy who experiences a varicella-zoster virus-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) (see the Appendix in the original guideline document). Any hematopoietic stem cell transplant recipient or candidate undergoing conditioning therapy who experiences a varicella-zoster virus-like rash after exposure to a varicella-zoster virus vaccinee with a rash should be administered intravenous acyclovir preemptively to prevent severe, disseminated varicella-zoster virus disease (BII). Acyclovir should be administered until 2 days after all lesions have crusted.

Long-term acyclovir prophylaxis to prevent recurrent varicella-zoster virus infection (e.g., during the first 6 months after hematopoietic stem cell transplant) is not routinely recommended (DIII); however, this therapy could be considered for use among hematopoietic stem cell transplant recipients with severe, long-term immunodeficiency (CIII). When acyclovir resistance occurs among patients, hematopoietic stem cell transplant physicians should use foscarnet for preemptive treatment of varicella-zoster virus disease (BIII). Researchers report valacyclovir use for preventing herpes simplex virus among hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipients. Controlled trial data regarding hematopoietic stem cell transplant recipients are limited, and the Food and Drug Administration has not approved valacyclovir for use among hematopoietic stem cell transplant recipients. Physicians wishing to use valacyclovir among hematopoietic stem cell transplant recipients with renal impairment should exercise caution and decrease doses as needed (BIII) (see the Appendix of the original guideline document). No data were found demonstrating safety and efficacy of preemptive treatment of famciclovir against herpes zoster among hematopoietic stem cell transplant recipients. Consequently, no recommendation for its use can be made.

**Live-Attenuated Varicella-Zoster Virus Vaccine.** Varicella-zoster virus vaccine use is contraindicated among hematopoietic stem cell transplant recipients <24 months after hematopoietic stem cell transplant (EIII). Use of varicella-zoster virus vaccine among hematopoietic stem cell transplant recipients is restricted to research protocols for recipients  $\geq$ 24 months after hematopoietic stem cell transplant who are presumed immunocompetent. Further research is needed to determine the safety, immunogenicity, and efficacy of varicella-zoster virus vaccine among hematopoietic stem cell transplant recipients.

#### Other Recommendations

An inactivated varicella-zoster virus vaccine has been used investigationaly among hematopoietic stem cell transplant recipients; however, more studies are needed before a recommendation regarding its use can be made. Recommendations for varicella-zoster virus prevention are the same for allogeneic or autologous recipients. Recommendations for preventing varicella-zoster virus disease among pediatric or adult hematopoietic stem cell transplant recipients are the same, except that appropriate dose adjustments for varicella-zoster immunoglobulin should be made for pediatric hematopoietic stem cell transplant recipients (AIII) (see the Appendix of the original guideline document).

**Recommendations Regarding Community-Acquired Respiratory Virus (CRV) Infections: Influenza, Respiratory Syncytial Virus, Parainfluenza Virus, and Adenovirus**

#### Preventing Exposure

Preventing community-acquired respiratory virus exposure is critical in preventing community-acquired respiratory virus disease. To prevent nosocomial community-acquired respiratory virus transmission, hematopoietic stem cell transplant recipients and their health-care workers should always follow hematopoietic stem cell transplant infection control guidelines (AIII). To minimize the risk for community-acquired respiratory virus transmission, health-care workers and visitors with upper respiratory infection (URI) symptoms should be restricted from contact with hematopoietic stem cell transplant recipients and hematopoietic stem cell transplant candidates undergoing conditioning therapy (AIII). At a minimum, active clinical surveillance for community-acquired respiratory virus disease should be conducted on all hospitalized hematopoietic stem cell transplant recipients and candidates undergoing conditioning therapy; this clinical surveillance should include daily screening for signs and symptoms of community-

acquired respiratory virus (e.g., upper respiratory infection or lower respiratory infection [LRI]) (AIII). Viral cultures of asymptomatic hematopoietic stem cell transplant candidates are unlikely to be useful. Hematopoietic stem cell transplant recipients with upper respiratory infection or lower respiratory infection symptoms should be placed under contact precautions to avoid transmitting infection to other hematopoietic stem cell transplant candidates and recipients, health-care workers, and visitors until the etiology of illness is identified (BIII). Optimal isolation precautions should be modified as needed after the etiology is identified (AIII). Hematopoietic stem cell transplant recipients and candidates, their family members and visitors, and all health-care workers should be informed regarding community-acquired respiratory virus infection control measures and the potential severity of community-acquired respiratory virus infections among hematopoietic stem cell transplant recipients (BIII). Physicians have routinely conducted culture-based community-acquired respiratory virus surveillance among hematopoietic stem cell transplant 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 to May) starting the season before hematopoietic stem cell transplant and continuing  $\geq 24$  months after hematopoietic stem cell transplant (AI) to prevent influenza exposure among the recipients or candidates. All family members and close or household contacts of hematopoietic stem cell transplant recipients who remain immunocompromised  $\geq 24$  months after hematopoietic stem cell transplant should continue to be vaccinated annually as long as the hematopoietic stem cell transplant recipient's immunocompromise persists (AI). Seasonal influenza vaccination is strongly recommended for all health-care workers of hematopoietic stem cell transplant recipients (AI).

If health-care workers, family members, or other close contacts of hematopoietic stem cell transplant recipients receive influenza vaccination during an influenza A outbreak, they should receive amantadine or rimantadine chemoprophylaxis for 2 weeks after influenza vaccination while the vaccinee experiences an immunologic response to the vaccine. Such a strategy is likely to prevent transmission of influenza A to health-care workers and other close contacts of hematopoietic stem cell transplant recipients, which could prevent influenza A transmission to hematopoietic stem cell transplant 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 health-care workers of hematopoietic stem cell transplant recipients and candidates should be administered influenza A chemoprophylaxis with amantadine or rimantadine until the end of the outbreak (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 hematopoietic stem cell transplant settings. However, health-care workers, family members, or other close contacts can be offered a neuroaminidase inhibitor (e.g., zanamivir or oseltamivir) using the same strategies outlined previously, if (a) rimantadine or amantadine cannot be tolerated, (b) the outbreak strain of influenza A is amantadine or rimantadine-resistant, or (c) the outbreak strain is influenza B

(BI). Zanamivir can be administered to persons aged  $\geq 12$  years, and oseltamivir can be administered to persons aged  $\geq 18$  years. Patients with influenza should be placed under droplet and standard precautions (AIII) to prevent transmission of influenza to hematopoietic stem cell transplant recipients. Health-care workers with influenza should be excused from patient care until they are no longer infectious (AIII).

## Preventing Disease

Hematopoietic stem cell transplant physicians should determine the etiology of an upper respiratory infection in an hematopoietic stem cell transplant recipient or candidate undergoing conditioning therapy, if possible, because respiratory syncytial virus (RSV), influenza, parainfluenza, and adenovirus upper respiratory infections can progress to more serious lower respiratory infection, and certain community-acquired respiratory viruses can be treated (BIII). Appropriate diagnostic samples include nasopharyngeal washes, swabs or aspirates, throat swabs, and bronchoalveolar lavage (BAL) fluid. Hematopoietic stem cell transplant candidates with upper respiratory infection symptoms at the time conditioning therapy is scheduled to start should postpone their conditioning regimen until the upper respiratory infections resolve, if possible, because certain upper respiratory infections might progress to lower respiratory infection during immunosuppression (BIII).

Recommendations Regarding Influenza. Life-long seasonal influenza vaccination is recommended for all hematopoietic stem cell transplant candidates and recipients, beginning during the influenza season before hematopoietic stem cell transplant and resuming  $\geq 6$  months after hematopoietic stem cell transplant (BIII). Influenza vaccinations administered to hematopoietic stem cell transplant recipients  $< 6$  months after hematopoietic stem cell transplant are unlikely to be beneficial and are not recommended (DII). Hematopoietic stem cell transplant recipients  $< 6$  months after hematopoietic stem cell transplant 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. During such outbreaks, hematopoietic stem cell transplant recipients 6 to 24 months after hematopoietic stem cell transplant, or  $> 24$  months after hematopoietic stem cell transplant and still substantially immunocompromised (i.e., receiving immunosuppressive therapy, have had a relapse of their underlying disease, or have graft-versus-host disease) 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 hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipients  $< 24$  months after hematopoietic stem cell transplant or  $\geq 24$  months after hematopoietic stem cell transplant and substantially immunocompromised regardless of vaccination history, because of their likely suboptimal immunologic response to influenza vaccine. 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 hematopoietic stem cell transplant recipients with unexplained acute upper respiratory infection or lower respiratory infection symptoms during a community or nosocomial outbreak of influenza A. However, the effectiveness in preventing influenza-related complications and the safety of this strategy have not been evaluated among hematopoietic stem cell transplant 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) have been proposed for investigational, preemptive treatment to prevent severe influenza disease among hematopoietic stem cell transplant recipients. However, because of lack of data, no recommendation for use of these strategies among hematopoietic stem cell transplant recipients can be made.

**Recommendations Regarding Respiratory Syncytial Virus.** Respiratory secretions of any hospitalized hematopoietic stem cell transplant candidate or recipient who experiences signs or symptoms of community-acquired respiratory virus infection should be tested promptly by viral culture and rapid diagnostic tests for respiratory syncytial virus (BIII). If two diagnostic samples taken  $\geq 2$  days apart do not identify a respiratory pathogen despite persistence of respiratory symptoms, bronchoalveolar lavage and further testing are advised (BIII). This testing is critical because of the high morbidity and case fatality of respiratory syncytial virus disease among hematopoietic stem cell transplant recipients. Hematopoietic stem cell transplant recipients, particularly those who are preengraftment and at highest risk for severe respiratory syncytial virus pneumonia, should have their illness diagnosed early (i.e., during respiratory syncytial virus upper respiratory infection), and their illness should be treated aggressively to prevent fatal respiratory syncytial virus disease (BIII).

Although a definitive, uniformly effective preemptive therapy for respiratory syncytial virus infection among hematopoietic stem cell transplant recipients has not been identified, certain strategies have been proposed, including use of aerosolized ribavirin, respiratory syncytial virus antibodies (i.e., passive immunization with high respiratory syncytial virus-titered intravenous immunoglobulin or respiratory syncytial virus immunoglobulin) in combination with aerosolized ribavirin, and respiratory syncytial virus monoclonal antibody. Clinical trials are currently underway to evaluate the efficacy of these strategies. No recommendation regarding the optimal method for respiratory syncytial virus 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 respiratory syncytial virus pneumonia among hematopoietic stem cell transplant recipients (DIII), and no commercially licensed vaccines against respiratory syncytial virus are currently available.

**Recommendations Regarding Parainfluenza Virus and Adenovirus.** Immunoprophylaxis, chemoprophylaxis, and preemptive treatment for parainfluenza virus and adenovirus infections among hematopoietic stem cell

transplant recipients have been proposed. 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 community-acquired respiratory virus infections and their recurrence are the same for allogeneic or autologous recipients. Generally, these recommendations apply to children or adults, but with appropriate adjustments in antiviral drug and influenza vaccine doses for children (see the Appendix of the original guideline document).

For pediatric hematopoietic stem cell transplant recipients and candidates aged >6 months, annual seasonal influenza vaccination is recommended hematopoietic stem cell transplant (BIII). Children aged <9 years who are receiving influenza vaccination for the first time require two doses administered  $\geq 1$  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,  $\geq 6$  months after hematopoietic stem cell transplant, and receiving their first influenza vaccination, should be administered  $\geq 6$  weeks of influenza A chemoprophylaxis after the first dose of influenza vaccine (BIII) (see the Appendix in the original guideline document). Amantadine and rimantadine are not Food and Drug Administration-approved for children aged <1 year (DIII).

To prevent respiratory syncytial virus disease, researchers report substituting respiratory syncytial virus-intravenous immunoglobulin for intravenous immunoglobulin during respiratory syncytial virus season (i.e., November to April) for pediatric recipients (i.e., children aged <18 years) who receive routine intravenous immunoglobulin therapy (i.e., those with hypogammaglobulinemia) (CIII) (see the Appendix in the original guideline document). Other researchers report that pediatric recipients with respiratory syncytial virus can be considered for preemptive therapy (e.g., during upper respiratory infection or early lower respiratory infection) with aerosolized ribavirin (CIII), although this therapy remains controversial (see the Appendix in the original guideline document). Droplet and contact precautions for the duration of illness are required for pediatric recipients for the duration of adenovirus (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, hematopoietic stem cell transplant 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., granulocyte-macrophage colony-stimulating factor and granulocyte colony-stimulating factor) shorten the duration of neutropenia after hematopoietic stem cell transplant; 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 hematopoietic stem cell transplant recipients (DII), but cultures should be obtained from symptomatic hematopoietic stem cell transplant 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. Consequently, methods of preventing exogenous yeast exposure usually do not prevent invasive yeast infections after hematopoietic stem cell transplant. However, because *Candida* species can be carried on the hands, health-care workers and others in contact with hematopoietic stem cell transplant 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 *Candida albicans* is the predominant cause of invasive fungal disease preengraftment (AI) (see the Appendix in the original guideline document). Because candidiasis occurs during phase I, fluconazole (400 mg/day by mouth or intravenously) should be administered from the day of hematopoietic stem cell transplant until engraftment (AII). Further studies are needed to determine the optimal duration of fluconazole prophylaxis. However, fluconazole is not effective against certain *Candida* species, including *Candida krusei* and *Candida 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 to 200 mg/day by mouth) among neutropenic patients has variable efficacy in preventing candidiasis. Therefore, this therapy is not recommended for hematopoietic stem cell transplant 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

Hematopoietic stem cell transplant candidates with candidemia or invasive candidiasis can safely receive transplants 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-chlorodeoxyadenosine recently (BIII). Recommendations regarding preventing invasive yeast infections among pediatric or adult hematopoietic stem cell transplant recipients are the same, except that appropriate dose adjustments for prophylactic drugs should be made for pediatric recipients (see the Appendix in the original guideline document).

## Recommendations Regarding Mold Infections

### Preventing Exposure

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

- high-efficiency (>90%) particulate air (HEPA) filtration (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 (BIII)
- correctly sealed rooms, including correctly sealed windows and electrical outlets (BIII)
- high rates of room air exchange (i.e., >12 air changes/hour) (BIII)
- 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 (BIII)

Additionally, hematopoietic stem cell transplant centers should be cleaned with care, particularly after hospital renovation or construction, to avoid exposing hematopoietic stem cell transplant recipients and candidates to mold spores (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, low-dose (0.1 to 0.25 mg/kg/day) amphotericin B, intranasal amphotericin B spray, lipid formulations of amphotericin B, and aerosolized amphotericin B have been administered for aspergillosis prophylaxis, but data are limited regarding the safety and efficacy of these formulations among hematopoietic stem cell transplant recipients. Additionally, itraconazole capsules are not recommended for fungal prophylaxis among hematopoietic stem cell transplant recipients (DII) for three reasons. First, itraconazole capsules are poorly absorbed gastrointestinally, particularly among patients who are fasting or receiving cytotoxic agents. Second, persons taking itraconazole capsules do not achieve steady-state serum levels for 2 weeks, and when achieved, these levels are lower than the average *Aspergillus* species minimum inhibitory concentration (MIC) among hematopoietic stem cell transplant recipients. Third, itraconazole has adverse interactions with other drugs (e.g., antiepileptics, rifampin, oral hypoglycemics, protease inhibitors, vinca alkaloids, cyclosporine, methylprednisolone, and warfarin-like anticoagulants). Trials assessing the efficacy of the recently licensed cyclodextrin oral solution and intravenous formulations of itraconazole in preventing invasive fungal disease among hematopoietic stem cell transplant recipients are in progress; however, no recommendations regarding its use for *Aspergillus* species infection prophylaxis can be made. For hematopoietic stem cell transplant recipients whose respiratory specimens are culture positive for *Aspergillus* species, acute invasive aspergillosis should be diagnosed presumptively 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 hematopoietic stem cell transplants were avoided among persons with uncontrolled, proven aspergillosis. However, hematopoietic stem cell transplant center personnel have recently reported successful allogeneic or autologous hematopoietic stem cell transplant among a limited number of persons who have had successfully treated, prior invasive pulmonary aspergillosis. Because of limited data, no recommendations regarding strategies for preventing aspergillosis recurrence can be made.

## Protozoal and Helminthic Infections

### Recommendations Regarding *Pneumocystis Carinii* Pneumonia

#### Preventing Exposure

Although a possible cause of *Pneumocystis carinii* pneumonia is reactivation of latent infection among immunocompromised persons, cases of person-to-person

transmission of *Pneumocystis carinii* pneumonia have been reported. Generally, standard precautions should be used for patients with *Pneumocystis carinii* pneumonia (BIII), but researchers have reported patients with *Pneumocystis carinii* pneumonia being isolated 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, hematopoietic stem cell transplant recipients should avoid exposure to persons with *Pneumocystis carinii* pneumonia (CIII).

### Preventing Disease and Disease Recurrence

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

Preferred *Pneumocystis carinii* pneumonia prophylaxis is trimethoprim-sulfamethasaxole (AII); however, if trimethoprim-sulfamethasaxole 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 hematopoietic stem cell transplant recipients are limited. For patients who cannot tolerate trimethoprim-sulfamethasaxole, physicians can choose to use alternative *Pneumocystis carinii* pneumonia prophylaxis regimens (e.g., dapsone) (BIII). Use of aerosolized pentamidine is associated with the lowest *Pneumocystis carinii* pneumonia prevention rates and should only be used if other agents cannot be tolerated. Atovaquone is a possible alternative drug for *Pneumocystis carinii* pneumonia prophylaxis among dapsone-intolerant persons with human immunodeficiency virus (HIV) infection; however, no recommendation regarding use of atovaquone among hematopoietic stem cell transplant recipients can be made because of lack of data. Although data are limited, concomitant use of leucovorin (folinic acid) and trimethoprim-sulfamethasaxole is not recommended (DIII). A patient's history of *Pneumocystis carinii* pneumonia should not be regarded as a contraindication to hematopoietic stem cell transplant (DIII).

Recurrent *Pneumocystis carinii* pneumonia among hematopoietic stem cell transplant recipients is rare; however, patients with continued immunosuppression should remain on *Pneumocystis carinii* pneumonia prophylaxis until their immunosuppression is resolved (AI). The regimen recommended for preventing toxoplasmosis recurrence among hematopoietic stem cell transplant recipients (i.e., trimethoprim-sulfamethasaxole) will also prevent *Pneumocystis carinii* pneumonia recurrence.

### Other Recommendations

Pneumocystis carinii pneumonia 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-chlorodeoxyadenosine (BIII).

Pneumocystis carinii pneumonia prophylaxis should be administered  $\geq 6$  months after hematopoietic stem cell transplant if substantial immunosuppression or immunosuppressive therapy (e.g., steroids) persists (CIII). Use of Pneumocystis carinii pneumonia prophylaxis among other autologous recipients is controversial (CIII). Generally, indications for Pneumocystis carinii pneumonia prophylaxis are the same among children or adults, but pediatric doses should be used (see the Appendix in the original guideline document).

## Recommendations Regarding Toxoplasma gondii

### Preventing Exposure

All hematopoietic stem cell transplant recipients should be provided information regarding strategies to reduce their risk for Toxoplasma species exposure. Researchers report that potential donors for allogeneic hematopoietic stem cell transplant be tested for Toxoplasma gondii antibodies by using Food and Drug Administration-licensed or -approved screening tests that include immunoglobulin G antibody testing because Toxoplasma gondii has been reported to be transmitted by leukocyte transfusion and hematopoietic stem cell transplant (CIII).

### Preventing Disease and Disease Recurrence

Because most toxoplasmosis among hematopoietic stem cell transplant recipients is caused by disease reactivation, researchers report that candidates for allogeneic hematopoietic stem cell transplant can be tested for immunoglobulin G antibody to determine whether they are at risk for disease reactivation after hematopoietic stem cell transplant (CIII). However, the value of such testing is controversial because a limited number of patients who were seronegative for Toxoplasma gondii pretransplant experienced the infection posttransplant. If testing is performed, only Food and Drug Administration-licensed or -approved screening tests should be used.

Researchers recommend toxoplasmosis prophylaxis for seropositive allogeneic recipients with active graft-versus-host disease or a prior history of toxoplasmic chorioretinitis, but data demonstrating efficacy are limited (CIII). The optimal prophylactic regimen for toxoplasmosis among hematopoietic stem cell transplant recipients has not been determined, but a proposed drug is trimethoprim-sulfamethasaxole (BII), although allogeneic recipients have experienced breakthrough clinical disease despite trimethoprim-sulfamethasaxole prophylaxis. For patients who are trimethoprim-sulfamethasaxole-intolerant, a combination of clindamycin, pyramethamine, and leucovorin can be substituted for Toxoplasma gondii prophylaxis (see the Appendix in the original guideline document). After therapy for toxoplasmosis, hematopoietic stem cell transplant recipients should continue receiving suppressive doses of trimethoprim-sulfamethasaxole or an alternate regimen for the duration of their immunosuppression (BIII) (see the Appendix in the original guideline document).

## Other Recommendations

Recipients of autologous transplants are at negligible risk for toxoplasmosis reactivation. 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 (see the Appendix in the original guideline document).

## 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 (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 hematopoietic stem cell transplant 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) (BIII). Hematopoietic stem cell transplant 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 hematopoietic stem cell transplant (BIII). Serologic testing with an enzyme-linked immunosorbent assay is the preferred screening method and has a sensitivity and specificity of >90% (BIII). Food and Drug Administration-licensed or -approved screening tests should be used. Although stool examinations for strongyloidiasis are specific, the sensitivity obtained from  $\geq 3$  stool examinations is 60% to 70%; the sensitivity obtained from concentrated stool exams is, at best, 80%. A total of  $\geq 3$  stool examinations should be performed if serologic tests are unavailable or if strongyloidiasis is clinically suspected in a seronegative patient (BIII).

Hematopoietic stem cell transplant candidates whose screening tests before hematopoietic stem cell transplant 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, preferably with ivermectin (BIII), even if seronegative or stool-negative (see the Appendix in the original guideline document).

To prevent recurrence among hematopoietic stem cell transplant candidates with parasitologically confirmed strongyloidiasis, cure after therapy should be verified with  $\geq 3$  consecutive negative stool examinations before proceeding with hematopoietic stem cell transplant (AIII). Data are insufficient to recommend a drug prophylaxis regimen after hematopoietic stem cell transplant to prevent recurrence of strongyloidiasis. Hematopoietic stem cell transplant recipients who had strongyloidiasis before or after hematopoietic stem cell transplant 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 hematopoietic stem cell transplant; however, the same screening precautions should be used among autologous recipients (BIII). Indications for empiric treatment for strongyloidiasis before hematopoietic stem cell transplant are the same among children or adults except for children weighing <15 kg, for whom the preferred drug is thiabendazole (BIII) (see Appendix in the original guideline document).

## Recommendations Regarding *Trypanosoma cruzi*

### Preventing Exposure

Hematopoietic stem cell transplant physicians should be aware that *Trypanosoma cruzi*, the etiologic agent of Chagas' disease, can be transmitted congenitally, through blood transfusion, and possibly through hematopoietic stem cell transplant. Additionally, treatment for persons infected with *Trypanosoma cruzi* is not always effective, even during the acute stage of infection. Therefore, potential donors who were born, received a blood transfusion, or ever lived for  $\geq 6$  months in a Chagas' disease endemic area (e.g., parts of South and Central America and Mexico) should be screened serologically for anti-*Trypanosoma cruzi* serum immunoglobulin G antibody (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 *Trypanosoma 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 immunoglobulin G anti-*Trypanosoma cruzi* antibodies (CIII). To decrease the risk for misdiagnosis by false-positive or false-negative serologic tests, *Trypanosoma cruzi* screening should consist of  $\geq 2$  conventional serologic tests (e.g., enzyme immunoassay, indirect hemagglutination, indirect fluorescent antibody) or  $\geq 1$  conventional serologic tests, followed by a confirmatory serologic test (e.g., radioimmunoassay) (BIII). Persons with active Chagas' disease should not serve as hematopoietic stem cell transplant donors (DIII). Researchers also recommend deferral of hematopoietic stem cell transplant donation for a past history of Chagas' disease (CIII).

### Preventing Disease

Hematopoietic stem cell transplant candidates who are at risk for being infected with *Trypanosoma cruzi* should be screened for serum immunoglobulin G anti-*Trypanosoma cruzi* antibody (BIII). *Trypanosoma cruzi* seropositivity is not a contraindication to hematopoietic stem cell transplant. However, if an acute illness occurs in a *Trypanosoma cruzi*-seropositive hematopoietic stem cell transplant recipient, particularly during neutropenia, *Trypanosoma cruzi* reactivation should be included in the differential diagnosis (BIII). Researchers have proposed use of beznidazole or nifurtimox for preemptive therapy or prophylaxis of recurrent *Trypanosoma cruzi* among seropositive hematopoietic stem cell transplant recipients, 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

Hematopoietic stem cell transplant center personnel should follow published guidelines for hospital room design and ventilation (BIII). Hematopoietic stem cell transplant centers should also prevent birds from gaining access to hospital air-intake ducts (AII). All allogeneic recipients should be placed in rooms with >12 air exchanges/hour and point-of-use high-efficiency (>90%) particulate air filters that are capable of removing particles  $\geq 0.3$  micrometer in diameter (AIII). Correct filtration is critical in hematopoietic stem cell transplant centers with ongoing construction and renovation. When portable high-efficiency (>90%) particulate air 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 high-efficiency (>90%) particulate air filtration for autologous recipients has not been established. However, high-efficiency (>90%) particulate air-filtered rooms should 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. Although laminar air flow has been demonstrated to protect patients from infection during aspergillosis outbreaks related to hospital construction, the value of routine laminar air flow room use for all hematopoietic stem cell transplant recipients is doubtful because substantial overall survival benefit has not been reported. During 1983, laminar air flow rooms were preferred for allogeneic recipients with aplastic anemia and human lymphocyte antigen-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 laminar air flow rooms. However, the survival of aplastic anemia hematopoietic stem cell transplant recipients during the late 1990s exceeds that reported during the early 1980s, and no studies have been done to determine whether hematopoietic stem cell transplant recipients with aplastic anemia still have an improved survival rate when treated in an laminar air flow room. Therefore, hematopoietic stem cell transplant centers need not construct laminar air flow rooms for each hematopoietic stem cell transplant recipient. Use of laminar air flow 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 (BIII). Each hospital room should also be well-sealed (e.g., around windows and electrical outlets) (BIII). To provide consistent positive pressure in the recipient's room, hematopoietic stem cell transplant 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) (BIII). Generally, hospital rooms for hematopoietic stem cell transplant 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. An exception is the hematopoietic stem cell transplant recipient with an active disease that has airborne transmission (e.g., pulmonary or laryngeal *Mycobacteria tuberculosis* [TB] or measles). These hematopoietic stem cell transplant patients should be placed in negative isolation rooms (BIII), and a room with an anteroom is recommended for such patients (BIII).

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

Hematopoietic stem cell transplant 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 (BIII). Additionally, infection control personnel should work with maintenance personnel to develop protocols to protect hematopoietic stem cell transplant 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. Therefore, persons responsible for hematopoietic stem cell transplant center construction or renovation should consult published recommendations regarding environmental controls during construction (AIII).

Whenever possible, hematopoietic stem cell transplant recipients, health-care workers, and visitors should avoid construction or renovation areas (AIII). Also, equipment and supplies used by hematopoietic stem cell transplant recipients or their health-care workers should not be exposed to construction or renovation areas. When planning for construction or renovation, the hematopoietic stem cell transplant 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 hematopoietic stem cell transplant center, the administration, and safety officers (BIII).

When constructing new hematopoietic stem cell transplant 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 hematopoietic stem cell transplant 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 (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 (BIII).

During hospital construction or renovation, hospitals should construct rigid, dust-proof barriers with airtight seals 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 (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 (BIII). Hematopoietic stem cell transplant 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, particularly those in the hematopoietic stem cell transplant center (BIII). If possible, specific corridors, entrances, and exits should be dedicated to construction use only. An elevator to which patients do not have access also should be dedicated to construction use only. 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 (BIII). Ideally, air from the construction or renovation areas should be exhausted to the outside of the hospital (BIII) or if recirculated, it should be high-efficiency (>90%) particulate air-filtered first (BIII).

Researchers have proposed that hematopoietic stem cell transplant 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%. For patients who cannot use or tolerate an N95 respirator, researchers have proposed using the powered air purifying respirator, 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 hematopoietic stem cell transplant 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 (AIII). Decontamination of fungal-contaminated areas that cannot be extracted and replaced should be done using copper-8-quinolate (BIII). Also, areas above false ceilings located under or adjacent to construction areas should be vacuumed (BIII). Additionally, the ventilation, direction of airflow, and room pressurization should be tested and correctly adjusted before patients are allowed to enter (BIII).

## Cleaning

Hematopoietic stem cell transplant centers should be cleaned  $\geq 1$  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 Food and Drug Administration- or Environmental Protection Agency (EPA)-registered hospital disinfectant (BIII). Thorough cleaning during and after any construction activity, including minor renovation projects, is critical (BIII).

Hematopoietic stem cell transplant 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) (AIII). Accordingly, doors to patient rooms should be closed when vacuuming hematopoietic stem cell transplant center corridors. All vacuum cleaners used in the hematopoietic stem cell transplant center should be fitted with high-efficiency ( $>90\%$ ) particulate air filters. An Food and Drug Administration- or Environmental Protection Agency-registered disinfectant should be used daily for environmental disinfection and when wet vacuuming is performed in the hematopoietic stem cell transplant center (BIII). If an hematopoietic stem cell transplant 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 bassinets or incubators (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 hematopoietic stem cell transplant patients care areas (BIII). If cleanup and repair are delayed  $\geq 72$  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 (BIII). For example, if the wall does not have  $<20\%$  moisture content  $\geq 72$  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 hematopoietic stem cell transplant centers should be scrubbable, nonporous, easily disinfected, and they should collect minimal dust (BIII).

## Isolation and Barrier Precautions

Hematopoietic stem cell transplant center personnel should follow published guidelines for hospital isolation practices, including CDC guidelines for preventing nosocomial infections (AIII). However, the efficacy of specific isolation and barrier

precautions in preventing nosocomial infections among hematopoietic stem cell transplant recipients has not been evaluated.

hematopoietic stem cell transplant 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. When indicated, hematopoietic stem cell transplant recipients should also be placed on airborne, droplet, or contact precautions in addition to standard precautions (AIII). Careful observation of isolation precautions is critical in preventing transmission of infectious agents among hematopoietic stem cell transplant recipients, health-care workers, visitors, and other hematopoietic stem cell transplant recipients. Physicians are cautioned that hematopoietic stem cell transplant recipients might have a prolonged or episodic excretion of organisms (e.g., cytomegalovirus).

Researchers have proposed that hematopoietic stem cell transplant recipients wear surgical mask and gloves when exiting their hospital rooms before engraftment (CIII). All hematopoietic stem cell transplant recipients who are immunocompromised (phases I to 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 community-acquired respiratory virus infections.

## Hand Hygiene

Hand washing is the single-most critical and effective procedure for preventing nosocomial infection. All persons, but particularly health-care workers, should wash their hands before entering and after leaving the rooms of hematopoietic stem cell transplant recipients and candidates undergoing conditioning therapy or before and after any direct contact with patients regardless of whether they were soiled from the patient, environment, or objects (AI). Hematopoietic stem cell transplant 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. If gloves are worn, health-care workers 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) and adhesive bandage strips, can create a nidus for pathogenic organisms that is difficult to clean. Thus, health-care workers should avoid wearing such items whenever possible (BII).

## Equipment

All hematopoietic stem cell transplant center personnel should sterilize or disinfect and maintain equipment and devices using only Environmental Protection Agency-registered compounds as directed by established guidelines (AIII). Hematopoietic stem cell transplant center personnel should monitor opened and unopened wound-dressing supplies (e.g., adhesive bandages and surgical and elastic adhesive tape) 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, 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 (DII). Hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipients.

#### Plants, Play Areas, and Toys

Although to date, exposure to plants and flowers has not been conclusively reported to cause fungal infections among hematopoietic stem cell transplant recipients, most researchers strongly recommend that plants and dried or fresh flowers should not be allowed in the rooms of hospitalized hematopoietic stem cell transplant candidates undergoing conditioning therapy and hematopoietic stem cell transplant recipients (phases I to 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 (BIII).

Play areas for pediatric hematopoietic stem cell transplant recipients and candidates undergoing conditioning therapy should be cleaned and disinfected  $\geq 1$  times/week and as needed (BIII). Only toys, games, and videos that can be kept clean and disinfected should be allowed in the hematopoietic stem cell transplant center (BIII). Hematopoietic stem cell transplant centers should follow published recommendations for washing and disinfecting toys (BIII). All hematopoietic stem cell transplant center toys, games, and videos should be routinely and thoroughly washed or wiped down when brought into the hematopoietic stem cell transplant center and thereafter  $\geq 1$  times/week and as needed by using a nontoxic Food and Drug Administration- or Environmental Protection Agency-registered disinfectant followed by a water rinse (BIII). Cloth or plush toys should be washed in a hot cycle of a washing machine or dry-cleaned  $\geq 1$  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. 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 to 20 minutes, rinsed again, and allowed to air dry. Alternatively, hard plastic toys can be washed in a dishwasher or hot cycle of a washing machine (BIII). Dolls (dolls are used to demonstrate medical procedures [e.g.,

insertion of BROVIAC® catheters] to children to lessen their fears) should be disassembled upon completion of play and washed with a nontoxic Food and Drug Administration- or Environmental Protection Agency-registered disinfectant, 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 (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).
- 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 Food and Drug Administration- or Environmental Protection Agency-registered disinfectant (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; therefore, these toys should not be used by immunocompromised hematopoietic stem cell transplant 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).

#### Health Care Workers

Hematopoietic stem cell transplant center personnel should have a written comprehensive policy regarding their immunizations and vaccinations, and that policy should meet current Centers for Disease Control and Prevention (CDC), Advisory Committee on Immunization Practices, and Healthcare Infection Control Practices Advisory Committee recommendations (BIII). Immunizations are needed to prevent transmission of vaccine-preventable diseases to hematopoietic stem cell transplant recipients and candidates undergoing conditioning therapy. All health-care workers with diseases transmissible by air, droplet, and direct contact (e.g., varicella-zoster virus, infectious gastroenteritis, herpes simplex virus lesions of lips or fingers, and upper respiratory infections) should be restricted from patient contact and temporarily reassigned to other duties (AI). Hematopoietic stem cell transplant center personnel should follow published recommendations regarding the duration of work restrictions for health-care workers with infectious diseases (BIII). Hematopoietic stem cell transplant center health-care workers 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 health-care worker's blood or body fluids. Work exclusion policies should be designed to encourage health-care workers to report their illnesses or exposures (AII).

## Hematopoietic Stem Cell Transplant Center Visitors

Hospitals should have written policies for screening hematopoietic stem cell transplant center visitors, particularly children, for potentially infectious conditions. Such screening should be performed by clinically trained health-care workers (BII). Visitors who might have communicable infectious diseases (e.g., upper respiratory infections, flu-like illnesses, recent exposure to communicable diseases, an active shingles rash whether covered or not, a varicella-zoster virus-like rash within 6 weeks of receiving a live-attenuated varicella-zoster virus vaccine, or a history of receiving an oral polio vaccine within the previous 3 to 6 weeks) should not be allowed in the hematopoietic stem cell transplant center or allowed to have direct contact with hematopoietic stem cell transplant recipients or candidates undergoing conditioning therapy (AII). No absolute minimum age requirement for hematopoietic stem cell transplant center visitors exists; however, all visitors must be able to understand and follow appropriate hand washing and isolation precautions (AIII). The number of hematopoietic stem cell transplant 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, hematopoietic stem cell transplant 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). Hematopoietic stem cell transplant 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, hematopoietic stem cell transplant 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 hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipients to avoid skin or mucosal breakdown (DIII).

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

All hematopoietic stem cell transplant candidates should receive a dental evaluation and relevant treatment before conditioning therapy begins (AIII). Likely sources of dental infection should be vigorously eliminated (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. Ideally, 10 to 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).

Hematopoietic stem cell transplant recipients with mucositis and hematopoietic stem cell transplant candidates undergoing conditioning therapy should maintain safe oral hygiene by performing oral rinses 4 to 6 times/day with sterile water, normal saline, or sodium bicarbonate solutions (AIII). Hematopoietic stem cell transplant recipients and candidates should brush their teeth  $\geq 2$  times/day with a soft regular toothbrush (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. Using toothpaste is optional, depending on the recipient's tolerance (CIII). Hematopoietic stem cell transplant 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 (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 hematopoietic stem cell transplant and during mucositis after hematopoietic stem cell transplant, 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

Hematopoietic stem cell transplant center personnel are advised to implement published guidelines for preventing intravascular device-related infections (AIII). Contact with tap water at the central venous catheter site should be avoided (BIII). For long-term central venous access among children, hematopoietic stem cell transplant 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 hematopoietic stem cell transplant 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 hematopoietic stem cell transplant.

To prevent bloodstream infections associated with needleless intravenous access devices, hematopoietic stem cell transplant 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 (BII). Also, hematopoietic stem cell transplant recipients and their caregivers should be educated regarding proper care of needleless intravenous access devices (BII). No recommendation regarding the use of antibiotic-impregnated central venous catheters among hematopoietic stem cell transplant recipients can be made because of lack of data.

## Control of Specific Nosocomial Infections

### Recommendations Regarding Legionella Species

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

The source of Legionella infection should be identified and decontaminated or removed (AIII). Extensive hospital investigations of an isolated case of possible nosocomial Legionnaires' disease might not be indicated if the patient has had limited contact with the inpatient center during most of the incubation period (CIII). Because hematopoietic stem cell transplant recipients are at much higher risk for disease and death from legionellosis compared with other hospitalized persons, 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 Legionnaires' disease in hematopoietic stem cell transplant centers (CIII). However, the optimal methodology (i.e., frequency or number of sites) for environmental surveillance cultures in hematopoietic stem cell transplant centers has not been determined, and the cost-effectiveness of this strategy has not been

evaluated. Because hematopoietic stem cell transplant recipients are at high risk for Legionnaires' disease 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 hematopoietic stem cell transplant recipients with nosocomial pneumonia even when environmental surveillance cultures do not yield Legionellae (AIII). If Legionella species are detected in the water supplying an hematopoietic stem cell transplant center, the following should be done until Legionella species are no longer detected by culture:

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

Hematopoietic stem cell transplant 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 (BII). Hematopoietic stem cell transplant 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 (DI) unless these humidifier or nebulizers are sterilized or subjected to daily high-level disinfection and filled with sterile water only (CIII).

When a new hospital with an hematopoietic stem cell transplant 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 (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 (BII).

Hematopoietic stem cell transplant physicians are encouraged to consult published recommendations regarding preventing nosocomial Legionellosis (BIII). No data were found to determine whether drinking tap water poses a risk for Legionella exposure among hematopoietic stem cell transplant recipients in the absence of an outbreak.

## Recommendations Regarding Methicillin-Resistant *Staphylococcus aureus*

Hematopoietic stem cell transplant center health-care workers 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 *Staphylococcus aureus* [MRSA] infected or colonized patient's room); these practices are essential for methicillin-resistant *Staphylococcus aureus* control (AII). If methicillin-resistant *Staphylococcus aureus* is a substantial problem in the hematopoietic stem cell transplant center and evidence exists of ongoing methicillin-resistant *Staphylococcus aureus* transmission, methicillin-resistant *Staphylococcus aureus* infected or colonized patients should be treated as a cohort (e.g., cared for exclusively by a limited number of health-care workers) (BIII). Hematopoietic stem cell transplant recipients with recurrent *Staphylococcus 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 methicillin-resistant *Staphylococcus aureus* 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 (see Appendix in the original guideline document). High-level mupirocin-resistant methicillin-resistant *Staphylococcus aureus* has been reported in Europe, the Middle East, and South America 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. For patients who fail mupirocin, physicians have used bacitracin, trimethoprim-sulfamethasazole, 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 cannulae or other implantable devices that are infected or colonized with methicillin-resistant *Staphylococcus aureus* should be removed (AIII). Patients with methicillin-resistant *Staphylococcus aureus* should be placed under contact precautions until all antibiotics are discontinued and until three consecutive cultures, taken  $\geq 1$  weeks apart, are negative (BIII). Screening cultures for methicillin-resistant *Staphylococcus aureus* include the anterior nares, any body site previously positive for methicillin-resistant *Staphylococcus aureus*, and any wounds or surgical sites.

## Recommendations Regarding *Staphylococcus* Species with Reduced Susceptibility to Vancomycin

All hematopoietic stem cell transplant centers should have sufficient laboratory capability to identify all *Staphylococci* isolates and their susceptibility patterns to antibiotics, including vancomycin (AIII). Additionally, all hematopoietic stem cell transplant center personnel should conduct routine surveillance for the emergence of *Staphylococcus* species strains with reduced susceptibility to vancomycin (AIII). Reduced susceptibility should be considered for all *Staphylococcus aureus* strains that have a vancomycin minimum inhibitory concentration of  $\geq 4$  micrograms/mL and all coagulase-negative *Staphylococci* that have a vancomycin minimum inhibitory concentration of  $\geq 8$  micrograms/mL. If repeat testing of the organism in

pure culture confirms the genus, species, and elevated vancomycin minimum inhibitory concentrations, the following steps should be taken:

- 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 the Centers for Disease Control and Prevention (CDC) Hospital Infections Program Help Desk ([404] 639-6106 or [800] 893-0485) (AIII).
- The hematopoietic stem cell transplant center's infection control personnel, in collaboration with appropriate authorities (i.e., state and local health departments and the Centers for Disease Control and Prevention [CDC]) should promptly initiate an epidemiologic and laboratory investigation (AIII) and follow published guidelines for the control of such species (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 health-care workers with secretions is likely) as recommended for multidrug-resistant organisms;
  - Minimize the number of persons with access to colonized or infected patients; and
  - treat as a cohort colonized or infected patients (e.g., care for them exclusively with a limited number of health-care workers) (AIII).
- If a patient in an hematopoietic stem cell transplant 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 (BIII).

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

#### Recommendations Regarding Vancomycin-resistant Enterococcus

Use of intravenous vancomycin is associated with vancomycin-resistant Enterococcus emergence. Vancomycin and all other antibiotics, particularly antianaerobic agents (e.g., metronidazole and third-generation cephalosporins) must be used judiciously (AII). Oral vancomycin use can be limited by treating recurrences of Clostridium difficile diarrhea with oral metronidazole instead of vancomycin (BIII). Physicians have placed patients with a history of vancomycin-resistant Enterococcus or vancomycin-resistant Enterococcus colonization into continuous isolation during clinic visits and hospitalizations; however, this practice is controversial because certain non-hematopoietic stem cell transplant recipients might clear vancomycin-resistant Enterococcus from their stools. No recommendation regarding use of continuous isolation among hematopoietic stem cell transplant recipients can be made because of lack of data. To control

vancomycin-resistant *Enterococcus* exposure, strict adherence to the following standard infection control measures is necessary (AI):

- Wash hands with antibacterial soap before entering and after leaving hematopoietic stem cell transplant recipients' rooms, particularly those who have vancomycin-resistant *Enterococcus* colonization or infection; alternatively, wash hands with a waterless antiseptic agent (e.g., an alcohol-based rinse or gel).
- Whenever possible, treat as a cohort patients who are known to be colonized or infected with vancomycin-resistant *Enterococcus*.
- Disinfect patient rooms and equipment, including surfaces of the hospital ward environment (e.g., floors, walls, bed frames, doors, bathroom surfaces) with an Food and Drug Administration- or Environmental Protection Agency-registered disinfectant. A nontoxic disinfectant should be used for pediatric areas (BIII).
- Place patients with vancomycin-resistant *Enterococcus* under contact precautions until all antibiotics are discontinued (CIII) and repeated cultures are negative (BIII). Health-care workers should always wear gloves when in the vancomycin-resistant *Enterococcus* patient or carrier's room and discard gloves in the patient's room before exiting.

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

#### Recommendations Regarding *Clostridium Difficile*

Hematopoietic stem cell transplant physicians should follow published recommendations for preventing and controlling *Clostridium difficile* disease, including minimizing the duration of antibiotic therapy and number of antibiotics used for any indication (AIII). All patients with *Clostridium difficile* disease should be placed under contact precautions for the duration of illness (AII). All health-care workers who anticipate contact with a *Clostridium difficile*-infected patient or the patient's environment or possessions should put on gloves before entering the patient's room and before handling the patient's secretions and excretions (AI). During *Clostridium difficile* outbreaks, hematopoietic stem cell transplant center personnel should restrict use of antibiotics (e.g., clindamycin) (BII). To prevent transmission of *Clostridium difficile* to patients during nosocomial *Clostridium difficile* outbreaks, hematopoietic stem cell transplant center health-care workers 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; and (c) perform surface sterilization of the hospital ward environment (e.g., floors, walls, bed frames,

doors, bathroom surfaces) with an Food and Drug Administration- or Environmental Protection Agency-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; or ethylene oxide) (BII). Additionally, physicians should treat patients with *Clostridium difficile* disease with antibiotics as recommended in published reports (BII).

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

The following practices are not recommended for *Clostridium difficile* control:

- routine stool surveillance cultures for *Clostridium difficile* for asymptomatic patients or health-care workers, even during outbreaks (DIII)
- culturing health-care workers' hands for *Clostridium difficile* (DIII)
- treating patients presumptively for *Clostridium difficile* disease pending toxin results (DIII), unless the patient is very sick with a compatible syndrome or the hospital has a high prevalence of *Clostridium 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 *Clostridium difficile* disease and has been associated with *Saccharomyces boulardii* fungemia (DII).

#### Recommendations Regarding Community Acquired Respiratory Virus (CRV) Infections

Physicians should institute appropriate precautions and infection control measures for preventing nosocomial pneumonia among hospitalized hematopoietic stem cell transplant recipients and candidates undergoing conditioning therapy, particularly during community or nosocomial community-acquired respiratory virus outbreaks (AIII). Patients with upper respiratory infection or lower respiratory infection 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 hematopoietic stem cell transplant candidates and recipients as well as to health-care workers and visitors (BIII). Identifying hematopoietic stem cell transplant recipients with respiratory syncytial virus infection and placing them under contact precautions immediately (AIII) to prevent nosocomial transmission is critical. When suctioning the respiratory tract of patients with upper respiratory infection or lower respiratory infection symptoms, health-care workers 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 (AIII). When caring for an hematopoietic stem cell transplant recipient or candidate undergoing conditioning therapy with upper respiratory infection or lower respiratory infection, health-care workers 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 (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 community-acquired respiratory virus infections.

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

Respiratory secretions of any hospitalized hematopoietic stem cell transplant candidate or recipient with signs or symptoms of community-acquired respiratory virus infection should be tested promptly by viral culture and rapid diagnostic tests for community-acquired respiratory virus (BIII). Appropriate samples include nasopharyngeal washes, swabs, aspirates, throat swabs, and bronchoalveolar lavage fluid. This practice is critical because preemptive treatment of certain community-acquired respiratory viruses (e.g., influenza and respiratory syncytial virus) might prevent severe disease and death among hematopoietic stem cell transplant recipients. Viral shedding among hematopoietic stem cell transplant recipients with community-acquired respiratory virus infection has been reported to last  $\leq 4$  months for influenza,  $\leq 2$  years for adenovirus, and  $\leq 22$  days for respiratory syncytial virus; however, respiratory syncytial virus viral shedding has been reported to last 112 days in a child with severe combined immunodeficiency. Therefore, to prevent nosocomial transmission of community-acquired respiratory virus, hematopoietic stem cell transplant center health-care workers should recognize that prolonged community-acquired respiratory virus shedding can occur when determining the duration of appropriate precautions for community-

acquired respiratory virus-infected hematopoietic stem cell transplant recipients or candidates undergoing conditioning therapy (CIII). Hematopoietic stem cell transplant 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 hematopoietic stem cell transplant physicians conduct routine community-acquired respiratory virus surveillance among hematopoietic stem cell transplant recipients to detect outbreaks and implement infection control measures as early as possible (CIII). During respiratory syncytial virus season, hematopoietic stem cell transplant recipients and candidates with signs or symptoms should be tested for respiratory syncytial virus infection (i.e., the presence of respiratory syncytial virus antigen in respiratory secretions, tested by enzyme-linked immunosorbent assay and viral culture) starting with admission to the hematopoietic stem cell transplant center. All patients who are respiratory syncytial virus-antigen positive should be treated as a cohort during nosocomial respiratory syncytial virus outbreaks because this practice reduces nosocomial respiratory syncytial virus transmission (BII). Symptomatic health-care workers should be excluded from patient contact until symptoms resolve. Health-care workers and visitors with infectious conjunctivitis should be restricted from direct patient contact until the drainage resolves (i.e., usually, 5 to 7 days for adenovirus) and the ophthalmology consultant concurs that the infection and inflammation have resolved (AII) to avoid possible transmission of adenovirus to hematopoietic stem cell transplant recipients.

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

#### Recommendations Regarding Mycobacteria tuberculosis (TB)

Hematopoietic stem cell transplant candidates should be screened for Mycobacteria tuberculosis by careful medical history and chart review to ascertain any history of prior Mycobacteria tuberculosis exposure (AIII) because immunocompromised persons have higher risk for progression from latent Mycobacteria tuberculosis infection to active disease. 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 tuberculin skin test is administered, either the Tubersol® or Aplisol® formulation of purified protein derivative can be used. Persons with a recently positive tuberculin skin test or a history of a positive tuberculin skin test and no prior preventive therapy should be administered a chest radiograph and evaluated for active Mycobacteria tuberculosis (AI). For immunocompromised persons, a positive tuberculin skin test is defined as  $\geq 5$  mm of induration because of their decreased ability to mount a delayed hypersensitivity response (CIII). Because immunosuppressive therapy decreases the sensitivity of the tuberculin skin test, hematopoietic stem cell transplant physicians should not rely solely on the tuberculin skin test to determine whether latent Mycobacteria tuberculosis infection is present and

whether preventive therapy should be administered to hematopoietic stem cell transplant recipients or candidates (DIII). Instead, a full 9-month course of isonicotinic acid hydrazide preventive therapy should be administered to immunocompromised hematopoietic stem cell transplant recipients or candidates who have been substantially exposed to someone with active, infectious (i.e., sputum-smear positive) pulmonary or laryngeal *Mycobacteria tuberculosis*, regardless of the hematopoietic stem cell transplant recipient's or candidate's tuberculin skin test status (BIII). A full 9-month course of isonicotinic acid hydrazide preventive therapy should also be administered to hematopoietic stem cell transplant recipients or candidates with a positive tuberculin skin test who were not previously treated and have no evidence of active *Mycobacteria tuberculosis* disease (AIII) (see Appendix in the original guideline document). Routine anergy screening might not be reliable among hematopoietic stem cell transplant recipients and candidates undergoing conditioning therapy and, therefore, is not recommended (DIII). An hematopoietic stem cell transplant should not be canceled or delayed because of a positive tuberculin skin test (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 *Mycobacteria tuberculosis*. 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 pyrazinamide/rifampin prophylactic regimen among hematopoietic stem cell transplant recipients is not recommended (DIII). However, this regimen can be used for hematopoietic stem cell transplant candidates who are not at risk for serious rifampin drug interactions and whose hematopoietic stem cell transplant is not scheduled until  $\geq 2$  weeks after completion of the 2-month pyrazinamide/rifampin course (CIII). This delay will diminish the possibility of adverse effects of rifampin on drugs used for routine hematopoietic stem cell transplant opportunistic infection prophylaxis (e.g., fluconazole). An hematopoietic stem cell transplant candidate or recipient who has been exposed to an active case of extrapulmonary, and therefore, noninfectious *Mycobacteria tuberculosis* does not require preventive therapy (DIII).

Hematopoietic stem cell transplant center personnel should follow guidelines regarding the control of *Mycobacteria tuberculosis* in health-care facilities, including instituting airborne precautions and negative-pressure rooms for patients with suspected or confirmed pulmonary or laryngeal *Mycobacteria tuberculosis* (AII). Health-care workers should wear N95 respirators, even in isolation rooms, to protect themselves from possible *Mycobacteria tuberculosis* transmission from patients with active pulmonary or laryngeal *Mycobacteria tuberculosis*, particularly during cough-inducing procedures (AIII). To be maximally effective, respirators (e.g., N95) must be fit-tested, and all respirator users must be trained to use them correctly (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 (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 *Mycobacteria tuberculosis* (DIII).

## Infection Control Surveillance

Hematopoietic stem cell transplant center personnel are advised to follow standard guidelines for surveillance of antimicrobial use and nosocomial pathogens and their susceptibility patterns (BIII). Hematopoietic stem cell transplant center personnel should not perform routine fungal or bacterial cultures of asymptomatic hematopoietic stem cell transplant recipients (DII). In the absence of epidemiologic clusters of infections, hematopoietic stem cell transplant center personnel should not perform routine periodic bacterial surveillance cultures of the hematopoietic stem cell transplant center environment or of equipment or devices used for respiratory therapy, pulmonary-function testing, or delivery of inhalation anesthesia (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 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. Furthermore, in the absence of a nosocomial fungal outbreak, hematopoietic stem cell transplant centers need not perform routine fungal cultures of devices and dust in the rooms of hematopoietic stem cell transplant recipients and candidates undergoing conditioning therapy (DIII). Hematopoietic stem cell transplant center personnel should routinely perform surveillance for the number of aspergillosis cases occurring among hematopoietic stem cell transplant 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 hematopoietic stem cell transplant center environment should be evaluated for breaks in infection control techniques and procedures and that the ventilation system should be investigated carefully (BIII).

### Strategies for Safe Living After Hematopoietic Stem Cell Transplant -- Preventing Exposure and Disease

#### Avoiding Environmental Exposures

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

#### Preventing Infections Transmitted by Direct Contact

Hematopoietic stem cell transplant 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
- before and after touching wounds (AIII)

Conscientious hand washing is critical during the first 6 months after hematopoietic stem cell transplant and during other periods of substantial immunosuppression (e.g., graft-versus-host disease, systemic steroid use, or relapse of the underlying disease for which the transplant was performed) (AIII). Pediatric hematopoietic stem cell transplant recipients and candidates should be supervised by adults during hand washing to ensure thorough cleaning (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. Hematopoietic stem cell transplant recipients who visit or live on farms should follow published recommendations for preventing cryptosporidiosis (BIII).

### Preventing Respiratory Infections

To prevent respiratory infections after hospital discharge, hematopoietic stem cell transplant recipients should observe the following precautions:

- Frequent and thorough hand washing is critical (BIII), but hematopoietic stem cell transplant recipients should also avoid touching their mucus membranes, unless they have washed their hands first, to avoid inoculating themselves with community-acquired respiratory virus.
- Hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipient can wear a surgical mask (CIII).
- Hematopoietic stem cell transplant recipients should avoid crowded areas (e.g., shopping malls or public elevators) where close contact with persons with respiratory illnesses is likely (BIII).
- Hematopoietic stem cell transplant 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 Mycobacteria tuberculosis 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 Mycobacteria tuberculosis exposure in the workplace, and the prevalence of Mycobacteria tuberculosis in the community. The decision to continue or terminate such activities should be made jointly between patient and physician (BIII). Hematopoietic stem cell transplant recipients should avoid exposure to persons with active tuberculosis, particularly during the first 6 months after hematopoietic stem cell transplant and during other periods of substantial immunosuppression (e.g., graft-versus-host disease, 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

hematopoietic stem cell transplant and during other periods of substantial immunosuppression (e.g., graft-versus-host disease, 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 hematopoietic stem cell transplant recipients should be advised of travel routes to the hematopoietic stem cell transplant center that will avoid or minimize exposure to construction sites (CIII).

Coccidioidomycosis is uncommon after allogeneic hematopoietic stem cell transplant; however, researchers report that hematopoietic stem cell transplant 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 hematopoietic stem cell transplant is also rare; however, researchers report that hematopoietic stem cell transplant recipients in histoplasmosis-endemic areas should avoid exposure to chicken coops and other bird-roosting sites and caves for the first 6 months after hematopoietic stem cell transplant and during periods of substantial immunosuppression (e.g., graft-versus-host disease, 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 community-acquired respiratory virus infections among healthy adults and children; consequently, logic dictates that physicians advise hematopoietic stem cell transplant 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 opportunistic infections among hematopoietic stem cell transplant recipients. Researchers have reported that marijuana smoking might be associated with generation of invasive pulmonary aspergillosis among immunocompromised persons, including hematopoietic stem cell transplant recipients. Therefore, hematopoietic stem cell transplant recipients should refrain from smoking marijuana to avoid *Aspergillus* species exposure (BIII).

#### Preventing Infections Transmitted Through Direct Contact and Respiratory Transmission

Researchers have proposed that immunocompromised hematopoietic stem cell transplant 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., *Toxoplasma gondii*, *Histoplasma capsulatum*, *Cryptococcus neoformans*, *Nocardia* species, and *Aspergillus* species) (CIII). Hematopoietic stem cell transplant recipients, particularly allogeneic recipients, could wear gloves while gardening or touching plants or soil (CIII), and they should avoid creating plant or soil aerosols (BIII). Additionally, they should always wash their hands afterwards 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 hematopoietic stem cell transplant recipients working in such settings, these exposures should be avoided during the first 6 months after hematopoietic stem cell transplant and during other periods of substantial immunosuppression (e.g., graft-versus-host disease, systemic steroid use, or relapse of the underlying disease for which the transplant was performed) (BIII).

## Safe Sex

Sexually active hematopoietic stem cell transplant recipients should avoid sexual practices that could result in oral exposure to feces (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 cytomegalovirus, herpes simplex virus, 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 hematopoietic stem cell transplant 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

Hematopoietic stem cell transplant physicians should advise recipients and candidates undergoing conditioning therapy of the potential infection risks posed by pet ownership; however, they should not routinely advise hematopoietic stem cell transplant recipients to part with their pets, with limited exceptions. Generally, immunocompromised hematopoietic stem cell transplant recipients and candidates undergoing conditioning therapy should minimize direct contact with animals, particularly those animals that are ill (e.g., with diarrhea) (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 (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 hematopoietic stem cell transplant 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 (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 (BIII).

If hematopoietic stem cell transplant recipients have contact with pets or animals, they should wash their hands after handling them (particularly before eating) and after cleaning cages; hematopoietic stem cell transplant recipients should avoid contact with animal feces to reduce the risk for toxoplasmosis, cryptosporidiosis, salmonellosis, and campylobacteriosis (BIII). Adults should supervise hand washing of pediatric hematopoietic stem cell transplant recipients (BIII). Immunocompromised hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipients and candidates should avoid adopting ill or juvenile pets (e.g., aged <6 months for cats) and any stray animals (BIII). Any pet that experiences diarrhea should be checked by a veterinarian for infection with *Cryptosporidium*, *Giardia* species, *Salmonella*, and *Campylobacter* (BIII).

Immunocompromised hematopoietic stem cell transplant recipients and candidates should not have contact with reptiles (e.g., snakes, lizards, turtles, or iguanas) (DII) to reduce their risk for acquiring salmonellosis. Additionally, patients should be informed that salmonellosis can occur from fomite contact alone. Therefore, hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipients and candidates should avoid contact with ducklings and chicks because of the risk for acquiring *Salmonella* or *Campylobacter* species infections (BIII). Immunocompromised hematopoietic stem cell transplant recipients and candidates should avoid contact with exotic pets (e.g., nonhuman primates) (BIII). Bird cage linings should be cleaned regularly (e.g., daily). All persons, but particularly immunocompromised hematopoietic stem cell transplant candidates and recipients, should wear gloves whenever handling items contaminated with bird droppings (BIII) because droppings can be a source of *Cryptococcus neoformans*, *Mycobacterium avium*, or *Histoplasma capsulatum*. However, routine screening of healthy birds for these diseases is not recommended (DIII). To minimize potential exposure to *Mycobacterium marinum*, immunocompromised hematopoietic stem cell transplant 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 (BIII).

### Preventing Toxoplasmosis

The majority of toxoplasmosis cases in the United States is acquired through eating undercooked meat. However, all hematopoietic stem cell transplant recipients and candidates, particularly those who are *Toxoplasma 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. Additionally, litter boxes should be cleaned daily by someone other than the hematopoietic stem cell transplant recipient during the first 6 months after hematopoietic stem cell transplant and during periods of substantial immunosuppression (e.g., graft-versus-host disease, steroid use, or relapse of the underlying disease for which the transplant was performed) to reduce the risk for transmitting toxoplasmosis to the hematopoietic stem cell transplant recipient (BIII). Daily litter box changes will minimize the risk for fecal transmission of *Toxoplasma gondii* oocysts, because fecal oocysts require  $\geq 2$  days of incubation to become infectious. If hematopoietic stem cell transplant recipients perform this task during the first 6 months after hematopoietic stem cell transplant and during subsequent periods of substantial immunocompromise (e.g., during graft-versus-host disease, systemic

steroid use, or relapse of the underlying neoplastic disease for which the transplant was performed), they should wear disposable gloves. Gloves should be discarded after a single use (BIII). Soiled, dried litter should be disposed of carefully to prevent aerosolizing the *Toxoplasma gondii* oocysts (BIII). Cat feces (but not litter) can be flushed down the toilet (BIII). Also, persons who clean cat litter, particularly hematopoietic stem cell transplant recipients, should wash their hands thoroughly with soap and water afterwards to reduce their risk for acquiring toxoplasmosis (BIII).

Hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipient (BIII). Pet cats of hematopoietic stem cell transplant 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). Hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipients, hematopoietic stem cell transplant 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. Hematopoietic stem cell transplant recipients should avoid walking, wading, swimming, or playing in recreational water (e.g., ponds or lakes) that is likely to be contaminated with *Cryptosporidium*, *Escherichia coli* O157:H7, sewage, or animal or human waste (BII). Hematopoietic stem cell transplant recipients should also avoid swallowing such water (e.g., while swimming) as well as any water taken directly from rivers and lakes (AIII).

Hematopoietic stem cell transplant 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  $\leq 1$  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  $\geq 2$  times/day for bacterial contamination. If hematopoietic stem cell transplant 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  $\geq 1$  minutes before it is consumed. Tap water might not be completely free of *Cryptosporidium*. To eliminate the risk for *Cryptosporidium* exposure from tap water, hematopoietic stem cell transplant recipients can boil tap water for  $\geq 1$  minutes before consuming it (e.g., drinking or brushing teeth) (CIII). Alternately, they can use certain types of water filters or a home distiller to reduce their risk for

Cryptosporidium and other waterborne pathogens (CIII). If a home water filter (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 [www.nsf.org/notice/crypto.html](http://www.nsf.org/notice/crypto.html)) is used, it should be capable of removing particles  $\geq 1$  micrometer 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-micrometer particulate absolute filtration. To confirm that a specific bottled water has undergone one of these processes, hematopoietic stem cell transplant recipients should contact the bottler directly (the International Bottled Water Association can be contacted at [703] 683-5213 from 9 a.m. to 5 p.m. Eastern Time or anytime at their Internet site, [www.bottledwater.org](http://www.bottledwater.org)) to obtain contact information regarding water bottlers. 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, fruit drinks made from frozen concentrate mixed with tap water, and iced tea or coffee made with tap water. Drinks that are likely to be Cryptosporidium safe for hematopoietic stem cell transplant recipients include nationally distributed brands of bottled or canned carbonated soft drinks and beers; 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); canned or bottled soda, seltzer or fruit drinks; steaming hot ( $\geq 175$  degrees F) tea or coffee; juices labeled as pasteurized; and nationally distributed brands of frozen fruit juice concentrate that are reconstituted with water from a safe source. Hematopoietic stem cell transplant recipients should not drink unpasteurized milk or fruit or vegetable juices (e.g., apple cider or orange juice) to avoid infection with Brucella species, Escherichia coli O157:H7, Salmonella species, Cryptosporidium, and others (DII).

## Food Safety

Hematopoietic stem cell transplant candidates and household or family members who prepare food for them after hematopoietic stem cell transplant should review food safety practices that are appropriate for all persons (AIII), and food preparers should be educated regarding additional food safety practices appropriate for hematopoietic stem cell transplant 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 hematopoietic stem cell transplant 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, 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 (AIII). Persons preparing food should follow published U.S. Department of Agriculture recommendations regarding safe food thawing (BIII).

Persons cooking food for hematopoietic stem cell transplant recipients should follow established guidelines for monitoring internal cooking temperatures for meats (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  $\geq 150$  degrees F (AII). Specifically, the U.S. Department of Agriculture recommends that poultry be cooked to an internal temperature of 180 degrees F; other meats and egg-containing casseroles and soufflés should be cooked to an internal temperature of  $\geq 160$  degrees F. Cold foods should be stored at  $< 40$  degrees F; hot foods should be kept at  $> 140$  degrees 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  $\geq 165$  degrees F throughout before serving (AII)
- bring leftover soups, sauces, and gravies to a rolling boil before serving (AIII)
- follow published guidelines for cold storage of food (AII)

#### Additional Food Safety Practices Appropriate for Hematopoietic Stem Cell Transplant Recipients

Hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipients (BIII). This diet should be continued for 3 months after hematopoietic stem cell transplant for autologous recipients. Allogeneic recipients should remain on the diet until all immunosuppressive drugs (e.g., cyclosporine, steroids, and tacrolimus) are discontinued. However, the hematopoietic stem cell transplant 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) (refer to Table 3

in the original guideline document for details). Hematopoietic stem cell transplant 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, hematopoietic stem cell transplant 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* (AII). Hematopoietic stem cell transplant recipients should not consume raw or undercooked seafood (e.g., oysters or clams) to prevent exposure to *Vibrio* species, viral gastroenteritis, and *Cryptosporidium parvum* (AII).

Hematopoietic stem cell transplant 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, hematopoietic stem cell transplant candidates undergoing conditioning therapy and hematopoietic stem cell transplant recipients with neutropenia (i.e., absolute neutrophil count  $<1,000/\text{mL}^3$ ), graft-versus-host disease, or immunosuppression should avoid exposures to naturopathic medicines that might contain molds (DIII). Hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipients, particularly allogeneic recipients chronically immunosuppressed. Hematopoietic stem cell transplant 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 to 12 months after hematopoietic stem cell transplant, particularly if graft-versus-host disease has occurred. Autologous recipients can travel to developing countries 3 to 6 months after hematopoietic stem cell transplant if their physicians agree.

Hematopoietic stem cell transplant 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 organization (AIII). Generally, while traveling in developing countries, hematopoietic stem cell transplant 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
- raw or undercooked eggs

Steaming hot foods, fruits peeled by oneself, bottled and canned processed drinks, and hot coffee or tea are probably safe. 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).

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

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

### Hematopoietic Stem Cell Transplant Recipient Vaccinations

Antibody titers to vaccine-preventable diseases (e.g., tetanus, polio, measles, mumps, rubella, and encapsulated organisms) decline during the 1 to 4 years after allogeneic or autologous hematopoietic stem cell transplant if the recipient is not revaccinated. Clinical relevance of decreased antibodies to vaccine-preventable diseases among hematopoietic stem cell transplant 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 hematopoietic stem cell transplant recipients; therefore, hematopoietic stem cell transplant recipients should be routinely revaccinated after hematopoietic stem cell transplant so that they can experience immunity to the same vaccine-preventable diseases as others (refer to Table 4 in the original guideline document).

Hematopoietic stem cell transplant center personnel have developed vaccination schedules for hematopoietic stem cell transplant recipients. One study determined that hematopoietic stem cell transplant center personnel used 3 to 11 different

vaccination schedules per vaccine; consequently, the study authors requested national guidelines for doses and timing of vaccines after hematopoietic stem cell transplant to eliminate confusion among hematopoietic stem cell transplant center personnel regarding how to vaccinate their patients. To address this need, an interim vaccination schedule for hematopoietic stem cell transplant recipients was drafted in collaboration with partner organizations, including the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices. The purpose of the vaccination schedule in these guidelines is to provide guidance for hematopoietic stem cell transplant centers (refer to Table 4 in the original guideline document). Although limited data were found regarding safety and immunogenicity (e.g., serologic studies of antibody titers after vaccination) among hematopoietic stem cell transplant recipients, no data were found regarding vaccine efficacy among hematopoietic stem cell transplant recipients (e.g., which determine whether vaccinated hematopoietic stem cell transplant recipients have decreased attack rates of disease compared with unvaccinated hematopoietic stem cell transplant recipients). Because certain hematopoietic stem cell transplant recipients have faster immune system recovery after hematopoietic stem cell transplant than others, researchers have proposed that different vaccination schedules be recommended for recipients of different types of hematopoietic stem cell transplant. However, to date, data are too limited to do so. Therefore, the same vaccination schedule is recommended for all hematopoietic stem cell transplant recipients (e.g., allogeneic, autologous, and bone marrow, peripheral, or umbilical cord blood grafts) until additional data are published. In the tables, vaccines have only been recommended for use among hematopoietic stem cell transplant recipients if evidence exists of safety and immunogenicity for those recipients. Vaccination of family members, household contacts, and health-care workers are also recommended to minimize exposure of vaccine-preventable diseases among hematopoietic stem cell transplant recipients (refer to Tables 5-8 in the original guideline document).

### Hematopoietic Stem Cell Safety

With allogeneic hematopoietic stem cell transplant, the life of the recipient might depend on the timely selection of an acceptable human lymphocyte antigen-matched donor. Only a limited number of human lymphocyte antigen-matched donors might be identified; hence, the transplant physician often has to accept a higher risk for transmission of an infectious agent through hematopoietic stem cell transplant than would be permitted for routine blood transfusion. This section provides strategies for the hematopoietic stem cell transplant 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 hematopoietic stem cell transplant, should be determined on a case-by-case basis (AIII) and is the final responsibility of the hematopoietic stem cell transplant 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 hematopoietic stem cell transplant 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 hematopoietic stem cell transplant procedure solely on the basis of the risk for an infectious disease. However, hematopoietic stem cell transplant physicians should avoid transplanting any infected or infectious donor hematopoietic stem cell product unless no other stem cell product can be obtained and 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 and the following should be noted in the recipient's chart:

- knowledge and authorization of the recipient's hematopoietic stem cell transplant physician regarding the potential for transmission of an infectious agent during hematopoietic stem cell transplant
- 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 hematopoietic stem cell transplant physician should include the infectious agent in the differential diagnosis of any illness that the hematopoietic stem cell transplant recipient experiences so that the infection, if transmitted, can be diagnosed early and treated preemptively, if possible. Infectious products (except those in which cytomegalovirus 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 Hematopoietic Stem Cell Transplant Donors to Recipients

All prospective hematopoietic stem cell transplant 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. To detect transmissible infections, all hematopoietic stem cell transplant 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 (AIII). Initial donor screening and physical exam should be performed  $\leq 8$  weeks before the planned donation (BIII). Donor serologic testing should be done  $\leq 30$  days before donation to detect potentially transmissible infections (BII); additionally, researchers recommend that donors be retested  $\leq 7$  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, Food and Drug Administration-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 hematopoietic stem cell transplant donors should be in good general health (BIII). Acute or chronic illness in the prospective donor should be investigated to determine the etiology. Generally, persons who are ill should not be hematopoietic stem cell transplant 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., Epstein-Barr virus, cytomegalovirus, *Toxoplasma gondii*) (BIII). Persons with a positive serum Epstein-Barr virus-viral capsid antigen immunoglobulin M but negative serum Epstein-Barr virus-viral capsid antigen immunoglobulin G should not serve as donors for allogeneic T-cell--depleted hematopoietic stem cell transplant, particularly for unrelated or mismatched transplants, until their serum Epstein-Barr virus-viral capsid antigen immunoglobulin G 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 asymptotically seropositive for *Toxoplasma gondii* might transmit this infection through hematopoietic stem cell transplant.

Prospective donors with symptoms of active *Mycobacteria tuberculosis* should be evaluated for that disease (BIII). Prospective donors with active *Mycobacteria tuberculosis* should not donate (EIII) until the *Mycobacteria tuberculosis* 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 *Mycobacteria tuberculosis* with Mantoux skin tests (DIII) is not necessary. Prospective hematopoietic stem cell transplant 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. 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 (CIII). Additionally, researchers have recommended deferring persons with acute human ehrlichiosis (e.g., human active human granulocytic ehrlichiosis, human monocytic ehrlichiosis, as well as any infections from *Ehrlichia ewingii*) from hematopoietic stem cell transplant donation (CIII).

The medical history of the prospective hematopoietic stem cell transplant donor should include the following:

- History of vaccinations during the 4 weeks before donation (AII). If the potential donor is unsure of vaccinations received, his or her records should be reviewed. Hematopoietic stem cell transplant 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 a hematopoietic stem cell transplant recipient. Hematopoietic stem cell transplant 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 (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.
- Travel history (BIII) to determine whether the donor has ever resided in or traveled to countries with endemic diseases that might be transmitted through hematopoietic stem cell transplant (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 hematopoietic stem cell transplant 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 hematopoietic stem cell transplant-transmitted malaria have been reported, persons who have had malaria and received appropriate treatment should be deferred from hematopoietic stem cell transplant donation for 3 years after becoming asymptomatic. Immigrants, refugees, citizens, or residents for  $\geq 5$  years of endemic countries can be accepted as hematopoietic stem cell transplant 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 hematopoietic stem cell transplant donors (DIII) because these diseases can be transmitted by transfusion. Researchers also recommend deferral of hematopoietic stem cell transplant donation if a past history exists of either of these diseases because the parasite can persist despite therapy (CIII).
  - History of any deferral from plasma or blood donation. The reason for such a deferral 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 hematopoietic stem cell transplant 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 hematopoietic stem cell transplant 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 (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 health-care workers 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 (BIII). Potential hematopoietic stem cell transplant 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  $\geq 6$  months during 1980 to 1996 or receipt of injectable bovine insulin since 1980, unless the product was not manufactured since 1980 from cattle in the United Kingdom (BIII). The clinical latency period for iatrogenic, classic Creutzfeldt-Jakob disease can be  $>30$  years, and transmission of classic

Creutzfeldt-Jakob disease by blood products is highly unlikely. Although no classic or new variant Creutzfeldt-Jakob disease has ever been reported among hematopoietic stem cell transplant recipients, persons with a history of classic or new variant Creutzfeldt-Jakob disease risk factors should be excluded from donation for unrelated hematopoietic stem cell transplant (DIII) if a choice exists between two otherwise equally suitable donors. The risk for transmitting classic or new variant Creutzfeldt-Jakob disease from an hematopoietic stem cell transplant donor to a recipient is unknown, but researchers believe that persons with new variant Creutzfeldt-Jakob disease risk factors could be at higher risk for transmitting new variant Creutzfeldt-Jakob disease to hematopoietic stem cell transplant recipients than persons with classic Creutzfeldt-Jakob disease 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), including:
  - men who have had sex with another man during the preceding 5 years (BIII);
  - persons who report nonmedical intravenous, intramuscular, or subcutaneous injection of drugs during the preceding 5 years (BIII);
  - persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates (BIII);
  - persons who have engaged in sex in exchange for money or drugs during the preceding 5 years (BIII);
  - persons who have had sex during the preceding 12 months with any person described previously or with a person known or suspected to have HIV 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 (BIII);
  - inmates of correctional systems 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 (BIII); and
  - persons who within 12 months have undergone tattooing, acupuncture, ear or body piercing 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-human T-lymphotropic virus-I and -II, hepatitis B surface antigen, total antihepatitis B core antigen, antihepatitis C, anti-cytomegalovirus, and a serologic test for syphilis (AIII). Potential donors who have repeatedly reactive screening tests for HIV-1 antigen, anti-HIV-1 or -2, anti-human T-lymphotropic virus-I or -II, antihepatitis C, hepatitis B surface antigen, or antihepatitis B core antigen should be excluded as hematopoietic stem cell transplant donors (EII). Persons who refuse infectious

disease testing should also be excluded as hematopoietic stem cell transplant donors (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 hematopoietic stem cell transplant donors. If nucleic acid tests are approved by the Food and Drug Administration, these tests should be incorporated into routine screening regimens for hematopoietic stem cell transplant donors. When nucleic acid testing is done for HIV and hepatitis C investigational, a positive result should exclude the potential donor.

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

Hematopoietic stem cell transplant center personnel should keep accurate records of all hematopoietic stem cell transplant received and the disposition of each sample obtained. 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 or distribution center supplying the hematopoietic stem cell transplant, recipient-identifying information, name of recipient's physician, and dates of a) receipt by the hematopoietic stem cell transplant center and b) either transplantation to the recipient or further distribution (AIII). All centers for donation, transplantation, or collection of hematopoietic stem cells should keep records of donor screening and testing, and hematopoietic stem cell transplant harvesting, processing, testing, cryopreservation, storage, and infusion or disposal of each aliquot of donated hematopoietic progenitor cells for  $\geq 10$  years after the date of implantation, transplantation, infusion, or transfer of the product (AIII). However, if that date is not known, records should be retained  $\geq 10$  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 (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 (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 hematopoietic stem cell transplant donors (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 (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 umbilical cord blood hematopoietic stem cells (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. The highest risk for extraneous microbial contamination of hematopoietic stem cells occurs during extensive manipulation and processing in the laboratory. Potential sources include unprotected hands and laboratory equipment and freezers, particularly the liquid phases of liquid nitrogen freezers. Therefore, stem cell processing should be performed according to current standards 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 (BIII). Additionally, water baths should be cleaned routinely (BIII) and certain researchers have proposed that the bath contain sterile water (CIII). Researchers also report sterilizing liquid nitrogen freezers before initial use for hematopoietic stem cell storage 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, donated hematopoietic stem cells should be cultured for aerobic bacteria and fungi  $\geq 1$  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 (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 hematopoietic stem cell transplant that might have been caused by exogenous contamination of donor stem cells (BIII) because this type of infection has been reported.

## In Utero or Fetal Hematopoietic Stem Cell Transplant

No national standards exist for in utero or fetal hematopoietic stem cell transplant, and the overall risks for transmitting infections to a fetus through

hematopoietic stem cell transplant have not been determined. However, in addition to precautions appropriate for adult recipients, physicians performing in utero or fetal hematopoietic stem cell transplant are advised to evaluate potential donors for evidence of active infectious diseases that could cause serious congenital infections (e.g., rubella, varicella, cytomegalovirus, syphilis, or *Toxoplasma gondii*) in the fetus (CIII).

Evidence-based rating system used to determine strength of recommendations

Category	Definition	Recommendation
A	Strong evidence for efficacy and substantial clinical benefit	Strongly recommend
B	Strong or moderate evidence for efficacy, but only limited clinical benefit	Generally recommend
C	Insufficient evidence against efficacy or for adverse outcome	Optional
D	Moderate evidence against efficacy or for adverse outcome	Generally not recommended
E	Strong evidence against efficacy or of adverse outcome	Never recommended

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

#### Categories and Definitions

- 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; or dramatic results from uncontrolled experiments.
- III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.

#### CLINICAL ALGORITHM(S)

None provided

### EVIDENCE SUPPORTING THE RECOMMENDATIONS

#### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations were based on a systematic review of currently available data and expert opinion.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- Reduced number and severity of opportunistic infections among hematopoietic stem cell transplant recipients.
- Decreased morbidity and mortality among hematopoietic stem cell transplant recipients.

### POTENTIAL HARMS

Not stated

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Staying Healthy

### IOM DOMAIN

Effectiveness  
Safety

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. *Biol Blood Marrow Transplant* 2000;6(6a):659-713; 715; 717-27; quiz 729-33. [410 references]

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 Recomm Rep* 2000 Oct 20;49(RR-10):1-125. [410 references] [PubMed](#)

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

American Society for Blood and Marrow Transplantation - Professional Association  
Centers for Disease Control and Prevention - Federal Government Agency [U.S.]  
Infectious Diseases Society of America - Medical Specialty Society

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GUIDELINE COMMITTEE

Guidelines Working Group

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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International Society for Hematotherapy and Graft Engineering - Professional Association

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [Centers for Disease Control and Prevention \(CDC\) Web site](#).

Print copies: Available from the CDC, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

#### AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Guidelines for Environmental Infection Control in Health-Care Facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC) (2003, Jun 6) available from the [Centers for Disease Control and Prevention \(CDC\) Web site](#). The new guideline supplements and updates the section of this guideline titled "Hospital Infection Control".

#### PATIENT RESOURCES

None available

#### NGC STATUS

This summary was completed by ECRI on January 24, 2001. The information was verified by the guideline developer as of May 23, 2001.

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