Immunizations for Children with HIV/AIDS

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Objectives

1. Describe the importance of immunizations for children with human immunodeficiency virus (HIV)/AIDS.
2. Discuss the specific types of immunizations that are available for HIV-infected patients.
3. Understand the side effects related to the administration of immunizations to HIV-infected patients.

Key Points

1. Immunizations play an important role in the prevention of childhood diseases.
2. It is recommended that children infected with HIV/AIDS follow an accelerated immunization schedule.
3. The bacille Calmette–Guérin vaccine is the most commonly used vaccine in the world and is the only vaccine available for Mycobacterium tuberculosis but should not be used in HIV-infected children.
4. The World Health Organization recommends the use of the oral polio vaccine in asymptomatic HIV-infected children in areas of the world where the inactivated polio vaccine is not available.
5. The measles and varicella vaccines are administered to HIV-infected children who are not severely immunocompromised.
6. The hepatitis B virus vaccine is recommended for HIV-infected children.
7. The yellow fever vaccine is recommended at 9 months of age and every 10 years thereafter for asymptomatic HIV-infected children living in or traveling to HIV-endemic areas of the world.

Importance of Immunizations for HIV-Infected Children

Immunization is one of the easiest ways to prevent dangerous diseases. Immunizations can also help human immunodeficiency virus (HIV)–infected children, who are more likely to acquire preventable diseases because of a compromised immune system. Appropriate immunizations vary by geographic location. There is limited information regarding routine immunization of HIV-infected children, but with some notable exceptions, immunization is generally safe and beneficial for HIV-infected patients.

Immune Response

Immune responses to vaccination vary, depending on the nature of the vaccine and the individual's immune status. Adult immune systems respond when exposed to a disease-causing antigen because of previous exposure to the antigen, either through vaccination or through acquisition of the infection. An unimmunized child who has never been exposed to the disease-causing antigen is reacting for the first time. The immune system dysfunction that occurs with advanced HIV infections can result in a blunted immune response to immunization, but this response does depend on how affected the immune system is at the time of vaccine receipt. Therefore, it is important to immunize HIV-infected children as quickly as possible so that they can mount protective responses prior to the failing of their immune system. One should consider HIV-infected patients with $CD4^+$ lymphocyte percentages of less than 15% or an absolute $CD4^+$ lymphocyte count that is lower than normal for age, those with a history of an AIDS-defining illness, or those with clinical manifestations of symptomatic HIV to have severe immunosuppression. Patients with $CD4^+$ lymphocyte counts from 15% to 25% or those patients older than 6 years with counts of 200-500 are considered to have limited immune deficits. Patients who have been severely immunosuppressed but have had immune reconstitution with highly active antiretroviral therapy can also usually respond to immunizations. Patients should therefore be categorized based upon the increase in their CD4 count, not the nadir count. The exact time at which the immune-reconstituted

lymphocytes become fully functional is not known; therefore, it is prudent to delay postreconstitution immunizations for at least 3 months to maximize the immune response. Increases in HIV viral loads have been observed after administration with several different vaccines (e.g., influenza), but the clinical significance of these increases is not known and they are usually transient. The possibility of transient increases in viral load is not a contraindication for immunization.

Immunization Schedule for HIV-Infected Children

The Expanded Program on Immunizations (EPI) of the World Health Organization (WHO), in collaboration with UNICEF, recommends a narrow and accelerated immunization schedule for HIV-infected children (**Table 1**). The immunization schedule may vary slightly in each country. The EPI schedule accounts for limited resources, barriers in the health care delivery system, and the urgency to better control morbidity and mortality related to infectious diseases. The WHO has also made recommendations that serve to guide whether particular vaccines should be used in the asymptomatic or symptomatic HIV-infected child (**Table 2**).

Specific Immunizations

Bacille Calmette–Guérin Vaccine

Bacille Calmette–Guérin (BCG) is the most widely used vaccine in the world and is the only vaccine available for prevention of *Mycobacterium tuberculosis*. This live vaccine is prepared from attenuated strains of *M. bovis* and is currently used in more than 100 countries. BCG is used to help prevent disseminated and other life-threatening forms of tuberculosis in infants and children. There are various BCG vaccines used throughout the world, and they differ in their composition and efficacy. Recent data have demonstrated, however, that children who are HIV infected when immunized with BCG at birth, and who later progress to AIDS, are at increased risk of developing disseminated BCG disease later in life. In 2007 the WHO recommended that BCG vaccine not be given to any child known to be HIV infected (symptomatic or asymptomatic). Infants born to mothers with an unknown HIV status or those born to mothers who are known to be HIV infected but without signs or symptoms suggestive of HIV can receive the vaccine.

Table 1. WHO Expanded Programme on Immunization for HIV-Exposed or -Infected Children

Vaccine	Birth	6 wks	10 wks	14 wks	9 mos
BCG[a]	x				
OPV[b]	x	x	x	x	
DTP		x	x	x	
Hepatitis B[c]	x	x	x	x	
Haemophilus influenzae, type B		x	x	x	
Yellow fever[d]					x
Measles[e]					x

[a] Not indicated for any infant or child known to be HIV infected.
[b] In polio-endemic countries.
[c] If perinatal transmission is not high can give at 6, 10, and 14 weeks.
[d] In countries where yellow fever poses a risk.
[e] A second opportunity to receive a dose of measles vaccine should be provided for all children. This can be done either as part of a routine schedule or in an immunization campaign.

Table 2. Immunizations for HIV-infected patients

Vaccine	Asymptomatic HIV infection	Symptomatic HIV infection
BCG	No	No
DTP	Yes	Yes
Hepatitis A	Yes	Yes
Hepatitis B	Yes	Yes
Haemophilus influenzae, type B	Yes	Yes
HPV	Yes	Yes
Influenza	Yes	Yes[a]
JBE	Yes	No[b]
Measles	Yes	No[b]
Neisseria meningitidis	Yes	Yes
Polio vaccine	Yes	Yes[c]
Rotavirus	Yes	No[b]
Streptococcus pneumoniae	Yes	Yes
Typhoid	Yes	Yes[d]
Varicella-zoster virus	Yes	No[b]
Yellow fever	Yes	No[a]

[a] Only the inactivated influenza vaccine that is given intramuscularly should be used.
[b] HIV-infected patients with $CD4^+$ lymphocyte percentages of less than 15% or an absolute $CD4^+$ lymphocyte count that is lower than normal for age, those with a history of an AIDS-defining illness, or those with clinical manifestations of symptomatic HIV should all be considered to have severe immunosuppression, and vaccine should not be given.
[c] The inactivated polio vaccine that is given intramuscularly should be used.
[d] The inactivated typhoid vaccine that is given intramuscularly should be used.

The recommended dose of BCG vaccine is 0.05 mL (0.05 mg) in children younger than 12 months and 0.1 mL (0.1 mg) in persons older than 12 months. It should be administered via the intradermal route. The best sites for injection are dorsogluteal and the lateral aspect of the upper arm, but in many countries the location is standardized. Attention should be given to how high on the upper arm one should give the injection. The higher the location, the greater the tendency for a scar to form. The best location is in the lower deltoid muscle. A papule with redness appears at the site of injection within 2-3 weeks. This improves slowly and is followed by a local lesion that may ulcerate 6-8 weeks later. This lesion will heal and leave a small flat scar 3-6 months after vaccination. Prolonged local reactions are common after receipt of the vaccine. The reactions usually consist of localized redness and swelling, which can last a few weeks to several months. Poor injection technique, such as giving the injection too deep, can cause the formation of large abscesses. In addition to the development of subcutaneous abscesses, regional lymphadenitis may also develop. Osteitis affecting the long bones underlying the injection site can occur up to several years after BCG immunization.

Diphtheria–Tetanus–Pertussis Vaccine

The diphtheria–tetanus–pertussis (DTP) vaccine is not contraindicated for HIV-infected children or their close contacts. Newer preparations of DTP vaccines using acellular pertussis (DTaP) for the primary series and booster doses or those including acellular pertussis for older adolescents and adults (Tdap) are available in many countries. When available, these are the preferred preparations to use. Recent recommendations providing acellular pertussis in the routine use of booster doses of diphtheria–tetanus immunizations (Tdap) to adolescents (>11 years) and adults (<65 years) also apply for symptomatic or asymptomatic HIV infected patients.

The vaccine is administered intramuscularly, usually in the anterolateral aspect of the thigh in infants and younger children and in the deltoid muscle in older children. Mild side effects after receipt of DPT vaccination include low-grade fever, mild irritability, and tenderness at the site of the injection. These side effects are usually due to the pertussis portion of the vaccine. Severe complications that may occur include fever; high-pitched, uncontrollable crying; febrile seizures; and shock. To help minimize postimmunization fever and muscle soreness, one may use acetaminophen (paracetamol) or ibuprofen every 4-6 h for the first 24 h after the vaccine is administered.

Parents should be instructed to return to the clinic if the child has a fever of more than 39.5°C, a seizure, or difficulty breathing or cries inconsolably for more than 3 h at a time.

Hepatitis A Vaccine

In the United States the hepatitis A vaccine is recommended for all children at 1 year and is given in a two-dose series, with the second dose being given 6-12 months after the first dose. There are both pediatric and adult formulations of the vaccine, and they differ in the dose of the hepatitis A antigen used. The adult formulations are recommended for persons aged at least 19 years. The vaccines are made from formalin-inactivated hepatitis A virus and are therefore safe for HIV-infected children and adults. As with other vaccines, however, patients with severe immunosuppression may have a suboptimal response. The need for booster doses has not been determined.

The hepatitis A vaccines are given intramuscularly, with the deltoid muscle being the preferred site of administration. The pediatric and adult forms vary based upon the amount antigen in the vaccine as well as the amount injected (e.g., 0.5 mL for pediatric and 1.0 mL for adult forms of the vaccine). The adverse reactions associated with the vaccine are mild and include local pain and induration at the injection site. There is a three-dose combination vaccine against hepatitis A and hepatitis B available for patients aged 18 or more years. Patients who have not had clinical disease or vaccine should receive immunoglobulin (0.02 mL/kg; 5-mL maximum) and hepatitis A vaccine for significant exposures occurring not more than 2 weeks in the past to prevent disease.

Hepatitis B Vaccine

Despite a short history of immunizing HIV-infected children with hepatitis B virus (HBV) vaccine, the WHO recommends the immunization for children and adults infected with HIV. To our knowledge, no adverse events associated with hepatitis vaccination of HIV-infected adults and children have been reported. However, in HIV-infected children, the antibody response mounted against HBV does not appear to be long lasting. For infants, two schedules are available. One is recommended in countries where perinatal transmission of HBV is frequent (birth,

6 weeks, 10 weeks, 14 weeks) and a second can be used where perinatal transmission is less frequent (6 weeks, 10 weeks, 14 weeks). For older children and adults, three doses would also be required (0, 1-2 months, 4-6 months).

There are two types of hepatitis vaccine available: plasma-derived vaccine and recombinant vaccine. The two are equal in terms of efficacy and length of immunogenicity. The hepatitis vaccine is available as a single-antigen or a combination-antigen product (e.g., hepatitis B–*Haemophilus influenzae*, type B; hepatitis A–hepatitis B) and should be administered intramuscularly, avoiding the dorsogluteal muscle because of possible reduced immunological response. Anaphylaxis (severe allergic reaction with symptoms that include swelling of the mouth, difficulty breathing, low blood pressure, and sometimes shock) is a rare but serious side effect of this or any immunization. In general, however, the HBV vaccine is well tolerated, with few reports of adverse events. If adverse events do occur, they are usually mild, consisting of irritability and soreness at the injection site. These symptoms usually appear within 24 h of receiving the vaccine and resolve within 1 or 2 days. For HIV-infected patients many experts suggest postvaccination antibody testing 1-2 months after the last dose is given. For patients who do not produce adequate anti-HBV titers (<10 mIU/mL) after the primary vaccine series, an additional three-dose series should be provided. Patients who remain anti-HBV negative after reimmunization are not likely to respond to additional doses. Unimmunized patients or those without a history of clinical disease should receive both HBV vaccine and hepatitis B immunoglobulin after a high-risk exposure to infected blood or body fluids (e.g., semen).

Haemophilus influenzae, Type B Vaccine

Haemophilus influenzae, type B (HIB) is a bacterium transmitted from person to person by sneezing and coughing, resulting in colonization of the nose and throat. Children whom this organism merely colonizes will be asymptomatic. In some children, however, the organism will cause significant and life-threatening disease. It can cause pneumonia, epiglottitis, bacteremia, meningitis, or pyogenic arthritis. Several HIB conjugate vaccines are available either as single-antigen products or in combination with other antigens (e.g., HBV–HIB, DTP–HBV–HIB). The immunization schedule for the HIB vaccine is a series of three injections that can be given on the same schedule as the DTP. An additional dose of HIB conjugate vaccine is given in some countries at 12-15 months of age regardless of which regimen was used for the primary series, though there is WHO recommendation for doing so at this time. One dose of the vaccine is sufficient for children aged 12-24 months who are late in receiving their vaccines.

The 0.5-mL dose is given intramuscularly in the outer mid thigh for infants and in the upper arm for older children. Adverse reactions to the vaccine are usually mild and involve simple pain, erythema, or swelling of the injection site. The HIB vaccine can be provided to asymptomatic or symptomatic HIV-infected children. Infants and children who are severely immunocompromised may not respond to the vaccine as well as those children who are immunocompetent.

Human Papillomavirus Vaccine

The transmission of genital human papillomavirus (HPV) is a common sexually transmitted infection. Although most of these infections are self-limited, persistent infection with HPV can cause anogenital cancers. Genital HPV types are categorized according to their epidemiologic association with cervical cancer. Infections with low-risk types (e.g., types 6 and 11) can cause benign or low-grade cervical cell changes, genital warts, and recurrent respiratory papillomatosis. High-risk types (e.g., types 16 and 18) can cause low-grade cervical cell abnormalities, high-grade cervical cell abnormalities that are precursors to cancer, and anogenital cancers. High-risk HPV types are detected in 99% of cervical cancers; approximately 70% of cervical cancers worldwide are caused by types 16 and 18. The quadrivalent HPV vaccine is a mixture of four HPV type–specific noninfectious viruslike particles prepared from the proteins of HPV types 6, 11, 16, and 18 combined with an aluminum adjuvant. Clinical trials indicate that the vaccine has high efficacy in preventing persistent HPV infection; cervical cancer precursor lesions; vaginal and vulvar cancer precursor lesions; and genital warts caused by HPV types 6, 11, 16, or 18 among females who have not already been infected with the respective HPV type. There are currently no data available on the immunogenicity, safety, and efficacy of the HPV vaccine in HIV-infected persons. But because the HPV vaccine is a noninfectious vaccine, one can administer it to HIV-infected (asymptomatic or symptomatic) women. However, the immune response might be less vigorous in those individuals who are severely immunocompromised.

The HPV vaccine is indicated for girls and women aged 9–26 years and should be administered intramuscularly (deltoid region of the arm or in the higher anterolateral area of the thigh). After the initial 0.5-mL dose, a second dose is required 2 months later and a third dose should be given 6 months after the initial dose. Fainting may occur after any dose of the vaccine, so vaccinees should be observed for approximately 15 min after administration. Other adverse effects include fever; nausea; and pain, swelling, erythema, or pruritus of the injection site.

Influenza Vaccine

Influenza can cause severe infections and complications in HIV-infected children. HIV-infected adults with influenza have a longer, more severe disease course and are more likely to suffer from lower levels of oxygen in the blood than healthy adults. In the United States, influenza immunization is indicated for all HIV-infected children aged 6 months or older, as well as their close contacts. There are two types of trivalent vaccines available: an inactivated and a live-attenuated, cold-adapted vaccine. Patients with HIV should not receive the live-attenuated, cold-adapted vaccine, which is given intranasally. The inactivated vaccine should be the only vaccine used for HIV-infected patients. It should be administered in the autumn and repeated annually because of the vaccine's low immunogenicity and changes in the type of influenza causing infection from year to year. For healthy close contacts of HIV-infected patients, the live-attenuated, cold-adapted vaccine can be used for contacts aged 5-49 years or the inactivated vaccine for those aged at least 6 months.

The influenza vaccine is administered as an intramuscular injection in the anterolateral upper side of the thigh in young children and the deltoid muscle in older children. A child receiving the influenza vaccine for the first time between the ages of 6 months and 8 years should receive a series of two shots separated by 1 month. Children aged 6-35 months should receive 0.25 mL, and those aged 3 years or older should receive 0.5 mL. Most adverse events are minor; they include fever, malaise, and soreness or redness at the injection site.

Japanese B Encephalitis Vaccine

Japanese B encephalitis (JBE) is the leading cause of viral encephalitis in Asia. Humans are dead-end hosts and become infected only through the bite of an infected mosquito. Most JBE infections are asymptomatic, but in its severe form patients may develop meningo-encephalitis, aseptic meningitis, or a polio-like flaccid paralysis. Most cases occur in children younger than 10 years.

Three types of JBE vaccine are currently available: (1) inactivated mouse brain–derived vaccine, (2) cell culture–derived inactivated vaccine, and (3) cell culture–derived live-attenuated vaccine. There are some countries that include inactivated JBE vaccination in the WHO EPI vaccination schedule for children (e.g., Thailand), and some countries are routinely using the live-attenuated vaccine (e.g., China). HIV-infected patients may receive the inactivated vaccines, but live-attenuated vaccine should not be used in patients who are severely immunocompromised.

The recommended primary series of the inactivated vaccine for patients older than 3 years is three doses (1.0 mL each dose) administered subcutaneously on days 0, 7, and 30. An abbreviated schedule can be used for those who may be traveling (0, 7, 14 days). The dose for children aged 1–3 years is usually 0.5 mL. Few data are available on vaccine safety and efficacy for infants.

Local and mild systemic reactions occur in 15%-25% of vaccine recipients. Fever, headache, and myalgia are the most common complaints. This vaccine, however, also has the unique ability to produce delayed (>72 h after immunization) allergic reactions that can be life threatening. Therefore, patients should not travel internationally for at least 7 days after receipt of the vaccine.

Measles Vaccine

In some developing countries, measles continues to cause serious illness and death in children younger than 5 years. HIV-infected children have an increased risk of developing severe complications when infected with measles. A review of reported cases of measles infections in children with HIV indicates a 40% death rate. The WHO recommends that HIV-infected children be offered measles vaccination as soon as possible. Therefore, children who are HIV infected can receive measles vaccine at 6 months of age, followed by a second dose at 9 months of age.

Recommendations in the United States are to immunize asymptomatic HIV-infected children against measles, mumps, and rubella at age 12-15 months and again at 4-6 years. Some experts suggest that the second dose should be given 1 month after the first dose instead of waiting until 4-6 years of age. Any children who are severely immunocompromised should be excluded. Because there are fewer cases of measles in the United States than in the developing world, and the risk of acquiring the disease is lower, making this recommendation practical in this small group of children. In many other parts of the world, however, the accelerated dosage schedule is recommended, because HIV progressively harms the immune system, and antibody responses to the vaccine are less likely to be effective as the disease progresses. Close contacts of children with HIV infection also should be vaccinated at routine intervals unless they are HIV infected and have severe immunosuppression. Measles vaccine is made from a live-attenuated strain and is available as a monovalent formulation (measles alone) or in combinations such as measles–rubella (MR), measles–mumps–rubella (MMR), or measles–mumps–rubella–varicella (MMRV). MMRV should not be administered as a substitute for the component vaccines in children with HIV until more data are available.

Severely immunocompromised and symptomatic patients with HIV should receive intramuscular immunoglobulin (0.5 mL/kg; maximum dose, 15 mL) if exposed to measles, regardless of vaccine status. Previously immunized HIV-infected children and adolescents have developed wild-type measles.

The measles vaccine is administered as a subcutaneous injection in the anterolateral region of the thigh or upper arm. Minor adverse reactions that may occur include fever (>39.4°C in 5%-15% of patients) 1-2 weeks after the injection. The fever generally lasts 1-2 days but may last as long as 5 days. Approximately 5% of vaccine recipients will develop a transient rash that is similar to the rash seen with wild-type measles. Other minor adverse effects include cough, nasal drainage, redness, swelling, and tenderness at the injection site. Serious adverse events include seizures, hypersensitivity reactions, thrombocytopenia, and subacute sclerosing panencephalitis.

Neisseria meningitidis *Vaccine*

Neisseria meningitidis is a gram-negative diplococcus that is responsible for many cases of bacteremia and meningitis among children and adults. At least 13 different serogroups exist, but most disease is caused by five of these serogroups (A, B, C, Y, and W-135). There are currently two types of meningococcal vaccines available: polysaccharide (PS) vaccines and conjugate vaccines. Both will cover either a single or multiple serogroups of *N. meningitidis*. The main PS vaccines currently available cover two (A and C), three (A, C, and W-135), or four (A, C, Y, and W-135) serogroups. The problem with the PS vaccines is that they are not immunogenic in children younger than 2 years, fail to induce immunological memory, and do not provide protection for more than 3-5 years.

Similar to the HIB and pneumococcal vaccines, newer vaccines have incorporated a PS conjugated to a protein carrier (e.g., diphtheria toxoid), resulting in a vaccine that not only is immunogenic in children younger than 2 years but also will induce long term-immunity. Current conjugate vaccines may be against a single serogroup (e.g., C) or multiple serogroups (A, C, Y, and W-135). In contrast to the other serogroups that tend to cause invasive disease, development of a vaccine against serogroup B remains problematic. Despite the type of vaccine or the number of serogroups involved, these vaccines are safe for asymptomatic or symptomatic HIV patients. The type of vaccine used will dictate the age of receipt and the type of vaccine used.

Meningococcal vaccines are given intramuscularly, and the most common adverse effects include localized pain, headache, and fatigue. There has been a temporal association with the quadrivalent conjugate vaccine (A, C, Y, and W-135) and Guillain–Barré syndrome; therefore, this vaccine should be avoided in patients who have a previous history of Guillain–Barré syndrome.

Polio Vaccine

Polio has been eradicated in much of the world. The risk of an adverse event after receipt of oral polio vaccine (OPV) by HIV-infected children is low, but there have been cases of children with primary immunodeficiency syndromes (problems with which they were born such as the B-cell disorder or X-linked agammaglobulinemia) who developed vaccine-associated paralytic polio after receiving OPV. Inactivated polio vaccine (IPV) is

considered the safer choice and is used for HIV-infected children and household contacts in countries where it is available. The U.S. Centers for Disease Control and Prevention endorses the use of IPV for all children. Because of the ease of administration, the ability to provide herd immunity, and few reported adverse events, the WHO continues to recommend the use of OPV in infants and children with an unknown HIV status or for those HIV-infected children who are asymptomatic in resource-limited areas. Symptomatic HIV-infected children can receive the IPV.

OPV is administered by mouth. IPV is administered via subcutaneous injection in the upper arm or thigh. There are no immediate side effects secondary to OPV administration. Vaccine-associated paralytic polio usually occurs within 2 months after immunization, but the risk is low, estimated at 1:7.8 million doses. Few adverse events secondary to receiving IPV have been reported.

Rotavirus Vaccine

Rotaviruses are the leading cause of severe diarrheal disease and dehydration in infants and young children in both developed and developing countries. Virtually all children are infected by the time they reach 2-3 years of age. Most symptomatic episodes occur between 3 months and 2 years of age, with a peak incidence between 7 and 15 months. Infants and young children are most at risk for the development of life-threatening dehydration from this infection.

The current licensed pentavalent rotavirus vaccine is an oral vaccine that contains five active reassortant rotaviruses. The rotavirus parent strains were isolated from human and bovine strains. Practitioners should consider the potential risks and benefits of administering rotavirus vaccine to infants with known or suspected HIV infection. No safety or efficacy data are available for the administration of rotavirus vaccine to infants who are HIV infected.

Three doses of the pentavalent rotavirus vaccine are administered orally at 2, 4, and 6 months of age. The first dose should be administered between 6 and 12 weeks of age; immunization should not be initiated for infants older than 12 weeks. Rotavirus vaccine can be given simultaneously with other childhood immunizations (e.g., DTP, HIB). If immunization with rotavirus vaccine is being considered for an HIV-infected infant, severe immunosuppression should be considered a contraindication to vaccine receipt. Rotavirus vaccine can be used for siblings living in the home of an HIV-infected patient. Fever and abdominal complaints are the most commonly reported adverse effects of the vaccine. Previous rotavirus vaccines were temporally associated with intussception, but this outcome has not been demonstrated with the current pentavalent vaccine.

Streptococcus pneumoniae *Vaccine*

Pneumococcus is the most common cause of bacterial invasive infections in children with HIV, causing frequent episodes of otitis media, sinusitis, and pneumonia. The pneumococcal conjugate vaccine (PCV7) and the pneumococcal polysaccharide vaccine (PPV23) are well tolerated in children with HIV. In the United States, PCV7 is recommended at 2, 4, 6, and 12-15 months of age, followed by PPV23 at 24 months of age and again 3-5 years later. If not previously vaccinated, patients aged at least 7 years should receive PPV23 with a single revaccination after 3-5 years. As the next generation of conjugate pneumococcal vaccines becomes available, countries that currently use PCV7 should assess the value of changing to the newer formulations to protect children against more invasive pneumococcal serotypes.

PCV7 is administered as a 0.5-mL dose by an intra-muscular injection in the upper anterior thigh or upper arm. It may be given simultaneously with other age-appropriate childhood immunizations.PPV23 is given as a 0.5-mL dose either subcutaneously or intramuscularly in the deltoid muscle region or the lateral mid thigh with appropriate precautions to avoid intramuscular administration. About half of the people who receive the vaccine develop mild adverse events, such as tenderness and redness at the injection site. Only about 1% of pneumococcal vaccine recipients develop fever, muscle pain, or severe local reactions.

Typhoid Vaccine

Typhoid fever is a febrile illness that can include bacteremia and death. It is encountered most often in resource-limited areas because infection occurs as a result either of fecal–oral contamination from an infected person or by contact with an item (e.g., food) contaminated by a carrier. Typhoid vaccines are not routinely provided to patients but may be used as part of an outbreak control or before travel.

There are currently two types of vaccines available: the live oral vaccine (LOV) and the polysaccharide vaccine (PSV). The LOV can be used in patients older than 6 years but should not be used for immunosuppressed HIV patients. The PSV is indicated for patients aged 2 or more years and is the vaccine of choice for immunocompromised HIV patients.

The LOV is given in four doses (one capsule every 2 days for a total of four capsules), whereas the PSV (0.5 mL) is intramuscular. Booster doses of the LOV in circumstances of continued or repeated exposure are every 5 years, whereas booster doses should be given every 2 years for the PSV. There are no data available for the efficacy of any typhoid vaccine in children younger than 2 years. The LOV requires replication in the gastrointestinal tract for effectiveness, so it should not be administered during gastrointestinal tract illness. Also, concomitant use with some antimalarial medications (e.g., atovaquone/proguanil) resulted in a poor immune response. Antimicrobial agents should also be avoided for at least 24 h prior to the first dose of vaccine and not until 7 days after the fourth dose.

Varicella (Chickenpox) Vaccine

In HIV-infected patients, chickenpox, or varicella-zoster virus, can cause serious complications, including pneumonia and encephalitis. The varicella live-attenuated vaccine can be administered to HIV-infected children without a history of clinical disease who are asymptomatic or mildly symptomatic and have age-specific $CD4^+$ lymphocyte percentages greater than 15%. Patients who are severely immunosuppressed should not receive the vaccine. Siblings of HIV-infected children should also be immunized with varicella vaccine. Combination vaccines such as the MMRV vaccine should not be used in HIV-infected patients.

The varicella vaccine is administered subcutaneously in the anterolateral region of the thigh or upper arm. HIV-infected patients who are eligible for the vaccine should receive two doses 3 months apart as soon as possible after their first birthday. HIV-infected adults without evidence of immunity or a history of clinical disease can also receive two doses 3 months apart, provided that they are not severely immunocompromised. Minor adverse events associated with varicella vaccine include fever; tenderness, redness, or swelling at the injection site; and a mild maculopapular or varicelliform rash at the injection site or elsewhere on the body. Serious adverse events that may occur include severe nausea and vomiting, loss of consciousness, dyspnea, and hives. A single dose of zoster vaccine can be given to HIV-infected adults aged at least 60 years, whether they report a prior episode of zoster (shingles) or not. This vaccine is a different product from the chickenpox vaccine and is not indicated for children. Like the chickenpox vaccine, however, it should not be used for adults who are severely immunocompromised.

HIV-infected patients who have neither received the vaccine nor have had clinical disease and who are exposed to chickenpox (varicella) should receive varicella-zoster immunoglobulin (VariZIG) within the first 96 h after exposure. If VariZIG is not available, intravenous immunoglobulin (IVIG) can be used. Acyclovir is beneficial in the treatment of varicella infection, and some experts recommend using acyclovir for a susceptible immunocompromised patient who has been exposed to varicella-zoster virus.

Yellow Fever Vaccine

Besides mosquito control, the yellow fever vaccine is the only measure available to prevent yellow fever. Immunity occurs within 1 week in 95% of people vaccinated, and immunity lasts for at least 10 years. The EPI of the WHO recommends immunization at 9 months or older for asymptomatic HIV-infected children who are living in or visiting disease-endemic areas. A booster vaccine should be administered every 10 years thereafter. Patients with symptomatic HIV infection or those with severe immune suppression should generally not receive the vaccine. Where the risk of disease is very high, medical practitioners may consider the risk to the patient from the vaccine to be less than that from acquiring the disease and elect to give the vaccine.

The vaccine is a live-attenuated vaccine that should be administered subcutaneously in a single dose of 0.5 mL for those living or traveling to areas with endemic yellow fever. It is required every 10 years by international regulations for travel to and from certain countries. Consideration for using the vaccine in an outbreak setting in patients aged 4-9 months must be weighed against the potential for life-threatening side effects. Infants younger than 4 months should not be immunized because of an increased risk of vaccine-associated encephalitis. Yellow fever vaccine–associated viscerotropic disease and yellow fever vaccine–associated neurotropic disease can occur

but are rare. Family members of immunocompromised patients can receive the vaccine.

Intravenous Immunoglobulin

IVIG has been used in the past as protection against bacterial infections, especially pneumococcal infections, for children infected with HIV. It is now no longer indicated. HIV-infected children receiving *Pneumocystis jirovecii* (formerly PCP [*Pneumocystis carinii*]) pneumonia prophylaxis with trimethoprim–sulfamethoxazole do not derive additional benefit from IVIG. Hyperimmune globulins are available that may be used for specific indications. The use of hyperimmune globulins is recommended for children who have been exposed to particular antigens to prevent an infection or shorten the course of the disease. For example, VariZIG is recommended for children who have been exposed to varicella-zoster virus. Other hyperimmune products include hepatitis B immunoglobulin, rabies immunoglobulin, tetanus immunoglobulin, cytomegalovirus intravenous immunoglobulin, and respiratory syncytial virus intravenous immunoglobulin.

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