



Immunization of immunocompromised persons

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Advances in medicine, science, and technology have led to increasing numbers of people in the general population with altered host defenses [1]. At the end of 2001, an estimated total of 344,178 persons were living with AIDS and a total of 161,976 persons were living with HIV infection in the United States [2]. Incident cases for selected immunocompromising conditions reported in the United States include the following: HIV infection, approximately 40,000 cases in 2001 [2]; cancer, 1,284,900 in 2002 [3]; solid organ transplants, 23,848 in 2002 [4], and hematopoietic stem cell transplantation (North America), approximately 20,000 in 1998 [5]. Vaccination represents a crucial approach for preventing infection in the general public and immunocompromised persons and has been recognized as one of the 10 great public health achievements in the United States between 1900 and 1999 [6]. This article reviews the benefits of and risks for immunization in immunocompromised persons and provides recommendations for the use of specific vaccines.

Principles for vaccinating immunocompromised people

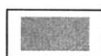
The risk for clinical infection in an immunocompromised host, such as a person who has received a solid organ transplant, is determined largely by the interaction between two factors: the epidemiologic exposures the person encounters and the person's net state of immunosuppression [7]. Community exposures of potential concern include respiratory viruses (eg, influenza A and B), *Mycobacterium tuberculosis*, geographically restricted systemic mycoses (ie, blastomycosis, coccidioidomycosis, histoplasmosis), *Streptococcus pneumoniae*, *Strongyloides*

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stercoralis, hepatitis A, B and C, HIV, and enteric pathogens, especially *Salmonella*. Immunocompromised patients also may be exposed to nosocomial pathogens, including *Legionella*, *Aspergillus*, respiratory viruses (especially influenza and respiratory syncytial virus), enteric pathogens (especially *Clostridium difficile*), antibiotic-resistant bacteria (especially oxacillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, drug-resistant *Streptococcus pneumoniae*, multidrug-resistant *M tuberculosis*, and multidrug-resistant gram-negative bacilli). The net immunosuppression in patients with transplants has been described as a complex function that is determined by the interplay of a number of

For all persons
in this group



Catch-up
childhood vaccination



For persons with
Medical/exposure indications



Contraindicated



Vaccine ►	Tetanus- diphtheria (Td)*	Influenza	Pneumococcal	Hepatitis B*	Hepatitis A	Measles, Mumps, Rubella (MMR)	Varicella*
Medical Conditions ▼							
Pregnancy		A					
Diabetes, heart disease, chronic pulmonary disease, chronic liver disease, including chronic alcoholism		B	C		D		
Congenital immunodeficiency, leukemia, lymphoma, generalized malignancy, therapy with alkylating agents, antimetabolites, radiation or large amounts of corticosteroids			E				F
Renal failure/end stage renal disease, recipients of hemodialysis or clotting factor concentrates			E	G			
Asplenia including elective splenectomy and terminal complement component deficiencies			E,H,I				
HIV infection			E,J			K	

factors, including the following: the nature of the immunosuppressive therapy being administered (dose, duration, temporal sequence), presence of defects in the mucocutaneous surfaces of the body, degree and duration of neutropenia, presence of metabolic abnormalities such as calorie malnutrition and hyperglycemia, and presence of infection with immunomodulating viruses (eg, cytomegalovirus, Epstein-Barr virus, hepatitis viruses, HIV) [7]. These same risk factors are present in recipients of hematopoietic stem cell transplants and persons receiving chemotherapy for cancer or other immunosuppressive medications.

Impaired host defense may result from a variety of acquired or congenital disorders that impair the body's immune system, such as infection with HIV, functional or anatomic splenectomy, renal insufficiency, cirrhosis and hepatic failure, and diabetes mellitus.

Features of infection in severely immunocompromised persons include susceptibility to a wider range of microorganisms than is encountered in normal hosts, more rapid progression of an infectious disease, increased disease severity, impaired clinical symptoms and signs of infection that often lead to delayed diagnosis, and poorer response to therapy. Specific host-defense defects often are associated with an increased risk for acquisition or severity of infection from specific microorganisms. For these reasons, prevention is superior to therapy. Immunization is an important method of prevention and should be tailored to the needs of each patient based on his or her underlying host defects and epidemiologic exposures (Fig. 1) [8,9]. The responsibility for determining whether a patient is severely immunocompromised ultimately lies with the physician.

The Centers for Disease Control and Prevention (CDC) includes the following conditions as severely immunosuppressive: congenital immunodeficiency (eg, IgA deficiency), HIV infection, leukemia, lymphoma, generalized malignancy or therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids [8]. For some of these conditions, all affected persons are immu-

Fig. 1. Recommended immunizations for adults with medical conditions, United States, 2002–2003. (A) If pregnancy is at second or third trimester during influenza season. (B) Although chronic liver disease and alcoholism are not indicator conditions for influenza vaccination, one dose should be given annually if patient is aged 50 or older, has other indications for influenza vaccine, or requests vaccination. (C) Asthma is an indication for influenza but not pneumococcal vaccination. (D) For all persons with chronic liver disease. (E) The patient should be revaccinated once after at least 5 years have elapsed since the initial vaccination. (F) Persons with impaired humoral but not cellular immunity may be vaccinated [39]. (G) For patients on hemodialysis, use special formulation of vaccine (40 µg/mL) or two 1.0 mL 20 µg/mL doses should be given at one site. Patients should be vaccinated early in the course of renal disease. Antibody titers should be assessed annually. Additional doses should be administered if anti-HBsAg levels decline to less than 10 mIU/mL. (H) Meningococcal vaccine also should be administered. (I) For patients who are undergoing elective splenectomy, vaccination should occur at least 2 weeks before surgery. (J) The patients should be vaccinated as close as possible to when the CD4 counts are highest. (K) MMR vaccine and other measles-containing vaccines should be withheld from persons with HIV infection and evidence of severe immunosuppression. (*Adapted from Recommendations for adult immunization schedule—United States, 2002–2003. MMWR Morb Mortal Wkly Rep* 2002; 51:904–8.)

nocompromised severely; for other conditions, such as HIV infection, the spectrum of disease severity caused by the disease or treatment stage determines the degree to which the immune system is compromised.

Immunocompromising conditions may alter vaccine recommendations in several ways. Patients with some immunocompromising conditions (eg, asplenia) may be increased risk for acquisition of certain infectious agents or at increased risk for severe disease (eg, *Neisseria meningitidis*, *S pneumoniae*); specific vaccines may be recommended (eg, pneumococcal and meningococcal vaccines). Immunocompromised persons frequently exhibit a reduced antibody response to immunization (Table 1) [10] and may require a higher dose, additional boosters,

Table 1
Response rates to immunization in persons with impaired immunity

Vaccine	Condition	Response rate (%) ^a
Measles	Malnutrition	83–86
	Bone marrow transplantation	77
	HIV infection	25–77
Mumps and rubella	Bone marrow transplantation	64–75
	Acute lymphoblastic leukemia	100
Poliovirus	HIV infection	>80 (IPV or OPV) 61–88 (IPV)
Varicella	Renal disease	100
	Acute lymphoblastic leukemia (acute)	88–91
	Acute lymphoblastic leukemia (remission)	88–98
	Cancer	77
	Elderly	67
	Collagen vascular disease	66
	Alcoholism	43–82
	End-stage liver disease	44–54
Hepatitis B virus	End-stage kidney failure with hemodialysis	50–80
	HIV infection	24–43
	Adults with cancer and on chemotherapy	73
	Advanced age	46
	Renal disease; chronic renal failure	66
	Renal disease, hemodialysis	25–100
	Renal disease; transplant	18–93
	Systemic lupus erythromyotosis	Normal, decreased if on immunosuppression
Influenza	Cancer	24–71
	Bone marrow transplant	18–60
	HIV infection	15–80

Abbreviations: IPV, inactivated poliovirus vaccine; OPV, oral poliovirus vaccine.

^a Rate denotes the percentage of patients who manifested an immunologic response (ie, as measured by serum antibody or skin testing). Response does not necessarily imply protection against infection. Adapted from Pirofski L-A, Casadevall A. Use of licensed vaccines for active immunization of the immunocompromised host. Clin Microbiol Rev 1998;11:1–26.

or postimmunization serologic testing for immunity (eg, hepatitis B virus vaccine in patients with chronic renal dysfunction). The immune response, however, may remain suboptimal, even with these modifications. Live virus or bacterial (eg, oral typhoid) vaccines may pose a risk to persons with severely immunocompromising conditions. In general, killed or inactivated vaccines do not represent a danger to immunocompromised persons and generally should be administered as recommended for healthy persons. Revaccination recommendations may depend on the type of immunocompromising condition and other factors (eg, recommendation for pneumococcal revaccination depends on underlying disease and age).

General recommendations for vaccinating immunocompromised persons

General recommendations regarding the immunization of adults, including those with altered host defenses, have been published by the Advisory Committee on Immunization Practices (ACIP) [11], the American College of Physicians [12], and the American College of Pediatrics [13]. Guidelines focusing specifically on vaccination of immunocompromised persons have been published by the CDC [8] and infectious-disease experts [10,14–19]. Detailed recommendations regarding the indications and contraindications have been published regarding vaccines for bacillus of Calmette and Guérin (BCG) [20], diphtheria-tetanus [21], hepatitis A virus [22], hepatitis B virus [23–25], influenza virus [26], measles [27], mumps [27], poliovirus [28], quadrivalent meningococcus [29,30], rabies [31], rubella [27,32], *S pneumoniae* [33,34], typhoid [35], vaccinia (smallpox) [36,37], and varicella [38,39]. Physicians who immunize persons with altered host defenses should be familiar with manufacturers' recommendations for use of specific vaccines. Immunocompromised persons may have altered indications for the use of immunoglobulin preparations (Table 2).

Specific altered host-defense conditions

For practical purposes, persons with immunocompromising conditions may be divided into the following groups [8]: (1) persons with HIV infection; (2) persons who are immunocompromised severely not as a result of HIV infection; and (3) persons with conditions that cause limited host-defense deficits (eg, asplenia, renal failure) that may require the use of special vaccines, require higher doses of vaccines, or lead to a less vigorous immunologic response (eg, diabetes) but that do not contraindicate use of any particular vaccine. Some nonimmunocompromising conditions may alter vaccine recommendations (eg, pregnancy, anticoagulation).

HIV infection

The World Health Organization has estimated that there are 42 million people with HIV or AIDS and that during 2002, 5 million people became infected with HIV and 3.1 million people died with AIDS [40]. Since the introduction of highly

Table 2

Use of immunoglobulins in immunocompromised adults

Immunoglobulin	Not immunocompromised	Severely immunocompromised ^a
IG	Recommended for adults with contraindication to measles vaccine when exposed to measles May be indicated for pre- and postexposure prophylaxis to hepatitis A virus	Recommended for persons exposed to measles regardless of immunization status ^b May be indicated for postexposure prophylaxis to hepatitis A virus
VZIG	Recommended for exposed pregnant women	Recommended for serosusceptible persons after significant exposure to VZV
TIG	Recommended for patients with serious wounds and <3 doses of tetanus toxoid vaccine	Same as for nonimmunocompromised patients
HBIG	Recommended for postexposure prophylaxis for susceptible HCWs after percutaneous or mucosal exposure to hepatitis B virus	Same as for nonimmunocompromised patients
HRIG	Recommended for postexposure prophylaxis of patients not previously vaccinated against rabies	Same as for nonimmunocompromised patients

Abbreviations: HBIG, hepatitis B immunoglobulin; HRIG, human rabies immunoglobulin; IG, immunoglobulin; VZIG, varicella-zoster immunoglobulin; VZV, varicella-zoster virus.

^a Severe immunosuppression can result from congenital immunodeficiency; HIV infection; leukemia; lymphoma; aplastic anemia, generalized malignancy; or therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids.

^b Recommended for symptomatic patients with HIV infection who have been exposed to measles, regardless of immunization status.

Adapted from Kontoyiannis DP, Rubin RH. Infection in the organ transplant recipient: an overview. *Infect Dis Clin North Am* 1995;9:811–822.

active antiretroviral therapy (HAART), the incidence of AIDS-related opportunistic infections and consequent morbidity and mortality have declined substantially [41–43]. An emphasis on preventing opportunistic infections remains important because of the recognized limitations of HAART, including noncompliance, inability to tolerate HAART, and failure of HAART in some patients to restore immunity to a level that substantially reduces the risk for opportunistic infection [44]. The US Public Health Service and Infectious Disease Society of America recommendations emphasize the continued need to focus on the prevention of infection in persons with HIV infection, including appropriate immunizations (Tables 3 and 4) [45,46]. Additional recommendations have been published by infectious disease experts [47,48].

Vaccine use in persons with HIV infection falls into four categories. Vaccines that specifically are indicated for such persons include the 23-valent polysaccharide pneumococcal vaccine, influenza vaccine, and hepatitis B virus vaccine (see Tables 3 and 4) [46]. Vaccines that are contraindicated include vaccines for oral typhoid [34], oral poliovirus [27], vaccinia (smallpox) [35,36,49]. Vaccines that are indicated only for persons with HIV infection that is early in the course of

illness include vaccines for measles, mumps, and rubella [46] and varicella [46] as defined by the child's immunologic status [50]. Vaccines whose indications are unaltered by HIV infection status include the diphtheria-tetanus toxoid (Td), hepatitis A virus, rabies, and quadrivalent meningococcal vaccines.

The rationale for immunizing persons with HIV infection is based on the following facts: The incidence of some vaccine-preventable diseases, most notably invasive pneumococcal disease (discussed later in this article) and measles [51], is increased in persons with HIV infection. Such persons may develop more serious disease after infection with vaccine-preventable diseases. Measles infection has resulted in significant morbidity and mortality in children [52–54] and adults [54] with HIV infection. Fatal measles pneumonia without a rash in a child with AIDS led to a nosocomial outbreak [55].

In general, symptomatic persons with HIV infection have reduced immunologic response to vaccines, including pneumococcal [56,57], poliovirus [58], tetanus [59,60], measles [60,61], *Haemophilus influenzae* type b [60], influenza [62], and hepatitis B virus [63] vaccines. The response to vaccine containing attenuated live viruses and inactivated antigens may decrease as HIV infection progresses [58,64,65]. For this reason, immunizations should be provided as early in the course of HIV infection as possible. Because most persons with HIV infection experience a significant rise in antibody levels with immunization, appropriate nonlive virus vaccines should be provided to all newly diagnosed persons, regardless of the stage of disease. Although higher doses or more frequent boosters may be considered for these patients, these interventions have not been studied systematically and cannot be recommended. Improved antibody response has been reported after the initiation of HAART. Revaccination [60] or administering vaccines after initiation of HAART [66] has been recommended.

The use live virus vaccines in persons with HIV infection generally is contraindicated. Limited studies of measles, mumps, and rubella (MMR) vaccination among asymptomatic and symptomatic patients with HIV infection who did not have evidence of severe immunosuppression have not demonstrated serious or unusual adverse events [48,67]. MMR vaccination is recommended for all children with HIV infection and without evidence of immunologic suppression or with moderate suppression. MMR vaccination should be avoided in children with severe immune suppression (ie, category 3), as defined by age-specific CD4⁺ T-lymphocyte counts and percentage of total lymphocytes: age ≤ 12 months, $<750/\mu\text{L}$ ($<15\%$); age 1 to 5 years, $<500/\mu\text{L}$ ($<15\%$); and age 6 to 12 years, $<200/\mu\text{L}$ ($<15\%$) [46]. Measles vaccine is not recommended for persons with HIV infection who have evidence of severe immunosuppression because a case of progressive measles pneumonia has been reported after administration of MMR vaccine to a person with AIDS and severe immunosuppression [68]; the incidence of measles in the United States is low; vaccination-related morbidity has been reported in severely immunocompromised persons without HIV infection; and a diminished antibody response to measles immunization occurs among severely immunocompromised persons with HIV infection.

Table 3
Recommended immunization schedule for children with HIV infection

Vaccine	Birth	1 mo	2 mo	4 mo	6 mo	12 mo	15 mo	18 mo	24 mo	4–6 y	11–12 y	14–16 y
Recommendations for these vaccines are the same as those for immunocompetent children												
Hepatitis B virus ^a	Hep B1											
		Hep B2			Hep B3						Hep B	
DTaP ^b			DTaP	DTaP	DTaP		DTaP			DTaP	Td	
Hib ^c			Hib	Hib	Hib	Hib						
IPV ^d			IPV	IPV	IPV					IPV		
Hepatitis A virus ^e										Hep A in selected areas		
Recommendations for these vaccines differ from those for immunocompetent children												
Pneumococcus ^f			PCV	PCV	PCV	PCV			PPV23	PPV23 (age 5–7 y)		
MMR ^g	Do not administer to severely immunocompromised (Category 3) children					MMR				MMR	MMR	
Varicella ^h	Administer only to asymptomatic nonimmuno- suppressed (Category 1) children, contraindicated for all other children with HIV infection					Var	Var				Var	
Influenza ⁱ						A dose is recommended every year starting at 3 months						

Vaccines noted by bold type to be administered if previously recommended doses missed or were administered at other than recommended minimum age. This schedule indicates the recommended ages for routine administration of licensed childhood vaccines as of November 1, 2000, for children aged birth to 18 years. Additional vaccines might be licensed and recommended in the future. Licensed combination vaccines might be used whenever any components of the combination are indicated and the vaccine's other components are not contraindicated. Providers should consult the manufacturer's package inserts for detailed recommendations.

^a Infants born to hepatitis B surface antigen (HBsAg) negative mothers should receive the first dose of hepatitis B vaccine (Hep B) at birth and no later than age 2 months. The second dose should be administered ≥ 1 month after the first dose. The third dose should be administered ≥ 4 months after the first dose and ≥ 2 months after the second dose, but not before age 6 months. Infants born to HBsAg-positive mothers should receive Hep B and 0.5 mL hepatitis B immune globulin (HBIG) ≤ 12 hours after birth at separate sites. The second dose is recommended at age 1–2 months and third dose at age 6 months. Infants born to mothers whose HBsAg status is unknown should receive Hep B ≤ 12 hours after birth. Maternal blood should be drawn at delivery to determine the mother's HBsAg status, if the HBsAg test is positive, the infant should receive HBIG as seen as possible (no later than age 1 week). All children and adolescents (through age 18 years) who have not been immunized against hepatitis B should begin this series during any visit. Providers should make special efforts to immunize children who were born in, or whose parents were born in, areas of the world where hepatitis B virus infection is moderately or highly endemic.

^b The fourth dose diphtheria and tetanus toxoids and acellular pertussis vaccines (DTaP) can be administered as early as 12 months, provided 6 months have elapsed since the third dose and the child is unlikely to return at age 15 to 18 months. Vaccination with tetanus and diphtheria toxoids (Td) is recommended at age 11 to 12 years if ≥ 5 years have elapsed since the last dose of diphtheria and tetanus toxoids and pertussis vaccine (DTP), DTaP, or diphtheria and tetanus toxoid (DT). Subsequent routine Td boosters are recommended every 10 years.

^c Three *Haemophilus influenzae* type b (Hib) conjugate vaccines are licensed for infant use. If Hib conjugate vaccine (polyribosylribitol phosphate-meningococcal outer membrane protein [PRP-OMP](PedvaxHB or ComVax [Merck and Company, Inc., Whitehouse Station, New Jersey]) is administered at ages 2 and 4 months, a dose at age 6 months is not required. Because clinical studies among infants have demonstrated that using certain combination products might induce a lower immune response to Hib vaccine component, DTaP/Hib combination products should not be used for primary immunization among infants at ages 2, 4, or 6 months, unless approved by the Food and Drug Administration for these ages.

^d An all-inactivated poliovirus (IPV) schedule is recommended for routine childhood polio vaccination in the United States. All children should receive four doses of IPV at age 2 months, age 4 months, ages 6 to 18 months, and ages 4 to 6 years. Oral poliovirus vaccine should not be administered to HIV-infected persons or their household contacts.

^e Hepatitis A vaccine (Hep A) is recommended for use in selected states or regions and for certain persons at high risk (e.g., those with hepatitis B or C infection). Information is available from local public health authorities.

^f Hepatavalent pneumococcal conjugate (PCV) is recommended for all HIV-infected children aged 2–59 months. Children aged ≥ 2 years should also receive the 23-valent pneumococcal polysaccharide vaccine; a single revaccination with the 23-valent vaccine should be offered to children after 3–5 years. Refer to MMWR 2000;49(RR-9):1–38.

^g Measles, mumps, and rubella (MMR) should not be administered to severely immunocompromised (category 3) children. HIV-infected children without severe immunosuppression would routinely receive their first dose of MMR as soon as possible after reaching their first birthdays. Consideration should be given to administering the second dose of MMR at age 1 month (ie, a minimum of 28 days) after the first dose rather than waiting until school entry.

^h Varicella-zoster virus vaccine should be administered only to asymptomatic, nonimmunocompromised children. Eligible children should receive two doses of vaccine with a ≥ 3 -month interval between doses. The first dose can be administered at age 12 months.

ⁱ Inactivated split influenza virus vaccine should be administered to all HIV-infected children aged ≥ 6 months each year. For children aged 6 months to < 9 years who are receiving influenza vaccine for the first time, two doses administered 1 month apart are recommended. For specific recommendations see MMWR 2003;52(RR-8):1–36.

Adapted from Centers for Disease Control and Prevention. Guidelines for preventing opportunistic infections among HIV-infected persons-2002. Recommendations of the US Public Health Service and the Infectious Disease Society of America. MMWR 2002;51(RR-8):1–51.

Table 4

Recommended immunizations for adults and adolescents with HIV infection

Vaccine	Definition of complete immunization	Recommendation ^a
Td	Primary series plus booster within past 10 years	Booster every 10 years
Influenza (inactivated trivalent)	1 dose annually	All patients (annually, before influenza season)
<i>H influenzae</i> type B (conjugate)	—	Not routinely recommended
Hepatitis A virus	2 doses	All susceptible patients at increased risk for hepatitis A virus infection (eg, illegal drug users) or patients with chronic liver disease (eg, hepatitis C virus infection)
Hepatitis B virus	3 doses	All susceptible patients (ie, antihepatitis B core antigen negative)
Meningococcal (quadrivalent)	—	Recommended only for patients at risk
Polio virus (inactivated)	3 doses plus 1 booster	Recommended only for patients at risk
<i>S pneumoniae</i> (23-valent polysaccharide)	1 dose (single revaccination after 5 years)	CD4 ⁺ count > 200/ μ L
Vaccinia	—	Contraindicated for preevent prophylaxis; consider the event of smallpox release
Varicella	—	Contraindicated

^a It is assumed that primary immunization (as per T3) has been provided.

Transient increases in HIV viral load have been observed after administration of some vaccines in some [69,70] but not all [71] studies. The clinical significance of these increases is not known but has not been reported to affect long-term survival.

Pneumococcal infection and use of the 23-valent pneumococcal polysaccharide vaccine

Bacterial pneumonia remains an important source of morbidity and mortality for persons with HIV infection [72–74]. Autopsy studies of such persons have reported that bacterial pneumonia is the most frequent pulmonary complication, although the incidence may be decreasing in the era of HAART [75,76]. In one study, pneumococcal pneumonia was 10 times more frequent and bacteremia was 100 times more frequent in patients with AIDS than in age-matched controls [77]. An episode of bacterial pneumonia has been associated with subsequent increased morbidity and decreased survival time [78]. The incidence of bacterial pneumonia increases with more advanced immunosuppression [79] and is increased among cigarette smokers and users of injectable drug [79,80]. *S pneumoniae* consistently has been found to be the most important cause of bacterial pneumonia, occurring in 20% to 70% of cases [72–74]. Pneumococcal bacter-

emia is more common in patients with HIV infection [81], and there seems to be a higher incidence of penicillin-resistant isolates in these patients [82,83]. More than 85% of *S pneumoniae* isolates in patients with HIV infection, pneumococcal pneumonia [84], and pneumococcal bacteremia [85] have been serotypes that are present in the pneumococcal vaccine.

Multiple studies have assessed the response of persons with HIV infection to the 23-valent pneumococcal polysaccharide vaccine [86]. Although most studies provide evidence that the antibody response was similar to HIV-seronegative controls or slightly impaired, some studies reported substantial impairment. Other studies suggested that the antibody response was dependent on the CD4 cell count. Several case-control studies have reported that receipt of the pneumococcal vaccine was protective for the development of invasive pneumococcal disease or pneumococcal illness [80,87,88]. The only randomized, controlled trial to assess the efficacy of vaccination to prevent invasive pneumococcal disease did not demonstrate a benefit in a cohort of Ugandan adults [85]; however, because of the benefits reported in observational and case-control studies and the safety of the vaccine, all persons with HIV infection should receive the 23-valent pneumococcal vaccine [46].

Immunization of transplant recipients

Advances in immunology, surgical techniques, and immuno-suppressive pharmacology have led to a steady growth in use of hemapoietic stem cell transplantation (HSCT) and solid organ transplantation. For both types of transplantation, infectious complications are frequent and represent a major cause of death. The different types of infections and their occurrence in relation to time of transplantation have been well characterized [17,89]. For patients with HSCT, the greatest risk for infectious complications occurs during the period of immune reconstitution with donor cells after ablative radiochemotherapy. As the patient with HSCT transitions from a state of profound humoral and cell-mediated immune deficiencies to a state capable of functional B- and T-cell responses, the recipient develops an improved ability to respond to vaccines. Recipients of solid organ transplants have a lifelong increased risk for infection as a result of the requirement for lifelong immunosuppression to prevent transplant rejection. The proper use of vaccines in transplant recipients continues to be an important preventative intervention to minimize their risk for infectious diseases.

Hemapoietic stem cell transplantation

Patients with HSCT are at increased risk for vaccine-preventable diseases from the encapsulated bacteria, including *H influenzae* type b, *N meningitidis*, and especially *S pneumoniae* [89]. These infections frequently occur in patients who underwent transplantation more than 6 months earlier. Although most cases occur in recipients of allogeneic HSCT, disease also has been reported in recipients of autologous HSCT. Because of the risk for infection with encapsulated bacteria, the 23-valent pneumococcal polysaccharide vaccine should be administered to

Table 5

Recommended vaccinations for hemapoietic stem cell transplantation recipients, of all ages, including allogeneic and autologous recipients

Time After HSCT				
Vaccine	12 mo	14 mo	24 mo	Rating
Inactivated or toxoid				
Diphtheria, tetanus, pertussis:				
Children aged <7 y ^a	DTaP or DT ^b	DTaP or DT	DTaP	BIII
Children aged ≥7 y ^c	Td	Td	Td	BII
Hib conjugate ^d	Hib conjugate	Hib conjugate	Hib conjugate	BII
Hepatitis B virus ^e	Hep B	Hep B	Hep B	BIII
PPV23 ^f	PPV23	—	PPV23	BIII
Hepatitis A virus ^g	Routine administration not indicated			Not rated because of limited data
Influenza ^h	Lifelong, seasonal administration, beginning before HSCT and resuming at ≥6 months after HSCT			BII
Meningococcal ⁱ	Routine administration not indicated			Not rated because of limited data
IPV ^j	IPV	IPV	IPV	BII
Rabies ^k	Routine administration not indicated			Not rated because of limited data
Live attenuated				
Measles ^{l,m,n}	MMR			BIII
Varicella ^o	Contraindicated for HSCT recipients			EIII

For these guidelines, HSCT recipients are presumed to be immunocompetent at more than 24 months after undergoing HSCT if they are not on immunosuppressed therapy and do not have GVHD. All indicated nonlive vaccines should be administered to HSCT recipients regardless of HSCT type or presence of GVHD. Live attenuated vaccines (eg, MMR, Bacillus Calmette-Guerin, yellow fever, and oral typhoid vaccines) should not be administered to any HSCT recipient with GVHD or immunosuppression. No contraindications to simultaneous administration of any vaccines exist, except cholera and yellow fever vaccines. If the HSCT recipient has lapsed immunizations after HSCT (ie, has missed one or more vaccine doses), the immunization schedule does not have to be restarted. The missing vaccine dose should be administered as soon as possible or during the next visit.

Abbreviations: DT, diphtheria toxoid-tetanus toxoid; DTaP, diphtheria toxoid, tetanus toxoid, and acellular pertussis; GVHD, graft-versus-host disease; Hib, *H influenzae* type B; IPV, inactivated poliovirus; PPV23, 23-valent polysaccharide pneumococcal.

^a Studies report that an HSCT recipient can be primed if the donor has had primary vaccination series. Studies also report that a recipient's antibody titer before HSCT might affect the titer 1 year after HSCT. No data were found regarding the safety and immunogenicity of pertussis vaccination among HSCT recipients.

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

^c HSCT recipients should be revaccinated with tetanus-diphtheria toxoid vaccines every 10 years as routinely recommended for all adolescents and adults.

^d Hib conjugate vaccination is recommended for HSCT recipients of any age.

^e Hepatitis B virus vaccination is recommended for all susceptible persons aged 18 years or younger and for adults who have risk factors for hepatitis B virus infection. ACIP recommendations for hepatitis B vaccination indicate that higher doses (40 µg/dose) are recommended for adult patients on dialysis

(continued on next page)

Notes to Table 5 (*continued*):

and other immunocompromised adults. No data were found regarding immunocompromised children and their response to higher doses of vaccine. Postvaccination testing for HBsAg is recommended 1 to 2 months after the third vaccine dose to ensure protection among immunocompromised persons. Persons who do not respond to the primary vaccine series (ie, anti-HBsAg titer, <10 mIU/mL) should complete a second three-dose series.

^f The PPV23 vaccine might not be protective against pneumococcal infection among HSCT recipients. The second dose of vaccine is not a booster dose, but provides a second chance for immunologic response among persons who failed to respond to the first dose. No data were found regarding the safety and immunogenicity of the seven-valent conjugate pneumococcal vaccine among HSCT recipients; no recommendation regarding use of this vaccine can be made.

^g No data were found regarding immunogenicity, safety, and efficacy of hepatitis A virus vaccine among HSCT recipients.

^h Children younger than 9 years receiving influenza vaccine for the first time require two doses. Children aged 12 years or younger should receive only split-virus influenza vaccine. Persons older than 12 years can receive whole- or split-virus vaccine. The ACIP's and the American Academy of Pediatrics's dosing schedule should be used. For optimal influenza prevention, vaccination and influenza chemoprophylaxis should be used among HSCT recipients.

ⁱ Administration of meningococcal vaccine should be evaluated for HSCT recipients who live in endemic areas or areas experiencing outbreaks. Meningococcal vaccine immunogenicity and efficacy among HSCT recipients has not been studied, however.

^j IPV vaccine is immunogenic among HSCT recipients, although no data were found regarding efficacy, and more data are needed regarding optimal methods and timing of immunization.

^k Clinicians can administer preexposure rabies vaccine to HSCT recipients with potential occupational exposures to rabies. The safety and immunogenicity of rabies vaccination among HSCT recipients has not been studied, however. Preexposure rabies vaccination probably should be delayed until 12 to 24 months after HSCT. Administration of rabies vaccine with human immunoglobulin after exposure can be administered anytime after HSCT, as indicated. Existing ACIP and the American Academy of Pediatrics guidelines for postexposure rabies immunoglobulin and vaccine administration should be followed, which include administering five doses of rabies vaccine administered on days 0, 3, 7, 14, and 28 after exposure. The first dose of MMR vaccine should be administered at least 24 months after HSCT if the recipient is presumed to be immunocompetent. The second MMR dose is recommended 6 to 12 months later; however, the benefit of a second dose among HSCT recipients has not been evaluated. During outbreaks, the second dose can be administered.

^l The first dose of MMR vaccine should be administered should be administered more than 24 months after HSCT if the recipient is presumed to be immunocompetent. The second MMR dose is recommended 6 to 12 months later; however, the benefit of a second dose among HSCT recipients has not been evaluated. During outbreaks, the second dose can be administered 4 weeks after the first dose.

^m The half-life of intravenous immunoglobulin is decreased among HSCT recipients, but its effect on vaccine immunogenicity has not been evaluated. The ACIP's recommendations regarding intervals between administration of immunoglobulin preparations for various indications and vaccines containing live virus should be used.

ⁿ Use of live vaccines (eg, MMR) is indicated only among immunocompetent persons and is contraindicated after HSCT in recipients who are not presumed to be immunocompetent.

^o To protect HSCT recipients from varicella exposure, all varicella-susceptible healthcare workers, family members, and close contacts of the recipient should be vaccinated against varicella.

Adapted from the Centers for Disease Control and Prevention. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients: recommendations of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation. MMWR Morb Mortal Wkly Rep 2000;49:1–125.

HSCT recipients at 12 to 24 months after transplantation [89]. The *H influenzae* type b conjugate vaccine should be administered at 12, 14, and 24 months after HSCT [89]. Meningococcal vaccination should be considered for HSCT recipients who live in endemic areas or areas experiencing outbreaks [89].

The immunization strategy used in patients with HSCT is based on careful studies of antibody concentrations and response to immunizations, relative to the time of transplantation (Table 5). Multiple studies have demonstrated that antibody concentrations to the childhood vaccines for tetanus toxoid [90,91], diphtheria [92], *H influenzae* type B [92], poliovirus [92–94], measles [95,96], mumps [95,96], and rubella [95,96] decrease over time in HSCT recipients; however, HSCT recipients are able to mount an immunologic response when revaccinated with the tetanus toxoid [90,91], *H influenzae* type b [97], inactivated poliovirus [93,94,98], and 23-valent pneumococcal polysaccharide vaccines at 6 to 12 months after transplantation [97]. HSCT recipients also have been demonstrated to respond to the quadrivalent meningococcal polysaccharide vaccine [99]. HSCT recipients without active graft-versus-host disease or ongoing immunosuppressive therapy can be reimmunized safely with live MMR vaccine 2 years after transplantation [95,96,100].

Molrine and Hibberd have summarized evolving strategies to enhance immune responses to immunizations in HSCT recipients, including donor immunizations 6 to 10 days before marrow harvest to produce antigen-specific immunity in the early transplant period and use of novel adjuvants, such as cytokines, local granulocyte macrophage colony stimulating factor (GM-CSF), lipid A, squalene, saponin (QS-21), and liposomes [17].

Solid organ transplantation

Vaccine-preventable diseases do not represent an important source of morbidity or mortality in recipients of solid organ transplants. Molrine and Hibberd have summarized the rationale for ensuring that patients who are likely to require a solid organ transplant remain up to date on their immunizations. Although the antibody titers that are achievable in transplant candidates are often suboptimal as a result of the immunosuppression that is associated with underlying liver or renal failure, antibody responses are even lower when vaccines are administered after transplantation [17]. The safety of live virus vaccines, such as those for MMR and varicella, has not been established, so these vaccines are contraindicated in transplant recipients receiving immunosuppressive medications. Because concern has been raised that immunization may trigger transplant rejection, many transplant recipients are not immunized after transplantation.

Unlike HSCT recipients, solid organ transplant recipients usually receive lifelong immunosuppression. Consensus recommendations regarding the timing, dose, and type of immunizations have not been published for solid organ transplant recipients. Molrine and Hibberd have published a well-thought-out guideline for adults (see Table 5) [17]. Because many vaccines are more immunogenic in the time period before transplantation than after transplantation, the vaccine should be administered before transplantation. Similarly, many vaccines are more effective

when administered early in the course of illness (eg, liver and renal failure) rather than when the patient has end-stage organ failure. Vaccines recommended for adults (if the immunizations are not up-to-date) include those for hepatitis B virus, hepatitis A virus (liver transplant recipients), yearly influenza (especially for patients with cardiac or pulmonary disease), MMR, inactivated poliovirus, varicella (seronegative patients), Td, *H influenzae* type b conjugate, 23-valent pneumococcal polysaccharide (especially for patients with cardiac or pulmonary disease), and meningococcus (patients entering college within 1 or 2 years) [101]. Recommendations for children (Table 6) [102] and adults (Table 7) [17] undergoing solid organ transplantation have been published.

Severely immunocompromised persons without HIV infection

In addition to HIV infection, severe immunosuppression can result from congenital immunodeficiency, leukemia, lymphoma, generalized malignancy or

Table 6

Recommendations for administration of childhood vaccines before and after solid organ transplantation

Vaccine	Recommended for use after transplantation	Reimmunization required after transplantation ^a	Assessment of immunity required after vaccination
Live attenuated			
Varicella	No	No	Yes
Measles	No	No	Yes
Mumps	No	No	No
Rubella	No	No	Yes ^b
BCG	No	No	Yes
Inactivated			
Poliovirus	IPV only	Yes	No
Acellular pertussis	Yes	Yes	No
Diphtheria	Yes	Yes	No
Tetanus	Yes	Yes	No
Hepatitis B virus	Yes	Yes ^c	Yes
<i>N meningitidis</i>	Yes ^d	Yes	No
Rabies ^e	Yes	Yes	No
Hepatitis A virus	Yes	Yes ^c	Yes
Influenza	Yes	Yes	No
<i>S pneumoniae</i>	Yes	Yes	No

Abbreviation: IPV, inactivated poliovirus.

^a Immunization schedule should be reinstituted once immunosuppression is decreased (typically 6 months to 1 year after transplantation). Once resumed, immunizations should follow the recommended schedule.

^b Documentation of immunity recommended for women of childbearing age.

^c Decision to reimmunize should be based on assessment of serologic response to vaccine.

^d Recommended for college students and other persons at risk.

^e Recommended for persons at risk because of avocation or vocation.

Adapted from Burroughs M, Moscona A. Immunization of pediatric solid organ transplant candidates and recipients. Clin Infect Dis 2000;30:857–69.

Table 7
Immunization for adults awaiting solid organ transplants

Vaccine ^a	Definition of Full Immunization	Visit 1	Visit 2 (1–2 mo after visit 1)	Visit 3 (6 mo after visit 2)	Routine schedule once fully immunized
Inactivated vaccines					
Td	3 doses, last within 10 years	Td-1	Td-2	Td-3	Td every 10 years
<i>H influenzae</i> type b conjugate ^b	Not routinely recommended	—	—	—	—
Hepatitis B virus	3 doses	Hep B-1	Hep B-2	Hep B-3	Booster if titer < 10 mIU/mL
Pneumococcal	2 doses of PPV23	PPV23-1	—	—	Complete 2 doses; second dose 5 years after first dose
Hepatitis A virus ^c	2 doses (at-risk patients only)	Hep A-1	—	Hep A-2	Recommended for at-risk patients; complete 2 doses
Influenza	Annual administration (every fall)	—	—	—	Annual (every fall)
Menigococcal ^d	1–2 doses (at-risk patients only)	Mening-1	—	—	Recommended for at-risk patients; complete 1–2 doses, second dose 5 years after first

IPV virus	3 doses plus 1 booster (at-risk patients only)	IPV-1	IPV-2	IPV-3	Recommended for at-risk patients
Live vaccines					
MMR	Up to 2 doses	Transplant candidates, MMR-1	Transplant candidates, MMR-2	—	Vaccine not recommended after transplant
Varicella ^c	2 doses (at-risk patients only)	Transplant candidates, varicella-1	Transplant candidates, varicella-1	—	Vaccine not recommended after transplant

Abbreviations: IPV, inactivated poliovirus; PPV23, 23-valent polysaccharide pneumococcal vaccine.

^a Absolute contraindications to all vaccines include anaphylactic reaction to previous dose or vaccine component; defer until resolution of acute moderate or severe illness.

^b Consider for lung-transplant candidates.

^c Consider for all patients waiting for liver transplant, all patients with chronic liver disease, and patients at risk for exposure to hepatitis A virus.

^d Consider for patients with anatomic or functional asplenia or travel exposure and college students.

^e Includes only varicella-seronegative patients.

Adapted from Molrine DC, Hibberd PL. Vaccines for transplant recipients. Infect Dis Clin North Am 2001;15:273–305; with permission.

therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids [8]. In such individuals, viral replication after administration of live, attenuated-virus vaccines can be enhanced [103,104]. In general, these patients should not receive live virus vaccines. Oral poliovirus vaccine should not be administered to any household contact of a severely immunocompromised person. MMR and varicella vaccines are not contraindicated for the close contacts of immunocompromised persons.

Persons with leukemia in remission who have not received chemotherapy for at least 3 months are not considered to be severely immunocompromised for the purposes of receiving live virus vaccines [8]. When cancer chemotherapy or immunosuppressive therapy is considered (eg, for patients with organ transplantation), vaccination ideally should precede the initiation of chemotherapy or immunosuppression by at least 2 weeks [8]. Vaccination during chemotherapy or radiotherapy should be avoided, because antibody responses are suboptimal. Patients who are vaccinated while on immunosuppressive therapy or in the 2 weeks before starting therapy should be considered unimmunized and should be revaccinated at least 3 months after discontinuing therapy. As with persons with HIV infection, severely immunocompromised persons respond less well to immunization than nonimmunocompromised persons.

Passive immunoprophylaxis with immune globulins may be indicated for immunocompromised persons instead of or in addition to vaccination. When exposed to a vaccine-preventable disease such as measles, severely immunocompromised persons should be considered susceptible regardless of their history of immunization.

Special conditions

Pregnancy

Although pregnancy is a normal state of health, pregnant women are discussed under the broad category of persons with altered host defenses. Pregnant women exhibit increased morbidity with several infectious diseases, including infection with influenza, hepatitis E virus [105], varicella [106], listeriosis [107], and malaria [108,109].

In general, all unnecessary medications or procedures that might jeopardize the fetus should be avoided. The risks from immunization during pregnancy are largely theoretical [11,12]. The benefit of immunization among pregnant women usually outweighs the potential risks for adverse reactions, especially when the risk for disease exposure is high, if infection would pose a special risk to the mother or fetus, or if the vaccine is unlikely to cause harm. New information continues to confirm the safety of vaccines that are given inadvertently during pregnancy.

Women of childbearing age should be immunized against measles, mumps, rubella, varicella, tetanus, diphtheria, and hepatitis B virus as adolescents before becoming pregnant [110,111]. Such women should be screened for immunity by a careful history of immunizations and childhood diseases. Many adolescents

and adults do not have reliable records or memories of childhood illnesses and immunizations. These factors are important for rubella because of the consequences of infection for the developing fetus. A history of rubella infection or undocumented immunization is often unreliable and should not be considered evidence of immunity. Hepatitis B virus can cause asymptomatic infection, and pregnant women may be carriers of the virus without being aware of infection, risking perinatal infection of their newborn infants. All pregnant women should be screened for rubella antibody and hepatitis B virus surface antigen (HBsAg). Women who are susceptible to rubella should be immunized immediately after delivery. Women who are HBsAg-positive should be followed carefully to ensure that the infant receives hepatitis B virus immunoglobulin, begins the hepatitis B virus vaccine series up to 12 hours after birth, and completes the recommended series.

Susceptible pregnant women should receive the combined Td vaccine [11,112]. Previously immunized pregnant women who have not received a Td immunization in the past 10 years should receive a booster dose. Pregnant women who are unimmunized or only are immunized partially against tetanus should complete the primary series. Women who are in their second or third trimester (>14 weeks' gestation) during respiratory virus season should receive influenza immunization [26]. There is no convincing evidence of risk from immunizing pregnant women with other inactivated virus or bacterial vaccines or toxoids. Susceptible pregnant women at high risk for specific infections should receive the following vaccines as indicated: hepatitis A virus vaccine, hepatitis B virus vaccine, influenza vaccine, polysaccharide pneumococcal vaccine, rabies vaccine, and inactivated poliovirus vaccine [11]. Thimerosal-free hepatitis B virus vaccine should be used. Several vaccines are recommended as part of postexposure prophylaxis, including those for hepatitis A virus, hepatitis B virus, and rabies. The same indications for use should be followed in pregnant women. Pregnant women should be immunized with meningococcal vaccine when there is a substantial risk for infection, such as during epidemics [29].

Breast-feeding does not affect adversely the response to immunization and is not a contraindication for any of the currently recommended vaccines. The indications for using immunoglobulins, intravenous immunoglobulin, and specific immunoglobulins (eg, tetanus immunoglobulin) in pregnant women are the same as those for women who are not pregnant.

Because of theoretical risks to the fetus, most attenuated live virus vaccines (eg, mumps, measles, varicella vaccines) should not be administered to pregnant women or to women are likely to become pregnant within 1 month. After rubella vaccination, a women should wait 28 days before becoming pregnant. Congenital disease from maternal immunization has not been reported for any current routine vaccine, including rubella [32] and varicella [113] vaccines. The presence of a pregnant woman in the household is not a reason for avoiding immunizations of household members for routine vaccines, including varicella [11]. However, vaccinia (smallpox) vaccine should not be administered to pregnant women or to persons with close contact (ie, household contact) with a pregnant woman as im-

munization with vaccinia during pregnancy may lead to congenital abnormalities in the fetus (~50 cases described). Routine pregnancy testing of women of childbearing age before administration of a live virus vaccine is not recommended. Yellow fever vaccine contains live attenuated virus but is not known to be teratogenic. If a pregnant woman must travel to an area where yellow fever is known to be prevalent, immunization should be considered. Vaccinia vaccination of pregnant women has resulted in congenital disease in their infants. Vaccinia vaccine should be avoided in pregnant women or in household members if there is a pregnant woman in the household [36,37].

The administration of a tetanus toxoid vaccine to pregnant women has been an effective method for the prevention of neonatal tetanus [114,115]. In the near future, it is likely that the use of maternal immunization will expand to provide passive immunity of infants to agents that produce life-threatening illnesses in the neonatal period [111,116]. Vaccines under development for this purpose include those for *H influenzae* type B, acellular pertussis, group B streptococcus conjugate, and respiratory syncytial virus.

Bleeding disorders

The CDC recommends that for persons with thrombocytopenia, hemophilia, or other bleeding disorders, one should consider the use of alternative vaccines that are recommended for administration by nonintramuscular routes (eg, intradermal human diploid cell vaccine (HDCV) in lieu of intramuscular HDCV or rabies vaccine absorbed (RVA) for rabies prophylaxis). One should weigh the comparative safety, immunogenicity, and efficacy of the alternative product in light of the patient's medical profile (eg, age, pregnancy, concurrent medications) and degree of exposure. For vaccines that normally are recommended for intramuscular use, the package insert should be checked for acceptability of alternative routes for the following reasons: (1) Subcutaneous or intradermal administration of some vaccines that normally are administered intramuscularly can result in reduced immune response (eg, hepatitis B virus and recombinant rabies vaccines); and (2) subcutaneous administration of intramuscularly administered vaccines that contain adjuvants (eg, aluminum-absorbed hepatitis B virus vaccine) can result in increased local reactions, granuloma formation, and necrosis.

The ACIP does not consider a history of bleeding disorder an absolute contraindication to the use of vaccines requiring intramuscular administration. Their guidelines are as follows: (1) When an intramuscular vaccine is indicated for a patient with a bleeding disorder, it can be administered intramuscularly if the physician who is knowledgeable about the patient's risk thinks this route is safe. (2) If the patient receives a blood-product infusion therapy or a similar therapy, intramuscular vaccination should be administered shortly after such treatment. (3) The patient or family member should receive instruction regarding the risk for hematoma from the injection. (4) A fine needle (23 gauge or smaller) should be used for the injection, with direct pressure applied (without rubbing) to the site for at least 2 minutes. The National Hemophilia Foundation Nursing Executive

Committee recommends that for persons with bleeding disorders, firm pressure be applied to the injection site for 7 to 10 minutes.

Concern has been raised that persons who are anticoagulated with warfarin may be at risk for an altered response to their anticoagulant or for clinically significant hematomas if they are administered a vaccine by the intramuscular route. Immunization with influenza vaccine [117–120] or pneumococcal [121] vaccine has been shown not to alter the prothrombin time in anticoagulated persons and not to lead to hematoma formation.

Some vaccines may be administered by the intradermal route, including rabies (only for preexposure prophylaxis) and typhoid vaccines. The hepatitis B virus vaccine also may be administered by the intradermal route at one tenth the standard dose; however, because titers are lower with intradermal than with intramuscular administration, this route is not recommended.

Chronic renal failure

As of 2000 there were more than 240,000 patients with chronic hemodialysis receiving care in approximately 3800 dialysis centers [122]. Patients with chronic renal failure on dialysis have impaired host defenses, including reduced antibody response to immunization [123,124] and abnormal cell-mediated immunity [125]. They exhibit transient neutropenia during hemodialysis as a result of complement activation by the dialyzer membrane and subsequent neutrophil margination and sequestration in the pulmonary circulation [126].

Patients with chronic renal failure on hemodialysis are at risk for several infectious syndromes, including sepsis related to vascular access, hepatitis B virus infection, invasive pneumococcal infection, and urinary tract infections. The incidence and prevalence of hepatitis B virus infection has decreased over the past 25 years as a result of improved infection control and use of the hepatitis B virus vaccine. In 2000, the incidence of hepatitis B virus infection was 0.05%, and the prevalence was 0.9% [122]. Recommendations to prevent such infection in patients on hemodialysis include routine serologic testing for hepatitis B virus, vaccination of susceptible patients against hepatitis B virus, and annual testing of anti-HBsAg titers with routine boosting if the titers is less than 10 mIU/mL [127]. Dialysis-dependent patients should receive a higher-than-standard dose (ie, 40 µg). After following the standard three-dose regimen, patients should be tested for adequacy of response (ie, anti-HBsAg titers, ≥ 10 mIU/mL). Patients with an inadequate response should receive an additional three doses of vaccine and be retested for a vaccine response. Patients without an appropriate response should be considered nonresponders. Because patients have been demonstrated to have an improved response to vaccine during the predialysis phase of illness, every attempt should be made to immunize patients with chronic renal failure who are likely to proceed to dialysis early in the course of illness. Many patients on dialysis still have not received the hepatitis B virus vaccine, despite the risk for infection.

The incidence of pneumonia in patients on dialysis has been reported as approximately 6 per 1000 patient-months; *S pneumoniae* is the causative agent in

more than 50% of cases. All patients on dialysis should receive the 23-valent pneumococcal polysaccharide vaccine. One study demonstrated that 83% of patients developed a sufficient antibody response after receiving the pneumococcal vaccine, but only 48% of patients had adequate antibody levels at 1 year [128]. Patients on dialysis also should receive yearly influenza immunization.

Specific vaccines

Measles, mumps, and rubella vaccine

The MMR vaccine should not be administered to severely immunocompromised persons, because case reports have linked vaccine-associated measles infection to the deaths of six severely immunocompromised persons [129]. The MMR vaccine should be considered for all asymptomatic persons with HIV infection who otherwise would be eligible for measles vaccination, because measles can result in severe disease in persons with HIV infection. MMR vaccination also should be considered for all symptomatic persons with HIV infection who do not have evidence of severe immunosuppression (ie, CD4⁺ T-lymphocyte count, <200/ μ L [$<14\%$ of total lymphocytes]). Limited studies of MMR vaccination among asymptomatic and symptomatic persons with HIV infection have not revealed an increased frequency of serious adverse events. Serious illness associated with the administration of rubella or mumps vaccine to severely immunocompromised persons with HIV infection has not been reported. MMR vaccination may be provided to HSCT recipients without graft-versus-host disease at 24 months and to children who are receiving low doses of corticosteroids (prednisone, <2 mg/kg/d or <20 mg/d if weight is >10 kg).

If administered within 6 days of exposure, immunoglobulin can prevent or modify measles in a nonimmune person. Severely immunocompromised persons and symptomatic persons with HIV infection who are exposed to measles should receive immunoglobulin, regardless of previous vaccination status. The recommended dose of immunoglobulin for measles prophylaxis of immunocompromised persons is 0.5 mL/kg of body weight (maximum dose, 15.0 mL). The immunogenicity of measles vaccine is decreased if the vaccine is administered less than 6 months after receiving immunoglobulin.

Hepatitis B virus vaccine

Hepatitis B virus vaccine is a universally recommended vaccine. It is recommended for patients on hemodialysis or with preexisting liver disease. For persons undergoing hemodialysis and for other immunocompromised patients, a higher dose of vaccine should be provided (ie, 40 μ g of HBsAg antigen). Immunocompromised persons should have a quantitative anti-HBsAg titer that is measured 1 to 2 months after completing the immunization series. Persons with a titer of less than 10 mIU/mL should receive up to three additional doses of vaccines. Persons who

do not seroconvert should be considered nonresponders and be provided with two doses of hepatitis B virus immunoglobulin (at initial injury and 1 month later) if they have a percutaneous, mucus membrane or nonintact skin exposure to blood from a person positive for HBsAg. In immunocompromised patients at high risk, titers should be monitored yearly, and revaccination considered if the titer is less than 10 mIU/mL.

Varicella vaccine

Varicella vaccination is contraindicated in persons who are immunocompromised severely, including persons with active malignancies or HIV infection or who are receiving chemotherapy, steroid therapy, or other immunosuppressive therapy. Transplant candidates who are seronegative for varicella should receive this vaccine before transplantation or onset of immunosuppression. It should be considered for children with HIV infection and without evidence of immune suppression (ie, age-specific CD4⁺ T-lymphocyte count [percentage of total lymphocytes]: age ≤ 12 months, $>1500/\mu\text{L}$ [$\leq 25\%$]; age 1–5 years, $>1000/\mu\text{L}$ [$>25\%$]; and age 6–12 years, $\geq 500/\mu\text{L}$ [$\geq 25\%$]) [46].

Travel vaccines

Immunocompromised patients considering international travel should have a complete medical evaluation before leaving. The risks and benefits of travel should be discussed. Patients should be counseled regarding safe travel, including risks from food and drink, motion sickness, altitude illness, possible injuries, swimming precautions, precautions against sexually transmitted diseases, methods to reduce risks for insect bites and arthropod-borne illnesses, and management of infections while abroad. Standard vaccine recommendations may need to be altered as follows:

- Only inactivated poliovirus vaccine should be provided.
- Yellow fever vaccine is a live virus vaccine and is contraindicated.
- Immunocompromised persons should receive the Vi capsular polysaccharide vaccine for typhoid infection; live oral typhoid vaccine is contraindicated.
- Rabies vaccine should be provided if indicated, but the response may be suboptimal; if exposure is likely, immunity should be assessed after immunization.
- The vaccine for Japanese B encephalitis is inactivated and can be provided if indicated.

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