

AMERICAN ACADEMY OF PEDIATRICS

Committee on Infectious Diseases and Committee on Pediatric AIDS

Measles Immunization in HIV-Infected Children

ABSTRACT. Children infected with human immunodeficiency virus (HIV) have had high rates of mortality attributable to measles, but until recently, measles vaccine was assumed to be safe for these children. A single fatal case of pneumonia attributable to vaccine type-measles virus has been documented in a young adult with acquired immunodeficiency syndrome. Because a protective immune response often does not develop in severely immunocompromised HIV-infected patients after immunization and some risk of severe complications exists, HIV-infected children, adolescents, and young adults who are severely immunocompromised (based on age-specific CD4 lymphocyte enumeration) attributable to HIV infection should not receive measles vaccine. All other HIV-infected children, adolescents, and young adults who are not severely immunocompromised should receive measles-mumps-rubella vaccine.

ABBREVIATIONS. HIV, human immunodeficiency virus; MMR, measles-mumps-rubella (vaccine); IGIV, intravenous immune globulin.

BACKGROUND

Live attenuated measles virus vaccine has been recommended for children, adolescents, and young adults with known human immunodeficiency virus (HIV) infection to prevent morbidity and mortality attributable to measles.^{1,2} The immunosuppressive effect of HIV predisposes to high mortality rates in HIV-infected children who develop measles. In developing nations, the mortality rate attributable to measles has been 50% for HIV-infected children.¹⁻³ From 1989 through 1991, 55 000 cases of measles occurred in the United States. New York City reported 19 deaths, 11 of which were known to be associated with HIV infection.² Measles-mumps-rubella (MMR) vaccine had been recommended for all HIV-infected children because it appeared to be safe without serious or unusual reactions.^{4,5} MMR vaccine should be administered to children 12 to 15 months of age, and knowledge of HIV status is not a prerequisite for immunization.⁶

A single report of a 21-year-old college student who received a second dose of measles vaccine in September 1992 has provided the first indication of potential harmful consequences of measles vaccine in a severely immunocompromised HIV-infected person.⁵ This man had a CD4 cell count of 10/ μ L at the time of immunization, and *Pneumocystis carinii*

pneumonia developed 1 to 2 months after he received the second dose of MMR vaccine. Approximately 1 year after vaccination, he was evaluated for progressive pulmonary disease. A transbronchial biopsy revealed multinucleated giant cells, and a measles virus was cultured that has been identified as vaccine-like by genomic sequencing. The patient died in December 1993, approximately 15 months after receipt of the vaccine. This patient had no identified measles rash, and progressive nodular disease was evident on the chest radiograph. Similar pulmonary disease associated with wild type and vaccine virus-induced disease has been reported in other immunocompromised patients.^{7,8} Progressive pulmonary disease attributable to wild type measles infection has developed in HIV-infected persons.^{9,10}

Measles as the cause of the pneumonia in this HIV-infected patient was not appreciated until 11 to 12 months after administration of MMR vaccine. This long incubation period is unique; however, wild type measles virus may establish a persistent infection. This raises the possibility that other HIV-infected patients with pulmonary disease might not have been evaluated for the presence of measles virus, although no other cases of MMR-associated pulmonary complications have been reported after immunization in HIV-infected children.

MEASLES IMMUNITY IN HIV-EXPOSED OR HIV-INFECTED INFANTS

HIV-infected women have lower concentrations of measles-specific antibodies and they transmit less measles antibody to their infants, resulting in susceptibility at a younger age than usual.¹¹

ADMINISTRATION OF MMR TO HIV-INFECTED CHILDREN, ADOLESCENTS, AND YOUNG ADULTS WITHOUT SEVERE IMMUNOSUPPRESSION

Several studies have substantiated a suboptimal and unpredictable response to MMR vaccine in HIV-infected children.¹²⁻¹⁴ Also, measles antibody titers decline more rapidly after immunization in HIV-infected children compared with uninfected children.^{15,16} However, the administration of MMR vaccine to HIV-infected children, adolescents, and young adults without severe immunosuppression continues to be important, and administration of vaccine before deterioration of the immunologic status provides the best opportunity to induce protection. Immunization of HIV-infected infants at 9 to 11 months was associated with somewhat better antibody responses^{17,18} than in children at 12 to 15 months in two small studies; this question of the

The recommendations in this statement do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

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optimal age of immunization is being addressed in a randomized study conducted by the AIDS Clinical Trial Group. Pending the results of this trial, HIV-infected children should be immunized as soon as they reach 12 months of age to induce an appropriate immune response. The second dose may be administered as soon as 30 days later in an attempt to induce early seroconversion. All persons in the household who are not HIV-infected and not otherwise immunocompromised should have immunity to measles. *Immunity* is defined as having been born before 1957, a history of physician-diagnosed measles, laboratory evidence of immunity, or age-appropriate immunization.

HIV-INFECTED CHILDREN, ADOLESCENTS, AND YOUNG ADULTS WITH SEVERE IMMUNOSUPPRESSION

Attenuated measles vaccine virus has caused fatal disease in one severely immunosuppressed HIV-infected patient. Because measles vaccine has been safely administered to >1000 HIV-infected children in the United States, we know that the risk of vaccine-induced virus disease is much less than that of wild type measles virus, but most of the children were not severely immunocompromised at the time of immunization. The antibody response to measles vaccine decreases as the level of immunosuppression increases.^{13,17,18} In one study, measles antibody developed after vaccination in 71% (12/17) of children without severe immunosuppression, but antibody developed in only 17% (3/18) of those with severe immunosuppression.¹⁵ In another study, 90% of HIV-infected children with CD4 lymphocyte counts <200/ μ L did not respond to measles vaccine, and severe disease after exposure to measles developed in some HIV-infected children who had been immunized.¹³ Thus, measles vaccine should not be administered to severely immunosuppressed HIV-infected children, adolescents, and young adults because they do not respond well to measles vaccine and there is some risk of serious complications. Whether a given CD4⁺ T-cell level achieved in response to antiretroviral therapy provides an equivalent assessment of the degree of immune system function or has the same predictive value for risk of opportunistic infections as do CD4⁺ T-cell levels obtained in the absence of therapy is unknown.

Mumps and rubella vaccine viruses have not been recognized to cause serious complications in HIV-infected persons, but these and other live vaccines should be withheld from severely immunocompromised persons as they are unlikely to benefit and complications could occur.

ASSESSMENT OF IMMUNOLOGIC STATUS OF HIV-INFECTED CHILDREN, ADOLESCENTS, AND YOUNG ADULTS

The HIV infection status of all infants born to HIV-infected women should be monitored.¹⁹ An HIV culture or a polymerase chain reaction are the preferred methods for diagnosing HIV infection among infants.^{19,20} The CD4 counts and percentages should be measured to assess the HIV-infected child's immune status, risk for disease progression, and need for antiretroviral therapy.²⁰⁻²² Quality standards for the enumeration of CD4 lymphocytes in children, adolescents, and young adults infected with HIV have been established.^{20,23} All HIV-infected children, adolescents, and young adults should have an initial CD4 lymphocyte count determined and repeated at least every 3 to 4 months if the initial count is >500/ μ L. If the initial count is between 200 and 500/ μ L and the patient is asymptomatic, the assay should be repeated at intervals determined by the physician but no less frequently than every 3 to 4 months.^{20,23}

Severe Immunosuppression

The definition of severe immunosuppression is currently based on CD4⁺ T-lymphocyte enumeration stratified by age^{24,25} (Table 1). Once a child has met the definition of severe immunosuppression, the child is always considered severely immunosuppressed.

Passive Immunization to Prevent Measles

Immunized HIV-infected children, adolescents, and young adults have contracted wild type measles and sustained severe disease. If exposed to measles, all HIV-infected infants, children, and adolescents, as well as children of unknown infectious status born to HIV-infected women, should receive 0.5 mL/kg (maximum dose, 15 mL) of immune globulin intramuscularly, regardless of their immunization status, because it is impossible to know in a timely fashion if the child has protective antibody. If the person exposed to measles is receiving intravenous immune globulin (IGIV) (400 mg/kg) and \geq 3 weeks have elapsed since the last dose, the person should receive IG (0.5 mL/kg) or IGIV (400 mg/kg) as soon as possible. Because of the uncertainty regarding measles antibody concentrations in IGIV and the rapid metabolism of IGIV in HIV-infected children, some experts have chosen to administer an additional dose of IGIV if 2 or more weeks have elapsed since IGIV has been administered at the time of measles exposure.

TABLE 1. Immunologic Categories Based on Age-Specific CD4⁺ T-Lymphocyte Counts and Percentage of Total Lymphocytes²³

Category	<12 Months		1-5 Years		\geq 6 Years	
	μ L	%	μ L	%	μ L	%
1. No evidence of immunosuppression	\geq 1500	(\geq 25)	\geq 1000	(\geq 25)	\geq 500	(\geq 25)
2. Evidence of moderate immunosuppression	750-1499	(15-24)	500-999	(15-24)	200-499	(15-24)
3. Severe immunosuppression	<750	(<15)	<500	(<15)	<200	(<15)

RECOMMENDATIONS

1. Severely immunosuppressed HIV-infected infants, children, adolescents, and young adults should not receive measles virus-containing vaccines.
2. HIV-infected children, adolescents, and young adults without evidence of severe immunosuppression should receive MMR vaccine. The first dose should be administered at 12 months of age. The second dose may be given as soon as 28 days after the first dose. In the event of an outbreak in the community, vaccination with monovalent measles vaccine (or MMR) is recommended for infants as young as 6 months when exposure to natural measles is considered likely. Children vaccinated before the first birthday should be revaccinated with MMR at 12 months, and an additional dose may be given as soon as 28 days later.
3. All members of the household of an HIV-infected person should receive measles vaccine *unless* they are HIV-infected and severely immunosuppressed, were born before 1957, have had physician-diagnosed measles, have laboratory evidence of measles immunity, have had age-appropriate immunizations, or have a contraindication to measles vaccine.
4. If they are exposed to wild type measles, immune globulin prophylaxis should be administered to all HIV-infected children and adolescents and to children of unknown infection status born to HIV-infected women, regardless of the degree of immunosuppression or measles immunization status.

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