Immunizations in Adults

Background

Providing appropriate immunizations is an important component of comprehensive HIV clinical care. There are numerous vaccines that are addressed in the adult immunization schedule (Table 1). Immunizing persons with HIV poses several challenges and concerns related to safety and efficacy. The Advisory Committee on Immunization Practices (ACIP) provides annual recommendations for routine immunizations of adults, including HIV-specific recommendations (Table 2). In addition, the Adult and Adolescent OI Guidelines provides recommendations for Immunizations for Preventable Diseases in Adults and Adolescents Living with HIV. This topic review will focus on immunization recommendations for adults with HIV. The immunizations topics discussed in this review are ordered alphabetically based on the vaccine.

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. These reports, however, involved persons with HIV who were not receiving potent antiretroviral therapy and investigators subsequently demonstrated that increases in HIV RNA levels following immunization 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.

Risk of Live Vaccines in Persons with HIV

Immunizations are generally safe in individuals with HIV, except for live virus vaccines in persons with low CD4 counts. In those individuals with HIV who have advanced immunosuppression, live vaccines can cause a potentially life-threatening disseminated infection with the live pathogen in the vaccine.

Challenges with Efficacy

Current or past advanced immunosuppression in persons with HIV is often associated with suboptimal responses to standard recommended vaccine doses; for several vaccines, the response appears to depend on current and nadir CD4 cell counts. In general, responses to immunization are better when the vaccine is given in persons with higher CD4 cell counts, including after immune reconstitution that has resulted from antiretroviral therapy.
COVID-19 Vaccines

Background

Persons living with HIV are at elevated risk for significant morbidity and mortality from COVID-19 infection, particularly persons who have untreated or advanced HIV (as evidenced by a low CD4 T-cell count or detectable HIV RNA) or other medical comorbidities.[9,10,11,12] Limited data exist on the specific safety and efficacy of COVID-19 vaccination for people living with HIV, but, based on available data and clinical experience, it is generally accepted that the benefits for reducing COVID-related morbidity and mortality far outweigh any vaccine-related risks.[13,14]

Vaccines

mRNA Vaccines

The United States Food and Drug Administration (FDA) has approved two COVID-19 vaccines: Pfizer-BioNTech mRNA COVID-19 vaccine and the Moderna mRNA COVID-19 vaccine. Both of these vaccines employ novel mRNA technology—the mRNA is delivered in a lipid nanoparticle to express a full-length viral spike protein (Figure 1).[15] These mRNA vaccines stimulate vigorous SARS-CoV-2 B-cell mediated neutralizing antibody responses and T-cell augmentation and memory immune responses against SARS-CoV2 (Figure 2).[15] The original mRNA vaccines from Pfizer-BioNTech and Moderna were monovalent vaccines, that is, they contained antigens from a single variant of SARS-CoV2 (alpha variant). More recently, both Pfizer and Moderna have developed bivalent vaccines. These contain antigens from both original and omicron BA.4/BA.5 strains of Sars-CoV2. As of April 2023, the monovalent Moderna and Pfizer-BioNTech COVID-19 vaccines are no longer authorized for use in the United States. Hence, in order to simplify the vaccination schedule, the bivalent vaccines are now recommended for use for both the primary series and booster doses.[16]

Protein Subunit Vaccines

The Novovax COVID-19 vaccine is available under an emergence use authorization from the FDA for use in individuals 12 years of age and older. This vaccine contains pieces of the SARS-CoV-2 spike protein as well as an adjuvant to boost immunogenicity. In the United States, the only current recommended use for the Novavax COVID-19 vaccine is for persons who are unable or unwilling to receive one of the mRNA vaccines.[16]

Adenovirus Vaccine

The Johnson & Johnson/Janssen COVID-19 vaccine, which utilizes a replication incompetent adenovirus vector that encodes viral spike protein, is no longer available in the United States and all remaining United States government stock of this vaccine expired on May 7, 2023.[16]

Recommendations for COVID-19 Vaccines In Persons with HIV

The Centers for Disease Control and Prevention (CDC) recommends that all adults with HIV receive COVID-19 vaccination, regardless of viral load or CD4 count.[16] All persons with HIV should receive a primary series and those with evidence of moderate to severe immune suppression should receive an additional dose as part of the primary series; for these recommendations, the CDC defines moderate to severe immune suppression as advanced or untreated HIV (e.g., CD4 count less than 200 cells/mm³, AIDS-defining illness, or symptomatic HIV infection), or may include other concomitant immunocompromising condition, such as treatment for malignancy, receipt of immunosuppressive medications (including high-dose corticosteroids), receipt of CAR T-cell therapy, past hematopoietic stem cell transplant, or primary immunodeficiency.[16] The vaccine recommendations for persons who have HIV depend on whether the individual is considered to have moderate-so-severe immune suppression. Because these vaccine recommendations are complicated and
frequently change, we recommend referring to the CDC web site Use of COVID-19 Vaccines in the United States: *Intermim Clinical Considerations* to view current recommendations.[16]
**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.[17] 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.[18] 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.[19]

### Vaccines

The currently three licensed *Haemophilus influenzae* type b (Hib) monovalent conjugate vaccines: *Hiberix*, *ActHIB*, and *PedvaxHIB*. In addition, there are four licensed combination conjugate vaccines that contain Hib: *Comvax* (Hib combined with hepatitis B vaccine), *Pentacel* (Hib combined with DTaP and inactivated poliovirus), *MenHibrix* (Hib combined with meningococcal vaccine), and *Vaxelis* (Hib combined with DTaP, inactivated poliovirus and hepatitis B vaccine IPV). Although none of these vaccines have FDA approval for use in adults, the ACIP has recommended that any of the monovalent conjugate Hib vaccines can be used for adults who have a specific indication to receive this vaccine.[18]

### 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.[20]
- Per the 2022 ACIP Adult Immunization Schedule any of the monovalent Hib vaccine should be administered to adults with HIV only if they have an indication for the vaccine, including hematopoietic stem cell transplant, anatomic asplenia, or functional asplenia (including sickle cell disease).[1] Persons who have undergone hematopoietic stem cell transplant should receive a 3-dose series (4 weeks apart starting 6 to 12 months after successful transplant), regardless of Hib vaccination history. For persons with functional or anatomic asplenia, one dose of Hib should be given if they have not previously received the vaccine; for persons undergoing elective splenectomy, the Hib vaccine should be administered, preferably at least 14 days prior to surgery.[1]
Hepatitis A Virus (HAV) Vaccine

Background

Hepatitis A virus (HAV) is transmitted through food, water, or objects contaminated with fecal matter.[21] Infection with HAV is usually an acute, self-limiting condition that does not require treatment though it can rarely cause fulminant liver failure.[21] Following the widespread use of the hepatitis A vaccine beginning in 1995, the number of HAV infections in the United States declined for nearly 2 decades, but during the last several years, there has been a dramatic increase in the number of cases as a result of multiple outbreaks, particularly those involving homeless persons, men who have sex with men, persons who inject drugs, and to a lesser degree, with consumption of imported contaminated food (Figure 3).[22,23] For persons with HIV, the hepatitis A vaccines are safe and usually 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, though rates were only 87% in patients with CD4 counts less than 300 cells/mm$^3$.[24]

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$^3$.[5]

Vaccines

Hepatitis A vaccine is an inactivated vaccine that can be given as one of the single-antigen preparations (Havrix or Vaqta) or as the combination vaccine (Twinrix). The two single-antigen brands of hepatitis A vaccine are potentially interchangeable, but ideally all doses in a vaccine series should be from the same manufacturer (Figure 4).[25]

- **Havrix**: this single-antigen vaccine contains 1,440 ELISA units (El.U) of hepatitis A antigen and is administered as a 2-dose schedule, with the second dose given 6 to 12 months after the initial dose.
- **Vaqta**: this single-antigen vaccine contains 50 units (U) of inactivated hepatitis A and is administered as a 2-dose schedule, with the second dose given 6 to 18 months after the initial dose.
- **Twinrix**: this combination vaccine contains 720 El.U of hepatitis A antigen (antigen component from Havrix, one-half amount) combined with 20 mcg of hepatitis B antigen (antigen component from Engerix-B standard dose); it is administered as a 3-dose series (0, 1, and 6 months).

Recommendations

The following summarizes the ACIP Adult Immunization Schedule and Adult and Adolescent OI Guidelines recommendations for administering the hepatitis A vaccine to persons with HIV who are not immune to HAV.[2,3,25]

- **General Approach and Timing of Administration**: The Hepatitis A vaccine series should be administered to all adolescents and adults with HIV if they are not immune to HAV, with the timing of administering the vaccine possibly depending on their CD4 count (Figure 5).[2,3,25] For persons with a CD4 count less than 200 cells/mm$^3$ and an ongoing risk of acquiring HAV infection, the HAV vaccine series should be administered without delay.[2] If the individual has a CD4 count less than 200 cells/mm$^3$ and no active risk of acquiring HAV, two options exist: either administer without delay or wait to give the vaccine series until the CD4 is greater than 200 cells/mm$^3$.[2,25,26]

- **Recommended Dosing Schedule**: Hepatitis A vaccine should be administered in two doses at 0 and 6-12 months (Havrix) or 0 and 6-18 months (Vaqta); the minimum interval before the first and second dose of these vaccines is 6 months.[1,2,25] The combined hepatitis A-hepatitis B vaccine (Twinrix) can also be administered as a 3-dose series (0, 1, and 6 months); for this combined vaccine, the minimum
intervals are 4 weeks between the first and second doses and 5 months between the second and third doses.[1,2,25] For non-immunized persons traveling to countries endemic for HAV, an accelerated dosing schedule with the combined hepatitis A-hepatitis B vaccine can be administered on days 0, 7, 21 to 30 days, with a booster dose given at 12 months.[1,2]

- **Postvaccination Serologic Testing and Revaccination:** Since persons with HIV may have an attenuated response to the vaccine, postvaccination serologic testing should be performed in these individuals at least 1-2 month after completing the HAV vaccination series.[2,25] If there is no evidence of immunity against HAV (e.g. antibody titer of at least 10 mIU/mL), then revaccination is recommended with the entire HAV vaccine series, preferably when the CD4 count is greater than 200 cells/mm³.[2,25] Postvaccination serology testing should be done again at least 1 to 2 months after completion of the additional HAV vaccination series.[25] If there is still no evidence of an adequate immune response, then further vaccination is not recommended, but the individual should receive counseling on the need to receive immune globulin after an exposure to HAV.[25]

- **Counseling:** Regardless of the initial immune response to the HAV vaccine series, all individuals with HIV should be counseled that the vaccine might not provide long-term protection against HAV infection.[25] Hence, immune globulin may need to be administered after a high-risk HAV exposure.[25,27,28]
Hepatitis B Virus (HBV) Vaccine

Background

Hepatitis B virus (HBV) is transmitted through percutaneous and mucosal exposure to infected blood or body fluids. Chronic HBV infection 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 with HIV and HBV coinfection 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 without HIV.[29,30] Thus, vaccination against HBV is very important for persons with HIV.

Vaccines

For adults, there are three U.S. Food and Drug Administration (FDA)-approved recombinant HBsAg single antigen (S) recombinant hepatitis vaccines: Recombivax-HB, Engerix-B, and Heplisav-B. In addition, in 2021 the FDA approved the 3-antigen (S, pre-S2, and preS1) recombinant HBsAg vaccine PreHevbrio. The following summarizes the hepatitis B vaccines.

- **Recombivax-HB**: This vaccine a recombinant, single-antigen that is available as an adult standard formulation (10 μg HBsAg per dose) and a high-dose dialysis formulation (40 μg per dose). Double-dose Recombivax-HB is 20 μg per dose.
- **Engerix B**: This vaccine is a single-antigen, recombinant vaccine, available as a standard 20 μg HBsAg per dose; double dose Engerix-B is 40 μg per dose).
- **Heplisav-B**: This vaccine consists of recombinant HBsAg conjugated to the cytosine phosphoguanine oligonucleotide (CpG 1018) adjuvant, is available in doses that each contain 20 μg of HBsAg and 3,000 μg of the 1018 adjuvant.[31]
- **PreHevbrio**: This recombinant hepatitis B vaccine contains 3 hepatitis B surface antigens: small (S), middle (pre-S2), and large (preS1). The vaccine contains 10 μg of each of these antigens.
- **Twinrix**: This combined hepatitis A-hepatitis B vaccine contains 720 El.U of hepatitis A (antigen component from Havrix) and 20 μg per dose of HBsAg (antigen component from Engerix-B). It is important to note that administering the Twinrix vaccine provides standard-dose, not double-dose strength hepatitis B antigen.

Using standard doses of older single antigen vaccines in adults with HIV generated significantly lower seroprotective response rates than in adults without HIV.[32,33] Lower HBV vaccine responses in persons with HIV have been associated with a recent or nadir CD4 count of less than 200 cells/mm$^3$, detectable HIV RNA levels, coinfection with hepatitis C virus, occult HBV, and overall health of the vaccine recipient.[8,32,34] Attempts to improve hepatitis B vaccine response rates have included giving a double dose, an increased number of doses, and the use of intradermal vaccines.[35,36] A recently published trial compared three doses (0, 1, and 6 months) of the Heplisav-B vaccine to placebo in persons with HIV who were hepatitis B vaccine naive and found 100% of those who received the vaccine had protective antibody levels (anti-HBs greater than 10 mIU/mL) at 28 weeks (Figure 6).[37] At week 8 (4 weeks after the second dose) 87% had protective antibody titers and this number increased to 98.5% at week 24, which was prior to receipt of the third vaccine dose.[37] Results from a second arm of this study, which involved giving this vaccine to hepatitis B vaccine non-responders, have not been published.

Recommendations

The recommendations for hepatitis B immunization in persons with HIV are outlined as follows and based on recommendations from the Adult and Adolescent OI Guidelines [2,3]

- **General Approach and Timing of Administration**: All persons with HIV who do not have active
HBV or evidence of immunity to HBV should receive the hepatitis B vaccine series if they have ongoing risk of acquiring HBV.[2,30] Although HBV non-immune individuals with CD4 less than 350 cells/mm³ may have decreased response to HBV vaccination, the deferring vaccination until CD4 rises to greater than 350 cells/mm³ is not recommended since many individuals a CD4 less than 350 cells/mm³ will mount an adequate antibody response to the HBV vaccine series.[2,30]

- **Prevaccine Screening**: Prevaccine screening should include HBsAg, anti-HBs, and anti-HBc. A positive HBsAg indicates active infection and no vaccine is indicated. If the individual has a positive test for both anti-HBs and anti-HBc, there is no need for hepatitis B immunization. In addition, if the anti-HBs alone is positive (with a titer greater than 10 mIU/mL), the person is considered immune and has no need for hepatitis B immunization.[30,31] The approach to patients with isolated anti-HBc is addressed below.

- **Dosing and Schedule for Hepatitis B Immunization**: The following are recommended options for hepatitis B immunization in persons with HIV who are not on hemodialysis (Figure 7):[2,30]
  - Double-dose, 3-series of recombinant hepatitis B vaccine with Engerix-B 40 (mcg of HBsAg) or Recombivax-HB (20 mcg HBsAg) given at 0, 1, 2, and 6 months (AII), or
  - For persons who need immunization against HAV and HBV, Combined hepatitis B and hepatitis A immunization (Twinrix) given as a 3-dose series (0, 1, and 6 months) (AII) (note that administering the Twinrix vaccine provides standard-dose, not double-dose strength of hepatitis B antigen), or
  - HpBCpG (Heplisav-B) given as a 2-dose series at 0 and 1 month (CIII). Note that Heplisav-B should not be used in pregnant individuals due to lack of safety data.

- **Postvaccine Antibody Testing**: Given the decreased response rate to hepatitis B vaccine among persons with HIV, postvaccine testing for antibody to hepatitis B surface antigen (anti-HBs) should be performed 1 to 2 months after completing the final dose of the vaccine series, with a titer of at least 10 mIU/mL considered protective; individuals who have a postvaccine anti-HB less than 10 mIU/mL are considered vaccine nonresponders.[26,30] Due to concerns of waning immunity, some experts recommend checking anti-HBs annually and giving a booster dose of hepatitis B vaccine if anti-HBs levels fall below 10 mIU/L, especially for individuals with ongoing risk of acquiring HBV who are not taking tenofovir DF or tenofovir alafenamide as part of their combination antiretroviral regimen.[30]

- **Vaccine Nonresponders**: If a postvaccine anti-HBs concentration of at least 10 mIU/mL is not attained, the following are considered as options for hepatitis B vaccine nonresponders (Figure 8):[2,30]
  - Revaccinate with a double-dose, 3-dose series with recombinant HBV vaccine (Engerix-B or Recombivax-HB) given at 0, 1, and 6 months (BIII). Note that some experts would give a double-dose, 4-dose series at 0, 1, 2, and 6 months, or
  - Revaccinate with the two-dose series of hepBCpG (Heplisav-B) vaccine (BIII), or
  - For persons with a CD4 count less than 200 cells/mm³, some experts would delay revaccination until after a CD4 count of 200 cells/mm³ or greater is achieved and sustained on antiretroviral therapy (CIII).

- **Isolated Core Antibody**: The optimal approach for persons with HIV who have 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 recommendations for the following approach to persons with HIV who have isolated anti-HBc. Administer one standard dose of hepatitis B vaccine and then check an anti-HBs titer 1 month later (Figure 9).[2,30] If the anti-HBs titer is greater than 100 mIU/mL, then no additional hepatitis B vaccine doses are needed and the person is considered immune to HBV.[2,30] If the anti-HBs titer is less than 100 mIU/mL (or if quantitative antibody titers are not available), then administer a full hepatitis B vaccine series (using 3-dose series of double-dose vaccine with Engerix-B or Recombivax or a 2-dose series with standard dose of Heplisav-B). One to two months after completing the vaccine series, a repeat anti-HBs titer should be obtained. Note: with this approach for persons with isolated core antibody, the cutoff representing immunity after the one vaccine dose (100 mIU/mL) is 10-fold higher than the 10 mIU/mL used to represent immunity following receipt of the HBV immunization series in persons who do not have isolated hepatitis B core antibody.[38]
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.[39, 40, 41] 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.[42, 43, 44] 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.[41, 45] More recent reports in persons with HIV have found a marked decline in cervical and anal cancer risk in women and men.[46] 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.[42] Another 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.[47] A population based study from Sweden found that quadrivalent HPV vaccination was associated with a substantially reduced risk of invasive cervical cancer in women between 10 and 30 years of age.[48] The study reported that the incidence of cervical cancer was reduced by 88% among women who were immunized before the age of 17 years, and by 53% in women immunized at 17 to 30 years of age, validating the benefit of HPV immunization.[48]

Vaccines

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 10).[49] In the United States, the 9-valent (9vHPV) vaccine is the only HPV vaccine currently manufactured; this vaccine provides protection against 7 cancer-causing HPV serotypes (16, 18, 31, 33, 45, 52, and 58) and 2 HPV serotypes 6 and 11, that cause genital warts (Figure 11).[50] The HPV serotypes 16 and 18 account for approximately 66% of cases of cervical cancer; the HPV serotypes 31, 33, 45, 52, and 58 combined account for approximately 15% of cervical cancers and 10% of invasive HPV-associated cancers.[50] The HPV serotypes 6 and 11 account for approximately 90% of genital warts.[50] The 9vHPV vaccine is FDA-approved for use for ages 9 through 45 years.[51] 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.[43, 44]

Recommendations

The following summarizes the [Guidelines] ACIP Child and Adolescent Immunization Schedule and Adult and Adolescent OI Guidelines recommendation for administering the HPV vaccine to persons with HIV.[2, 3]

- **General Approach**: The 9vHPV vaccine series should be given to all persons with HIV who are 9 through 26 years of age.[2, 3] The 9vHPV vaccine is not routinely recommended for persons with HIV who are older than 26 years of age, but it can be considered in this age group using a shared decision-making process.[2]

- **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).[2] A 2-dose schedule should not be used in persons with HIV.[2, 3, 52]

- **HPV Vaccine in Pregnancy**: The HPV vaccine is not recommended for pregnant people, but pregnancy testing is not needed prior to vaccination.[50] If a person is found to be pregnant after receiving a dose of HPV vaccine while they are pregnant, no intervention is needed. In addition, if an
individual 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.[50,53]

- **Use as Therapeutic Vaccine**: The HPV vaccine is not recommended for therapeutic purposes for persons 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.[54] Larger antigenic change, termed antigenic shift, has the potential to cause a worldwide pandemic since there is no preexisting 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 persons without HIV.[55] Studies in individuals with HIV suggest a single dose of inactivated vaccine generates a good humoral immune response, except in those with a low CD4 cell count.[6]

Vaccines

All adults with HIV, including pregnant women, can receive inactivated influenza vaccine (IIV) or recombinant quadrivalent influenza vaccine (RIV4). The recommended inactivated and recombinant influenza vaccine are quadrivalent vaccines (contains two strains of both influenza A and B).[56] All influenza vaccines expected to be available for the current influenza season are quadrivalent vaccines, containing two strains both of influenza A and B.[56] In addition, a high dose inactivated influenza vaccine (HD-IIV), a modified adjuvant inactivated influenza vaccine (all4V) and/or recombinant quadrivalent influenza vaccine (RIV4) can be used in individuals who are 65 years of age and older.[3] A recombinant quadrivalent influenza vaccine (RIV4) that does not contain any egg protein is available for adults. The quadrivalent live attenuated influenza vaccine (LAIV4), also known as the nasal spray flu vaccine, is approved for use in healthy adults 18 through 49 years of age, but is not recommended for persons with HIV due to concern that attenuated virus could lead to influenza virus infection.

Recommendations

The following summarizes the ACIP Adult Immunization Schedule and the Adult and Adolescent OI Guidelines for administering influenza vaccine to persons with HIV.[2,3,20]

- **General Approach**: All people with HIV should receive a single annual dose of influenza vaccine.
- **Recommended Vaccines for People Younger than 65 Years of Age**: Recommended routine influenza vaccines for people with HIV who are younger than 65 years of age include inactivated influenza vaccine (IIV) or recombinant influenza vaccine (RIV4).
- **Pregnant People**: Individuals with HIV who are pregnant can receive inactivated influenza vaccine or recombinant influenza vaccine at any time during pregnancy.
- **Recommended Vaccines for persons 65 Years of Age and Older**: People with HIV who are 65 years of age and older should receive either a dose of the high-dose inactivated influenza vaccine (HD-IIV) or the adjuvant inactivated influenza vaccine (all4V); these vaccines are recommended over the use of standard-dose unadjuvanted vaccines
- **Contraindicated Vaccine**: The live attenuated influenza vaccine (LAIV) is contraindicated in all people with HIV.
- **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.
Measles-Mumps-Rubella (MMR) Vaccine

Background

Measles, mumps, and rubella are highly contagious viruses that can cause a wide range of clinical manifestations, 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 good MMR vaccine coverage in the United States, outbreaks continue to occur. Between January 1 and December 31, 2019, more than 1,200 cases of measles were diagnosed in the United States, which is the largest number of annual cases reported in the United States since 1992. In the United States, for the years 2021 and 202, there were 49 and 121 confirmed measles cases, respectively.

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. 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 is modest at best, and the protection of the vaccine in persons with HIV 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, the MMR vaccine became available in 1971 and is still widely used. There is also an FDA-approved quadrivalent measles-mumps-rubella-varicella (MMRV) vaccine, but it is rarely used in adults. All currently used measles vaccines contain live attenuated measles virus, and thus pose significant risk to severely immunocompromised individuals, including persons with HIV who have low CD4 cell counts. There have been case reports of fatal pneumonitis in persons with HIV and advanced immunosuppression who received the MMR vaccine.

Recommendations

The following summarizes the ACIP Adult Immunization Schedule and Adult and Adolescent OI Guidelines recommendation for administering the MMR vaccine to persons with HIV.

- **General Approach**: The MMR vaccine should only be administered to persons with HIV if (1) they lack immunity to measles, mumps, and rubella and (2) for at least 6 months, they have a CD4 count of at least 200 cells/mm$^3$ and a CD4 percentage of at least 15%. Persons are considered to have immunity to measles if any of the following are met: they were born before 1957; they have documentation of receipt of the MMR vaccine, or they have laboratory evidence of immunity (AIII).
- **Recommended Dosing Schedule**: Give the two-dose MMR vaccine series, with the doses administered at least 4 weeks apart.
- **Quadrivalent Measles-Mumps-Rubella-Varicella (MMRV) Vaccine**: The quadrivalent MMRV vaccine is not recommended in persons with HIV, regardless of CD4 cell count.
- **Persons with Advanced Immunodeficiency**: The MMR and MMRV vaccines are contraindicated in persons with HIV who have a CD4 count less than 200 cells/mm$^3$ or a CD4 percentage less than 15%.
- **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. Pregnant people without evidence of rubella immunity who have a CD4 count of at least
200 cells/mm³ and CD4 percentage of at least 15% should receive the MMR vaccine upon completion or termination of pregnancy.[2]

- **Persons who Received Measles Vaccine During 1963 through 1967**: Receipt of an inactivated measles vaccine, which was an option during 1963 through 1967, but was ineffective, does not count as a dose of measles vaccine.[60] In addition, if the type of measles vaccine received during 1963-1967, is not known, then it does not count as a dose.[60]

- **Vaccine Nonresponders**: There are some data that suggest persons with HIV have an attenuated antibody response to the MMR vaccine.[59,62,63] Currently, there is no guidance on whether to obtain post-MMR vaccine serologic titers to document vaccine response. If post-MMR vaccine titers are checked and demonstrate lack of immunity, the recommendation is to consider repeating the 2-dose MMR series, especially if the person did not have suppressed HIV RNA levels at the time they received the MMR vaccine.[2]
Meningococcal Vaccine

Background

Meningococcal meningitis, which is caused by *Neisseria meningitidis*, can cause severe complications, including hearing loss, brain damage, and death. Available data from population studies suggest that persons with HIV have a 5- to 24-fold higher risk of developing meningococcal disease than persons without HIV; the highest risk in persons with HIV occurs in those with low CD4 cell counts and high HIV RNA levels.\[2,64,65\] In addition, several local outbreaks of meningococcal meningitis have been reported in the United States involving gay and bisexual men.\[66,67,68\] Unpublished CDC data from 62 cases of meningococcal disease in persons with HIV found that serogroup C was the most common isolate, followed next by serogroup Y (Figure 13).\[64\] As with other vaccines given to individuals with HIV, low CD4 count and HIV RNA above 10,000 copies/mL are associated with decreased meningococcal vaccine response rate.\[69\]

Vaccines

Three quadrivalent meningococcal conjugate vaccines (MenACWY) covering groups A, C, W-135, and Y have been licensed in the United States: MenACWY-D, MenACWY-CRM, and MenACWY-TT.\[65\] The production of the MenACWY-D vaccine was discontinued in 2022. The MenACWY vaccine is approved for use in persons 2 months through 55 years of age, and MenACWY-TT is approved for persons at least 2 years of age.\[1,65\] Two 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 years and older who have an increased risk for meningococcal disease. If both the Men-ACWY and Men-B vaccines are indicated for an individual with HIV, the vaccines can be administered simultaneously, but, if feasible, they should be administered at 2 different anatomic sites.\[2,3\]

Recommendations

The following summarizes recommendations from ACIP Adult Immunization Schedule and the Adult and Adolescent OI Guidelines for administering conjugate meningococcal vaccines to adolescents and adults with HIV.\[2,3\]

Meningococcal Conjugate Vaccine (A, C, W, Y)

- **General Approach:** Routine administration of either of the quadrivalent meningococcal conjugate vaccines (MenACWY-CRM, and MenACWY-TT) is recommended for all adolescents and adults with HIV (AIII).\[2\] If possible, the same meningococcal vaccine product should be used for all doses.\[3,65\]
- **Dosing Recommendations:** For adolescents and adults with HIV, give 2 doses (at least 8 weeks apart); follow-up booster doses should be given every 5 years beginning 5 years after completing the initial series (Figure 14) (BIII).\[3,65\]

Meningococcal B Vaccine

- **General Approach:** Administration of conjugate meningococcal B (MenB) vaccine is not routinely recommended for adults with HIV. The MenB vaccine may be administered to individuals with HIV if they have an additional indication for receiving meningococcal B vaccine, such as functional or anatomic asplenia,\[3\] persistent complement component deficiency, or receipt of a complement inhibitor (e.g. eculizumab, ravulizumab).\[2,3\] The MenB vaccine should be avoided during pregnancy unless the individual is at increased risk of meningococcal infection. In addition, for those individuals with HIV 16-23 years of age, Men B vaccination may be given using shared clinical decision making, for short-term protection against most strains of serogroup B meningococcal disease and/or for patients at increased risk, such as those living in dormitories or barracks, and during meningococcal B outbreaks. The MenB vaccine should be avoided during pregnancy, unless the individual is at...
increased risk of meningococcal infection.

- **Dosing Recommendations:** If MenB-4C is used, 2 doses should be given at least 1 month apart.\[2, 3\] If MenB-FHbp is used, then give 3 doses at 0, 1-2, and 6 months.\[2, 3\] If the second dose of MenB-FHbp was administered 6 months after the first dose in the series, then a third dose is not required.\[3\] People with HIV should not receive the two-dose series of MenB-FHbp vaccine.\[2\] In addition, the MenB-4C and the MenB-FHbp should not be used interchangeably. Persons should receive one booster dose of the MenB vaccine 1 year after completing the initial vaccine series, followed by booster doses every 2 to 3 years if there is persistent risk of meningococcal infection.\[3\]
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.\[^{70}\] 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.\[^{71,72,73}\] 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.\[^{74}\]

Efficacy of Pneumococcal Immunization in Persons with HIV

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.\[^{75,76}\] 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) 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\(^3\).\[^{77}\] The safety and immunogenicity 1 of PCV15 compared to PCV13 was evaluated in approximately 300 adults with HIV in a phase 3, randomized, controlled clinical trial conducted at multiple sites internationally.\[^{78}\] This study demonstrated the PCV15 vaccine was well-tolerated and induced adequate antibody responses to all 15 pneumococcal serotypes included in the vaccine.\[^{78,79}\] The PCV20 has also been shown to be safe and immunogenic in clinical trials involving adults with some medical conditions, but HIV and other immunocompromising conditions were excluded from the study.\[^{79}\]

Vaccines

Four pneumococcal vaccines are currently available for use in the United States: PPSV23, PCV13, PCV15, and PCV20.\[^{70,79}\] The PCV13 contains antigens from 13 common *S. pneumoniae* serotypes.\[^{80}\] The PCV15 and PCV20 contain all the PCV13 serotypes, with two additional serotypes in PCV15 and seven additional serotypes in PCV20 (Figure 15).\[^{79,80}\] The PCV15 is administered as a single dose with one PPSV23 follow-up dose given at least 8 weeks later; no additional doses are recommended after that. The PCV20 requires one dose only; there are no additional doses needed.

Recommendations

The following summarizes recommendations from Adult and Adolescent OI Guidelines ACIP Adult Immunization Schedule recommendations for pneumococcal immunization in persons with HIV, with the exact schedule based on age and whether the individual has previously received pneumococcal vaccine.\[^{2,3}\]

- **General Approach:** Initial pneumococcal immunization for persons with HIV should now utilize the newer conjugate vaccines— PCV15 or PCV20 (AII).\[^{2}\] If PCV15 is given, a dose of PPSV23 should be administered at least 8 weeks later (AII).\[^{2}\] These new recommendations for pneumococcal immunization in persons with HIV provide a markedly simplified approach compared with older recommendations.

- **No Prior Pneumococcal Immunization:** Adults with HIV who have never received pneumococcal
vaccine (or their pneumococcal immunization status is unknown) should receive either (1) a single
dose of PCV20 or (2) a single dose of PCV15 followed by a dose of PPSV23 at least 8 weeks later
\textbf{(All)} \footnote{2, 3} Regardless of which of these two approaches is used, no further doses of
pneumococcal vaccine are needed.\footnote{2, 79}

- **Prior Receipt of PCV13 Only:** For persons with HIV who have received PCV13 only, there are two
  options recommended in the ACIP Adult Immunization Schedule: (1) receive 1 dose of PCV20 at least 1
  year after the PCV13 dose or (2) complete the recommended PPSV23 series (receive the remaining
  additional doses of PPSV23, which consists of one dose PPSV23 at least 8 weeks after the dose of
  PCV13, followed by PPSV23 at least 5 years after the first dose of PPSV23, followed by receipt of a
  final dose of PPSV23 after age 65 years and at least 5 years after the prior dose of PPSV23) \footnote{3}
  \textbf{(Figure 16).} \footnote{2, 79} Note, for this situation, the Adult and Adolescent OI Guidelines recommend completing the
  recommended PPSV23 series (as noted above).\footnote{2}

- **Prior Receipt of PCV13 and One or More Doses of PPSV23:** For persons with HIV who have
  received PCV13 and at least 1 dose of PPSV23, but have not completed the vaccine series, two options
  exist as recommended in the ACIP Adult Immunization Schedule: (1) receive 1 dose of PCV20 at least 5
  years after the last pneumococcal dose, or (2) complete the recommended PPSV23 series (receive the
  additional doses of PPSV23) \footnote{3} \textbf{(Figure 18).} \footnote{3} Note, for this situation, the Adult and Adolescent OI
  Guidelines recommend completing the recommended PPSV23 series (receive the remaining additional
doses of PPSV23).\footnote{2}

- **Prior Receipt of PPSV23 Only:** For persons with HIV who have received one or more doses of
  PPSV23 previously without receiving PCV13, the recommenced approach is to receive one dose of
  PCV20 or PCV15, with this dose given at least 1 year after the prior dose of PPSV23 \footnote{2, 3}
  \textbf{(Figure 19).} \footnote{2, 3} After the PCV20 or PCV15 dose is administered, no further vaccine doses are recommended.\footnote{2, 3} This
  recommendation is the same in the ACIP Adult Immunization Schedule and Adult and Adolescent OI
  Guidelines.\footnote{2, 3}
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 prevaccine 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.[81] Most individuals with HIV mount adequate antibody responses to tetanus and diphtheria toxins, but responses are often lower among those with CD4 count less than 300 cells/mm³.[6,82]

Vaccines

Several tetanus and diphtheria toxoid vaccines (Td) are currently licensed by the FDA.[81] 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. 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.[81,83]

Recommendations

The following summarizes recommendation from the ACIP Adult Immunization Schedule and Adult and Adolescent OI Guidelines for administering Tdap and Td for adults with HIV.[2,3]

- **General Approach:** Adults and adolescents with HIV should receive immunization with Tdap and Td per the same schedule as nonpregnant adults without HIV.[2,3] 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 and adolescents with HIV who have not received the primary vaccination series for tetanus, diphtheria, or pertussis, give an initial three dose series consisting of one dose Tdap, followed by one dose Td or Tdap at least 4 weeks after Tdap, and another dose Td or Tdap 6 months to 12 months after the last Td or Tdap.

- **No Tdap After Age 11 Years:** For adults and adolescents with HIV who received the primary vaccine series for tetanus, diphtheria, or pertussis, but have not received a dose of Tdap after age 11 years, give a one-time dose of Tdap, followed by a Td or Tdap booster every 10 years (AII).[2] Adults and adolescents 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 During Pregnancy:** Give Tdap during every pregnancy in persons with HIV 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 person’s prior history of receiving Tdap.[2,3]
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.[84]

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).[85,86]

Recommendations

The following summarizes recommendations from the ACIP Adult Immunization Schedule and the Adult and Adolescent OI Guidelines for administering varicella vaccine to adults with HIV.[1,84]

• General Approach: The Adult and Adolescent OI Guidelines recommend adults with HIV should receive varicella vaccine if (1) they do not have immunity to VZV, and (2) they have a CD4 count of at least 200 cells/mm³ and a CD4 percentage of at least 15%.[2] If all of these criteria are met, the ACIP Adult Immunization Schedule recommends considering administering varicella vaccine based a shared-decision process.[3] The varicella vaccine does not need to be given to those born in the United States before 1980 (except health care personnel), or to those with VZV immunity.
• Varicella Serologic Screening: To identify persons with HIV who lack immunity to VZV, some experts would obtain varicella antibody titers (quantitative IgG) if the individual does not have any of the following: prior varicella immunization, prior clinical varicella (or zoster) infection, or a documented protective varicella IgG titer. The varicella titer does not have optimal sensitivity, especially in persons who have previously received varicella vaccine.
• Dosing Recommendation: Two doses of varicella vaccine should be given at least 3 months apart.
• Varicella Vaccine in Pregnancy: The varicella vaccine is contraindicated during pregnancy, regardless of HIV status. Pregnant people without evidence of varicella immunity and a CD4 count of at least 200 cells/mm³ and a CD4 percentage of at least 15% should receive (or complete) the varicella vaccine series upon completion or termination of pregnancy and before discharge from the health facility; varicella vaccine for these women should be administered as outlined, regardless of whether they were United States born before 1980.
• Contraindications: Varicella vaccine is contraindicated in persons with HIV who have a CD4 count less than 200 cells/mm³ or a CD4 percentage less than 15%. In addition, as noted above, the varicella vaccine is contraindicated in pregnant persons. Further, the quadrivalent measles-mumps-rubella-varicella vaccine is not recommended for individuals with HIV. The zoster vaccine should not be used interchangeably with the varicella vaccine.
Zoster Vaccine

Background

Although primary varicella-zoster virus infection is unusual in persons with HIV, the incidence of zoster among adults with HIV who are not receiving antiretroviral therapy is at least 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$^3$.[84,87,88] Individuals with HIV have additional increased risk in the first 4 months after starting effective antiretroviral therapy, likely as a result of immune reconstitution.[89] Following the widespread use of potent antiretroviral therapy, the incidence rate of zoster has markedly decreased compared with early years of the HIV epidemic.[90] 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.[91] 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

There are two zoster vaccines that have been approved for use in the United States: recombinant zoster vaccine (RZV) and zoster vaccine live (ZVL). The RZV vaccine contains varicella-zoster glycoprotein E combined with a novel adjuvant (AS01B), whereas ZVL contains high titers of attenuated live varicella-zoster virus (Figure 20).[92,93] As of June 30, 2020, the ZVL vaccine was no longer manufactured and sold in the United States. Therefore, the following discussion will address only the RZV vaccine. The RZV is licensed as a 2-dose vaccine series, given 2 to 6 months apart (minimum interval allowed 4 weeks).[1,93] In July 2021, the FDA expanded the indicated use of RZV to include individuals aged 18 years and older who are or will be at increased risk of developing herpes zoster because of immunodeficiency or immunosuppression.[94] The RZV has shown efficacy of greater than 95% in preventing herpes zoster in phase 3 trials that enrolled immunocompetent older adults.[95,96,97] A phase 1/2a trial evaluated RZV in persons with HIV and found it was safe and immunogenic, but this trial did not evaluate the impact of RZV in preventing zoster.[98] Giving RZV to persons who previously received ZVL may provide significant benefit. The RZV does not contain live varicella-zoster virus and therefore poses no risk of causing varicella-zoster infection.

Recommendations

The following summarizes recommendations in the Adult and Adolescent OI Guidelines for the use of RZV in persons with HIV.[2]

- **General Approach:** The RZV is recommended for adults with HIV who are 18 years of age or older. Note that ACIP uses 19 years and older as the age cut off for people with HIV to receive RZV, but this 19 year age cut-off was set to align with the age range in the general adult immunization schedule from ACIP, rather than a scientific indication.[3] This vaccine is considered safe regardless of the CD4 cell count.
- **Vaccine Schedule:** The RZV vaccine should be administered as a 2-dose series given 2 months apart (Figure 21) (AIII). The two-dose series should ideally be administered 2 to 6 months apart; if more than 6 months have elapsed by the second dose, the RZV series does not need to be restarted. If, however, the second dose is administered sooner than 4 weeks after the first dose, then another (third) RZV dose should be administered (more than 4 weeks after the dose that was given too early).[94]
- **Timing of Vaccine Administration:** In general, the RZV vaccine is recommended regardless of CD4 count. To maximize immunologic response to the vaccine, some experts recommend delaying vaccination until the individual has started antiretroviral therapy and (1) achieved virologic suppression and/or (2) obtained immune reconstitution, with a CD4 count recovery of at least 200 cells/mm$^3$ (CIII).
- **Prior History of Zoster:** The RZV vaccine is recommended regardless of whether the person with
HIV has a history of zoster, but the RZV vaccine should not be given during an episode of acute herpes zoster (AIII).

- **Prior Receipt of ZVL**: If an individual with HIV has previously received ZVL, they should undergo revaccination and receive the standard two dose series of RZV.
- **Contraindications**: The RZV vaccine should be deferred in persons who are pregnant, breastfeeding, or who have a current episode of herpes zoster.[94]
Travel Vaccines

Background

An estimated 8% of travelers to resource-limited regions of the world require treatment during travel, and major disease risks include vaccine-preventable illnesses.[99] Vaccines related to travel are generally not part of the initial evaluation process of persons with HIV. Many persons with HIV may at some point 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.[100]

Recommendations

All persons with HIV 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.[100,101] The Adult and Adolescent OI Guidelines provide information for vaccines to prevent cholera, typhoid, and yellow fever.[2]
Contraindicated Vaccines

The following summarizes vaccines that are available in the United States that are contraindicated in some or all adolescents and adults with HIV.[2] In general, caution should be exerted when considering the use of a live vaccine in any person with HIV.

The following live vaccines are contraindicated in all people with HIV regardless of CD4 cell count.

- Live intranasal influenza vaccine (LIAV) (*Flumist*)
- Live smallpox/mpox vaccine (ACAM2000) vaccine
- Quadrivalent measles-mumps-rubella-varicella vaccine

The following live vaccines are contraindicated in adults with HIV who have a CD4 count less than 200 cells/mm$^3$, a CD4 percentage less than 15%, or uncontrolled HIV.

- Live attenuated oral Typhoid vaccine (*Vivotif*)
- Live measles, mumps, and rubella (MMR) vaccine
- Live varicella vaccine (*Varivax*)
- Live yellow fever vaccine (*YF-VAX*) due to the theoretical risk of developing encephalitis in severely immune compromised patients

The following live vaccine has inadequate safety and efficacy data in persons with HIV.

- Live cholera vaccine (lyophilized CVD 103-HgR) (*Vaxchora*)

The following live vaccine is considered safe in adults with HIV.

- Live smallpox/mpox vaccine (*JYNNEOS*); this vaccine contains nonreplicating virus and is considered safe to give to adults with HIV, regardless of CD4 cell count.
Summary Points

- Immune responses to vaccinations among persons with HIV are enhanced in persons with higher levels of CD4 cell counts and with suppressed HIV RNA levels while taking antiretroviral therapy.
- Hepatitis A vaccine is recommended for all persons with HIV who are not immune to HAV. Postvaccination antibody testing should be performed 1 to 2 months after completion of the primary hepatitis A vaccine series.
- When giving the hepatitis B vaccine to adults with HIV, the preferred initial option is to use a double-dose of Engerix-B or Recombivax-HB given at a standard dosing schedule (3 doses), with 2 doses of Heplisav-B considered an alternative option. Postvaccination 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 persons with HIV who are 9 through 26 years of age. For persons with HIV who are 27 through 45 years of age, shared decision-making should be used to determine whether to administer this vaccine.
- All adults with HIV should receive two doses of conjugate meningococcal vaccine and booster doses every 5 years thereafter.
- MMR and varicella vaccines are indicated for asymptomatic persons with HIV who have a CD4 count of at least 200 cells/mm$^3$ and a CD4 percentage of at least 15%, if they lack immunity to these vaccine-preventable viruses.
- Pneumococcal vaccine-naïve persons should receive a single dose of either PCV15 or PCV20. If they receive PCV15, a follow-up dose of PPSV23 should be given at least 8 weeks later. Persons who have received PCV13, but not completed the series of PPSV23 doses, should complete the vaccine with PCV20 or complete those doses as originally planned.
- Two doses of RZV are recommended for persons with HIV who are 18 years of age and older, regardless of CD4 cell count and prior history of zoster.
- Some live virus vaccines are contraindicated in all persons with HIV and other live vaccines are contraindicated in persons with HIV who have a CD4 count less than 200 cells/mm$^3$.
- 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. Some travel vaccines are contraindicated in persons with HIV.
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COVID-19 mRNA vaccines consist of mRNA surrounded by a lipid nanoparticle (LNP). The LNP protect the mRNA from being degraded and it facilitates cellular uptake of the mRNA. The coding region (orange) is a genetically engineered sequence of nucleoside modified mRNA that encodes for the prefusion-stabilized SARS-CoV-2 spike protein. The Cap 5’ and 3’ UTR elements enhance the stability and translation of the mRNA.

Illustration: Cognition Studio, Inc.
Figure 2 COVID-19 mRNA Vaccines and Immune Responses

The immune system responds to the antigens on the surface of the cell produced by the COVID-19 mRNA vaccines. These vaccines generate cellular immune responses (T-cell) and humoral responses (B-cell). The immune response includes: activation of B cells to produce antibodies against SARS-CoV-2; activation of cytotoxic CD8 T-cells that can destroy cells infected with SARS-CoV-2; activation of CD4 T-cells that augment both CD8 T-cell and B-cell responses; generation of memory T and B cells that can quickly respond to future SARS-CoV-2 infection.

Illustration: Cognition Studio, Inc.
Figure 3 Number of Reported Cases of Hepatitis A Virus Infections — United States, 2013-2020

### Figure 4 Hepatitis A Vaccine Doses and Schedule for Adults

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Dose and Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis A Vaccines</strong></td>
<td></td>
<td></td>
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<tr>
<td><em>Havrix</em></td>
<td>1440 ELISA Units (IM)</td>
<td>2 doses given at 0, 6-12 months</td>
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<tr>
<td><em>Vaqta</em></td>
<td>50 U (IM)</td>
<td>2 doses given at 0, 6-18 months</td>
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<tr>
<td><strong>Combined Hepatitis A and B Vaccine</strong></td>
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<tr>
<td><em>Twinrix</em></td>
<td><em>Havrix 1440 ELISA Units plus Engerix 20 µg (IM)</em></td>
<td>Standard: 3 doses given at 0, 1, 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*Accelerated: Days 0, 7, 21-30 and 12 months</td>
</tr>
</tbody>
</table>

*For travelers, consider accelerated dosing*
**Figure 5 Recommendations for Hepatitis A Vaccine in People with HIV Based on CD4 Cell Count and Risk of Acquiring Hepatitis A Virus**

Source: Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Immunizations for Preventable Diseases in Adults and Adolescents Living with HIV. Last updated: April 13, 2023.
Figure 6 Heplisav-B Vaccine in HBV Vaccine-Naive People With HIV

This bar graph shows the seroprotective response rates to three doses of Heplisav-B vaccine given at 0, 4, and 24 weeks.

Figure 7 HBV Vaccine Schedule Options in Persons with HIV

Note: A 1.0 mL dose of Twinrix contains 720 ELISA units of inactivated hepatitis A virus [antigen component from Havrix] and 20 µg HBsAg [antigen component from Engerix-B]. Twinrix can be given on an accelerated schedule, but the accelerated schedule requires a total of 4 doses (days 0, 7, and 21 to 30 followed by a booster dose at 12 months).

Source: Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Immunizations for Preventable Diseases in Adults and Adolescents Living with HIV. Last updated: April 13, 2023.

*Combined hepatitis A and B vaccine for or individuals susceptible to both hepatitis A and hepatitis B

SD = standard dose; DD = double dose
Figure 8 Recommended Approach to Hepatitis B Vaccine Nonresponders in Persons with HIV

Source: Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Hepatitis B virus infection. Last Updated: April 14, 2023.

*If CD4 count <200 cells/mm³ at first vaccine series, some experts would delay revaccination until CD4 count ≥200 cells/mm³.
Figure 9 Approach to Isolated Anti-HBc in Persons with HIV

This approach is based on recommendations in the Adult and Adolescent Opportunistic Infections Guidelines.
*The full vaccine series options include the 3-dose series with double dose vaccine using Engerix-B or Recombivax or the 2-dose series using standard dose Heplisav-B.

Source: Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Hepatitis B virus infection. Last Updated: April 14, 2023.
Figure 10 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 capsomers to form viral-like particles (VLPs). The assembled pseudovirus is very similar to the native human papillomavirus and is highly immunogenic.

Illustration: David H. Spach, MD
Figure 11 9-valent Human Papillomavirus Vaccine

Illustration: David H. Spach, MD
Figure 12 Number of Measles Cases in United States, Reported by Year, 2010-2021

Source: Centers for Disease Control and Prevention
Figure 13 *Neisseria meningitidis* Isolates in Persons with HIV—United States, 1995-2014

Figure 14 Recommendation for Conjugate Quadrivalent Meningococcal Vaccine in Persons with HIV

Source: Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Immunizations for Preventable Diseases in Adults and Adolescents Living with HIV. Last updated: April 13, 2023.
Figure 15 Serotypes in the Pneumococcal Conjugate Vaccines (PCV): PCV13, PCV15, and PCV20

Serotypes with a yellow outside border indicate serotypes in PCV15 and PCV20 that were not included in PCV13. As shown, the two serotypes in PCV15 that are not in PCV13 are 22F and 33F; the five serotypes in PCV20 that are not in PCV13 are 8, 10A, 11A, 12F, 15B, 22F, and 33F.

Figure 16 Recommendations for Pneumococcal Immunization in Adults with HIV and No Prior Pneumococcal Immunization

Source: Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Immunizations for Preventable Diseases in Adults and Adolescents Living with HIV. Last updated: April 13, 2023.

### Pneumococcal Vaccine-Naïve Adults

- **PCV15** → **≥ 8 weeks** → **PPSV23**

  or

- **PCV20**
Figure 17 Recommended ACIP Approach to Persons with HIV and Prior Receipt PCV13 Only

Note: the red box represents receipt of prior pneumococcal vaccine.

Source: Advisory Committee on Immunization Practices (ACIP). Recommended Immunization Schedule for Ages 19 Years or Older, United States, 2023.
Figure 18 Recommended ACIP Approach to Persons with HIV and Prior Receipt PCV13 and ≥1 Dose PPSV23

Source: Advisory Committee on Immunization Practices (ACIP). Recommended Immunization Schedule for Ages 19 Years or Older, United States, 2023.
Figure 19 Recommended ACIP Approach to Persons with HIV and Prior Receipt of ≥1 Dose of PPSV23 (without PCV13)

Source: Advisory Committee on Immunization Practices (ACIP). Recommended Immunization Schedule for Ages 19 Years or Older, United States, 2023.
Figure 20 Herpes Zoster Vaccines

Illustration: David H. Spach, MD
Figure 21 Recommendation for Zoster Vaccine in Persons with HIV

Table 1.

**Vaccines in the Adult Immunization Schedule**

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Abbreviations</th>
<th>Trade Names</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Haemophilus influenzae</em> type b</td>
<td>Hib</td>
<td>ActHIB, Hiberix, PedvaxHIB</td>
</tr>
<tr>
<td>Hepatitis A vaccine</td>
<td>HepA</td>
<td>Havrix, Vaqta</td>
</tr>
<tr>
<td>Hepatitis A and hepatitis B vaccine</td>
<td>HepA-HepB</td>
<td>Twinrix</td>
</tr>
<tr>
<td>Hepatitis B vaccine</td>
<td>HepB</td>
<td>Engerix-B, Recombivax HB, Heplisav-B, Prehevbrio</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>LAIV4</td>
<td>FluMist Quadrivalent</td>
</tr>
<tr>
<td>Influenza vaccine, recombinant</td>
<td>RIV4</td>
<td>Flublok Quadrivalent</td>
</tr>
<tr>
<td>Measles, mumps, and rubella vaccine</td>
<td>MMR</td>
<td>M-M-R II</td>
</tr>
<tr>
<td>Meningococcal serogroups A, C, W, Y vaccine</td>
<td>MenACWY</td>
<td>Menevo, MenQuadfi</td>
</tr>
<tr>
<td>Meningococcal serogroup B vaccine</td>
<td>MenB-4C, MenB-FHbp</td>
<td>Bexsero, Trumenba</td>
</tr>
<tr>
<td>Pneumococcal conjugate vaccines</td>
<td>PCV13, PCV15, PCV20</td>
<td>Prevnar 13, Vaxneuvance, Prevnar 20</td>
</tr>
<tr>
<td>Pneumococcal 23-valent polysaccharide vaccine</td>
<td>PPSV23</td>
<td>Pneumovax 23</td>
</tr>
<tr>
<td>Tetanus and diphtheria toxoids</td>
<td>Td</td>
<td>Tenivac, Td vaccine</td>
</tr>
<tr>
<td>Tetanus and diphtheria toxoids and acellular pertussis vaccine</td>
<td>Tdap</td>
<td>Adacel, Boostrix</td>
</tr>
<tr>
<td>Varicella vaccine</td>
<td>VAR</td>
<td>Varivax</td>
</tr>
<tr>
<td>Zoster vaccine, recombinant</td>
<td>RZV</td>
<td>Shingrix</td>
</tr>
</tbody>
</table>

Source:

- Centers for Disease Control and Prevention. Vaccines in the Adult Immunization Schedule. [CDC]
Table 2.
2023 ACIP Recommended Immunizations for Adults with HIV, United States, 2022

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Abbreviations</th>
<th>CD4 count</th>
<th>Recommended/Contraindicated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;15% or &lt;200 cells/mm³</td>
<td></td>
</tr>
<tr>
<td><strong>Haemophilus influenza type b</strong></td>
<td>Hib</td>
<td>Recommended with an additional risk factor or other indication</td>
<td>1 or 3 doses, depending on indication</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>HepA</td>
<td><strong>Recommended</strong></td>
<td>2 or 3 doses depending on vaccine</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>HepB</td>
<td><strong>Recommended</strong></td>
<td>2, 3, or 4 doses depending on vaccine</td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td>9vHPV</td>
<td><strong>Recommended</strong></td>
<td>3 doses through age 26 years (0, 1-2, and 6 months)</td>
</tr>
<tr>
<td>Influenza inactivated 4, or Hepatitenza B recombinant 4</td>
<td>IIV4 or RIV4</td>
<td><strong>Recommended</strong></td>
<td>1 or 3 doses depending on vaccine</td>
</tr>
<tr>
<td>Influenza live, attenuated</td>
<td>LAIV4</td>
<td>Contraindicated</td>
<td>With measles-mumps-rubella: 2 doses (at least 8 weeks apart)</td>
</tr>
<tr>
<td>Measles-mumps-rubella</td>
<td>MMR</td>
<td>Contraindicated</td>
<td>With measles-mumps-rubella: 2 doses (at least 8 weeks apart)</td>
</tr>
<tr>
<td>Meningococcal serogroups A, C, W, Y</td>
<td>MenACWY-CRM, MenACWY-TT</td>
<td><strong>Recommended</strong></td>
<td>2 doses (at least 8 weeks apart), then revaccinate every 5 years</td>
</tr>
<tr>
<td>Meningococcal serogroup B</td>
<td>MenB-4C, MenB-FHbp</td>
<td>Recommended with an additional risk factor or other indication</td>
<td>2 or 3 doses</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>PCV15, PCV20, PPSV23</td>
<td>*<em>Recommended</em></td>
<td>1 dose PCV15 followed ≥8 weeks by 1 dose PPSV23</td>
</tr>
<tr>
<td>Tetanus-diphtheria-acellular pertussis</td>
<td>Tdap, Td</td>
<td><strong>Recommended</strong></td>
<td>1 dose Tdap then Td or Tdap booster every 10 years</td>
</tr>
<tr>
<td>Tetanus-diphtheria</td>
<td>VAR</td>
<td>Contraindicated</td>
<td>With varicella: Consider based on Shared Decision Making 2 doses (3 months apart)</td>
</tr>
<tr>
<td>Zoster, recombinant</td>
<td>RZV</td>
<td><strong>Recommended</strong></td>
<td>2 doses (2-6 months apart) at age ≥19 years</td>
</tr>
</tbody>
</table>

†This table is based on the 2023 ACIP Recommended Adult Immunization Schedule by Medical Condition and Other Indications, United States.

&Recommended if CD4 count greater than 200 cells/mm³ for at least 6 months with no evidence of immunity to measles-mumps-rubella.

Source:
- Advisory Committee on Immunization Practices (ACIP). Recommended Immunization Schedule for Ages 19 Years or Older, United States, 2023. [ACIP]