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Recommendations of the Advisory Committee on Immunization Practices (ACIP): Use of Vaccines and Immune Globulins in Persons with Altered Immunocompetence

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Questions relating to the content of these recommendations should be addressed to the following persons in the Division of Immunization, NCPS, CDC:

Stephen C. Hadler, M.D.
Mark Grabowsky, M.D., M.P.H
Robert T. Chen, M.D.

Recommendations of the Advisory Committee on Immunization Practices (ACIP): Use of Vaccines and Immune Globulins for Persons with Altered Immunocompetence

INTRODUCTION

This statement summarizes current recommendations by the Advisory Committee on Immunization Practices (ACIP) on the use of active and passive immunization for persons with altered immunocompetence. The purpose of this statement is to make ACIP recommendations more accessible for clinicians by consolidating them into a single document. ACIP statements on individual vaccines or immune globulins should be consulted for more details on safety and efficacy and on the epidemiology of the diseases. Recommendations on immunization following bone marrow transplantation will be published in a separate ACIP statement.

These recommendations are for use in the United States and its territories and are appropriate for the epidemiologic setting and program priorities of these areas. Other organizations, particularly the Expanded Programme on Immunization of the World Health Organization, have made different recommendations, particularly with respect to the use of oral polio vaccine (OPV) and Bacille Calmette-Guerin (BCG) for immunocompromised persons. Those recommendations are appropriate for populations, particularly in developing countries, with higher risks of exposure to wild poliovirus infection and tuberculosis.

This statement is divided into four sections. The first is a brief summary of principles for vaccinating immunocompromised persons. The second section discusses how specific immunocompromising conditions may alter recommendations for vaccination. The third section discusses each vaccine and how recommendations for use may be altered in immunocompromised persons. The final section contains summary tables on the use of vaccines and immune globulins, arranged by immunocompromising condition.

SUMMARY OF PRINCIPLES FOR VACCINATING IMMUNOCOMPROMISED PERSONS

The degree to which an individual patient is immunocompromised should be determined by a physician. Severe immunosuppression can be due to a variety of conditions, including congenital immunodeficiency, human immunodeficiency virus (HIV) infection, leukemia, lymphoma, generalized malignancy or therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids. For some of these conditions, all affected persons will be severely immunocompromised; for others, such as HIV infection, the spectrum of disease severity due to disease or treatment stage will determine the degree to which the immune system is compromised. The responsibility for determining whether a patient is severely immunocompromised ultimately lies with the physician.

Killed or inactivated vaccines do not represent a danger to immunocompromised persons and generally should be administered as recommended for healthy persons. For specific immunocompromising conditions (e.g., asplenia), such patients may be at higher risk for certain diseases, and additional vaccines, particularly bacterial polysaccharide vaccines [*Haemophilus influenzae* type b (Hib), pneumococcal and meningococcal], are recommended for them. Frequently, the immune response of immunocompromised persons to these vaccine antigens is not as good as that of immunocompetent persons; higher doses or more frequent boosters may be required, although even with these modifications, the immune response may be suboptimal.

Steroid therapy usually does not contraindicate administration of live-virus vaccines when such therapy is short term (<2 weeks); low to moderate dose; long-term, alternate-day treatment with short-acting preparations; maintenance physiologic doses (replacement therapy); or administered topically (skin or eyes), by aerosol, or by intra-articular, bursal, or tendon injection. The exact amount of systemic corticosteroids and the duration of their administration needed to suppress the immune system of an otherwise healthy child are not well defined. The immunosuppressive effects of steroid treatment vary, but many clinicians consider a dose equivalent to either 2 mg/kg of body weight or a total of 20 mg/day of prednisone as sufficiently immunosuppressive to raise concern about the safety of immunization with live-virus vaccines. Corticosteroids used in greater than physiologic doses also may reduce the immune response to vaccines. Physicians should wait at least 3 months after discontinuation of therapy before administering a live-virus vaccine to patients who have received high-dose, systemic steroids for ≥2 weeks.

SPECIFIC IMMUNOCOMPROMISING CONDITIONS

For practical considerations, persons with immunocompromising conditions may be divided into three groups:

A. Persons who are severely immunocompromised not as a result of HIV infection;
B. Persons with HIV infection; and
C. Persons with conditions that cause limited immune deficits (e.g., asplenia, renal failure) that may require use of special vaccines or higher doses of vaccines but that do not contraindicate use of any particular vaccine.

These groups differ primarily in the recommendations for use of live-virus vaccines, which are contraindicated for all persons in group A, for some vaccines and some persons in group B, and are not contraindicated in group C.

A. Severely Immunocompromised, Non-HIV-Infected Persons

Severe immunosuppression not associated with HIV can be the result of congenital immunodeficiency, leukemia, lymphoma, generalized malignancy or therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids (*1–3*). Virus replication after administration of live, attenuated-virus vaccines can be enhanced in severely immunocompromised persons (*4–6*). In general, these patients should not be administered live vaccines, with the exceptions noted below. *In addition, OPV should not be administered to any household contact of a severely immunocompromised person.* Measles-mumps-rubella (MMR) vaccine is not contra-

indicated for the close contacts (including health-care providers) of immunocompromised persons.

Persons with leukemia in remission who have not received chemotherapy for at least 3 months are not considered severely immunosuppressed for the purpose of receiving live-virus vaccines (*7*). When cancer chemotherapy or immunosuppressive therapy is being considered (e.g., for patients with Hodgkin's disease or organ transplantation), vaccination ideally should precede the initiation of chemotherapy or immunosuppression by ≥2 weeks. Vaccination during chemotherapy or radiation therapy should be avoided because antibody responses are suboptimal. Patients 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 discontinuation of therapy.

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

B. HIV-Infected Persons

In general, persons known to be HIV infected should not receive live-virus or live-bacteria vaccines. However, evaluation and testing for HIV infection of asymptomatic persons are not necessary before decisions concerning vaccination with live-virus vaccines are made. Limited studies of MMR vaccination among both asymptomatic and symptomatic HIV-infected patients have not documented serious or unusual adverse events (see discussion under MMR vaccine) (*8*). Therefore, MMR vaccination is recommended for all children and for adults when otherwise indicated, regardless of their HIV status. Enhanced inactivated polio vaccine (eIPV) is the preferred polio vaccine for persons known to have HIV infection. Pneumococcal vaccine is indicated for all HIV-infected persons ≥2 years of age. Children <2 years of age with known HIV infection should receive Hib vaccine according to the routine schedule. Clinicians deciding whether to administer Hib vaccine to HIV-infected persons should take into consideration the individual patient's risk of Hib disease and the effectiveness of the vaccine for these persons. In some settings, the incidence of Hib disease may be higher among HIV-infected adults than non-HIV-infected adults (*9,10*), and the disease can be severe in these patients.

In general, symptomatic HIV-infected children and adults have suboptimal immunologic responses to vaccines (*8,11–15*). The response to both live and killed antigens may decrease as the HIV disease progresses (*8*). However, the response to higher doses of vaccine and the persistence of antibody in HIV-infected patients have not been systematically evaluated. Although higher doses or more frequent boosters may be considered for these patients, firm recommendations cannot be made at this time.

C. Medical Conditions Associated Only with Special Indications for Vaccines

Certain medical conditions, such as renal failure, diabetes, alcoholic cirrhosis, or asplenia, may increase the patient's risk for certain diseases. Some antigens, particularly bacterial polysaccharide vaccines, are recommended for such patients. Frequently, the immune response of these patients to these antigens is not as good as

that of immunocompetent persons, and higher doses or more frequent boosters may be required. Persons with these conditions are generally not considered immunosuppressed for the purposes of vaccination and should receive routine vaccinations with both live and inactivated vaccines according to the usual schedules.

Renal Failure

Patients with renal failure have an increased risk of infection with a variety of pathogens, particularly pneumococcus and hepatitis B (*16–19*). The efficacy of pneumococcal vaccination for some of these patients, including those on dialysis, may be considerably lower than for immunocompetent patients (*20,21*), their antibody levels may be lower (*22*), and they may require repeat vaccination (*23,24*) or an increased dose of vaccine. Because secondary antibody responses are less affected than primary antibody responses, immunization strategies should be formulated early in the course of progressive renal disease. This approach is particularly important if transplantation and chronic immunosuppressive therapy are being considered. Nephrotic syndrome is the renal disease most clearly associated with an increased risk for pneumococcal infection. See the discussion under Influenza and Hepatitis B vaccine for recommendations on the use of those antigens.

Diabetes

Although several in vitro tests of immunologic function are known to be abnormal among diabetic patients, these defects may be of little clinical importance. However, because patients with longstanding diabetes mellitus often have cardiovascular, renal, and other end-organ dysfunction, one-time pneumococcal vaccination and annual influenza vaccination are recommended. Pneumococcal vaccine is safe and effective for these patients and does not interfere with insulin levels or glucose control (*25,26*). Patients receiving either insulin or oral antidiabetic agents respond normally to influenza vaccination without impairment of diabetic control (*27*).

Alcoholic Cirrhosis

Patients with alcoholism and alcoholic liver disease have an increased incidence of infections, especially pneumonia. Such patients have many defects in host defenses, although the clinical importance of any one defect as measured in the laboratory is often uncertain. Many of these patients have leukopenia, decreased complement activity, chemotactic defects, and impaired cell-mediated immunity. In cirrhotic patients, portosystemic shunting can diminish the clearance of bacteria and increase the severity of infection. Patients with alcoholism or alcoholic liver disease should receive one-time pneumococcal and yearly influenza vaccination.

Asplenia

Persons who have anatomic or functional asplenia have an increased risk for fulminant bacteremia, associated with a high mortality rate. Polyvalent pneumococcal vaccine is recommended for all asplenic persons ≥2 years of age. In some instances, reimmunization with pneumococcal vaccine is indicated (see discussion under Pneumococcal vaccine). Quadrivalent meningococcal polysaccharide vaccine also should be administered to asplenic children ≥2 years of age. Immunization with Hib vaccine

should be initiated in infancy at the same dosage and schedule as recommended for otherwise healthy children. Hib vaccines are immunogenic in splenectomized adults and may be considered for this group. When elective splenectomy is planned, vaccination with pneumococcal, meningococcal, and Hib vaccines should precede surgery by at least 2 weeks, if possible.

SPECIFIC CONSIDERATIONS FOR USE OF VACCINES

Live, Attenuated Vaccines

Measles-Mumps-Rubella (MMR/MR/M/R) Vaccine

MMR vaccine should not be administered to severely immunocompromised persons. For HIV-infected children, MMR should routinely be administered at 15 months of age. MMR should be considered for all symptomatic HIV-infected persons who would otherwise be eligible for measles vaccine, since measles can affect these patients severely (*28*). Evaluation and testing for HIV infection of asymptomatic children are not necessary before decisions concerning immunization with live-virus vaccines are made. Limited studies of MMR vaccination among both asymptomatic and symptomatic HIV-infected patients have not documented serious or unusual adverse events (*8*). If there is risk of exposure to measles, single-antigen measles vaccine should be administered at 6–11 months of age with a second dose (of MMR) at >12 months of age. Severely immunocompromised patients and symptomatic HIV-infected patients who are exposed to measles should receive immune globulin (IG), regardless of prior vaccination status. The recommended dose of IG for measles prophylaxis of immunocompromised persons is 0.5 mL/kg of body weight (maximum dose, 15 mL). The immunogenicity of measles vaccine is decreased if vaccine is administered <6 months after IG.

Oral Polio Vaccine (OPV)

OPV should not be used to immunize immunocompromised patients, their household contacts, or nursing personnel in close contact with such patients; eIPV is recommended for such persons. Immunocompromised patients may be unable to limit replication of vaccine virus effectively, and administration of OPV to children with congenital immunodeficiency has resulted in severe, progressive neurologic involvement (*29–32*). Although a protective immune response to eIPV in the immunocompromised patient cannot be assured, the vaccine is safe and may confer some protection. If OPV is inadvertently administered to a household or intimate contact (regardless of prior immunization status) of an immunocompromised patient, close contact between the patient and the recipient of OPV should be avoided for approximately 1 month after vaccination, the period of maximum excretion of vaccine virus. Because of the possibility of immunodeficiency in other children born to a family in which there has been one such case, OPV should not be administered to a member of a household in which there is a history of inherited immunodeficiency until the immune status of the recipient and other children in the family is documented. Although OPV has not been harmful when administered to asymptomatic HIV-infected children (*8*), eIPV is the vaccine of choice for a child who is known to be infected.

Evaluation and testing for HIV infection of asymptomatic children are not necessary before decisions concerning immunization with live-virus vaccines are made.

BCG

BCG vaccine is not routinely recommended for use in the United States for prevention of tuberculosis (TB). BCG vaccine is strongly recommended for infants and children with negative tuberculin skin tests who are a) at high risk of intimate and prolonged exposure to persistently untreated or ineffectively treated patients with infectious pulmonary TB, cannot be removed from the source of exposure, and cannot be placed on long-term preventive therapy; or b) continuously exposed to persons with TB who have bacilli resistant to isoniazid and rifampin. BCG is also recommended for tuberculin-negative infants and children in groups in which the rate of new infections exceeds 1% per year and for whom the usual surveillance and treatment programs have been attempted but are not operationally feasible.

BCG should be administered with caution to persons in groups at high risk for HIV infection or persons known to be severely immunocompromised. Although limited data suggest that the vaccine may be safe for use for asymptomatic children infected with HIV (*33*), BCG vaccination is not recommended for HIV-infected adults or for persons with symptomatic disease (*34–36*). Until further research can clearly define the risks and benefits of BCG vaccination for this population, vaccination should be restricted to persons at exceptionally high risk for tuberculosis infection. HIV-infected persons thought to be infected with *M. tuberculosis* should be strongly recommended for tuberculosis preventive therapy.

Typhoid Vaccine

Live, attenuated TY21a typhoid vaccine should not be administered to immunocompromised persons, including those known to be infected with HIV. Parenteral inactivated vaccine is a theoretically safer alternative for this group.

Yellow Fever Vaccine

Yellow fever vaccine virus poses a theoretical risk of encephalitis to those with severe immunosuppression or known HIV infection, and such patients should not receive the vaccine. If travel to an area endemic for yellow fever is necessary, patients should be advised of the risk, instructed in methods for avoiding vector mosquitos, and supplied with vaccination waiver letters by their physicians. Persons who are known to be HIV infected and who cannot avoid potential exposure to yellow fever virus should be offered the choice of vaccination. Vaccinees should be monitored for possible adverse effects. Since the vaccination of such persons may be less effective than that for non-HIV-infected persons, it may be desirable to measure their neutralizing antibody responses before travel. (For these tests, contact the appropriate state health department or CDC [303-221-6400]). Family members of immunosuppressed persons who themselves have no contraindications may receive yellow fever vaccine.

Vaccinia

The only persons for whom vaccinia vaccine is recommended are laboratory personnel working with orthopox viruses and certain health-care workers involved in

clinical trials of vaccinia recombinant vaccines. Vaccinia should not be administered to severely immunocompromised persons or those with symptomatic HIV infection. Disseminated vaccinia has been reported in a military recruit with HIV infection (*37*).

Killed or Inactivated Vaccines

Diphtheria-Tetanus-Pertussis (DTP/DTaP/DT/Td)

For children who are severely immunocompromised or who are infected with HIV, DTP vaccine is indicated in the same schedule and dose as for immunocompetent children, including the use of acellular pertussis-containing vaccines (DTaP) as a booster. Although no specific studies with pertussis vaccine are available, if immunosuppressive therapy is to be discontinued shortly it would be reasonable to defer immunization until at least 3 months after the patient last received therapy; otherwise, the patient should be vaccinated while still receiving therapy.

Enhanced Inactivated Polio Vaccine (eIPV)

If polio immunization is indicated, immunocompromised infants, their household members, nursing personnel in close contact, and other close contacts should receive eIPV rather than OPV. (See the discussion under OPV.) For unvaccinated adults at increased risk of exposure to poliovirus, a primary series of enhanced-potency eIPV is recommended. This recommendation applies to both immunologically normal and immunocompromised adults.

Haemophilus influenzae *b Conjugate Vaccine (Hib)*

Immunocompromised children should receive Hib conjugate vaccines in the same dosage and schedule as for immunocompetent children. Unimmunized children ≥5 years of age with a chronic illness known to be associated with increased risk of *Haemophilus influenzae* type b disease, specifically, persons with anatomic or functional asplenia or sickle-cell anemia or those who have undergone splenectomy, should receive Hib vaccine. One dose may be insufficient to induce immunity in children >5 years of age with sickle cell disease, but the data are insufficient to recommend whether persons suffering from this or other immunosuppressive disorders should receive more than one dose. Clinicians deciding whether to administer Hib vaccine to HIV-infected persons should take into consideration the individual patient's risk of Hib disease and the effectiveness of the vaccine for these persons. In some settings, the incidence of Hib disease may be higher among HIV-infected adults than non-HIV-infected adults (*9,10*), and the disease can be severe in these patients. Patients with Hodgkin's disease should be vaccinated at least 2 weeks before the initiation of chemotherapy or, if this is not possible, ≥3 months after the end of chemotherapy. Hib vaccine can be administered simultaneously with pneumococcal or meningococcal vaccine in separate syringes at different sites.

Influenza Vaccine

Because influenza may result in serious illness and complications for immunocompromised persons, vaccination is recommended and may result in protective antibody levels in many immunocompromised recipients (*38*). Influenza vaccine is recom-

mended for children with symptomatic HIV infection. However, the antibody response to vaccine may be low in persons with advanced HIV-related illnesses; a booster dose of vaccine has not been shown to improve the immune response for these persons (*39*). There is currently little information regarding the frequency and severity of influenza illness in HIV-infected persons (*40*).

Patients with chronic renal failure should receive annual influenza immunization. Uremic patients on chronic hemodialysis may often have an impaired but adequate antibody response to influenza vaccination (*41–43*). Antibody response in renal transplant patients after influenza immunization is lower in those receiving cyclosporine A than in those on azathioprine (*44,45*). Amantadine prophylaxis or treatment also should be considered during periods of increased type A influenza activity in the community. However, strict attention must be given to administering reduced doses of amantadine to patients with renal failure.

Pneumococcal Vaccine

Pneumococcal vaccine is recommended for use in persons ≥2 years of age with chronic illnesses specifically associated with increased risk of pneumococcal disease or its complications (e.g., anatomic or functional asplenia [including sickle cell disease], nephrotic syndrome, cerebrospinal fluid leaks, and conditions associated with immunosuppression, including HIV infection) (*46*). Revaccination after 3–5 years should be considered for children with nephrotic syndrome, asplenia, or sickle cell anemia who would be ≤10 years old at revaccination.

Pneumococcal vaccine is recommended for use in immunocompetent adults who are at increased risk of pneumococcal disease or its complications because of chronic illness (e.g., cardiovascular disease, pulmonary disease, diabetes mellitus, alcoholism, cirrhosis, or cerebrospinal fluid leaks). Vaccination is also recommended for immunocompromised adults at increased risk of pneumococcal disease or its complications (e.g., persons with splenic dysfunction or anatomic asplenia, Hodgkin's disease, leukemia, lymphoma, multiple myeloma, chronic renal failure, nephrotic syndrome, or conditions such as organ transplantation associated with immunosuppression). Revaccination should be strongly considered ≥6 years after the first dose for those patients at highest risk of fatal pneumococcal infection (e.g., asplenic patients) or for those at highest risk of rapid decline in antibody levels (e.g., those with chronic renal failure, nephrotic syndrome, or transplanted organs).

Hepatitis B Vaccine

Hepatitis B vaccination is recommended for susceptible hemodialysis patients. Although seroresponse to hepatitis B vaccine is lower in hemodialysis patients than in healthy persons, for those patients who do respond, hepatitis B vaccine will protect them from hepatitis B virus infection and reduce the necessity for frequent serologic screening (*47*). Hepatitis B vaccine is also indicated for patients whose renal disease is likely to lead to dialysis or transplantation. Such patients are at increased risk for hepatitis B because of their need for blood products and hemodialysis. Patients with uremia who were vaccinated before they required dialysis have been shown to have higher seroconversion rates and antibody titers (*48*). The response may also be better in children (*49*). In addition, periodic booster doses are usually necessary following

successful immunization, with their timing determined by serologic testing at 12-month intervals.

For patients undergoing hemodialysis and for other immunosuppressed patients, higher vaccine doses or increased number of doses are required. A special formulation of one vaccine is now available for such persons (Recombivax HB, 40 μg/mL). Persons with HIV infection have an impaired response to hepatitis B vaccine. The immunogenicity of higher doses of vaccine is unknown for this group, and firm recommendations on dosage cannot be made at this time (*50*). The anti-Hbs response of such persons should be tested after they are vaccinated, and those who have not responded should be revaccinated with 1–3 additional doses.

Meningococcal Vaccine

Routine immunization with the quadrivalent vaccine is recommended for certain high-risk groups, including persons with terminal complement component deficiencies and those with anatomic or functional asplenia. Persons splenectomized because of trauma or nonlymphoid tumors and those with inherited complement deficiencies have acceptable antibody responses to meningococcal vaccine, although its clinical efficacy has not been documented in these patients.

Rabies Vaccine

Corticosteroids, other immunosuppressive agents, and immunosuppressive illnesses can interfere with the development of active immunity and predispose the patient to developing rabies if exposed. Immunosuppressive agents should not be administered during postexposure therapy, unless essential for the treatment of other conditions. When rabies postexposure prophylaxis is administered to persons receiving steroids or other immunosuppressive therapy, it is especially important that serum be tested for rabies antibody to ensure that an adequate response has developed.

Other Killed Antigens

Other vaccines containing killed antigens, including cholera, plague, and anthrax, do not pose a risk to immunocompromised persons and should be used for the same indications as for immunologically normal persons.

USE OF IMMUNE GLOBULINS

Immunocompromised persons may benefit from protection by passive immunization. The use of immune globulin preparations in these patients is described below.

Immune Globulin (IG)

For immunocompromised persons, IG is indicated to prevent measles following exposure. If immediate protection against measles is required for immunocompromised persons with contraindications to measles vaccination, including exposed infants <1 year of age, passive immunization with IG, 0.5 mL/kg of body weight (maximum dose = 15 mL), should be administered intramuscularly as soon as possible after exposure. Exposed *symptomatic* HIV-infected and other severely immunocom-

promised persons should receive IG regardless of their previous vaccination status, because measles vaccine may not be effective in such patients and the disease may be severe. For immunocompromised persons, the recommended dose is 0.5 mL/kg of body weight if IG is administered intramuscularly (maximum dose = 15 mL). This corresponds to a dose of protein of approximately 82.5 mg/kg (maximum dose = 2,475 mg). Intramuscular IG may not be necessary if a patient with HIV infection is receiving 100–400 mg/kg IGIV at regular intervals and the last dose was administered within 3 weeks of exposure to measles. Because the amounts of protein administered are similar, high-dose IGIV may be as effective as IG administered intramuscularly. However, no data are available concerning the effectiveness of IGIV in preventing measles.

For immunocompromised persons receiving IG for measles prophylaxis (0.50 mL/kg [82 mg/kg] intramuscularly), measles vaccination should be delayed for 6 months following IG administration. For persons receiving IG for replacement of humoral immune deficiencies (320 mg/kg intravenously), measles vaccination should be delayed until 8 months following IG administration.

For the prevention of hepatitis A, IG should be administered in the same dose and schedule to both immunocompromised and immunocompetent persons.

Varicella-Zoster Immune Globulin (VZIG)

The most important use of VZIG is for passive immunization of neonates and susceptible, severely immunocompromised persons after significant exposure to chickenpox or zoster. (Significant exposure to a person with varicella is defined to include household contact, close contact indoors of >1 hour, sharing the same two- to four-bed hospital room, or prolonged direct, face-to-face contact such as occurs with nurses or doctors who care for the patient *[51].*) Immunocompromised patients who are exposed to varicella and receive VZIG may have lower rates of complications and infections. Varicella-susceptible pregnant women may be at higher risk for serious complications than are adults in general. Of especial concern is the risk to the fetus when a woman develops varicella-zoster infection during the first half of pregnancy. Whether the fetus will be protected against development of malformations if VZIG is administered to a pregnant, susceptible woman after exposure is unknown.

When deciding to administer VZIG to an immunocompromised patient, the clinician must determine whether the patient is likely to be susceptible and whether the exposure is likely to result in infection. The risks of VZIG administration appear to be negligible, but the costs of administration can be substantial. A physician should carefully evaluate the susceptibility of patients to varicella before administering VZIG. Both immunocompetent and immunocompromised adults and children who are believed to have had varicella on the basis of a carefully obtained history by an experienced interviewer can be considered immune. Laboratory determination of susceptibility to varicella is often impractical. Modern antibody assays may detect either nonspecific antibody or antibody levels that may not be protective.

Hepatitis B Immune Globulin (HBIG)

Immunocompromised persons should receive HBIG for the same indications (perinatal, needlestick, or sexual exposure to a person positive for hepatitis B surface antigen) and in the same doses as immunocompetent persons. The HB vaccine series should be started concurrently with HBIG treatment.

Vaccinia Immune Globulin (VIG), Tetanus Immune Globulin (TIG), and Human Rabies Immune Globulin (HRIG)

Immunocompromised persons should receive VIG, TIG, and HRIG for the same indications and in the same doses as immunocompetent persons.

References

1. Infections in immunocompromised infants and children, section II. In: Disorders of host defense. Patrick CC, ed. New York: Churchill Livingstone, 1992.
2. Hibberd PL, Rubin RH. Approaches to immunization in the immunocompromised host. Infectious Disease Clinics of North America 1990; 4:123–42.
3. Vessal S, Kravis LP. Immunologic mechanisms responsible for adverse reactions to routine immunizations in children. Clin Pediatr 1976;15:688–96.
4. Mitus A, Holloway A, Evans AE, Enders JF. Attenuated measles vaccine in children with acute leukemia. Am J Dis Child 1962;103:243–8.
5. Bellini WJ, Rota JS, Greer PW, Zaki SR. Measles vaccination death in a child with severe combined immunodeficiency: report of a case. Lab Investig 1992;66:91A.
6. Mawhinni H, Van Allen I, Beare JM, et al. Dysgammaglobulinemia complicated by disseminated measles. Br Med J 1971;2(758):380–1.
7. Committee on Infectious Diseases, American Academy of Pediatrics. Report of the Committee on Infectious Diseases, 22nd edition. Peter G, ed. Elk Grove, IL: American Academy of Pediatrics, 1991, p. 48.
8. Onorato IM, Markowitz LE, Oxtoby MJ. Childhood immunization, vaccine-preventable diseases and infection with human immunodeficiency virus. Pediatr Infect Dis J 1988;6:588–95.
9. Farley MM, Stephens DS, Brachman PS Jr, Harvey RC, Smith JD, Wenger JD. Invasive *Haemophilus influenzae* disease in adults. A prospective, population-based surveillance. CDC meningitis surveillance group. Ann Intern Med 1992;116:806—12.
10. Steinhart R, Reingold AL, Taylor F, Anderson G, Wenger JD. Invasive *Haemophilus influenzae* infections in men with HIV infection. JAMA 1992;268:3350-2.
11. Opravil M, Fierz W, Matter L, Blaser J, Lüthy R. Poor antibody response after tetanus and pneumococcal vaccination in immunocompromised, HIV-infected patients. Clin Exp Immunol 1991;84(2):185–9.
12. Borkowsky W, Steele CJ, Grubman S, et al. Antibody responses to bacterial toxoids in children infected with human immunodeficiency virus. J Pediatr 1987;110:563–6.
13. Huang KL, Ruben FL, Rinaldo CR Jr, et al. Antibody responses after influenza and pneumococcal immunization in HIV-infected homosexual men. JAMA 1987;257:2047–50.
14. Klein RS, Selwyn PA, Maude D, et al. Responses to pneumococcal vaccine among asymptomatic heterosexual partners of persons with AIDS and intravenous drug users infected with human immunodeficiency virus. J Infect Dis 1989;160:826–31.
15. Vardinon N, Handsher R, Burke M, Zacut V, Yust I. Poliovirus vaccination responses in HIV-infected patients: correlation with T4 cell counts. J Infect Dis 1990;162:238–41.
16. Schwebke J, Mujais S. Vaccination in hemodialysis patients (editorial). Int J Artif Organs 1989;12:481–4.
17. Johnson DW, Fleming SJ. The use of vaccine in renal failure. Clin Pharmacokin 1992;22:434–46.
18. Linneman CC Jr, First MR. Risk of pneumococcal infections in renal transplant patients. JAMA 1979;241:2619–21.
19. Alter MJ, Farrero MS, Maynard JG. Impact of infection control strategies on the incidence of dialysis-associated hepatitis in the United States. J Infect Dis 1986;153:1149–51.
20. Simberkoff MS, Schiffman G, Katz LA, et al. Pneumococcal capsular polysaccharide vaccination in adult chronic hemodialysis patients. J Lab Clin Med 1980;96:363–70.
21. Cosio FG, Giebink GS, Le CT, Schiffman G. Pneumococcal vaccination in patients with chronic renal disease and renal allograft recipients. Kidney Int 1981;20:254–8.
22. Linneman CC Jr, First MR, Schiffman G. Response to pneumococcal vaccine in renal transplant and hemodialysis patients. Arch Intern Med 1981;141:1637–40.
23. Rytel MW, Dailey MP, Schiffman G, Hoffman RG, Piering WF. Pneumococcal vaccine immunization of patients with renal impairment. Proc Soc Exp Biol Med 1986;182:468–73.

24. Linneman CC Jr, First MR, Schiffman G. Revaccination of renal transplant and hemodialysis recipients with pneumococcal vaccine. Arch Intern Med 1986;146:1554–6.
25. Beam TR Jr, Crigler ED, Goldman JK, Schiffman G. Antibody response to polyvalent pneumococcal polysaccharide vaccine in diabetics. JAMA 1980;244:2621–4.
26. Lederman MM, Schiffman G, Rodman HM. Pneumococcal immunization in adult diabetics. Diabetes 1981;30:119–21.
27. Feery BJ, Hartman LJ, Hampson AW, Proietto J. Influenza immunization in adults with diabetes mellitus. Diabetes Care 1983;6:475–8.
28. Kaplan LJ, Daum RS, Smaron M, McCarthy CA. Severe measles in immunocompromised patients. JAMA 1992;267:1237–41.
29. Sixbey JW. Routine immunization and the immunosuppressed child. Adv Pediatr Infect Dis 1987;2:79–114.
30. Wright PF, Hatch MH, Kasselberg AG, et al. Vaccine-associated poliomyelitis in a child with sex-linked agammaglobulinemia. J Pediatr 1977;91:408–12.
31. Wyatt HV. Poliomyelitis in hypogammaglobulinemics. J Infect Dis 1973;128:802–6.
32. Davis LE, Bodian D, Price D, Butler IJ, Vickers JH. Chronic progressive poliomyelitis secondary to vaccination of an immunodeficient child. N Engl J Med 1977;297:241–5.
33. Bregere P. BCG vaccination and AIDS. Bull Int Union Tuberc Lung Dis 1988;63:40–1.
34. Quinn TC. Interactions of the human immunodeficiency virus and tuberculosis and the implications for BCG vaccination. Rev Infect Dis Suppl 2, 1989;2:s379–84.
35. CDC. Disseminated *Mycobacterium bovis* infection from BCG vaccination of a patient with acquired immunodeficiency syndrome. MMWR 1985;34:227–8.
36. Ninane J, Grymonprez A, Burtonboy G, Francois A, Cornu G. Disseminated BCG in HIV infection. Arch Dis Child 1988;63:1268–9.
37. Redfield RR, Wright DC, James WD, et al. Disseminated vaccinia in a military recruit with human immunodeficiency virus (HIV) disease. N Engl J Med 1987;316:673–6.
38. Hodges GR, Davis JW, Lewis HD, et al. Response to influenza A vaccine among high-risk patients. South Med J 1979;72:29–32.
39. Gross PA, Lee H, Wolff JA, Hall CB, Minnefore AB, Lazicki ME. Influenza immunization in immunosuppressed children. J Pediatr 1978;92:30–5.
40. Safrin S, Rush JD, Mills J. Influenza in patients with human immunodeficiency virus infection. Chest 1990;98:33–7.
41. Cappel R, Van Beers D, Liesnard C, Dratwa M. Impaired humoral and cell-mediated immune responses in dialyzed patients after influenza vaccination. Nephron 1983;33:21–5.
42. Jordan MC, Rousseau WE, Tegtmeier GE, et al. Immunogenicity of inactivated influenza virus vaccine in chronic renal failure. Ann Intern Med 1973;79:790–4.
43. Osanloo EO, Berlin BS, Popli S, et al. Antibody responses to influenza vaccination in patients with chronic renal failure. Kidney Int 1978;14:614–8.
44. Huang KL, Armstrong JA, Ho M. Antibody response after influenza immunization in renal transplant patients receiving cyclosporine A or azathioprine. Infect Immun 1983;40:421–4.
45. Versluis DJ, Beyer We, Masurel N, Wenting GJ, Weimar W. Impairment of the immune response to influenza vaccination in renal transplant recipients by cyclosporine, but not by azathioprine. Transplantation 1986;42:376–9.
46. Landesman SH, Schiffman G. Assessment of the antibody response to pneumococcal vaccine in high-risk populations. Rev Infect Dis 1981;3:suppl:s184–97.
47. CDC. Routine screening for viral hepatitis in chronic hemodialysis centers. Hepatitis surveillance report no. 49. Atlanta: CDC, 1985:5–6.
48. Seaworth B, Drucker J, Starling J, et al. Hepatitis B vaccine in patients with chronic renal failure before dialysis. J Infect Dis 1988;157:332–7.
49. Callis LM, Clanxet J, Fortuny G, et al. Hepatitis B virus infection and vaccination in children undergoing hemodialysis. Acta Pediatr Scand 1985;74:213–8.
50. Collier AC, Corey L, Murphy VL, Handsfield HH. Antibody to human immunodeficiency virus (HIV) and suboptimal response to hepatitis B vaccination. Ann Intern Med 1988;109:101–5.
51. CDC. Update on adult immunization: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1991:41(No. RR-12):49.

ORGANIZATION OF THE SUMMARY TABLES

The following tables summarize recommendations for vaccine use in immunocompromised persons. A "Recommended" entry denotes that the vaccine is either recommended as part of the routine schedule or the medical condition represents an indication for use of the vaccine. A "Use if Indicated" entry in the table denotes that the category of immunosuppression is not a contraindication to the use of the vaccine if otherwise indicated. A "Contraindicated" entry denotes that the medical condition represents either an absolute or relative contraindication to the use of the vaccine. A "Considered" entry indicates that the decision to use the vaccine should include consideration of the individual patient's risk of disease and the likely effectiveness of the vaccine. See section on "Principles for vaccinating immunocompromised persons" for a discussion of categories of immunosuppression.

Abbreviations

BCG = bacille Calmette Guerin
DTP = diphtheria, tetanus, pertussis
eIPV = enhanced inactivated polio vaccine
HAV = hepatitis A virus
HBIG = hepatitis B immune globulin
Hib = *Haemophilus influenzae* b
HIV = human immunodeficiency virus
HRIG = human rabies immune globulin
IG = immune globulin
MMR = measles, mumps, rubella
OPV = oral polio vaccine
TIG = tetanus immune globulin
VZIG = varicella zoster immune globulin

TABLE 1. Summary of ACIP recommendations on immunization of immunocompromised infants and children

Vaccine	Routine (not immunocompromised)	HIV infection/AIDS	Severely immunocompromised (non-HIV related)*	Asplenia	Renal Failure	Diabetes
			Routine infant immunizations			
DTP (DT/T/Td)†	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended
OPV	Recommended	**Contraindicated**	**Contraindicated**	Recommended	Recommended	Recommended
eIPV	Use if indicated	Recommended	Recommended	Use if indicated	Use if indicated	Use if indicated
MMR (MR/M/R)	Recommended	Recommended /considered§	**Contraindicated**	Recommended	Recommended	Recommended
Hib	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended
Hepatitis B¶	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended
			Other childhood immunizations			
Pneumococcal**	Use if indicated	Recommended	Recommended	Recommended	Recommended	Recommended
Influenza††	Use if indicated	Recommended	Recommended	Recommended	Recommended	Recommended

*Severe immunosuppression can be the result of congenital immunodeficiency, HIV infection, leukemia, lymphoma, aplastic anemia, generalized malignancy or therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids.
†Including DTaP boosters.
§See discussion of MMR.
¶HB vaccine is now recommended for all infants.
**Recommended for persons ≥2 years of age.
††Not recommended for infants <6 months of age.

TABLE 2. Summary of ACIP recommendations on immunization of immunocompromised adults

Vaccine	Routine (not immuno-compromised)	HIV infection/AIDS	Severely immuno-compromised (non-HIV related)*	Post-solid organ transplant on chronic immunosuppressive therapy	Asplenia	Renal failure	Diabetes	Alcoholism and alcoholic cirrhosis
Td	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended
MMR(MR/M/R)	Use if indicated	Recommended/ considered†	**Contraindicated**	**Contraindicated**	Use if indicated	Use if indicated	Use if indicated	Use if indicated
Hepatitis B	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Recommended§	Use if indicated	Use if indicated
Hib	Not recommended	Considered¶	Recommended	Recommended	Recommended	Use if indicated	Use if indicated	Use if indicated
Pneumococcal	Recommended if ≥65 years of age	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended
Meningococcal	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Recommended	Use if indicated	Use if indicated	Use if indicated
Influenza	Recommended if ≥65 years of age	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended

* Severe immunosuppression can be the result of congenital immunodeficiency, HIV infection, leukemia, lymphoma, generalized malignancy or therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids.
† See discussion of MMR.
§ Patients with renal failure on dialysis should have their anti-Hbs response tested after vaccination, and those found not to respond should be revaccinated.
¶ See discussion of HIV.

TABLE 3. Summary of ACIP recommendations on nonroutine immunization of immunocompromised persons

Vaccine	Not immunocompromised	HIV infection/AIDS	Severely immunocompromised (non-HIV related)*	Post-solid organ transplant or chronic immunosuppressive therapy	Asplenia, renal failure, diabetes, alcoholism, and alcoholic cirrhosis
			Live vaccines		
BCG	Use if indicated	**Contraindicated**	**Contraindicated**	**Contraindicated**	Use if indicated
OPV	Use if indicated	**Contraindicated**	**Contraindicated**	**Contraindicated**	Use if indicated
Vaccinia	Use if indicated	**Contraindicated**	**Contraindicated**	**Contraindicated**	Use if indicated
Typhoid, Ty21a	Use if indicated	**Contraindicated**	**Contraindicated**	**Contraindicated**	Use if indicated
Yellow fever†	Use if indicated	**Contraindicated**	**Contraindicated**	**Contraindicated**	Use if indicated
			Killed or inactivated vaccines		
eIPV	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated
Cholera	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated
Plague	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated
Typhoid, inactivated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated
Rabies	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated
Anthrax	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated

*Severe immunosuppression can be the result of congenital immunodeficiency, HIV infection, leukemia, lymphoma, aplastic anemia, generalized malignancy, or therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids.
†Yellow fever vaccine should be considered for patients when exposure to yellow fever cannot be avoided (see text).

TABLE 4. Summary of ACIP recommendations on use of immune globulins in immunocompromised persons

Immune globulin	Not immunocompromised	HIV infected	Severely immunocompromised*
IG	Recommended for infants and adults with contraindication to measles vaccine exposed to measles	• Recommended for symptomatic patients exposed to measles regardless of immunization status • Recommended for persons with exposure to hepatitis A or who will travel to HAV-endemic areas	Recommended for patients exposed to measles regardless of immunization status
VZIG†	• Recommended for newborns of mothers who develop chickenpox within 5 days before and 48 hours after delivery • Recommended for exposed newborns (≥28 weeks gestation) of susceptible mothers • Recommended for exposed pre-term infants (<28 weeks or <1000 g) • May be used for exposed, susceptible adults, exposed pregnant women, and infants <28 days	Recommended for susceptible infants and adults after significant exposure to V-Z	Recommended for susceptible infants and adults after significant exposure to V-Z
TIG	Recommended for those with serious wounds and <3 doses of tetanus toxoid	Same as for non-immuno-compromised	Same as for non-immuno-compromised
HBIG	Recommended for prophylaxis of infants born to HBsAg+ mothers and susceptible persons with percutaneous, sexual, or mucosal exposure to HB virus	Same as for non-immuno-compromised	Same as for non-immuno-compromised
HRIG	Recommended for post-exposure prophylaxis of persons not previously vaccinated against rabies.	Same as for non-immuno-compromised	Same as for non-immuno-compromised

*Severe immunosuppression can be the result of congenital immunodeficiency, HIV infection, leukemia, lymphoma, aplastic anemia, generalized malignancy or therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids.

† See Section III for a discussion of issues to be considered before using VZIG.

MMWR

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