# Background

Providing appropriate immunizations is an important component of comprehensive HIV clinical care. Immunizing persons with HIV poses several challenges and concerns related to safety and efficacy. The immunizations topics discussed in this review are ordered alphabetically based on the vaccine.

## Recommendations by Organizations

The Advisory Committee on Immunization Practices (ACIP) provides annual recommendations for routine immunizations of adults, including HIV-specific recommendations.[1] In 2013, the Infectious Disease Society of America (IDSA) issued IDSA Vaccine Guidelines for the Immunocompromised Host, but these guidelines have not been updated.[2] Unfortunately, some differences exist in the recommendations provided by the different organizations, which creates a challenge for clinicians. This topic review will focus on common adult immunizations (Table 1),[3] with a discussion of specific recommendations for adults living with HIV (Table 2).[1]

## Safety Concerns

Early in the HIV epidemic, several reports generated concern that vaccinations in persons with HIV could activate their cellular immune system and enhance HIV replication, thereby increasing HIV RNA levels and potentially accelerating the course of HIV disease.[4] These reports, however, involved persons with HIV who were not receiving potent antiretroviral therapy and investigators subsequently demonstrated that post-immunization increases in HIV RNA levels were transient and clinically insignificant. Further, in persons taking modern highly potent antiretroviral therapy, immunizations generally do not cause any detectable increases in plasma HIV RNA levels. Current guidelines recommend that immunizations should not be withheld in persons with HIV due to concerns of increases in HIV RNA levels.[2,5]

## Risk of Live Vaccines in Persons with HIV Infection

Immunizations are generally safe in individuals with HIV, with the exception of live virus vaccines in patients with low CD4 counts. In persons with HIV who have advanced immunosuppression, live vaccines can cause a potentially life-threatening disseminated infection with the live pathogen in the vaccine.[6]

## Challenges with Efficacy

Unfortunately, current or past advanced immunosuppression in persons with HIV is often associated with suboptimal responses to standard recommended vaccine doses; response to several vaccines
appears to depend on current and nadir CD4 cell counts.[7, 8, 9, 10] In general, responses to immunization are better when the vaccine is given as early as possible in the course of HIV infection or after immune reconstitution that has resulted from antiretroviral therapy.
**Haemophilus influenzae type b (Hib) Vaccine**

**Background**

*Haemophilus influenzae* infection is more common in adults with HIV than in the general population, but the annual incidence remains relatively low at 41/100,000 adults with HIV.[11] Only about one-third of cases of invasive *H. influenzae* involve type b, which is the type in the currently licensed vaccines. Multiple identifiable subtypes of *H. influenzae* and other unidentifiable types (called nontypeable *H. influenzae*) can cause a wide range of clinical disease, including bacteremia, meningitis, pneumonia, epiglottitis, cellulitis, and infectious arthritis. Infants and children younger than five years of age, adults over the age of 65, and Native American and Alaskan Indian populations are all at higher risk of disease.[12] Certain medical conditions also predispose individuals to *H. influenzae* disease, such as HIV, sickle cell disease, asplenia, complement and antibody deficiency syndromes, and receipt of chemotherapy, radiation or hematopoietic stem cell transplant. The conjugate *H. influenzae* type b vaccine is safe and effective in all age groups.[13]

**Vaccines**

The currently licensed *Haemophilus influenzae* type b conjugate vaccines are *Hiberix, ActHIB*, and *PedvaxHIB*. Additional Hib conjugate vaccines are licensed in combination with other vaccines, including *Comvax* (Hib combined with hepatitis B vaccine), *Pentacel* (Hib combined with DTaP and inactivated polio virus), and *MenHibrix* (Hib combined with meningococcal vaccine).

**Recommendations**

- Due to the low incidence of *H. influenzae* type b infections among adults with HIV, *H. influenzae* type b immunization is not recommended for routine administration to adults with HIV.[14]
- Per the 2019 ACIP Adult Immunization Schedule, one dose of Hib vaccine should be administered to adults with HIV only if they have an indication for the vaccine, namely sickle cell disease, leukemia, or anatomic or functional asplenia.[1]
Hepatitis A Virus (HAV) Vaccine

Background

Hepatitis A virus (HAV) is transmitted through food, water, or objects contaminated with fecal matter. Infection with HAV is usually an acute, self-limiting condition that does not require treatment though it can rarely cause fulminant liver failure. Rates of HAV infection in the United States have markedly declined in the past 20 years, likely due to the widespread use of the hepatitis A vaccine since 1995. During the last several years, however, rates have increased dramatically as a result of multiple outbreaks that have primarily involved homeless persons, men who have sex with men, persons who inject drugs, and to a lesser degree, with consumption of imported contaminated food. For persons with HIV, the hepatitis A vaccines are safe and moderately effective, though seroconversion rates may be diminished for individuals with lower CD4 cell counts. One randomized control study found seroconversion rates of 94% in persons with HIV compared to 100% in persons without HIV infection, though rates were only 87% in patients with CD4 counts less than 300 cells/mm$^3$. In another randomized control trial, after two doses of hepatitis A vaccine, seroconversion rates were observed in 68% of persons with HIV who had a CD4 count greater than or equal to 200 cells/mm$^3$ compared to only 9% of those with CD4 counts less than 200 cells/mm$^3$.

Vaccines

Hepatitis A vaccine is an inactivated vaccine that can be given either as Havrix or Vaqta, or as part of a combination vaccine (Twinrix) that contains both inactivated hepatitis A and recombinant hepatitis B vaccine. Havrix contains 1,440 ELISA units (El.U) of hepatitis A antigen and Vaqta contains 50 units (U) of inactivated hepatitis A; Twinrix contains 720 El.U of hepatitis A antigen (half of the Havrix dose) combined with 20 mcg of hepatitis B antigen (the full Engerix-B dose). The two brands of hepatitis A are interchangeable.

Recommendations

The following summarizes the 2019 ACIP Adult Immunization Schedule for administering hepatitis A vaccine to persons with HIV.

- **General Approach:** Administer Hepatitis A vaccination to all persons with HIV at risk of encountering hepatitis A virus, including men who have sex with men, homeless individuals, health care workers, persons with hemophilia, persons who inject drugs, persons working in or traveling to parts of the world that have high or intermediate hepatitis A endemicity, and patients with chronic liver disease.

- **Timing of Vaccine:** Persons with HIV should be vaccinated against hepatitis A prior to a decline in CD4 counts (and after virologic response to antiretroviral therapy) to improve the likelihood of an adequate response, but vaccination should not be delayed in individuals at risk for hepatitis A acquisition. For patients with advanced immunosuppression, most experts recommend deferring the hepatitis A immunization until the CD4 count has increased to greater than 200 cells/mm$^3$ in response to highly effective antiretroviral therapy. In the context of the ongoing outbreak of HAV infection in the United States, the CDC has suggested administering a one-time hepatitis A vaccination, with age-appropriate dosing, to individuals at risk for HAV acquisition and in whom prior immunity cannot be verified in a timely fashion.

- **Recommended Dosing Schedule:** The ACIP Adult Immunization Schedule recommends administering hepatitis A vaccine in two doses at 0 and 6 to 12 months (Havrix) or 0 and 6 to 18 months (Vaqta); the minimum interval before the first and second dose of these vaccines is 6 months. The combined hepatitis A-hepatitis B vaccine (Twinrix) can also be administered as a 3-dose series (0, 1, and 6 months); the minimum intervals are 4 weeks.
between the first and second doses and 5 months between the second and third doses. \[1\]
**Hepatitis B Virus (HBV) Vaccine**

**Background**

Hepatitis B virus (HBV) is transmitted through percutaneous and mucosal exposure to infected blood or body fluids. Chronic infection with HBV can cause cirrhosis, liver failure, hepatocellular cancer, and death. Individuals with HIV have an increased risk of acquiring HBV through injection drug use and/or condomless sex. When compared to persons with HBV monoinfection, those coinfected with HIV and HBV have an increased likelihood of establishing chronic HBV after initial infection, accelerated progression of liver disease, and significantly higher rates of liver-related mortality compared with individuals not infected with HIV.\[20,21\] In light of these risks, vaccination against HBV is very important for persons with HIV infection. Unfortunately, hepatitis B vaccine response rates in adults with HIV are significantly lower than in adults without HIV, with response rates in persons with HIV, ranging from 18 to 71% in persons with HIV compared to 60 to 80% in those without HIV.\[22,23\] Lower HBV vaccine response in persons with HIV have been associated with a recent or nadir CD4 count less than 200 cells/mm\(^3\), detectable HIV RNA levels, and coinfection with hepatitis C virus.\[10,22\] Attempts to improve hepatitis B vaccine response rates have included giving a double dose (40 mcg of the hepatitis B surface antigen [HBsAg] instead of 20 mcg), increased number of doses (four instead of three), and using intradermal rather than intramuscular dosing.\[24,25,26\]

**Vaccines**

For adults, there are three FDA-approved HBsAg recombinant vaccines hepatitis that are widely used: *Recombivax-HB*, *Engerix-B*, and *Heplisav-B*). The *Engerix-B* vaccine is available in doses that contain 20 mcg of HBsAg. The *Recombivax-HB* is available as a standard 10 mcg HBsAg per dose and a high-dose dialysis formulation (40 mcg per dose). A combined hepatitis A-hepatitis B (*Twinrix*) vaccine is also available, which contains 20 mcg per dose of HBsAg and 720 El.U of hepatitis A. The *Heplisav-B*, which includes the CpG adjuvant, is available in doses that each contain 20 mcg of HBsAg and 3,000 μg of the 1018 adjuvant;\[27\] four randomized trials performed in immunocompetent persons have shown that two doses of *Heplisav-B* vaccine generated a higher rate of seroprotection than three doses of the *Engerix-B* vaccine.\[28,29,30,31\]

**Recommendations**

The recommendations for hepatitis B immunization in persons with HIV differ among several existing guidelines as outlined below.\[2,20,32\]

- **General Approach**: All persons with HIV who do not have active HBV or evidence of immunity to HBV should be vaccinated with a hepatitis B vaccine.
- **Prevaccine Screening**: Pre-vaccine screening should include HBsAg, anti-HBs, and anti-HBc. A positive HBsAg indicates active infection and no vaccine is indicated. If the patient has a positive anti-HBs and anti-HBc, the patient does not need immunization. In addition, if the anti-HBs alone is positive (with a titer greater than 10 IU/mL), the patient is considered immune and has no need for hepatitis B immunization.\[20\] The approach to patients with isolated anti-HBc is addressed below.
- **Timing of Vaccine**: The Adult and Adolescent Opportunistic Infection Guidelines recommend providing hepatitis B vaccine to non-immune individuals at entry into care and before CD4 count declines to less than 350 cells/mm\(^3\).\[20\] In addition, the guidelines recommend that patients who initially present with a low CD4 count should receive hepatitis B vaccine without delay, since some patients with a low CD4 will respond to the vaccine.
- **Dose and Schedule**: Expert recommendations regarding the dose and schedule of hepatitis
B vaccine administration in persons with HIV infection range from giving a standard vaccine dose for *Engerix-B* and *Recombivax-HB* on a three-vaccine dose schedule (0, 1, and 6 months) to double-dose vaccine strength on a three- or four-dose schedule. Although low CD4 count and high HIV RNA levels are associated with poorer vaccine response, there are no specific guidelines as to timing of vaccination relative to CD4 count or HIV RNA status. The hepatitis B vaccine conjugated to CpG (*Heplisav-B*) vaccine in healthy adults requires only 2 doses, given intramuscularly 1 month apart, and in April 2018, the ACIP recommended the *Heplisav-B* for use in persons 18 years of age and older.[27]

- **ACIP Dosing Recommendation:** The 2019 ACIP Adult Immunization Schedule does not give any specific hepatitis B dosing recommendations for persons with HIV.[1]
- **Opportunistic Infections Guideline Dosing Recommendation:** The Adult and Adolescent Opportunistic Infection Guidelines recommend the following for hepatitis B vaccine in persons with HIV:[20]
  - Standard 3-dose series of hepatitis B vaccine (*Engerix-B* or *Recombivax-HB*) given at 0, 1, and 6 months (*AII*), or
  - Double doses of hepatitis B vaccine given as a 4-dose series at 0, 1, 2, and 6 months (*BII*), or
  - Combined hepatitis A and B vaccine given as a 3-dose series (0, 1, 2, and 6 months) or a 4-dose series (0, 7, and 21 to 30 days, and 6 months) (*AII*), or
  - Vaccine conjugated to CpG (*Heplisav-B*) given as a 2-dose series at 0 and 1 months;
    this 2-dose series is only recommended if both doses given are *Heplisav-B* (*CIII*).

- **Post-vaccine Antibody Testing:** Given the decreased response rate to hepatitis B vaccine in the setting of HIV infection, persons with HIV infection should have testing for antibody to hepatitis B surface antigen (anti-HBs) 1 to 2 months after completing the final dose of the vaccine series, with a titer of at least 10 mIU/mL considered protective; persons with post-vaccine anti-HB less than 10 mIU/mL are considered as vaccine nonresponders.[2, 20]
- **Repeat Immunization for Vaccine Nonresponders:** If a post-vaccination anti-HBs concentration of at least 10 mIU/mL is not attained, the Adult and Adolescent Opportunistic Infection Guidelines recommend the following as options for these vaccine nonresponders:
  - Administer a 4-dose series of double-dose hepatitis B vaccine given at 0, 1, 2, and 6 months (*BII*).
  - Give a second hepatitis B vaccine series (using a standard dose) (*BIII*).
  - If the CD4 cell count was less than 200 cells/mm$^3$ at the time of the initial vaccine series, some experts would recommend delaying the second vaccine series until the patient has a sustained increase in CD4 count in response to antiretroviral therapy (*CIII*).
- **Isolated Core Antibody:** The optimal approach for patients with HIV infection with isolated anti-HBc (positive anti-HBc, negative anti-HBs, and negative HBsAg) is unclear since this pattern may signify a false positive result, exposure in the distant past with waning anti-HBs, or occult HBV infection. The Adult and Adolescent Opportunistic Infection Guidelines recommend administering one standard dose of hepatitis B vaccine and then checking an anti-HBs titer 1 month later. If the anti-HBs titer is greater than 100 IU/mL then no additional hepatitis B vaccines need to be administered and the person is considered immune to HBV. If the anti-HBs titer is less than 100 IU/mL, then a full hepatitis B vaccine series should be administered and post-vaccine anti-HBs titer checked.
Human Papillomavirus (HPV) Vaccine

Background

Individuals with HIV have a high burden of human papillomavirus (HPV)-associated disease compared to persons who do not have HIV: genital warts are more common in women and men, abnormal cervical cytology is nearly 11 times more common in women, and anal cancer is approximately 30-fold higher among men.[33,34,35] For persons with HIV, the impact of the widespread use of antiretroviral therapy on the incidence of cervical cancer in women and anal cancer in men is uncertain.[36,37,38] Early studies reported unchanged or increasing incidence of these cancers, suggesting a reversal of HIV-induced immunosuppression does not overcome the long latency of the carcinogenic effects of HPV.[35,39] More recent reports in persons with HIV have found a marked decline in cervical and anal cancer risk in women and men.[40] In addition, population level analyses of large HPV vaccination programs have demonstrated a reduced prevalence of HPV subtypes responsible for cervical cancer and genital warts in adolescent girls and boys, thereby signaling significant future benefit, both directly from immunization and indirectly through herd immunity.[36] Further, a recent study that examined the prevalence of vaccine-type oral HPV in a large sample of unvaccinated men, aged 18 to 59 years, noted a 37% decline between 2009-2010 and 2015-2016.[41]

Vaccines

Three HPV vaccines have been approved by the United States FDA: bivalent (2vHPV), quadrivalent (4vHPV), and 9-valent (9vHPV).[42] In the United States, the 9vHPV vaccine is the only HPV vaccine currently manufactured. The 9vHPV vaccine includes the same 4 serotypes included in 4vHPV (6, 11, 16, and 18) and 5 additional cancer-causing HPV types (31, 33, 45, 52, and 58).[42] The HPV types 16 and 18 account for approximately 66% of cases of cervical cancer, HPV types 6 and 11 account for approximately 90% of genital warts, and serotype 31, 33, 45, 52, and 58 combined account for approximately 15% of cervical cancers and 10% of invasive HPV-associated cancers.[42] The HPV vaccines are prepared from recombinant noninfectious virus-like particles and are considered safe for immunocompromised individuals since they do not pose any risk of transmitting infection (Figure 1). The 9vHPV vaccine is FDA-approved for use in females and males 9 through 45 years of age.[43] Use of HPV vaccination in persons with HIV is safe and effective, with seroconversion rates of 95% in men 18 years of age and older who received the quadrivalent vaccine, and seroconversion rates of 92.3 to 100% among women with HIV aged 16 to 23 years who received the quadrivalent vaccine.[37,38] Being on suppressive antiretroviral therapy may improve vaccine response.[37]

Recommendations

- **General Approach:** The 2019 ACIP Adult Immunization Schedule and the updated recommendations of the ACIP for HPV vaccination of adults recommend administering the 9vHPV vaccine routinely for females and males with HIV who are 9 through 26 years of age.[1,44] The 9vHPV vaccine is recommended to start in children at age 11 years, but can be given at any time through 26 years of age. Administering the 9vHPV vaccine is based on the patient's age and not on past sexual history, HPV or Pap smear testing, or history of genital warts.
- **Dosing Recommendation:** For persons with HIV, the HPV vaccination should be given in a 3-dose series (given at 0, 1-2, and 6 months).[42] A 2-dose schedule is now recommended for healthy boys and girls 9 through 14 years of age, but this 2-dose series should not be used in persons with HIV.[45]
- **Recommendation for Adults Older than 26:** On October 5, 2018, the U.S. FDA approved the expanded use of the 9vHPV vaccine in persons 27 through 45 years of age.[43] The ACIP recommends that persons 27 to 45 years of age who have not previously received HPV vaccine engage in shared decision making with their clinician regarding vaccination with
9vHPV, as the public health benefit of 9vHPV in older individuals is not clear since many individuals in this age range have already been infected with multiple HPV types.[44] Currently, however, the Adult and Adolescent Opportunistic Infection Guidelines have not extended the HPV vaccination to persons with HIV who are older than age 26 years.[46]

- **HPV Vaccine in Pregnancy**: The ACIP Adult Immunization Schedule recommends against administering HPV vaccine to pregnant women, but pregnancy testing is not needed prior to vaccination.[1,42] If a woman is found to be pregnant after vaccination, no intervention is needed; if a woman has started the vaccine series and becomes pregnant, the remainder of the 3-dose series should be delayed until completion of pregnancy. The largest HPV vaccine pregnancy registry to date shows no adverse signals and at this time, pregnancy registries for the bivalent and quadrivalent vaccines have been closed.[42,47] In addition, recent data with 4vHPV suggest that HPV vaccine is safe when given during pregnancy.

- **Use as Therapeutic Vaccine**: The HPV vaccine is not recommended for therapeutic purposes in patients with HPV-related abnormal cervical or anal cytology.
Influenza Vaccine

Background

Influenza viruses typically circulate widely in the United States annually from the late autumn through early spring. Influenza A and influenza B are the types of viruses that cause human epidemic disease. New variants emerge due to frequent antigenic change (i.e. antigenic drift) resulting from point mutations and recombination events that occur during viral replication; antigenic drift is the virologic basis for seasonal epidemics and necessitates adjustment of the vaccine components each year.\[48\] Larger antigenic change, termed antigenic shift, has the potential to cause a worldwide pandemic since there is no pre-existing immunity among humans to the novel virus in this situation. Annual influenza vaccination is the primary means of preventing influenza and its complications. Persons with HIV have a higher risk of influenza-associated morbidity and mortality compared to the general population.\[49\] Studies in individuals with HIV suggest a single dose of inactivated vaccine generates a good humoral immune response, which does not improve significantly with the second dose. In persons with HIV who have a low CD4 cell count, the influenza vaccine does not generate good immune responses.\[8\]

Vaccines

Adults with HIV, including pregnant women, can receive inactivated influenza vaccine (IIV). The inactivated influenza vaccine options now include trivalent (contains two strains of influenza A and one of influenza B) and quadrivalent vaccines (contains two strains of both influenza A and B). A recombinant quadrivalent influenza vaccine (RIV) that does not contain any egg protein is approved for adults 18 to 49 years of age. The quadrivalent live attenuated influenza vaccine (LAIV), also known as the nasal spray flu vaccine, has not been adequately studied for use in immunocompromised individuals, including patients with HIV infection, and experts do not recommend giving living attenuated influenza vaccine to persons with HIV infection due to concern that attenuated virus could lead to actual infection and result in prolonged viral shedding.

Recommendations

The following summarizes the 2019 ACIP Adult Immunization Schedule for administering influenza vaccine to persons with HIV infection.\[1\]

- **General Approach**: All persons with HIV should receive a single annual dose influenza vaccine.
- **Recommended Vaccines**: Recommended routine influenza vaccines for persons with HIV infection include inactivated influenza vaccine (IIV) or recombinant influenza vaccine (RIV).
- **Contraindicated Vaccine**: The live attenuated influenza vaccine (LAIV) should not be administered to persons with HIV infection.
- **Persons with Egg Allergy**: The recombinant influenza vaccine (RIV), which does not use an egg-based culture system, is available and safe for persons with an egg allergy.
- **Persons 65 and Older**: Adults with HIV infection aged 65 years or older can receive the standard-dose inactivated influenza vaccine (IIV), adjuvanted inactivated quadrivalent influenza vaccine, or quadrivalent high-dose inactivated influenza vaccine.
**Measles-Mumps-Rubella (MMR) Vaccine**

**Background**

Measles, mumps, and rubella are highly contagious viruses that can cause a wide range of clinical disease, including congenital syndromes. Since the introduction of the measles-mumps-rubella (MMR) vaccine, the incidence of these viral diseases has decreased by 99%. Nevertheless, despite excellent MMR vaccine coverage in the United States, sporadic outbreaks continue to occur. Due to low immunization rates, measles cases in Europe reached 41,000 cases during the first half of 2018, more than twice the reported number compared to years 2010 through 2017, thus posing a risk to United States travelers. Similarly, between January and July 2019, more than 1,100 cases of measles were diagnosed in the United States, which is the largest number of annual cases reported in the United States since 1992 (Figure 2).

**Impact of Measles in Persons with HIV**

Measles can cause significant morbidity and mortality in healthy individuals, and the impact is even greater in immunosuppressed persons, with one case report citing 40% mortality in patients with HIV infection. Studies suggest that most individuals with HIV in the United States have adequate antibody titers to measles, although data from an ongoing observational cohort of United States Department of Defense beneficiaries found a seroprevalence of measles immunity of only 67%. Adults born before 1957 are considered immune to measles. Based on limited available data, the immunologic responses to the MMR vaccine among individuals with HIV infection is modest at best, and the protection of the vaccine in these persons is not well established; MMR does not appear to have any significant detrimental impact on either CD4 count or HIV RNA levels.

**Measles Vaccines**

In the United States, in 1963 both live attenuated measles vaccine and the inactivated measles vaccine became available for use. In 1967, the inactivated vaccine was discontinued after it was shown to be ineffective. In 1971, the MMR vaccine became available and is still widely used. There is also a quadrivalent measles-mumps-rubella-varicella (MMRV) vaccine that is approved by the FDA, but it is rarely used in adults. All measles vaccines that are currently used contain live attenuated measles virus and thus pose significant risk to severely immunocompromised individuals. There have been case reports of fatal pneumonitis in patients with advanced immunosuppression who received the MMR vaccine.

**Recommendations**

The following summarizes the 2019 ACIP Adult Immunization Schedule recommendation for administering MMR to persons with HIV.

- **General Approach**: For persons with HIV and a CD4 count of 200 cells/mm$^3$ or greater (for at least 6 months) and who do not have immunity to measles, give the two-dose MMR vaccine series, with the doses administered at least 4 weeks apart.
- **Persons with CD4 Count Less than 200 cells/mm$^3$**: The MMR and MMRV vaccines are contraindicated in persons with HIV infection who have a CD4 count less than 200 cells/mm$^3$.
- **Quadrivalent Measles-Mumps-Rubella-Varicella (MMRV) Vaccine**: The quadrivalent MMRV vaccine is not recommended in persons with HIV, regardless of CD4 cell count.
- **MMR in Pregnancy**: The MMR vaccine is contraindicated during pregnancy, and pregnancy should be avoided for 28 days after vaccination to minimize the theoretical risk of congenital rubella syndrome. Women without evidence of rubella immunity and a CD4 count of at least 200 cells/mm$^3$ should receive MMR vaccination upon completion or termination of pregnancy and before discharge from the health facility.
• **Persons who Received Measles Vaccine During 1963 through 1967**: Receipt of the inactivated (ineffective) measles vaccine, which was an option during 1963 through 1967, does not count as a dose of measles vaccine.\[54\] In addition, if the type of measles vaccine received during 1963-1967, is not known, then it does not count as a dose.\[54\]
Meningococcal Vaccine

Background

Meningococcal meningitis, which is caused by *Neisseria meningitidis*, can cause severe complications, including brain damage, hearing loss, and learning disabilities. Risk factors that can increase a person’s risk of acquiring meningitis include very young age (infants are at highest risk), community setting (college dormitory, military barracks), travel to endemic regions, and certain medical conditions, including HIV. Available data from population studies suggest that persons with HIV infection have an increased risk of developing meningococcal disease, with the relative risk estimated at 5- to 13-fold higher than in persons without HIV infection; the risk in persons with HIV infection appears to be higher with low CD4 cell counts and high HIV RNA levels.\[56\] In addition, several local outbreaks of meningococcal meningitis have been reported in the United States involving gay and bisexual men.\[57, 58, 59\] Unpublished CDC data from 62 cases of meningococcal disease in persons with HIV infection found that serogroup C was the most common isolate, followed next by serogroup Y (Figure 3).\[56\] As with other vaccines given to individuals with HIV infection, low CD4 count and HIV RNA above 10,000 copies/mL are associated with decreased meningococcal vaccine response rate.\[60\]

Vaccines

Two quadrivalent meningococcal conjugate vaccines (MenACWY) covering groups A, C, W-135, and Y are licensed and available for use in the United States: MenACWY-D and MenACWY-CRM.\[56\] MenACWY is preferred for use in adults 55 years of age and younger as well as for adults aged 56 years and older who were either previously vaccinated with MenACWY and are recommended for revaccination, or in whom multiple doses are anticipated. Meningococcal polysaccharide vaccine (MPSV4) is preferred for adults 56 years of age and older who have not received MenACWY previously and who require a single dose only (e.g. travelers). In addition, serogroup B meningococcal vaccines (MenB) are now available, including MenB-4C, given as a 2-dose series and MenB-FHbp given as a 3-dose series. Both of the MenB vaccines are approved for persons aged 10 to 25 years old who have increased risk for meningococcal disease.

Recommendations

The following summarizes the recommendations in the 2019 ACIP Adult Immunization Schedule regarding administering conjugate meningococcal vaccine to persons with HIV.\[1\] The recommendation to routinely administer conjugate meningococcal vaccine was first published by the ACIP in 2016.\[56\]

- **General Approach**: Routine administration of meningococcal conjugate vaccine (serogroups A, C, W, Y) is recommended for persons with HIV infection; if possible, the same product of the meningococcal vaccine should be used for all doses.

- **Dosing Recommendations**: For persons 2 years or older, give 2 doses (8 to 12 weeks apart) of either MenACWY-D or MenACWY-CRM.

- **Booster Doses**: For persons who were at least 7 years of age when they received the primary vaccine series, follow-up booster doses should be given every 5 years beginning 5 years after the initial series.

- **Conjugate Meningococcal B Vaccine**: Routine administration of conjugate meningococcal B vaccine is not recommended for persons with HIV infection.
Pneumococcal Vaccine

Background

In the general population, *Streptococcus pneumoniae* causes significant disease, including bacteremia, meningitis, and pneumonia, and is responsible for approximately 4,000 deaths each year in the United States. In the early years of the HIV epidemic, the risk of invasive pneumococcal disease in persons with HIV was approximately 20 times higher than in adults without high-risk conditions.\[61\] Subsequently, the incidence of invasive pneumococcal disease has decreased in persons with HIV, likely due to (1) the widespread use of potent antiretroviral therapy that resulted in improved immune function and improved humoral responses to pneumococcal antigens during clinical infections, and (2) population herd protection against invasive strains of *S. pneumoniae* following the widespread use of conjugate pneumococcal vaccines in children since 2000.\[62,63,64,65,66\] A study that examined the risk of invasive pneumococcal disease in persons with HIV during 1996 through 2011 at a large integrated healthcare system in the United States reported a sevenfold increased risk of invasive pneumococcal disease in adults with HIV compared with adults without HIV.\[67\]

Efficacy of Pneumococcal Immunization in Persons with HIV Infection

There are limited data that have addressed the efficacy of pneumococcal vaccination in persons with HIV. Retrospective studies indicate the 23-valent pneumococcal polysaccharide vaccine (PPSV23) alone has modest clinical benefit, if any, in reducing rates of pneumococcal infections in persons with HIV. In addition, the immunologic response to PPSV23 is impaired in persons with CD4 counts below 200 cells/mm\(^3\).\[65,68\] Based on the lack of convincing data with PPSV23, significant interest emerged in using the conjugate pneumococcal vaccine, in combination with PPSV23. Further interest was generated after investigators demonstrated enhanced antibody responses to PPSV23 after initial immunization with the 7-valent conjugate pneumococcal vaccine (PCV7).\[69\] There are no published trials using the 13-valent pneumococcal conjugate vaccine (PCV13) in adults with HIV, but a randomized controlled trial in Malawi that used two doses of PCV7 given 1 month apart in 496 adults (88% with HIV infection) demonstrated a vaccine efficacy of 74% in preventing invasive pneumococcal disease; this study included a large number of patients with a CD4 count less than 200 cells/mm\(^3\).\[70\] No data exist regarding the efficacy of the combined PCV13 plus PPSV23 vaccine regimen—the combination recommended for persons with HIV infection.

Vaccines

Two different pneumococcal vaccines are now available for use in the United States: PCV13 and PPSV23.\[61\] The PCV13 contains antigens from 13 common *S. pneumoniae* serotypes.\[71\] The PCV13 was approved by the United States Food and Drug Administration (FDA) in 2011 and it replaced the previously used PCV7. Of note, the PCV13 serotypes include all 7 serotypes in PCV7 (Figure 4).\[71\]

Recommendations

The ACIP Adult Immunization Schedule for pneumococcal immunization in adults with HIV infection combines the use of PCV13 and PPSV23, with the exact schedule based on age and whether the individual has previously received pneumococcal vaccine (Figure 5).\[1,61\]

- **General Approach**: In general, pneumococcal immunization should be given to all adults with HIV, ideally prior to CD4 decline and preferably after receipt of suppressive antiretroviral therapy. For individuals who have already experienced advanced immunosuppression and have a CD4 count less than 200 cells/mm\(^3\), the PCV13 should be given without delay. In contrast, the timing of when to initiate PPSV23 in patients with advanced immunosuppression...
(CD4 count less than 200 cells/mm$^3$) remains unclear. Many experts would defer PPSV23 component until the individual achieves an increase in the CD4 count to greater than 200 cells/mm$^3$ as a result of suppressive antiretroviral therapy.[14, 72]

- **No Prior Pneumococcal Immunization:** Adults with HIV who have never received pneumococcal vaccine should first receive one dose of PCV13, regardless of CD4 count, followed by a dose of PPSV23 (at least 8 weeks later). Note that if the CD4 count is less than 200 cells/mm$^3$, it may be preferable to defer PPV23 until after the CD4 count increases to greater than 200 cells/mm$^3$ on suppressive antiretroviral therapy. Revaccination with a dose of PPSV23 should occur at least 5 years after the first dose of PPSV23. If the person received their revaccination dose of PPSV23 prior to age 65, they should receive a third dose of PPSV23 after age 65 (and at least 5 years after the last dose of PPSV23).

- **Received One Prior Dose of PPSV23:** Adults with HIV who have already received one dose of PPSV23 (but no dose of PCV13) should receive one dose of PCV13 (at least 1 year after PPSV23). Revaccination with a dose of PPSV23 should be administered at least 5 years after the first dose of PPSV23 and at least 8 weeks after the PCV13 dose. If the individual has received two doses of PPSV23 prior to age 65, they should receive a third PPSV23 dose after age 65 and at least 5 years after the prior dose of PPSV23.

- **Received Two Prior Doses of PPSV23:** Adults with HIV who have already received two doses of PPSV23 (but no dose of PCV13) should receive one dose of PCV13 (at least 1 year after the last dose of PPSV23). If the individual has received the two doses of PPSV23 prior to age 65, they should receive a third dose of PPSV23 after age 65 and at least 5 years after the prior dose of PPSV23 (and at least 8 weeks after the PCV13 dose).

- **Received Prior Dose of PPSV23 after Age 65:** Adults with HIV who have already received two doses of PPSV23 prior to age 65 and one dose after age 65 (but no dose of PCV13) should receive one dose of PCV13 (at least 1 year after the last dose of PPSV23).

- **Persons 65 and Older:** All persons with HIV who have received PPSV23 prior to age 65 should receive one additional dose of PPSV23 at age 65, or later, but this must be given at least 5 years after the last dose of PPSV23 and at least 8 weeks after a dose of PCV13.
Tetanus, Diphtheria and Pertussis (Tdap) Vaccine

Background

Tetanus, diphtheria, and pertussis are vaccine-preventable bacterial diseases that can lead to serious complications. Tetanus (lockjaw) can potentially cause muscle paralysis and carries a 20% mortality rate. Diphtheria causes a thick coating to form in the posterior pharynx that can lead to breathing difficulty, and, in some instances, death. Pertussis (whooping cough) causes severe coughing spells that can lead to pneumonia, hypoxia, sleeping problems, and rarely death.

Widespread childhood vaccination has markedly reduced the number of serious complications related to tetanus, diphtheria, and pertussis in the United States among all age groups. Although pertussis vaccine has reduced the incidence of pertussis compared with the pre-vaccine era, the number of reported cases of pertussis has increased since the 1980s, primarily due to lack of long-term immunity with the pertussis vaccine.[73] In recent years, the ACIP has recommended expanding the use of Tdap to improve community immunity against pertussis and reduce the burden of disease among the general population.[73] Most individuals with HIV mount adequate antibody responses to tetanus and diphtheria toxins, though it is a T-cell dependent vaccine and the titers are often lower among those with CD4 count less than 300 cells/mm$^3$.[8,74]

Vaccines

Several tetanus and diphtheria toxoid vaccines (Td) are currently licensed by the FDA.[73] In addition, two tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccines are approved by the FDA: Boostrix (for persons aged 10 and older) and Adacel (for persons aged 11 to 64 years). Both the Tdap and Td vaccines contain inactivated bacteria and thus are unlikely to pose any risk to individuals with HIV infection. When the Tdap vaccine was initially licensed, concern existed regarding the safety of administering the Tdap vaccine within 5 years of the Td vaccine. Subsequently, studies reported that administering the Tdap to an individual who had recently received Td (21 days to 2 years) was safe, other than a mild local reaction.[73,75]

Recommendations

The following summarizes the 2019 ACIP Adult Immunization Schedule for administering Tdap and Td for adults with HIV.[1]

- **General Approach:** Adults with HIV should receive immunization with Tdap and Td per the same schedule as non-pregnant adults without HIV.[1] The timing and dosing of the Tdap and Td vaccination in persons with HIV is not altered based on CD4 count.

- **No Prior Tdap:** For adults with HIV who have not previously received Tdap, give a one-time dose of Tdap, followed by a Td booster every 10 years.[1] Adults who previously received Td but have not had a Tdap dose should receive the Tdap vaccine regardless of the interval since Td was last administered.

- **Tdap for Pregnant Women with HIV:** Give Tdap during every pregnancy to prevent pertussis morbidity and mortality in infants. The dose of Tdap should be given preferably during gestational weeks 27 to 36 and it should be administered regardless of the pregnant woman’s prior history of receiving Tdap.[1]
Varicella Vaccine

Background

Varicella-zoster virus (VZV), or the chickenpox virus, is a highly contagious virus that causes rash, fever, and potentially severe, disseminated disease in persons with weakened immune systems. Prior to the introduction of the varicella vaccine and the incorporation of this vaccine into the routine childhood immunization schedule, chickenpox was very common in the United States general population, causing infection in more than 4 million persons each year. Primary varicella zoster virus infection is uncommon in adults with HIV since most have acquired immunity through childhood infection.[76]

Vaccine

The varicella vaccine is a live attenuated vaccine that poses significant risk to persons with HIV who have advanced immunosuppression. The duration of protection from varicella vaccine is not known. In addition to providing protection against primary varicella infection, the varicella vaccine has also been shown in studies to reduce the risk of herpes zoster (when compared with wild-type infection).[77,78]

Recommendations

The following summarizes the 2019 ACIP Adult Immunization Schedule and the Adult and Adolescent Opportunistic Infection Guidelines recommendations for administering varicella vaccine to adults with HIV.[1]

- **General Approach**: Adults with HIV and no evidence of immunity to VZV and a CD4 count of 200 cells/mm³ or greater should receive varicella vaccine. The vaccine does not need to be given to those born in the United States before 1980, or to those with VZV immunity.
- **Dosing Recommendation**: Two doses of varicella vaccine should be given 3 months apart.
- **Contraindications**: Varicella vaccine is contraindicated in persons with HIV who have a CD4 count less than 200 cells/mm³. In addition, the quadrivalent measles, mumps, rubella, and varicella vaccine is not recommended for individuals with HIV. The zoster vaccine should not be used interchangeably with the varicella vaccine, since the zoster vaccine has a much higher titer of live, attenuated VZV.
Zoster Vaccine

Background

Although primary varicella-zoster virus infection is unusual in persons with HIV, the incidence of zoster among adults with HIV is 15-fold higher than among age-matched immunocompetent adults, and the risk is highest in persons with a CD4 count less than 200 cells/mm$^3$. Individuals with HIV have additional increased risk in the first 4 months after starting effective antiretroviral therapy, likely as a result of immune reconstitution. Following the widespread use of potent antiretroviral therapy, the incidence rate of zoster has markedly decreased compared with early years of the HIV epidemic. Zoster is typically limited to a painful, dermatomal vesicular rash but can result in severe and complicated disease in adults with HIV, especially those with a low CD4 count. The goal of using zoster vaccine in persons with HIV is twofold: prevent zoster and reduce the severity of zoster if it does occur.

Zoster Vaccines

Recombinant Zoster Vaccine (RZV)

This recombinant zoster vaccine (RZV) contains varicella-zoster glycoprotein E combined with a novel adjuvant (AS01B) (Figure 6). The RZV is licensed as a 2-dose vaccine series, given 2 to 6 months apart, for persons 50 years of age and older. The ACIP also recommends RZV for adults who are 50 years of age and older and it is considered the preferred zoster vaccine. The RZV has shown efficacy of greater than 95% in preventing herpes zoster in phase 3 trials that enrolled immunocompetent older adults. In addition, a phase 1/2a trial evaluated RZV in persons with HIV and found that it was safe and immunogenic; this trial, however, did not evaluate the impact of RZV in preventing zoster. Giving RZV to persons who previously received ZVL may provide significant benefit; the minimum acceptable interval between giving RZV to a person who previously received ZVL is 2 months. The RZV does not contain live varicella-zoster virus and therefore poses no risk of causing varicella-zoster infection.

Zoster Vaccine Live (ZVL)

The live attenuated zoster (shingles) vaccine, which is now referred to as zoster vaccine live (ZVL), is a live virus vaccine that contains high titers of varicella-zoster virus. The ZVL is currently licensed in the United States for the prevention of shingles in adults over age 50, but the ACIP recommends use only in adults 60 years of age and older. This vaccine requires only one dose given subcutaneously and it requires freezing for storage. In a study involving 296 adults with HIV and a CD4 count of at least 200 cells/mm$^3$, two doses of ZVL was safe and immunogenic.

Opportunistic Infections Guideline Recommendations

The following summarizes recommendation from the Adult and Adolescent Opportunistic Infection Guidelines for use of RZV and ZVL in persons with HIV; for persons with HIV RZV is preferred over ZVL for preventing herpes zoster.

Recombinant Zoster Vaccine (RZV) In Persons with HIV

- The RZV vaccine is recommended for adults with HIV who are 50 years of age or older, regardless of CD4 cell count.
- The RZV vaccine is not recommended for persons younger than 50 years of age.
- The RZV vaccine should be given as a 2-dose series 2 to 6 months apart.
- The RZV vaccine should not be given during an episode of acute herpes zoster.
- To maximize immunologic response to RZV, some experts would defer administering RZV...
until virologic suppression on antiretroviral therapy has been achieved or until CD4 count recovery has occurred.

**Zoster Live Vaccine (ZVL) in Persons with HIV**

- If RZV is not available or cannot be given because of allergy or intolerance, ZVL can be administered (1 dose)
- The ZVL vaccine is contraindicated for persons with CD4 count less than 200 cells/mm$^3$

**ACIP Recommendations**

As of September 16, 2019, there were conflicting published versus the on-line 2019 ACIP recommendations regarding zoster vaccine for persons with HIV.[1,89]

**Recombinant Zoster Vaccine (RZV) in Persons with HIV**

The published ACIP 2019 Recommended Adult Immunization by Medical Condition and Other Indications lists RZV as recommended for persons with HIV 50 years of age and older, regardless of CD4 count, but the online 2019 version lists a “no recommendation” for RZV for persons with HIV (at all CD4 cell counts).[1,89] If RZV vaccine is administered, it requires 2 doses given 2 to 6 months apart.

**Zoster Live Vaccine (ZVL) in Persons with HIV**

The 2019 ACIP published and on-line recommendations are also conflicting for ZVL.[1,89] For both the published and on-line 2019 ACIP recommendations, ZVL is contraindicated for persons with HIV if they have a CD4 count less than 200 cells/mm$^3$, but for persons with HIV who have a CD4 count of at least 200 cells/mm$^3$ and are 60 years of age or older, the published version recommends ZVL whereas the on-line version lists a no recommendation.[1,89] If ZVL is given, it required only 1 dose.
Travel Vaccines

Background

An estimated 8% of travelers to the resource-limited regions of the world require treatment during travel, and major disease risks include vaccine-preventable illnesses.[90] Vaccines related to travel are generally not part of the initial evaluation process of persons with HIV. Newly diagnosed, treatment-naïve individuals with CD4 counts less than 200 cells/mm$^3$ should delay travel until CD4 counts have been reconstituted with antiretroviral therapy in order to avoid immune reconstitution illness while traveling.[90] Many persons with HIV will eventually travel to regions of the world that require multiple preventive vaccinations, such as typhoid fever, cholera, yellow fever virus, Japanese encephalitis virus, and rabies virus. Recommendations for appropriate travel-related vaccines can be very complex and depend on numerous factors, including the immune status of the person with HIV, the specific region of travel, and the types of exposure likely to occur in that region.[91]

Recommendations

All persons with HIV infection who are planning international travel should undergo an evaluation by a medical provider who has expertise in travel-related issues, and this travel evaluation should occur well in advance of the travel date to allow time for all appropriate immunizations to be given. The CDC provides an online resource for general information regarding HIV and travel.[91, 92]
Contraindicated Vaccines

Background

In general, caution should be exerted when administering any live virus vaccine to any immunocompromised individual, including persons with HIV. Certain live vaccines—Bacillus Calmette Guérin (BCG), vaccinia (smallpox), typhoid (21a) and live intranasal influenza—are contraindicated for all persons with HIV, regardless of CD4 cell count. In many resource-poor settings, BCG continues to be routinely administered to the general population in an effort to reduce the risk of tuberculosis infection. Unfortunately, persons with HIV who receive BCG as part of a general population vaccine program are at risk for subsequently developing disseminated vaccine-related tuberculosis, even years after receiving the vaccine. The CDC recommends against the use of BCG for persons with HIV. Vaccinia immunization confers protection against smallpox and is still recommended for lab or healthcare workers who come into contact with the virus or attenuated strains through cultures or contact with infected animals or contaminated materials. Due to case reports of severe smallpox infection in persons with HIV infection after exposure to smallpox vaccine, the ACIP recommends against smallpox vaccination in persons with HIV in all non-emergency situations.

Recommendations

The 2013 IDSA Vaccine Guidelines for the Immunocompromised Host recommends the following regarding use of live vaccines for adults and adolescents with HIV:

- Live influenza vaccine is contraindicated, at any CD4 cell count.
- Quadrivalent measles, mumps, rubella and varicella vaccine is contraindicated regardless of CD4 count.
- Measles, mumps and rubella (MMR) and varicella vaccines are contraindicated with a CD4 count less than 200 cells/mm$^3$, but indicated for a non-immune individual with a CD4 count of 200 cells/mm$^3$ or greater.
- Zoster vaccine live (ZVL) is contraindicated for persons with HIV who have a CD4 count less than 200 cells/mm$^3$. 
Summary Points

- Adults with HIV should receive immunizations according to the ACIP Recommended Adult Immunization Schedule by Medical Condition and Other Indications, which includes recommendations for persons with HIV.
- Immune responses to vaccinations among persons with HIV are enhanced when the vaccines are given as early as possible in the course of HIV infection, or after immune reconstitution has occurred as a result of suppressive antiretroviral therapy.
- Vaccination is generally safe in persons with HIV, with the exception that live virus vaccines in persons with a CD4 count less than 200 cells/mm³ can cause serious infectious complications.
- When giving the hepatitis B vaccine to adults with HIV, consideration should be given to using high dose (40 mcg) vaccine and/or using a four-dose schedule instead of the standard three-dose schedule. Post-vaccination antibody titers should be checked 1 to 2 months after completion of the primary hepatitis B vaccine series.
- Three doses of 9vHPV should be administered to all males and females through 26 years of age. The vaccine should ideally be given at age 11 or 12, but can be given as early as 9 years of age. At this time, there is no clear recommendation for administering 9vHPV to persons with HIV who are 27 through 45 years of age.
- MMR and varicella vaccines are indicated for asymptomatic persons with HIV who have a CD4 count greater than 200 cells/mm³ if they lack immunity to these vaccine-preventable illnesses.
- All adults with HIV should receive two doses of conjugate meningococcal vaccine and booster doses every 5 years thereafter.
- Pneumococcal vaccine-naïve persons should receive both the conjugate 13-valent (PCV13) and the 23-valent polysaccharide pneumococcal vaccine (PPSV23), and the recommended sequence and spacing of these vaccines depends on whether the individual has previously received any doses of polysaccharide pneumococcal vaccine.
- The recombinant zoster vaccine (RZV) is preferred over zoster vaccine live (ZVL). Two doses of RZV are recommended for persons with HIV who are 50 years of age and older. The ZVL should be avoided in persons who have a CD4 count below 200 cells/mm³ due to the risk of developing disseminated varicella-zoster virus infection, but it can be used (one dose required) in persons with HIV who are 60 years of age and older and have a CD4 count of 200 cells/mm³ or greater.
- Persons with HIV who plan to travel outside the United States should undergo an evaluation by a medical provider who has expertise in travel-related issues well in advance of planned travel.
- Expert consultation is advised for management of immunizations in children with HIV.
Citations


3. Centers for Disease Control and Prevention. Vaccines in the Adult Immunization Schedule. [CDC]


12. Briere EC, Rubin L, Moro PL, Cohn A, Clark T, Messonnier N. Prevention and control of haemophilus influenzae type b disease: recommendations of the advisory committee on...


43. U.S. Food and Drug Administration. FDA News Release: FDA approves expanded use of Gardasil 9 to include individuals 27 through 45 years old. [U.S. FDA] -


46. Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the


52. Centers for Disease Control and Prevention. Measles Cases and Outbreaks. 


89. Advisory Committee on Immunization Practices (ACIP). Recommended Immunization Schedule for Adults Aged 19 Years or Older by Medical Conditions and Other Indications, United States, 2019. [ACIP]


92. Kotton CN, Freedman DO. Immunocompromised travelers. In: CDC Health Information for International Travel (The Yellow Book). 2014 [CDC] -


References


• Toft L, Storgaard M, Müller M, et al. Comparison of the immunogenicity and reactogenicity of Cervarix and Gardasil human papillomavirus vaccines in HIV-infected adults: a randomized,
[PubMed Abstract] -

[MMWR] -

[PubMed Abstract] -
Figures

Figure 1 Production of Human Papillomavirus Subunit Vaccine

Conceptual rendition of production of human papillomavirus vaccine. The vaccine process involves recombinant synthesis of major capsid L1 proteins that self-assemble as a shell of 72 pentameric capsomeres to form viral-like particles (VLPs). The assembled pseudovirus is very similar to the native human papillomavirus and is highly immunogenic.

Illustration by David H. Spach, MD
Figure 2 Number of Measles Cases in United States, Reported by Year, 2010-2019*

*The data for 2019 are through July 11.

Source: Centers for Disease Control and Prevention
Figure 3 Neisseria meningitidis Isolates in Persons with HIV—United States, 1995-2014

Figure 4 Serotypes in the Pneumococcal Conjugate Vaccine 13 (PCV13)

Figure 5 Recommendations for Pneumococcal Immunization in Adults with HIV Infection

Note green rectangles indicate administer PCV13 and dark blue rectangles indicate administer PPSV23. Light blue rectangles indicate prior receipt of PPSV23.


### Pneumococcal Vaccine-Naïve Adults

- **≥ Age 65**
  - PCV13 → PPSV23
  - PPSV23 → PPSV23

### PPSV23-Immunized Adults

- **≥ Age 65**
  - PPSV23
  - PCV13
  - PPSV23

- **≥ 5 yrs**
  - PPSV23
  - PCV13
  - PPSV23

- **≥ 8 wks**
  - PPSV23
  - PCV13
  - PPSV23

- **≥ 1 yr**
  - PPSV23
  - PCV13
  - PPSV23

- **≥ 8 wks**
  - PPSV23
  - PCV13
  - PPSV23

- **≥ 5 yrs**
  - PPSV23
  - PCV13
  - PPSV23

- **≥ 1 yr**
  - PPSV23
  - PCV13
  - PPSV23
Figure 6 Herpes Zoster Vaccines

Illustration by David H. Spach, MD

Varicella-Zoster Virus

Attenuated VZV

Glycoprotein E

AS01e Adjuvant

Zoster Vaccine Live (ZVL)
Zostavax

Recombinant Zoster Vaccine (RZV)
Shingrix
<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Abbreviations</th>
<th>Trade Names</th>
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<tr>
<td><em>Hemophilus influenza</em> type b</td>
<td>Hib</td>
<td>ActHIB</td>
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<td></td>
<td></td>
<td>Hiberix</td>
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<td>HepA</td>
<td>Havrix</td>
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<td></td>
<td></td>
<td>Vaqta</td>
</tr>
<tr>
<td>Hepatitis A and hepatitis B vaccine</td>
<td>HepA-HepB</td>
<td>Twinrix</td>
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<td>Hepatitis B vaccine</td>
<td>HepB</td>
<td>Engerix-B</td>
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<td></td>
<td></td>
<td>Recombivax HB</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Heplisav-B</td>
</tr>
<tr>
<td>Human papillomavirus vaccine</td>
<td>HPV vaccine</td>
<td>Gardasil 9</td>
</tr>
<tr>
<td>Influenza vaccine, inactivated</td>
<td>IIV</td>
<td>Many brands</td>
</tr>
<tr>
<td>Influenza vaccine, live, attenuated</td>
<td>LAIV</td>
<td>FluMist Quadrivalent</td>
</tr>
<tr>
<td>Influenza vaccine, recombinant</td>
<td>RIV</td>
<td>Flublok Quadrivalent</td>
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<td>Measles, mumps, and rubella vaccine</td>
<td>MMR</td>
<td>M-M-R II</td>
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<td>MenACWY</td>
<td>Menactra</td>
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<td></td>
<td></td>
<td>Mencevo</td>
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<td>Meningococcal serogroup B vaccine</td>
<td>MenB-4C</td>
<td>Bexsero</td>
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<tr>
<td></td>
<td>MenB-FHbp</td>
<td>Trumemba</td>
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<td>Pneumococcal 13-valent conjugate vaccine</td>
<td>PCV13</td>
<td>Prevnar 13</td>
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<td>Pneumococcal 23-valent polysaccharide vaccine</td>
<td>PPSV23</td>
<td>Pneumovax</td>
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<td>Tetanus and diphtheria toxoids</td>
<td>Td</td>
<td>Tenivac</td>
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<td></td>
<td></td>
<td>Td vaccine</td>
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<tr>
<td>Tetanus and diphtheria toxoids and acellular pertussis vaccine</td>
<td>Tdap</td>
<td>Adacel</td>
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<td></td>
<td></td>
<td>Boostrix</td>
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<tr>
<td>Varicella vaccine</td>
<td>VAR</td>
<td>Varivax</td>
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<td>Zoster vaccine, recombinant</td>
<td>RZV</td>
<td>Shingrix</td>
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<tr>
<td>Zoster vaccine, live</td>
<td>ZVL</td>
<td>Zostavax</td>
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Source:
- Centers for Disease Control and Prevention. Vaccines in the Adult Immunization Schedule. [CDC]
<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Abbreviations</th>
<th>CD4 count &lt;200 cells/mm³</th>
<th>CD4 count ≥200 cells/mm³</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Haemophilus influenza</em> type b</td>
<td>Hib</td>
<td>Recommended with an additional risk factor or other indication 1 dose</td>
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<tr>
<td><em>Hepatitis A</em></td>
<td>HepA</td>
<td>Recommended with an additional risk factor or other indication 2 or 3 doses depending on vaccine</td>
<td></td>
</tr>
<tr>
<td><em>Hepatitis B</em></td>
<td>HepB</td>
<td>Recommended 2 or 3 doses depending on vaccine</td>
<td></td>
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<td><em>Human papillomavirus, female</em></td>
<td>9vHPV</td>
<td><strong>Recommended</strong> 3 doses through age 26 (0, 1-2, and 6 months)</td>
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<tr>
<td><em>Human papillomavirus, male</em></td>
<td></td>
<td><strong>Recommended</strong> 1 dose annually</td>
<td></td>
</tr>
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<td>Influenza, inactivated, or Influenza, recombinant</td>
<td>IIV RIV</td>
<td><strong>Contraindicated</strong></td>
<td></td>
</tr>
<tr>
<td><em>Influenza vaccine, live, attenuated</em></td>
<td>LAIV</td>
<td></td>
<td></td>
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<tr>
<td><em>Measles-mumps-rubella</em></td>
<td>MMR</td>
<td><strong>Contraindicated</strong> 6<strong>Recommended</strong> 2 doses (at least 4 weeks apart)</td>
<td></td>
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<td><em>Meningococcal serogroups A, C, W, Y</em></td>
<td>MenACWY-D MenACWY-CRM</td>
<td><strong>Recommended</strong> 2 doses (at least 8 weeks apart), then revaccinate every 5 years</td>
<td></td>
</tr>
<tr>
<td><em>Meningococcal serogroup B</em></td>
<td>MenB-4C MenB-FHbp</td>
<td>Recommended with an additional risk factor or other indication 2 or 3 doses</td>
<td></td>
</tr>
<tr>
<td><em>Pneumococcal 13-valent conjugate</em></td>
<td>PCV13</td>
<td><strong>Recommended</strong> 1 dose</td>
<td></td>
</tr>
<tr>
<td><em>Pneumococcal 23-valent polysaccharide</em></td>
<td>PPSV23</td>
<td><strong>Recommended</strong> 2 doses before age 65 years and 1 dose after age 65 years</td>
<td></td>
</tr>
<tr>
<td><em>Tetanus-diphtheria-acellular pertussis</em></td>
<td>Tdap Td</td>
<td><strong>Recommended</strong> 1 dose Tdap then Td booster every 10 years</td>
<td></td>
</tr>
<tr>
<td><em>Varicella</em></td>
<td>VAR</td>
<td><strong>Contraindicated</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Zoster, recombinant (preferred)</strong></td>
<td>RZV</td>
<td><strong>Recommended</strong> 2 doses (3 months apart)</td>
<td></td>
</tr>
<tr>
<td><strong>Zoster, live</strong></td>
<td>ZVL</td>
<td><strong>Contraindicated</strong></td>
<td></td>
</tr>
</tbody>
</table>

| Recommended if CD4 count greater than 200 cells/mm³ for at least 6 months with no evidence of immunity to measles, mumps, or rubella |
| The dosing of PCV13 and PPSV23 depend on whether the person has previously received any |

† This table is based on the 2019 ACIP Recommended Adult Immunization Schedule by Medical Condition and Other Indications, United States.
Vaccines

Abbreviations | CD4 count <200 cells/mm$^3$ | CD4 count ≥200 cells/mm$^3$

Note: As of September 16, 2019, there are conflicting 2019 ACIP recommendations regarding zoster vaccine—the published version (as shown here) recommends 2 doses of RZV for persons with HIV 50 years of age and older, regardless of CD4 count, but the online 2019 version lists a no recommendation for RZV for persons with HIV (at all CD4 cell counts). Similarly the 2019 ACIP published and on-line recommendations are conflicting for ZVL. For both the published and on-line 2019 ACIP recommendations, ZVL is contraindicated for persons with HIV if they have a CD4 count less than 200 cells/mm$^3$, but for persons with HIV who have a CD4 count of at least 200 cells/mm$^3$ and are 60 years of age or older, the published version recommends one dose of ZVL whereas the on-line version lists a no recommendation. The table shown here is the published version.

Source:
