

IMMUNIZATIONS FOR CHILDREN WITH HIV/AIDS

IMMUNIZATIONS

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Objectives

The purposes of this module are to:

1. Describe the importance of immunizations for children with HIV/AIDS.
2. Review the mechanisms involved in the immune response.
3. Identify the accelerated immunization schedule for HIV-infected children.
4. Discuss the specific types of immunizations administered to HIV-infected children.
5. Understand the side effects related to the administration of immunizations to HIV-infected children.
6. The hepatitis B 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 endemic areas of the world.

Key Points

1. Immunizations play an important role in the prevention of childhood diseases.
2. Children infected with HIV/AIDS should receive an accelerated immunization schedule.
3. BCG is the most commonly used vaccine in the world and is the only vaccine available for *Mycobacterium tuberculosis*.
4. The World Health Organization (WHO) recommends the use of the oral polio vaccine (OPV) in asymptomatic and symptomatic HIV-infected children in areas of the world where the inactivated polio vaccine (IPV) is not available.
5. The measles vaccine is administered to HIV-infected children who are not severely immunocompromised.

Importance of Immunizations for HIV-Infected Children

Immunization is one of the easiest ways to prevent dangerous diseases. Immunizations can also help HIV-infected children who are more likely to acquire preventable diseases because of a compromised immune system. Appropriate immunizations vary by geographic location. It is important to consider several questions regarding immunization of HIV-infected children: Should the child be immunized early before HIV has caused damage to the immune system? When should a child be immunized according to an accelerated schedule? Will an immune system that takes two to five years to fully mature benefit from a routine immunization schedule? What will be the risk to an already weakened immune system if certain vaccines accelerate HIV replication? Will this increase in viral replication hasten HIV disease progression? Should live attenuated vaccines be used in HIV-infected children?

There is limited information regarding routine immunization of HIV-infected children. However, the fact that very few adverse events have been reported leads us to believe that the benefits associated with immunization outweigh the possible risks.

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 particular 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 response is usually and least expensively assessed by measurement of humoral (antibody) immunity, but this may be blunted in an HIV-infected person because of the damage HIV has done to the immune system.

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 and women of childbearing age (see Table 1). The immunization schedule may vary slightly in each country. The EPI schedule takes into consideration limited resources, barriers in the health-care delivery system, and the urgency to better control morbidity and mortality related to infectious diseases.

Specific Immunizations

Bacille Calmette-Guérin (BCG) Vaccine

BCG is the most widely used vaccine in the world and is the only vaccine available for prevention of Mycobacterium tuberculosis. Use of the vaccine in immunocompromised children has triggered concerns of disseminated BCG infection. Many authorities believe that the possible complications of receiving

the BCG vaccine, such as lymphadenitis, fistula formation at the site of injection, osteomyelitis, and disseminated disease, outweigh the benefits. Where the risk of tuberculosis is high, the WHO recommends BCG at birth or as soon as possible thereafter, in accordance with standard policies for immunization of non-HIV-infected children.

The recommended dose of BCG vaccine is 0.5ml per dose and should be administered via the intradermal route. The best sites for injection are dorsogluteal and the lateral aspect of the upper arm. 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 two to three weeks. This improves slowly and is followed by

Table 1: WHO/UNICEF Recommendations for the Immunization of HIV-Infected Children and Women of Childbearing Age

Vaccine	Asymptomatic HIV Infection	Symptomatic HIV Infection	Optimal Timing of Immunization
BCG	Yes	No	Birth
DPT	Yes	Yes	6, 10, 14 weeks
OPV*	Yes	Yes	0, 6, 10, 14 weeks
Measles	Yes	Yes	6 and 9 months
Hepatitis B	Yes	Yes	Same as uninfected child: flexible 3- or 4-shot series starting at birth or 6 weeks
Yellow fever	Yes	No**	9 months
Tetanus toxoid	Yes	Yes	5 doses***

* IPV can be used as an alternative for children with symptomatic HIV infection

** Pending further studies

*** 5 doses of tetanus toxoid (TT) for women of childbearing age as for non-HIV-infected persons. TT₁: as early as possible in pregnancy; TT₂: 4 weeks after TT₁; TT₃: 6 months after TT₂; TT₄: 2 years after TT₃ or during subsequent pregnancy; TT₅: 1 year after TT₄ or during subsequent pregnancy.

a local lesion that may ulcerate six to eight weeks later. This lesion will heal and leave a small flat scar three to six 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 pus-filled abscesses. Another short-term complication that may occur is suppurative lymphadenitis. Serious, long-term complications after vaccination are rare. The most serious adverse event related to BCG vaccination is the development of disseminated BCG infection. This can occur anywhere from four months to two years after vaccination.

Diphtheria, Pertussis, Tetanus (DPT)

The DPT vaccine protects against these diseases. The vaccine is not contraindicated for HIV-infected children or their close contacts. 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 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 post-immunization fever and muscle soreness, acetaminophen or ibuprofen may be used every four to six hours for the first 24 hours 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 degrees C, a seizure, or difficulty breathing or cries inconsolably for more than three hours at a time.

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) 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 (CDC) endorses the use of IPV for all children.² The WHO continues to recommend OPV in asymptomatic HIV-infected children, with very few reported cases of adverse events.¹

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 two months after immunization, but the risk is low, estimated at 1:7.8 million doses. Very few adverse events secondary to receiving IPV have been reported.

Measles Vaccine

In some developing countries, measles continues to cause serious illness and death in children under the age of 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 percent death rate. This risk is serious enough for the WHO to recommend immunization of HIV-infected children with measles vaccine at 6 months of age, followed by a second dose at 9 months of age.

Recommendations for HIV-infected children in the United States are to immunize against measles at 12-15 months of age, and again at 4-6 years of age, unless the youngsters have a CD4+ lymphocyte percentage of less than 15 percent or an absolute CD4+ lymphocyte count that is lower than normal for age. Children in these categories have severely impaired immune systems, and public health officials recommend that they not receive the vaccine. Because there are fewer cases of measles in the United States than in the developing world, 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 does harm to 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.

Severely immunocompromised and symptomatic patients with HIV should receive measles serum immune globulin 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 low-grade fever one to two weeks after the injection, cough, nasal drainage, rash, redness, and swelling and tenderness at the injection site. Serious adverse events include seizures, dyspnea, and severe skin rash. Parents should be instructed to call their health care provider if the child has seizures, rash, or fever greater than 39.5 degrees C.

Hepatitis B Vaccine

Despite a short history of immunizing HIV-infected children with hepatitis B vaccine, the WHO recommends the immunization for children and adults infected with HIV.¹ 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 hepatitis B does not appear to be long-lasting.

The hepatitis vaccine should be administered intramuscularly, avoiding the dorsogluteal muscle because of possible reduced immunological response. Anaphylaxis is a very rare but serious side effect. Anaphylaxis is a severe allergic reaction with symptoms that include swelling of the mouth, difficulty breathing,

low blood pressure, and sometimes shock. But generally the vaccine is well tolerated, with very 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 hours of receiving the vaccine and resolve within one or two days.

Yellow Fever Vaccine

Besides mosquito control, the yellow fever vaccine is the only measure available to prevent yellow fever. Immunity occurs within one week in 95 percent of people vaccinated, and immunity lasts for at least 10 years. The EPI of the WHO recommends immunization at 9 months of age or older for asymptomatic HIV-infected children who are living in or visiting endemic areas. A booster vaccine should be administered every 10 years thereafter.

The vaccine is a live attenuated vaccine that should be administered subcutaneously in a dose of 0.5 ml. Adverse events related to immunization against yellow fever are very rare.

Varicella or Chickenpox Vaccine

In HIV-infected patients, chickenpox or varicella zoster virus can cause serious complications, including pneumonia and encephalitis. The CDC recommends that the varicella live attenuated vaccine be administered to HIV-infected children who are asymptomatic or mildly symptomatic in CDC Class N1 or A1 and have age-specific CD4+ lymphocyte percentages of at least 25 percent. Siblings of HIV-infected children should also be immunized with varicella vaccine.³

The varicella vaccine is administered subcutaneously in the anterolateral region of the thigh or upper arm. 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.

HIV-infected children who have not received the vaccine and who are exposed to chickenpox (varicella) should receive varicella zoster immune globulin (VZIG) within the first few days after exposure. Acyclovir is beneficial in the treatment of varicella infection.

Influenza Vaccine

Influenza can cause severe infections and complications in HIV-infected children. Studies have shown that 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 vaccination is indicated for all HIV-infected children ages 6 months or older as well as their close contacts.⁴ The vaccine should be administered in the fall and repeated annually because of the vaccine's low immunogenicity and changes in the type of influenza causing infection from year to year.

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 one month. Most adverse events are minor; they include fever, malaise, and soreness or redness at the injection site.

Pneumococcal Vaccine

Pneumococcus is the most common cause of bacterial invasive infections in children with HIV, causing frequent episodes of otitis media, sinusitis, and pneumonia. Preventing the disease is increasingly important, because research indicates that some forms of the bacteria are resistant to penicillin, cephalosporins, and other antibiotics, and their numbers are increasing. 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 three to five years later.⁵

The pneumococcal vaccine is administered as an intramuscular or subcutaneous injection in the upper anterior thigh or upper arm. Approximately 50 percent of people who receive the vaccine develop mild adverse events, such as tenderness and redness at the injection site. Only about 1 percent of pneumococcal-vaccine recipients develop fever, muscle pain, or severe local reactions.

Immunoglobulin

Intravenous immunoglobulin (IVIG) has been used as protection against bacterial infections, especially pneumococcal infections, for children infected with HIV. It is now no longer indicated. Studies have shown that HIV-infected children receiving *P. 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, VZIG is recommended for children who have been exposed to varicella. Other hyperimmune products include hepatitis B immunoglobulin (HBIG), rabies immunoglobulin (RIG), tetanus immunoglobulin (TIG), cytomegalovirus intravenous immunoglobulin (CMV-IVIG), and respiratory syncytial virus intravenous immunoglobulin (RSV-IVIG).

Review Questions

1. Review the importance of immunizations for children infected with HIV/AIDS.
2. Describe the steps involved in the immune response to disease.
3. What is BCG used for, and why is it so important for vaccination in developing countries?
4. Why is measles a concern in children infected with HIV/AIDS?
5. What are the concerns related to administering OPV rather than IPV to immunocompromised children?
6. What are the side effects related to each of the immunizations given to HIV-infected children?
7. What is the accelerated immunization schedule for HIV-infected children?

Exam Questions

1. According to the EPI schedule for immunizations, which vaccines should be administered to a newborn at birth?
 - a. DPT, OPV, hepatitis B
 - b. BCG, OPV, hepatitis B
 - c. Measles, OPV
 - d. BCG, measles
2. A 6-week-old infant was immunized yesterday with his second DPT vaccination. His mother brings him back to the clinic with a high fever (>39.5 degrees C) and says he cried all night. He continues to breastfeed every three hours. What should you do?
 - a. Administer hydration fluids
 - b. Admit to the hospital for observation
 - c. Give acetaminophen every 4 to 6 hours
 - d. Discontinue breastfeeding for 24 hours
3. When should the first measles vaccine be administered to an HIV-infected child living in an area with a high prevalence of measles??
 - a. At birth
 - b. 6 months of age
 - c. 5 years of age
 - d. 2 years of age
4. You are about to administer the measles vaccine to a young child. How and where should you give the vaccine?
 - a. Subcutaneous injection in the anterolateral region of the thigh
 - b. Intramuscular injection in the deltoid muscle
 - c. By mouth
 - d. Intramuscular injection in the ventrogluteal region of the buttock
5. What concern exists for vaccination with OPV?
 - a. Seizures
 - b. Paralysis
 - c. Bleeding
 - d. Blindness

Case Studies

Case Study #1

A mother brings her 9-month-old asymptomatic HIV-positive son to the clinic for his first well-baby check. Which immunizations would you administer at this time?

Question: Which immunizations would you administer at this time?

- DPT, OPV, hepatitis B
- DPT, OPV, BCG, tetanus toxoid
- Measles, OPV, hepatitis B, BCG, yellow fever.
- Measles, hepatitis B.

Answer: c. Like children without HIV, children who are HIV-positive should receive immunizations to prevent disease. Measles continues to cause serious illness and death in young children in many developing countries. An HIV-infected child's risk of developing complications from measles is so high that the WHO recommends measles immunization of HIV-infected children.

The child's risk of an adverse event related to OPV is low; the WHO continues to recommend OPV for HIV-infected children.

The WHO recommends hepatitis B vaccine for people infected with HIV. There have been no reported adverse events associated with immunizing an HIV-positive person with hepatitis vaccine.

BCG and yellow fever vaccine should be administered to asymptomatic HIV-positive children in regions where *M. tuberculosis* and yellow fever are widespread.

Question: The mother brings her baby back to the clinic the next day and says he was irritable all night and had a fever. You take the baby's temperature; it is 37 degrees C. What should you do for the mother and the baby?

- Tell the mother her baby is having a life-threatening reaction to the immunizations and needs to be admitted to the hospital.
- Educate the mother about mild and serious side effects associated with administration of some immunizations.
- Tell the mother that her baby's symptoms should resolve within the next 24 hours but that she should call if they persist.
- b and c

Answer: d. Caregivers should be educated at the time of immunization about the possible side effects associated with the immunizations being administered. Most mild adverse events, such as muscle soreness and low-grade fever, appear within 24 hours of receiving a vaccine and resolve within one or two days. Acetaminophen or ibuprofen may be used every four to six hours for the first 24 hours after vaccination to help minimize post-immunization fever and muscle soreness.

Case Study #2

A 25-year-old HIV-positive woman arrives in your clinic for a routine visit. You notice that she is extremely thin. She is barefoot and says she walks barefoot several kilometers daily. In assessing her immunization status, which immunization would be your highest priority?

Question: In assessing her immunization status, which immunization would be your highest priority?

- Measles
- BCG
- Tetanus toxoid
- None. She is an adult and no longer needs immunizations.

Answer: c. Tetanus toxoid should be administered to women of childbearing age every 10 years. Other immunizations are not recommended at this time. This woman probably received the immunizations at a

younger age or contracted the disease at some point in her life and developed antibodies, allowing her immune system to respond from memory when exposed to a particular antigen.

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