

8. Altered Immunocompetence

Updates

This section incorporates general content from the Infectious Diseases Society of America policy statement, 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host (1), to which CDC provided input in November 2011. The evidence supporting this guidance is based on expert opinion and arrived at by consensus.

General Principles

Altered immunocompetence, a term often used synonymously with immunosuppression, immunodeficiency, and immunocompromise, can be classified as primary or secondary. Primary immunodeficiencies generally are inherited and include conditions defined by an inherent absence or quantitative deficiency of cellular, humoral, or both components that provide immunity. Examples include congenital immunodeficiency diseases such as X-linked agammaglobulinemia, SCID, and chronic granulomatous disease. Secondary immunodeficiency is acquired and is defined by loss or qualitative deficiency in cellular or humoral immune components that occurs as a result of a disease process or its therapy. Examples of secondary immunodeficiency include HIV infection, hematopoietic malignancies, treatment with radiation, and treatment with immunosuppressive drugs. The degree to which immunosuppressive drugs cause clinically significant immunodeficiency generally is dose related and varies by drug. Primary and secondary immunodeficiencies might include a combination of deficits in both cellular and humoral immunity. Certain conditions like asplenia and chronic renal disease also can cause altered immunocompetence.

Determination of altered immunocompetence is important to the vaccine provider because incidence or severity of some vaccine-preventable diseases is higher in persons with altered immunocompetence; therefore, certain vaccines (e.g., inactivated influenza vaccine, pneumococcal vaccines) are recommended specifically for persons with these diseases (2,3). Administration of live vaccines might need to be deferred until immune function has improved. This is primarily a safety concern, because persons who have altered immunocompetence and receive live vaccines might be at increased risk for an

adverse reaction because of uninhibited growth of the attenuated live virus or bacteria. Vaccines might be less effective during the period of altered immunocompetence. Non-live vaccines might best be deferred during a period of altered immunocompetence; in this circumstance, the concern is with effectiveness and not safety. Additionally, if a non-live vaccine is administered during the period of altered immunocompetence, it might need to be repeated after immune function has improved.

The degree of altered immunocompetence in a patient should be determined by a physician. The challenge for clinicians and other health-care providers is assessing the safety and effectiveness of vaccines for conditions associated with primary or secondary immunodeficiency, especially when new therapeutic modalities are being used and information about the safety and effectiveness of vaccines has not been characterized fully in persons receiving these drugs ([Table 8-1](#)). Laboratory studies can be useful for assessing the effects of a disease or drug on the immune system. Tests useful to assess humoral immunity include immunoglobulin (and immunoglobulin subset) levels and specific antibody levels (e.g., tetanus and diphtheria). Tests that demonstrate the status of cellular immunity include lymphocyte numbers (i.e., a complete blood count with differential), a test that delineates concentrations and proportions of lymphocyte subsets (i.e., B and T lymphocytes, CD4+ B lymphocytes versus CD8+ T lymphocytes), and tests that measure T-cell proliferation or function in response to specific or nonspecific stimuli (e.g., lymphocyte proliferation assays) (4,5). The ability to characterize a drug or disease condition as affecting cellular or humoral immunity is only the first step; using this information to draw inferences about whether particular vaccines are indicated or whether caution is advised with use of live or non-live vaccines is more complicated and might require consultation with an infectious diseases or immunology specialist.

Altered Immunocompetence as an Indication to Receive a Vaccine Outside of Routinely Recommended Age Groups

This section describes situations in which vaccines are recommended outside of the routine-age-based recommendation because the risk for vaccine-preventable disease is increased due to altered immunocompetence.

Persons with altered immunocompetence generally are recommended to receive polysaccharide-based vaccines (PCV13, PPSV23, and Hib), on the basis of increased risk for disease if the vaccine is withheld. For certain specific categories of altered immunocompetence, patients are also recommended to receive polysaccharide based vaccines (MenACWY, Hib-MenCY, and MPSV4).

Pneumococcal Vaccines

Two types of vaccine against invasive pneumococcal disease are available in the United States: PCV13 and PPSV23. PCV13 is recommended routinely for all children beginning at age 2 months through age 59 months and for adults aged 65 years or older. PCV13 is also recommended for children, adolescents, and adults with conditions that place them at high risk for invasive disease from *Streptococcus pneumoniae*. PCV13 is recommended for persons aged 6-64 years who have not previously received PCV13 and have congenital immunodeficiency disorders (including B- or T-lymphocyte deficiency, complement deficiencies, and phagocytic disorders), anatomic or functional asplenia (including sickle cell disease and other hemoglobinopathies), HIV infection, cochlear implant, cerebrospinal fluid leak, chronic renal failure, nephrotic syndrome, iatrogenic immunosuppression, or other immunocompromising conditions.

PPSV23 is licensed for use in persons aged ≥ 2 years and recommended routinely for adults aged 65 years and older. PPSV23 is also recommended for persons age 2 through 64 years with congenital immunodeficiency disorders, anatomical and functional asplenia, HIV infection, cochlear implant, cerebrospinal fluid leak, and iatrogenic immunosuppression. Complete recommendations on use of PCV13 and PPSV23 are available in the Recommended Immunization Schedules for Persons Aged 0 Through 18 Years and the Recommended Adult Immunization Schedule (2,6).

Meningococcal Vaccines

Three types of meningococcal vaccines are licensed in the United States: meningococcal conjugate (MenACWY and Hib-MenCY), meningococcal polysaccharide (MPSV4), and serogroup B meningococcal (MenB) vaccines.

Persons with functional or anatomic asplenia (including sickle cell disease), HIV infection and persistent complement component deficiency (including persons taking eculizumab [Soliris]) (7) are at increased risk for meningococcal disease and should receive MenACWY vaccine. Persons with functional or anatomic asplenia (including sickle cell disease) and persistent complement component deficiency (including persons taking eculizumab [Soliris]) should receive MenB vaccine. For children 2 months through 23 months of age, an age-appropriate series of meningococcal conjugate vaccine should be administered. If MenACWY-D (Menactra) is administered to a child with asplenia or HIV, it should be after 2 years of age and at least 4 weeks after the completion of all PCV13 doses. A 2-dose primary series of either MenACWY-CRM (Menveo) or MenACWY-D (Menactra) should be administered to persons 2 years of age or older with asplenia or complement deficiency. Following the primary series of vaccine, a 3-year interval to the next dose is recommended for persons who received their previous dose at younger than 7 years. A 5-year interval is recommended for persons who received their previous dose at age 7 years or older. Although MPSV4 is the only meningococcal vaccine licensed for persons older than 55 years of age, adults 56 years and older with asplenia or complement deficiency should be vaccinated with MenACWY-CRM or MenACWY-D rather than MPSV4 (8). Meningococcal serogroup B vaccines are licensed for persons 10-25 years of age and are recommended for persons 10 years of age or older for persons with high-risk conditions like functional or anatomic asplenia or persistent complement component deficiency. There are presently no recommendations for booster doses of either MenB vaccine (9,10). Complete recommendations for use of meningococcal vaccines are available in the Recommended Immunization Schedules for Persons Aged 0 Through 18 Years and the Recommended Adult Schedule (2,6).

Hib Vaccines

Hib conjugate vaccines are available in single or combined antigen preparations. Hib vaccine is recommended routinely for all children through age 59 months.

Children 12 through 59 months who are at high risk for invasive Hib disease (i.e., recipients of chemotherapy or radiation for malignant neoplasms, or those with functional or anatomic asplenia, HIV infection, immunoglobulin deficiency, or early complement component deficiency) and who are unvaccinated or received only one dose of Hib vaccine before 12 months of age should receive 2 additional doses of Hib vaccine; those who received 2 or more doses of Hib before 12 months of age should receive one additional dose.

A child younger than 5 years of age receiving chemotherapy or radiation therapy should have Hib doses repeated if the doses were received during therapy or within 14 days of starting therapy; repeat doses should be started at least 3 months after completion of therapy. Recipients of hematopoietic cell transplants should be revaccinated with 3 doses of Hib vaccine, starting 6-12 months after successful transplant, regardless of vaccination history or age.

Children 5-18 years of age with HIV who are unimmunized(a) should receive a dose of Hib vaccine; Hib vaccination is not recommended in HIV-infected adults. Unimmunized(a) asplenic patients older than 59 months of age or adults should receive a dose of Hib vaccine. Anyone 15 months of age or older who is undergoing a splenectomy and is unimmunized(a) should receive a dose of Hib vaccine (11). Complete recommendations for use of Hib vaccine are available in the *Recommended Immunization Schedules for Persons Aged 0 Through 18 Years and the Recommended Adult Immunization Schedule* (2,6).

Zoster (Shingrix) Vaccine

Zoster (Shingrix) vaccine is recommended for persons 19 years old and older who have altered immunocompetence.

Vaccination of Contacts of Persons with Altered Immunocompetence

Household contacts and other close contacts of persons with altered immunocompetence should receive all age- and exposure-appropriate vaccines, with the exception of smallpox vaccine (12,13).

Receipt of vaccines will prevent the vaccine-preventable disease, so there can be no potential transmission to the contact with altered immunocompetence. The live MMR, varicella, and rotavirus vaccines should be administered to susceptible household contacts and other close contacts of immunocompromised patients when indicated. No specific precautions are needed unless the varicella vaccine recipient has a rash after vaccination, in which case direct contact with susceptible household contacts with altered immunocompetence should be avoided until the rash resolves (14,15). All members of the household should wash their hands after changing the diaper of an infant who received rotavirus vaccine.

This minimizes rotavirus transmission, as shedding may occur up to one month after the last dose (16,17). Household and other close contacts of persons with altered immunocompetence should receive annual influenza vaccination. Introduction of low levels of vaccine viruses into the environment likely is unavoidable when administering LAIV. LAIV vaccine viruses are cold-adapted, so they can replicate in the nose and generate an immune response without entering the lungs (i.e., they are temperature sensitive and replicate poorly at core body temperatures). No instances have been reported of illness caused by attenuated vaccine virus infections among health-care providers or immunocompromised patients. LAIV may be administered to healthy household and other close contacts of persons with altered immunocompetence unless the person with altered immunocompetence is in a protective environment, typically defined as a specialized patient-care area with a positive airflow relative to the corridor, high-efficiency particulate air filtration, and frequent air changes (3). No preference exists for inactivated influenza vaccine use by health-care workers or other persons who have close contact with persons with lesser degrees of immunosuppression (e.g., persons with diabetes, persons with asthma taking high-dose corticosteroids, or persons infected with HIV), and no preference exists for inactivated influenza vaccine use by health-care workers or other healthy persons aged 5-49 years in close contact with all other groups at high risk.

Non-live Vaccines: Safety

All non-live vaccines can be administered safely to persons with altered immunocompetence, whether the vaccine is a killed whole-organism or a recombinant, subunit, split-virus, toxoid, polysaccharide, or polysaccharide protein-conjugate vaccine.

Non-live Vaccines: Effectiveness

Except for inactivated influenza vaccine, vaccination during chemotherapy or radiation therapy should be avoided if possible because antibody response might be suboptimal.

Patients vaccinated within a 14-day period before starting immunosuppressive therapy or while receiving immunosuppressive therapy should be considered unimmunized and should be revaccinated at least 3 months after therapy is discontinued if immune competence has been restored. Patients who have quantitative B-cell deficiencies and are receiving immunoglobulin therapy should not receive either non-live or live vaccines while receiving the immunoglobulin therapy because of concerns about effectiveness of the vaccines. Patients on chemotherapy with anti-B cell antibodies (e.g., rituximab) should wait at least 6 months after therapy before being vaccinated with non-live vaccines. Some experts recommended longer than 6 months for some anti-B cell antibodies. For other forms of altered immunocompetence, if non-live vaccines are indicated, the usual schedules are recommended. However, the effectiveness of such vaccinations might be suboptimal (1).

Live, Attenuated Viral and Bacterial Vaccines: Effectiveness

The same rationale regarding effectiveness that exists with non-live vaccines also exists with live vaccines.

Live, Attenuated Viral and Bacterial Vaccines: Safety

Severe complications have followed vaccination with certain live, attenuated viral and live, attenuated bacterial vaccines among persons with altered immunocompetence (18-26).

Persons with most forms of altered immunocompetence should not receive live vaccines (MMR, varicella, MMRV, LAIV, yellow fever, Ty21a oral typhoid, BCG, smallpox, and rotavirus). However, exceptions exist, and are discussed in this section.

Patients with any defect in phagocytic function (e.g., chronic granulomatous disease, leukocyte adhesion deficiency, myeloperoxidase deficiency, Chediak-Higashi syndrome) should NOT receive live bacterial vaccines. Patients with a specific type of defect in phagocytic function—chronic granulomatous disease—should receive recommended live attenuated viral vaccines in addition to non-live vaccines but should NOT receive live bacterial vaccines.

Patients with defects in phagocytic function that are undefined or known to be accompanied by defects in T-cell and natural killer cell function (e.g., leukocyte adhesion deficiency, myeloperoxidase deficiency, Chediak-Higashi syndrome) should NOT receive live attenuated viral or bacterial vaccines. These conditions include specific deficits in T-cell and natural killer cell function, reducing the response to live viral vaccine antigens to an extent not seen in chronic granulomatous disease (1). Children with deficiencies in complement should receive recommended live, attenuated viral and live, attenuated bacterial vaccines. Children with asplenia should not receive LAIV, but can receive recommended live, attenuated viral and live, attenuated bacterial vaccines.

Persons with severe cell-mediated immunodeficiency should not receive live, attenuated viral or bacterial vaccines. Patients with defects of the interferon-gamma/interleukin-12 axis should not receive live bacterial vaccines. Patients with deficiencies of interferon-gamma or interferon-alpha should not receive live viral or live bacterial vaccine. These defects involve a deficiency in cytokine production which affects the immune response to a wide scope of antigens, both bacterial and viral (1). Two factors support vaccination of HIV-exposed or HIV-infected infants with rotavirus vaccines: 1) the HIV diagnosis might not be established in infants born to HIV-infected mothers before the age of the first rotavirus vaccine dose (only 1.5%-3% of HIV-exposed infants in the United States will be determined to be HIV-infected), and 2) the vaccine strains of rotavirus are considerably attenuated. Patients taking exogenous interferon as therapy should not receive live bacterial or live viral vaccines.

Children with HIV infection are at increased risk for complications from varicella and herpes zoster infection compared with immunocompetent children (27, 28). Limited data among HIV-infected children younger than 8 years (specifically, those individuals with CDC class N, A, or B with age-specific CD4+ T-lymphocyte percentages of $\geq 15\%$) indicate that single-component varicella vaccine is immunogenic, effective, and safe (14,28). Data on use of varicella vaccine in HIV-infected adolescents and adults are lacking. However, on the basis of expert opinion, the safety of varicella vaccine in HIV-infected persons older than 8 years with comparable levels of immune function (CD4+T-lymphocyte count greater than 200 cells/mm³) is likely to be similar to that of children aged younger than 8 years (14).

Varicella vaccine should be considered for persons who meet these criteria. Eligible HIV-infected persons 12 months of age or older should receive 2 doses of single-component varicella vaccine with a 3-month interval between doses (14,28). MMRV vaccine should not be administered to any HIV-infected person.

Persons with HIV infection are at increased risk for severe complications if infected with measles. No severe or unusual adverse events have been reported after measles vaccination among HIV-infected persons who did not have evidence of severe immunosuppression (29-32). Two doses of MMR vaccine are recommended for all HIV-infected individuals aged ≥ 12 months who do not have evidence of current severe immunosuppression (i.e., individuals aged ≤ 5 years must have CD4+T lymphocyte [CD4+] percentages $\geq 15\%$ for ≥ 6 months, and individuals aged > 5 years must have CD4+percentages $\geq 15\%$ and CD4+ ≥ 200 lymphocytes/mm³ for ≥ 6 months) and do not have current evidence of measles, rubella, and mumps immunity. In cases when only CD4+cell counts or only CD4+percentages are available for those > 5 years, the assessment of severe immunosuppression can be based on the CD4+values (count or percentage) that are available. In cases when CD4+percentages are not available for those aged ≤ 5 years, the assessment of severe immunosuppression can be based on age-specific CD4+counts at the time CD4+counts were measured; i.e., absence of severe immunosuppression is defined as ≥ 6 months above age-specific CD4+count criteria: CD4+count > 750 lymphocytes/mm³ while aged ≤ 12 months and CD4+count ≥ 500 lymphocytes/mm³ while aged 1 through 5 years (33).

Similarly, repeat doses of MMR vaccination are recommended for individuals with perinatal HIV infection who were vaccinated prior to establishment of effective combination antiretroviral therapy (cART). They should receive 2 appropriately spaced doses of MMR vaccine once effective cART has been established (individuals aged ≤ 5 years must have CD4+percentages $\geq 15\%$ for ≥ 6 months; individuals aged > 5 years must have CD4+percentages $\geq 15\%$ and CD4+ ≥ 200 lymphocytes/mm³ for ≥ 6 months) unless they have other acceptable current evidence of measles, rubella, and mumps immunity.

HIV-infected persons who are receiving regular doses of IGIV are unlikely to respond to varicella vaccine or MMR vaccine because of the continued presence of passively acquired antibody.

However, because of the potential benefit, MMR and varicella vaccines should be considered approximately 14 days before the next scheduled dose of IGIV (if not otherwise contraindicated), although an optimal immune response might not occur depending on the presence of neutralizing antibodies against the vaccine virus. Vaccination should be repeated (if not otherwise contraindicated) after the recommended interval (see [Table 3-6 in the Timing and Spacing of Immunobiologics](#) of this document). In most cases, this is after the therapy has been discontinued.

Patients with leukemia, lymphoma, or other malignancies whose disease is in remission, who have restored immunocompetence, and whose chemotherapy has been discontinued for at least 3 months can receive live-virus vaccines. Persons with impaired humoral immunity (e.g., hypogammaglobulinemia or dysgammaglobulinemia) may be vaccinated with varicella vaccine (14). However, most persons with these disorders also receive periodic doses of IGIV. Appropriate spacing should be maintained between administration of IGIV and varicella vaccine in an attempt to prevent an inadequate response to vaccination caused by the presence of neutralizing antibodies from the IGIV.

Zoster incidence is higher in persons with altered immunocompetence (34). Adults with most types of altered immunocompetence are expected to maintain residual immunity to varicella-zoster virus because of chronic latent infection that protects against primary varicella but provides incomplete protection against zoster. Zoster vaccine is not recommended in persons with primary or acquired immunodeficiency (e.g., lymphoma,

leukemia, tumors involving bone marrow, and patients receiving chemotherapy) and some

HIV infected patients (34). Zoster vaccine may be administered to certain persons age 50 or older with altered immunocompetence, such as persons receiving low dosages of immunosuppressive medications, those with isolated B-cell deficiencies (i.e., impaired humoral immunity), or those with HIV infection who have CD4+ T-lymphocyte counts >200 cells/mm³.

Recipients of Hematopoietic Cell Transplants

A hematopoietic stem cell transplant (HSCT) results in immunosuppression because of the hematopoietic ablative therapy administered before the transplant, drugs used to prevent or treat graft-versus-host disease, and, in some cases, from the underlying disease process necessitating transplantation (35-37). HSCT involves ablation of the bone marrow followed by reimplantation of the person's own stem cells or stem cells from a donor. The ablation caused by the HSCT will also gradually remove immune memory from previous vaccination. Antibody titers to vaccine-preventable diseases (e.g., tetanus, poliovirus, measles, mumps, rubella, and encapsulated bacteria) decrease 1-4 years after autologous or allogeneic HSCT if the recipient is not revaccinated. HSCT recipients of all ages are at increased risk for certain vaccine-preventable diseases, including diseases caused by encapsulated bacteria (e.g., pneumococcal and Hib infections). As a result, HSCT recipients who received vaccines prior to their HSCT should receive repeat doses routinely after HSCT, regardless of the source of the transplanted stem cells (35-37). Revaccination doses following HSCT are indicated with pneumococcal vaccines, DTaP vaccine, Tdap vaccine, Hib vaccine, hepatitis A vaccine, hepatitis B vaccine, IPV, inactivated influenza vaccines, meningococcal conjugate vaccine (for individuals 11 through 18 years or at high-risk), serogroup B meningococcal vaccine (for individuals 16 through 23 years or at high-risk), and human papillomavirus (HPV) vaccines (for individuals aged 9-26 years, or 27 through 45 years of age based on shared clinical decision-making) (1, 35). Recombinant zoster vaccine may be re-administered 6-12 months after an allogeneic HSCT, and may be re-administered 3-12 months after an autologous HSCT. For more specificity on the precise timing of re-administration of RZV, note that this should optimally occur 2 months prior to cessation of prophylactic antiviral therapy (acyclovir, famciclovir, and valacyclovir). Varicella and MMR vaccines may be re-administered after HSCT if 24 months have passed since HSCT, the patient does NOT have graft-vs-host disease, and is considered immunocompetent.

Yellow fever vaccine, rabies vaccine, tick-borne encephalitis vaccine, and Japanese encephalitis vaccine are not routinely administered vaccines, so their use post-HSCT will be driven by a disease-specific risk such as exposure or travel. If someone has received yellow fever vaccine prior to an HSCT, another dose should be re-administered post-HSCT (38). BCG, LAIV, typhoid vaccine, and rotavirus vaccine are not recommended after HSCT. Most non-live vaccines should be re-initiated 6 months after the HSCT (37). Inactivated influenza vaccine should be administered beginning at least 6 months after HSCT and annually thereafter for the life of the patient. A dose of inactivated influenza vaccine can be given as early as 4 months after HSCT, but a second dose should be considered in this situation (37). A second dose is recommended routinely for all children younger than 9 years receiving influenza vaccine for the first time. Revaccination of HSCT patients with pneumococcal vaccines is recommended regardless of whether doses were administered prior to HSCT. For those HSCT recipients that were vaccinated prior to HSCT with PCV7, PCV13, PCV15, or PCV20, sequential administration of 4 doses of PCV20 is recommended, beginning 3-6 months after the transplant. The first three doses should be separated by 4 weeks and the fourth dose of PCV20 should be administered 6 months after the third dose or 1 year after the HSCT, whichever is later. As an alternative to PCV20, three doses of PCV15 separated by 4 weeks, followed by PPSV23 one year after the last dose of PCV15 (and at least 4 weeks after the third dose of PCV15) may be administered. If the patient has graft-versus-host disease, substitute a fourth dose of PCV15 for PPSV23. For doses of pneumococcal conjugate vaccine administered after HSCT consisting of PCV13 or PCV15, these doses count as post-HSCT doses, so one always has the option to transition FROM PCV15 to PCV20 for the post-HSCT dosing regimen. A 3-dose regimen of Hib vaccine should be administered beginning 6 months after transplant; at least 1 month should separate the doses (37). The revaccination schedule for pertussis-containing vaccines includes 3 doses of DTaP for patients <7 years (14). For patients ≥7 years, providers have 3 options for revaccination: 1) 3 doses of DTaP; 2) one dose of Tdap and 2 doses of DT; or 3) one dose of Tdap and 2 doses of Td (1).

Providers need to make a clinical judgment whether they will follow the revaccination schedules described above in circumstances where particular vaccines were NOT administered prior to the HSCT. In this circumstance, providers may just vaccinate according to routine recommendations for post-HSCT vaccination. For instance, there are

specific recommendations for Hib and pertussis-containing vaccines. Use of the 3-dose Hib schedule following HSCT is supported for both patients that received Hib prior to HSCT and those who did not receive Hib prior to HSCT (6, 11). For children >6 years who did not receive previous doses of pertussis-containing vaccine prior to the HSCT, the preferred schedule following HSCT is a dose of Tdap followed by 2 doses of Td (personal communication, subject matter experts).

This is identical to one of the alternative regimens for revaccination doses, described above.

Conditions or Drugs that Might Cause Immunodeficiencies

Asplenia and use of corticosteroids or certain drugs have the potential to be immunosuppressive and are presumed to cause some degree of altered immunocompetence.

Anatomic or Functional Asplenia

Persons with anatomic asplenia (e.g., surgical removal or congenital absence of the spleen) or functional asplenia (as occurs in persons with sickle cell disease) are at increased risk for infection by encapsulated bacteria, especially *S. pneumoniae* (pneumococcus), *N. meningitidis* (meningococcus), and Hib (7-8, 39).

Children should receive an age-appropriate series of PCV13. Unvaccinated children 2-5 years should receive 2 doses of PCV13. Children ≥ 6 years should receive a dose of PCV13 if they have not previously received a dose of PCV13. Persons aged ≥ 2 years should receive 2 doses of PPSV23 separated by 5 years, beginning 8 or more weeks after completing all recommended doses of PCV13 (6-7, 40-41). In circumstances where both PCV13 and PPSV23 are indicated, doses of PCV13 should be administered first followed by PPSV23 8 weeks after the last dose of PCV13.

Meningococcal conjugate (MenACWY) and serogroup B (MenB) vaccines are recommended for persons with anatomic or functional asplenia (including sickle cell disease). For children 2-23 months of age, a series of MenACWY-CRM (Menveo) or Hib-MenCY (MenHibrix) should be administered. For persons ≥ 2 years of age, a 2-dose

primary series of either MenACWY-CRM or MenACWY-D (Menactra) should be administered. If a person with functional or anatomic asplenia is catching up on pneumococcal conjugate vaccine (PCV13), and the provider only carries MenACWY-D, indicated doses of PCV13 should be completed first and MenACWY-D should be given 4 weeks after the PCV13 series is completed. Following the primary series of vaccine, a 3-year interval to the next dose is recommended for asplenic children who received their last previous dose at age younger than 7 years. A 5-year interval for asplenic persons is recommended for persons who received their last previous dose at age 7 years or older. Meningococcal B (MenB) vaccine should be administered as either a 2-dose series of MenB-4C (Bexsero) or a 3-dose series of MenB-FHbp (Trumenba). The same vaccine product must be used for all doses. Based on available data and expert opinion, MenB-4C or MenB-FHbp may be administered concomitantly with MenACWY vaccines, but at a different anatomic site, if feasible. There are presently no recommendations for booster doses of either MenB vaccine.

Hib vaccine is recommended routinely for all children through age 59 months. Children 12-59 months with functional or anatomic asplenia and who are unvaccinated or who received only one dose of Hib disease before 12 months of age should receive 2 doses of Hib vaccine; those who received 2 or more doses of Hib before 12 months of age should receive one additional dose. Unimmunized(a) asplenic patients older than 59 months of age should receive one dose of Hib vaccine. Anyone ≥ 15 months of age who is undergoing a splenectomy and is unimmunized(a) should receive one dose of Hib vaccine.

Pneumococcal, meningococcal, and Hib vaccinations should be administered at least 14 days before elective splenectomy, if possible. If the vaccinations are not administered before surgery, they should be administered after the procedure as soon as the patient's condition is stable.

Corticosteroids

The amount of systemically absorbed corticosteroids and the duration of administration needed to suppress the immune system of an otherwise immunocompetent person are not well defined. Although the immunosuppressive effects of steroid treatment vary, the majority of clinicians consider a dose equivalent to either ≥ 2 mg/kg of body weight or ≥ 20

mg/day of prednisone or equivalent for persons who weigh >10 kg when administered for ≥14 consecutive days as sufficiently immunosuppressive to raise concern about the safety of vaccination with live-virus vaccines (37). This dosage is referred to as “high-dose corticosteroids”. Corticosteroids used in greater than physiologic doses also can reduce the immune response to vaccines.

Vaccination providers should defer live-virus vaccination for at least 1 month after discontinuation of high-dose systemically absorbed corticosteroid therapy administered for ≥14 days. Following vaccination, the decision needs to be made when to restart immunosuppressive therapy. There are no specific recommendations about when to restart immunosuppressive medicines. However, when initiating immunosuppressive therapy, providers should wait 4 weeks after a live vaccine and 2 weeks after a non-live vaccine. However, if patients require therapy for chronic inflammatory conditions, this therapy should not be delayed because of past administration of vaccines (1).

Corticosteroid therapy usually is not a contraindication to administering live-virus vaccine when administration is 1) short term (i.e., <14 days); 2) a low to moderate dose (i.e., <20 mg of prednisone or equivalent per day or <2mg/kg body weight per day for a young child); 3) long-term, alternate-day treatment with short-acting preparations; 4) maintenance physiologic doses (replacement therapy); or 5) topical (skin or eyes), inhaled, or by intra-articular, bursal, or tendon injection (37). No evidence of an increased risk for more severe reactions to live, attenuated viral vaccines has been reported among persons receiving corticosteroid therapy by aerosol, and such therapy is not a reason to delay vaccination.

Other Immunosuppressive Drugs

When feasible, clinicians should administer all indicated vaccines before initiation of chemotherapy, before treatment with other immunosuppressive drugs, and before radiation or splenectomy. Persons receiving chemotherapy or radiation for leukemia and other hematopoietic malignancies, or for solid tumors, should be assumed to have altered immunocompetence. Live, attenuated vaccines should not be administered for at least 3 months after such immunosuppressive therapy. Non-live vaccines administered during chemotherapy should be readministered after immune competence is regained. Children

vaccinated before receiving chemotherapy for leukemia, lymphoma, other malignancies, or radiation generally are thought to retain immune memory after treatment, although revaccination with the common childhood vaccines after chemotherapy for acute lymphoblastic leukemia might be indicated (42).

In general, revaccination of a person after chemotherapy or radiation therapy is considered unnecessary if the previous vaccination occurred before therapy and not during therapy, with the exception of recipients of HSCT, who should be revaccinated as recommended previously. Determination of the level of immune memory and the need for revaccination should be made by the treating physician.

Certain immunosuppressive medications are administered to prevent solid organ transplant rejection. Live vaccines should be withheld for 2 months following discontinuation of anti-rejection therapies in patients with a solid organ transplant.

Other immunosuppressive medications include human immune mediators like interleukins and colony-stimulating factors, immune modulators, and medicines like tumor necrosis factor-alpha inhibitors and anti-B cell agents. Non-live and live vaccines should be administered 2 or more weeks before initiating such therapies. Live vaccines should be withheld 3 months following such therapies, and both non-live and live vaccines should be withheld at least 6 months following therapy with anti-B cell agents. Some experts recommend longer than 6 months following anti-B cell agents.

Anti-B cell agents suppress antibody-producing cells for a prolonged duration, hence the longer interval recommended before administering vaccines (17).

Zoster vaccine is an exception and should be withheld 1 month following anti-B cell agents. After vaccination, anti-B cell agents can be resumed 1 month later.

^(a) Patients who have not received a primary series and booster dose or at least 1 dose of Hib vaccine after 14 months of age are considered unimmunized.

Table 8-1. Vaccination of persons with primary and secondary immunodeficiencies				
Category	Specific types	Contraindications ^(a)	Risk-specific recommended vaccines ^(a)	Effectiveness and comments
Primary: B-lymphocyte (humoral)	Severe antibody deficiencies (e.g., X-linked agammaglobulinemia and common variable immunodeficiency)	OPV ^(b) Smallpox [©] LAIV BCG Ty21a (live typhoid) Yellow fever MMR MMRV DEN4CYD	Pneumococcal Hib (children 12–59 months of age) ^(d) Recombinant zoster vaccine ^(e)	The effectiveness of any vaccine is uncertain if it depends only on the humoral response (e.g., PPSV23) IGIV interferes with the immune response to measles vaccine and possibly varicella vaccine
	Less severe antibody deficiencies (e.g., selective IgA deficiency and IgG subclass deficiency)	OPV ^(b) BCG DEN4CYD Yellow fever ^(f) Other live vaccines appear to be safe	Pneumococcal Hib (children 12–59 months of age) ^(d) Recombinant zoster ^(e)	All vaccines likely effective; immune response might be attenuated
Primary: T-lymphocyte (cell-mediated)	Complete defects (e.g., SCID disease, complete DiGeorge syndrome)	All live vaccines ^{(g), (h), (i)}	Pneumococcal Hib (children 12–59 months of age) ^(d)	Vaccines unlikely to be effective

and humoral)			Recombinant zoster ^(e)	
	Partial defects (e.g., most patients with DiGeorge syndrome, Wiskott-Aldrich syndrome, ataxia-telangiectasia)	All live vaccines ^{(g),(h),(i)}	Pneumococcal Meningococcal Hib (children 12-59 months of age) ^(d) Recombinant zoster ^(e)	Effectiveness of any vaccine depends on degree of immune suppression
	Interferon-alpha deficiencies, interferon-gamma deficiencies	All live vaccines ^{(g), (h)}	Recombinant zoster ^(e)	
	Interferon-gamma/interleukin-12 axis deficiencies	Live bacterial vaccines ^(g)	Recombinant zoster ^(e)	
Primary: phagocytic function	Chronic granulomatous disease	Live bacterial vaccines ^(g)	Recombinant zoster ^(e)	Live viral vaccines likely safe and effective
	Phagocytic deficiencies that are undefined or accompanied by defects in T-cell and NK cell dysfunction (such as a Chediak-Higashi syndrome, Leukocyte Adhesion Deficiency [LAD], and myeloperoxidase deficiency)	Live vaccines ^{(g),(h)}	Pneumococcal Recombinant zoster ^(e)	All non-live vaccines safe and likely effective
Primary: complement	Persistent complement, properdin, or Factor B deficiency	None	Pneumococcal Meningococcal Hib (children 12-59 months of age) ^(d)	All routine vaccines likely effective

Secondary	HIV/AIDS	<p>OPV^(b) Smallpox BCG LAIV Ty21a MMRV DEN4-CYD</p> <p>Withhold MMR, and varicella in severely immunocompromised persons</p> <p>Yellow fever vaccine might have a contraindication or a precaution depending on clinical parameters of immune function^(j)</p>	Pneumococcal Hib ^{(d),(k)} HepB MenACWY Recombinant zoster ^(e)	MMR and Varicella vaccine in those with mild immunosuppression, rotavirus, and all non-live vaccines, including inactivated influenza as per routine vaccination schedule, might be effective ^(l)
	Generalized malignant neoplasm, transplantation, immunosuppressive or radiation therapy	Live viral and bacterial, depending on immune status ^{(g),(h),(m)}	Pneumococcal Hib ^(m) Recombinant zoster ^(e)	Effectiveness of any vaccine depends on degree of immune suppression
	Taking eculizumab (Solaris), and/or ravulizumab (Ultomiris)	None	Meningococcal	
	Asplenia	LAIV	Pneumococcal Meningococcal Hib ^{(d),(o)}	
	Chronic renal disease	None	Pneumococcal HepB ^(p)	All routine vaccines likely effective

Abbreviations: AIDS = acquired immunodeficiency syndrome; BCG = bacille Calmette-Guérin; HepB = hepatitis B; Hib = *Haemophilus influenzae* type b; HIV = human immunodeficiency virus; IG = immunoglobulin; IGIV = immune globulin intravenous; IgA = immune globulin A; IgG = immune globulin G; LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella; MMRV = measles, mumps, rubella, and varicella; OPV = oral poliovirus vaccine (live); PPSV23= pneumococcal polysaccharide vaccine; SCID = severe combined immunodeficiency; Ty21a = live oral typhoid vaccine.

Source: (43).

- (a) Other vaccines that are universally or routinely recommended should be given if not contraindicated. An exception is patients with B-cell deficiencies receiving immunoglobulins, who should not receive either live or non-live vaccines, due to safety (live vaccines) and efficacy (live and non-live vaccines) concerns.
- (b) OPV is no longer available in the United States.
- (c) This table refers to contraindications for nonemergency vaccination (i.e., the ACIP recommendations); emergency response recommendations are addressed in the clinical guidance for smallpox vaccine use in an emergency.
- (d) Children 12-59 months: if unimmunized or received zero or only 1 dose, and that dose was administered before 12 months of age, should receive 2 Hib doses, 8 weeks apart; if received 2 or more doses before age 12 months, and none after 12 months, should receive 1 Hib dose 8 weeks after the last dose; if completed a primary series and received a booster dose at age 12 months or older, no additional Hib doses are recommended.
- (e) 19 years and older only.
- (f) There are no data to support IgA deficiency as a contraindication for yellow fever vaccine.
- (g) Live bacterial vaccines: BCG and oral Ty21a *Salmonella Typhi* vaccine.
- (h) Live viral vaccines: MMR, MMRV, OPV, LAIV, yellow fever, rotavirus, varicella, and vaccinia (smallpox). Nonemergency smallpox vaccination is not recommended for children younger than 18 years or the general public.
- (i) Regarding T-lymphocyte immunodeficiency as a contraindication for rotavirus vaccine, data exist only for SCID.
- (j) Symptomatic HIV infection or CD4+ T-lymphocyte count of $<200/\text{mm}^3$ or $<15\%$ of total lymphocytes for children aged <6 years is a contraindication to yellow fever vaccine administration. Asymptomatic HIV infection with CD4+ T-lymphocyte count of $200-499/\text{mm}^3$ for persons aged ≥ 6 years or $15\%-24\%$ of total lymphocytes for children aged <6 years is a precaution for yellow fever vaccine administration. Details of yellow fever vaccine recommendations are available from CDC (44)
- (k) Patients 5-18 years of age who have not received a Hib primary series and a booster dose or at least one Hib dose after 14 months of age.
- (l) HIV-infected children should be considered for varicella vaccine if CD4+ T-lymphocyte count is $\geq 15\%$ and should receive MMR vaccine if they are aged ≥ 12 months and do not have 1) evidence of current severe immunosuppression (i.e.,

individuals aged ≤ 5 years must have CD4+T lymphocyte [CD4] percentages $\geq 15\%$ for ≥ 6 months; and individuals aged > 5 years must have CD4+percentages $\geq 15\%$ and CD4+ ≥ 200 lymphocytes/mm³ for ≥ 6 months) and 2) other current evidence of measles, rubella, and mumps immunity. In cases when only CD4+cell counts or only CD4+percentages are available for those older than age 5 years, the assessment of severe immunosuppression can be based on the CD4+values (count or percentage) that are available. In cases when CD4+percentages are not available for those aged ≤ 5 years, the assessment of severe immunosuppression can be based on age-specific CD4+counts at the time CD4+counts were measured; i.e., absence of severe immunosuppression is defined as ≥ 6 months above age-specific CD4+count criteria: CD4+count > 750 lymphocytes/mm³ while aged ≤ 12 months and CD4+count ≥ 500 lymphocytes/mm³ while aged 1 through 5 years (33).

(m) Withholding non-live vaccines also is recommended with some forms of immunosuppressive therapy, like anti-CD20 antibodies, induction or consolidation chemotherapy, or patients with major antibody deficiencies receiving immunoglobulins. Inactivated influenza vaccine is an exception, but consideration should be given to repeating doses of any non-live vaccine administered during these therapies.

(n) Persons younger than 60 months undergoing chemotherapy or radiation therapy who have not received a Hib primary series and a booster dose or at least one Hib dose after 14 months of age; HSCT patients of any ages, regardless of Hib vaccine history.

(o) Persons older than 59 months who are asplenic and persons 15 months or older who are undergoing elective splenectomy who have not received a Hib primary series and a booster dose or at least one Hib dose after 14 months of age.

(p) Hepatitis B vaccine is recommended for all persons birth through 59 years of age. Hepatitis B vaccine is also recommended for patients with chronic renal disease in all age groups (including 60 years old and older) based on the risk from dialysis-based bloodborne transmission.

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