

## Evaluation and Medical Treatment of the HIV-Exposed Infant

**ABSTRACT.** As a result of the expanding human immunodeficiency virus (HIV) infection epidemic and recently published recommendations for routine HIV testing with consent for all pregnant women in the United States, pediatricians are becoming increasingly involved in providing care to infants born to HIV-infected women. This article provides guidelines about counseling the parent or care giver of the infant, use of antiretroviral therapy to reduce the risk of infection in the infant, medical treatment of the HIV-exposed infant, laboratory testing to determine the infection status of the infant, laboratory monitoring of hematologic and immunologic parameters, prophylaxis for *Pneumocystis carinii* pneumonia, and recommendations for immunizations and tuberculosis screening.

**ABBREVIATIONS.** HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; ACTG-076, AIDS Clinical Trials Group Protocol 076; CBC, complete blood count; PCP, *Pneumocystis carinii* pneumonia; PCR, polymerase chain reaction; CDC, Centers for Disease Control and Prevention; IVIG, intravenous immune globulin; TB, tuberculosis; PPD, purified protein derivative; BCG, Bacille Calmette-Guérin.

The expanding human immunodeficiency virus (HIV) infection epidemic and recently published recommendations regarding routine HIV testing with consent for all pregnant women in the United States<sup>1,2</sup> ensure the increasing involvement of pediatricians in providing care to infants born to HIV-infected women. During 1994 an estimated 7000 infants were born in the United States to HIV-infected women.<sup>3</sup> Seroprevalence of HIV infection in pregnant women nationwide is .16%, although some individual hospitals report seroprevalence rates in pregnant women as high as 6% to 8%.<sup>4</sup> The epidemic of HIV infection is no longer localized to major metropolitan areas, and HIV infection is being identified in women from rural areas and smaller communities more often. A rural health care setting in Florida reported a 5% seroprevalence rate for pregnant women.<sup>5</sup>

Women are most often infected through heterosexual contact with an infected partner or through drug use. Pediatric HIV infection is now overwhelmingly a result of perinatal transmission. More than 90% of pediatric acquired immunodeficiency syndrome (AIDS) reported in 1994 occurred as a consequence of maternal to infant transmission.<sup>6</sup> Transmission to the

infant may occur during the pregnancy, during labor and delivery, or postnatally by breastfeeding. The maternal to infant transmission rate is approximately 20% to 30%, with the majority of infants who are born to an infected mother being ultimately uninfected.<sup>7</sup> Recent research (AIDS Clinical Trials Group Protocol 076 [ACTG-076]) has shown that for selected HIV-infected women, zidovudine may lower the perinatal HIV transmission rate by two-thirds.<sup>8</sup>

### REDUCING THE RISK OF PERINATAL HIV INFECTION

The ACTG-076 demonstrated that a regimen of zidovudine given orally during the second and third trimesters of pregnancy, intravenously during labor and delivery, and orally to the infant during the first 6 weeks postnatally resulted in a dramatic two-thirds reduction in the risk of perinatal transmission (from 25% in the placebo group to 8% in the group receiving the regimen of zidovudine). The zidovudine regimen used in the clinical trial was as follows:

- Pregnancy: zidovudine, 100 mg orally, five times a day, beginning between 14 and 34 weeks' gestation;
- Labor and delivery: zidovudine, 2 mg/kg intravenously over 1 hour followed by a continuous infusion of zidovudine, 1 mg/kg per hour until delivery; and
- Postnatal (infant): zidovudine syrup, 2 mg/kg per dose orally every 6 hours, beginning 8 to 12 hours after birth and continuing until 6 weeks of age.

The results of this clinical trial are only directly applicable to HIV-infected pregnant women who have characteristics similar to those of the women who entered the trial (14 to 34 weeks of gestation at enrollment, a CD4<sup>+</sup> lymphocyte count >200, no prior antiretroviral therapy during the current pregnancy, and no other maternal clinical indication for antiretroviral therapy). The US Public Health Service has published recommendations for use of zidovudine to reduce perinatal HIV transmission that include considerations for its use in HIV-infected women who meet the ACTG-076 study criteria and in other clinical populations.<sup>9</sup> These recommendations were intended as a basis for discussion between an infected woman and her health care provider regarding use of the zidovudine regimen; such discussions must be tailored to the woman's individual clinical situation. All HIV-infected pregnant women should be counseled about the possible use of this regimen.

General principles were delineated to assist clinicians in assessing the appropriateness of the regimen

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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**TABLE 1.** US Public Health Service Recommendations for Use of Zidovudine to Reduce Perinatal HIV Transmission

Clinical Scenario	Recommendations
CD4 <sup>+</sup> ≥200/mm <sup>3</sup> 14–34 weeks of gestation No maternal clinical indication for zidovudine	Risk vs benefit discussion Recommend full ACTG-076 zidovudine regimen
CD4 <sup>+</sup> ≥200/mm <sup>3</sup> >34 weeks of gestation No maternal clinical indication for zidovudine No extensive history (>6 mo) of prior zidovudine	Risk vs benefit discussion Recommend full ACTG-076 zidovudine regimen  May be less effective because therapy is initiated late
CD4 <sup>+</sup> <200/mm <sup>3</sup> 14–34 weeks of gestation No extensive history (>6 mo) of prior zidovudine	Risk vs benefit discussion Recommend antenatal zidovudine therapy for woman's health Recommend intrapartum and neonatal components of ACTG-076 zidovudine regimen
Significant prior administration of zidovudine or other antiretroviral therapy (>6 mo)	Risk vs benefit discussion Recommend zidovudine therapy on a case-by-case basis Issues to consider Likelihood of resistance to therapy Duration of prior zidovudine therapy Reason alternative therapy was given, if received (intolerance vs progression of disease despite therapy)
Woman is in labor and has not had antepartum zidovudine therapy	Risk vs benefit discussion Discuss and offer intrapartum and neonatal ZDV if clinical situation permits
Infant is born to a woman who has not received intrapartum zidovudine	Risk vs benefit discussion If ≤24 h old and clinical situation permits: Discuss and offer neonatal zidovudine Start zidovudine as soon as possible after birth If >24 h old: no data support offering zidovudine therapy

for individual patients (Table 1). Important considerations include the gestational age of the fetus at the time therapy is considered, maternal CD4<sup>+</sup> lymphocyte count and clinical disease stage, and prior use and duration of antiretroviral therapy. Determination of maternal serostatus during the first trimester will provide maximal opportunity to prevent perinatal transmission of HIV infection (with initiation of maternal zidovudine therapy at 14 weeks of gestation). Communication is critical between obstetricians and pediatricians about the use of the ACTG-076 zidovudine regimen in HIV-infected pregnant women because administration of zidovudine to infants for 6 weeks is also required.

Pediatricians may be consulted about the use of the intrapartum and/or newborn components of the zidovudine regimen in women and their infants when the antepartum component of the zidovudine regimen has not been received. The US Public Health Service recommends that zidovudine therapy during labor, with subsequent administration to the newborn, should be discussed and offered when the clinical situation permits. Because at least 50% to 70% of perinatal transmission may occur during the intrapartum period, it is theoretically possible that administration of zidovudine during labor followed by administration to the newborn could offer some protection. However, the benefit is likely to be less than that observed in the ACTG-076 trial.

In women who have not received zidovudine during pregnancy or labor, the postpartum component of the regimen (6 weeks of therapy for infants) should be offered if therapy can be started within 24 hours of birth. In such situations, infants have not

had zidovudine present in their bloodstream at the time of intense viral exposure during delivery; therefore, administration of zidovudine provides only postexposure prophylaxis. There are no data to suggest that initiation of zidovudine therapy after 24 hours of age will reduce perinatal HIV transmission.

The only adverse effect observed more frequently in infants in the group receiving zidovudine was a mild, transient anemia that reached nadir at 6 weeks of age and resolved without therapy by 12 weeks of age. Therefore, a complete blood count (CBC) and differential leukocyte count should be performed initially at birth as a baseline and again at 4 and 6 weeks of age. Infants with anemia at birth or with blood group incompatibility hemolysis should have more frequent hematologic monitoring during administration of zidovudine. Therapy with zidovudine is completed at 6 weeks and prophylaxis for *Pneumocystis carinii* pneumonia (PCP) begins at 6 weeks. Prophylaxis for PCP should be provided for all infants born to HIV infected women regardless of the results of the infant's initial tests for HIV infection (see Prophylaxis for *Pneumocystis carinii* pneumonia on page 912).

In ACTG-076, zidovudine was not associated with an increase in congenital abnormalities or preterm births. Long-term follow-up of these infants is ongoing. For uninfected infants followed up until at least 1 year of age, no differences in immune status, growth, or neurodevelopment have been observed when infants receiving zidovudine were compared with those receiving placebo.<sup>10</sup> However, the long-term effects of in utero exposure to zidovudine are unknown.

## BREASTFEEDING

Several reports indicate that breastfeeding can transmit HIV infection to infants.<sup>11-13</sup> Thus, in the United States where suitable alternative sources of nutrition are readily available, HIV-infected women must be counseled not to breastfeed or provide expressed breast milk to any infant.<sup>14,15</sup>

## CARE OF THE HIV-EXPOSED NEWBORN IN THE HOSPITAL

Adherence by health care providers to standard (universal) precautions is recommended for all infant deliveries, and includes use of gowns, gloves, masks, and goggles or face shields. Only wall suction or bulb suction should be used, and mouth-to-mouth or mouth-to-DeLee catheter suction should be avoided.

Most HIV-exposed infants are born at term of normal birth weight and have normal physical examination findings at birth. There may be a slight increase in the incidence of preterm and low birth weight infants, although it is unclear whether HIV infection or other confounding variables account for this.<sup>16</sup> Marion et al<sup>17</sup> originally suggested dysmorphic facial features in HIV-infected infants, but these findings have since been refuted.<sup>18</sup> Because a substantial portion of HIV infection in infants is believed to occur at delivery,<sup>7</sup> physical findings (eg, adenopathy or hepatosplenomegaly), which may later suggest HIV infection, are usually absent in the newborn period. Infants who are small for gestational age or have microcephaly, adenopathy, or hepatosplenomegaly should have a thorough assessment for other causative factors.

The mother's medical records should be thoroughly reviewed for documentation of other infections (eg, herpes simplex virus, cytomegalovirus, toxoplasmosis, syphilis, gonorrhea, or tuberculosis) that may affect the infant.<sup>19</sup> Maternal history should also be reviewed for psychosocial factors (eg, poverty, substance abuse, depression, or domestic violence) that may affect the need for additional services for the mother and infant.

If information about other maternal infections cannot be obtained, the infant should undergo serologic screening for syphilis and toxoplasmosis and culture of a urine specimen for cytomegalovirus. A CBC and differential leukocyte count should be performed to provide baseline data and to assess the possible effect of maternal pharmacologic therapy (such as zidovudine) on the infant's hematologic parameters. All infants born to HIV-infected women should receive hepatitis B vaccine. Hepatitis B immune globulin should also be administered to the infant if the mother tests positive for hepatitis B surface antigen.

## DIAGNOSIS OF HIV INFECTION IN THE INFANT

The HIV antibody as measured by enzyme-linked immunoabsorbent assay and Western blot analysis includes immunoglobulin G antibody, which crosses the placenta. Thus, an HIV-positive antibody test in an infant younger than 18 months indicates maternal infection but does not diagnose infection in the infant. By the time the child is 18 months old, generally

the maternal antibody is gone and an HIV-positive antibody test indicates infection in the child.<sup>20,21</sup> In rare instances, a false-negative result may occur in serologic testing for HIV infection if the child has hypogammaglobulinemia.<sup>22,23</sup>

Because standard HIV antibody testing alone cannot provide early diagnosis of HIV infection in infants, additional testing, such as HIV DNA polymerase chain reaction (PCR) or viral cultures for HIV, should be performed. Testing by PCR or viral cultures should be performed at birth and again at 1 to 2 months of age. Umbilical cord blood should not be used for HIV testing. If the PCR or viral culture is positive for HIV, the test should be repeated immediately and confirmed before a diagnosis of HIV infection is made. If the PCR or viral cultures performed at birth and at 1 to 2 months of age do not indicate infection and the infant remains asymptomatic, testing by PCR or viral culture should be repeated at 4 months of age. (Another test should be performed earlier than 4 months of age if symptoms develop in the infant or results of hematologic or immunologic testing are suggestive of HIV infection.) If the PCR and viral culture are unavailable, the p24 antigen may be used to assess HIV infection status in infants older than 1 month, but the sensitivity of p24 antigen testing is substantially less.<sup>24,25</sup> Thus, the absence of the p24 antigen does not rule out HIV infection in the infant. An infant who is 4 months of age or older with no positive test for HIV by PCR or viral cultures (with both tests performed at 1 month of age or older and one test performed at 4 months of age or older) has a greater than 95% chance of being uninfected.<sup>26</sup> Continued follow-up with serologic testing to document disappearance of the HIV antibody is indicated for all HIV-exposed children 12 months of age or older who are believed to be uninfected based on negative PCR or viral cultures performed at 4 months of age or later. An HIV-exposed infant is considered uninfected when there are no physical findings to suggest HIV infection, immunologic test results are normal, virologic tests are negative for infection, and, after the infant is 12 months of age, two or more HIV antibody tests are negative for infection. Even though an infant has two or more negative HIV antibody tests, the National Pediatric HIV Resource Center recommends a final HIV antibody test at 24 months of age for the HIV-exposed infant whose previous testing has been negative.<sup>27</sup>

## MONITORING OF IMMUNOLOGIC AND HEMATOLOGIC PARAMETERS

Children who are born to HIV-infected women should undergo monitoring of the CD4<sup>+</sup> lymphocyte count and percentage, CBC, differential leukocyte count, and platelet count during the first 6 months of life. Monitoring should continue in children found to be infected and in those whose infection status is unclear at 6 months of age.<sup>28</sup> The CD4<sup>+</sup> lymphocyte count and percentage should be monitored at 1 and 3 months of age in all HIV-exposed infants. Infants identified as infected or whose infection status is unclear should continue to undergo monitoring of

the CD4<sup>+</sup> lymphocyte count and percentage at 3-month intervals (at 6, 9, and 12 months of age) or more frequently if the CD4<sup>+</sup> lymphocyte count or percentage declines rapidly. Quantitative immunoglobulins should also be measured by the time the infant is 4 to 6 months of age. Hematologic abnormalities, hypergammaglobulinemia, and an abnormally low CD4<sup>+</sup> lymphocyte count and percentage (below the age-related normal levels) are frequently seen in HIV-infected children. The CD4<sup>+</sup> lymphocyte count and percentage are no longer used as guidelines for prophylaxis for PCP during the first year of life, but results obtained during that first year are used to guide prophylaxis for HIV-infected children during the second 12 months of life (Tables 2 and 3).<sup>28</sup>

### PROPHYLAXIS FOR *PNEUMOCYSTIS CARINII* PNEUMONIA

*Pneumocystis carinii* pneumonia, frequently the "AIDS indicator" for HIV-infected children, occurs most often between 3 and 6 months of age when many HIV-exposed infants have not yet been identified as being infected.<sup>29</sup> In 1991, the Centers for Disease Control and Prevention (CDC) published recommendations for PCP prophylaxis in infants and children based on the CD4<sup>+</sup> lymphocyte count and percentage.<sup>30</sup> Because of the continuing infant morbidity and mortality due to PCP,<sup>28,31</sup> revised recommendations for PCP prophylaxis were published in 1995 by the CDC (see Table 4).<sup>28</sup>

#### Initiating PCP Prophylaxis for HIV-Exposed Infants

- Prophylaxis for PCP for all infants born to HIV-infected women should be initiated at 4 to 6 weeks of age, regardless of the infant's CD4<sup>+</sup> lymphocyte count (Table 3). Infants who are first identified as being HIV-exposed after 6 weeks of age should begin prophylaxis at the time of identification. These recommendations are based on the following: (1) most cases of PCP among HIV-infected children occur during the first year of life; (2) the risk for PCP begins to increase dramatically at 2 months of age (when HIV infection cannot yet be reasonably excluded, see PCP Prophylaxis for Infants 4 to 12 Months of Age); and (3) the reliability of CD4<sup>+</sup> lymphocyte counts in predicting risk for PCP is relatively low during infancy, particularly

**TABLE 2.** CD4<sup>+</sup> T-Lymphocyte Counts and Percentage of Total Lymphocytes Corresponding to Level of Immunosuppression in Children,\* by Age at CD4<sup>+</sup> Measurement<sup>32</sup>

Age at CD4 <sup>+</sup> Measurement	Level of Immunosuppression		
	No Evidence of Immunosuppression	Moderate	Severe
CD4 <sup>+</sup> count (cells/ $\mu$ L)			
≤12 mo	≥1500	750–1499	<750
1–5 y	≥1000	500–999	<500
6–12 y	≥500	200–499	<200
CD4 <sup>+</sup> percentage			
<13 y	≥25	15–24	<15

\* Persons younger than 13 years of age.

among infants 6 months of age or younger, the age at which the peak incidence of PCP occurs.

- Prophylaxis for PCP should not be administered to infants younger than 4 weeks of age because they are at low risk for PCP and the use of sulfa drugs among infants at this age is not advised because immature bilirubin metabolism may result in adverse drug effects. Additionally, the concurrent use of sulfa drugs among infants receiving zidovudine during the first 6 weeks of life to prevent perinatal HIV transmission could exacerbate the anemia that some infants receiving zidovudine experience. Therefore, to avoid the potential for adverse drug reactions in infants receiving zidovudine, prophylaxis against PCP should be started at 6 weeks of age, the age at which zidovudine is discontinued.

#### PCP Prophylaxis for Infants 4 to 12 Months of Age

- Prophylaxis for PCP should continue until at least 12 months of age for all HIV-infected infants and infants whose infection status has not yet been determined.
- Prophylaxis for PCP should be discontinued in infants in whom two or more viral diagnostic tests have been negative for infection (ie, culture or PCR), both of which were performed when the infant was 1 month of age or older and one was performed when the infant was 4 months of age or older). In some clinical centers, these viral diagnostic tests are not available. For children who do not have access to such testing, prophylaxis should be continued until 12 months of age unless HIV infection has been reasonably excluded on the basis of two or more negative HIV antibody tests performed at 6 months of age or later.

#### Prophylaxis for HIV-Infected Children 12 Months of Age and Older

- All HIV-infected children 12 months of age and older should continue to undergo regular monitoring of CD4<sup>+</sup> lymphocyte count and percentage, and PCP prophylaxis should be provided in accordance with the guidelines in Table 3.
- HIV-infected children who are 12 months of age or older and are not receiving prophylaxis (eg, children whose infection was not identified previously or whose PCP prophylaxis was discontinued) should begin prophylaxis if the CD4<sup>+</sup> lymphocyte count or percentage indicates severe immunosuppression (Table 2).<sup>28,32</sup>
- Children who have received PCP prophylaxis from 12 to 24 months of age should be evaluated again at 24 months of age. Prophylaxis should be provided in accordance with guidelines in Table 3.

#### Prophylaxis Against Recurrence of PCP

- Children infected with HIV who have had an episode of PCP should receive lifelong prophylaxis to prevent recurrence, regardless of CD4<sup>+</sup> lymphocyte count or percentage or clinical status.

**TABLE 3.** Recommendations for PCP Prophylaxis and CD4<sup>+</sup> Lymphocyte Monitoring<sup>28</sup> for HIV-Exposed Infants\* and HIV-Infected Children by Age and HIV Infection Status\*

Age and HIV Infection Status	PCP Prophylaxis	CD4 <sup>+</sup> Monitoring
Birth to 4–6 wk, HIV-exposed	No prophylaxis	1 mo of age
4–6 wk to 4 mo, HIV-exposed	Prophylaxis	3 mo of age
4–12 mo, HIV-infected or indeterminate	Prophylaxis	6, 9, and 12 mo of age
HIV infection reasonably excluded†	No prophylaxis	None
1–2 y, HIV-infected	Prophylaxis if CD4 <sup>+</sup> count <750 cells/μL in first 12 mo or <500 cells/μL at 12–24 mo, or CD4 <sup>+</sup> percentage <15§	Every 3–4 mo‡
2–5 y, HIV-infected	Prophylaxis if CD4 <sup>+</sup> count <500 cells/μL or CD4 <sup>+</sup> percentage <15§	Every 3–4 mo‡
6–12 y, HIV-infected	Prophylaxis if CD4 <sup>+</sup> count <200 cells/μL or CD4 <sup>+</sup> percentage <15§	Every 3–4 mo‡
All ages, HIV-infected, prior PCP infection	Prophylaxis§	Every 3–4 mo‡

\* PCP indicates *Pneumocystis carinii* pneumonia; HIV, human immunodeficiency virus; and PCR, polymerase chain reaction.

† HIV infection can be reasonably excluded among children who have had two or more viral diagnostic tests negative for infection (ie, culture or PCR), both of which are performed at 1 month of age or older, and one of which is performed at 4 months of age or older, or two or more negative HIV antibody tests performed at 6 months of age or older among children who have no clinical evidence of HIV infection.

‡ More frequent monitoring (eg, monthly) is recommended for children whose CD4<sup>+</sup> counts or percentages are approaching the threshold at which prophylaxis is recommended.

§ Prophylaxis should be considered on a case-by-case basis for children who may otherwise be at risk for PCP, such as children with rapidly declining CD4<sup>+</sup> counts or percentages or children with category C conditions (severely symptomatic). Children who have had PCP should receive lifelong prophylaxis.

**TABLE 4.** Drug Regimens for PCP Prophylaxis for Children 4 Weeks of Age or Older<sup>28</sup>

Recommended regimen
Trimethoprim-sulfamethoxazole, 150 mg/m <sup>2</sup> /d of trimethoprim with 750 mg/m <sup>2</sup> /d of sulfamethoxazole (or 5 mg/kg/d of trimethoprim with 25 mg/kg/d of sulfamethoxazole), orally in divided doses two times a day, 3 times per week on consecutive days (eg, Monday, Tuesday, and Wednesday)
Acceptable alternative trimethoprim-sulfamethoxazole dosage schedules
150 mg/m <sup>2</sup> /d of trimethoprim with 750 mg/m <sup>2</sup> /d of sulfamethoxazole, orally as a single daily dose, 3 times per week on consecutive days (eg, Monday, Tuesday, and Wednesday)
150 mg/m <sup>2</sup> /d of trimethoprim with 750 mg/m <sup>2</sup> /d of sulfamethoxazole, orally in divided doses two times a day, administered 7 days per week
150 mg/m <sup>2</sup> /d of trimethoprim with 750 mg/m <sup>2</sup> /d of sulfamethoxazole, orally in divided doses two times a day, 3 times per week on alternate days (eg, Monday, Wednesday, and Friday)
Alternative regimens when therapy with trimethoprim-sulfamethoxazole is not tolerated†
Dapsone, 2 mg/kg (not to exceed 100 mg), orally once a day
Aerosolized pentamidine (for children ≥5 y of age), 300 mg administered via Respigard II inhaler, once a month

\* PCP indicates *Pneumocystis carinii* pneumonia.

† If neither dapsone nor aerosolized pentamidine is tolerated, some clinicians administer 4 mg/kg of pentamidine intravenously every 2 or 4 weeks.

### Recommended Chemoprophylaxis Regimens

The recommended chemoprophylaxis regimen for PCP for children is trimethoprim-sulfamethoxazole (Table 4). When initiating prophylaxis with this drug combination, a baseline CBC, differential leukocyte count, and platelet count should be obtained. These measurements should be obtained monthly while the child receives prophylaxis.

If prophylaxis with sulfamethoxazole-trimethoprim is not tolerated, alternative regimens should be followed. On the basis of recently compiled pharmacokinetic data, the revised recommended dosage of dapsone as an alternative regimen is 2 mg/kg per day.

- Prophylaxis for PCP is an approved label indication by the US Food and Drug Administration (FDA) for oral trimethoprim-sulfamethoxazole but not for the various other alternative regimens for PCP prophylaxis. Therapy with trimethoprim-sulfamethoxazole substantially reduces the risk for PCP among HIV-infected children,<sup>33</sup> although some children have experienced PCP despite receiving recommended prophylaxis.<sup>34</sup>

### PREVENTION OF OTHER OPPORTUNISTIC INFECTIONS

The US Public Health Service has recently published guidelines for the prevention of opportunistic infections in HIV-infected individuals.<sup>35</sup> Pediatricians should counsel parents or care givers of HIV-exposed infants about the need to avoid consumption of raw or undercooked food to decrease the risk of enteric infection such as salmonella. The risk of acquiring infection with *Cryptosporidium* or *Giardia* species can be reduced by not drinking or swimming in lake or river water. Contact with young farm animals should also be avoided to reduce the risk of cryptosporidiosis. Parents and care givers should also be advised of the potential risks of infection from pets, particularly cats (eg, toxoplasmosis and bartonellosis). The benefits of good hand washing also should be emphasized. Decisions about using prophylactic medication for opportunistic infections (those caused by *Mycobacterium avium-intracellulare* complex; *Cryptococcus*, *Histoplasma*, or *Coccidioides* species; or *Cytomegalovirus*) in severely immunocompromised infants and children should be made after consultation with a physician with expertise in pediatric HIV infection.

### ANTIRETROVIRAL THERAPY

Recommendations for antiretroviral therapy (beyond 6 weeks postnatally when used prophylactically) in HIV-infected children have been based on the CD4<sup>+</sup> lymphocyte count and percentage and clin-

ical conditions.<sup>19,36</sup> Due to rapidly expanding knowledge concerning the dynamic interaction of the HIV virus with the host's immune system and due to the availability of multiple new antiretroviral drugs, recommendations for antiretroviral therapy are being revised. Thus, decisions regarding antiretroviral therapy in HIV-infected children should be made in conjunction with a physician with expertise in pediatric HIV infection.

### IMMUNIZATIONS

Recommendations for immunizations for HIV-exposed and HIV-infected children have been published by the American Academy of Pediatrics and the Advisory Committee on Immunization Practices of the Centers for Disease Control.<sup>36-39</sup> HIV-exposed and infected infants and children should receive standard pediatric immunizations, such as vaccines for hepatitis B, diphtheria-pertussis-tetanus, and *Haemophilus influenzae*. Administration of tetanus immune globulin is recommended for tetanus-prone wounds in HIV-infected children regardless of tetanus immunization status. Inactivated polio vaccine should be given instead of oral polio vaccine, and even if the child is ultimately uninfected, inactivated polio vaccine should be continued if the child resides with HIV-infected persons. Because of the severity of live measles infection in HIV-infected children, measles-mumps-rubella vaccination is recommended for HIV-exposed and HIV-infected children who are not severely immunocompromised (based on CD4<sup>+</sup> lymphocyte count and percentage). Immune globulin should also be used when HIV-exposed, or HIV-infected children have been exposed to measles regardless of the child's measles vaccine history unless intravenous immune globulin (IVIG) was administered during the previous 3 weeks.

Influenza vaccine should be administered seasonally and repeated annually for children who are at least 6 months of age and are infected with HIV or reside with HIV-infected persons. Pneumococcal vaccine should be provided at 2 years of age for HIV-infected children. **Varicella vaccine is not recommended for HIV-infected children.** If a rash develops in a household contact who received varicella vaccine, direct contact with an HIV-infected person should be avoided until the rash resolves. HIV-infected children and HIV-exposed children whose HIV infection status is unclear should receive varicella zoster immune globulin for exposure to live varicella unless IVIG was administered during the previous 3 weeks.

### TUBERCULOSIS PREVENTION AND DETECTION

The expanding HIV infection epidemic and the resurgence of tuberculosis (TB) are interrelated.<sup>40-43</sup> Because of the profound effect of HIV infection on cell-mediated immunity, TB is more likely to reactivate in people with HIV infection. Similarly, exposure of HIV-infected persons to infectious TB may result in an explosive outbreak such as that which occurred when TB developed in 35% of the residents in a facility for HIV-infected persons within 4 months of exposure to an index case.<sup>44</sup>

Because of household exposure to immunocompromised individuals and the overlap in the population at risk for TB and HIV infection, infants and children of HIV-infected women may be at increased risk of TB regardless of the child's own HIV status. Before an infant is discharged from the nursery, but preferably during the woman's pregnancy, an assessment of the mother's TB status should be made, keeping in mind that anergy frequently occurs with HIV infection. Information about the TB status of other household contacts should be requested.

If the mother has hematogenous dissemination of TB, the infant should be evaluated for congenital TB. If the mother or a household contact has active tuberculous pulmonary disease that is believed to be contagious, the infant should, if possible, be separated from that person until the person is considered noncontagious. Any infant or young child exposed to a person with contagious TB should undergo tuberculin skin testing and a chest radiograph in accordance with guidelines of the American Academy of Pediatrics.<sup>45</sup> Even if the baseline skin test is nonreactive and the chest radiograph shows no abnormalities, the infant or young child should receive prophylaxis with isoniazid for 3 months until a skin test is repeated. If the skin test is then positive ( $\geq 5$ -mm induration), antituberculous therapy is continued. In the event the index case is infected with a resistant strain of *Mycobacterium tuberculosis*, consultation should be obtained from a physician with expertise in pediatric infectious diseases.

All HIV-infected children and uninfected children

**TABLE 5.** Definition of a Positive Mantoux Skin Test (5TU-PPD) in Children<sup>\*45</sup>

Reaction $\geq 5$ mm	Children in close contact with persons who have known or suspected infectious cases of TB: Households with active or previously active cases if (1) treatment cannot be verified as adequate before exposure, (2) treatment was initiated after contact with the child occurred, or (3) reactivation is suspected.
	Children suspected to have tuberculous disease: Chest radiograph shows active or previously active TB Clinical evidence of TB
	Children with immunosuppressive condition† or HIV infection
Reaction $\geq 10$ mm	Children at increased risk of dissemination from: Young age: <4 y Other medical risk factors, including Hodgkin's disease, lymphoma, diabetes mellitus, chronic renal failure, and malnutrition
	Children with increased environmental exposure: Born or with parents born in regions of the world where TB is endemic Frequent exposure to adults who are HIV-infected, homeless, users of intravenous and other street drugs, poor and medically indigent city dwellers, residents of nursing homes, incarcerated or institutionalized persons, or migrant farm workers
Reaction $\geq 15$ mm	Children $\geq 4$ y of age without any risk factors

\* The Mantoux skin test contains 5 tuberculin units of purified protein derivative (5TU-PPD). These recommendations should apply regardless of whether bacille Calmette-Guérin (BCG) has been previously administered. TB, tuberculosis; HIV, human immunodeficiency virus.

† Including immunosuppressive dose of corticosteroids.

**TABLE 6.** Laboratory Monitoring and Immunization for the HIV-Exposed Infant (Birth to 6 Months of Age)\*

	Age								
	Birth	2 wk	4 wk	6 wk	2 mo	3 mo	4 mo	5 mo	6 mo
Assess risk of other diseases†	x								
Continuation of ACTG-076 regimen‡	x	x	x	x					
CBC and differential leukocyte counts§	x		x	x	x	x	x		
PCR for HIV DNA and/or viral culture for HIV	x		x				x		
T-cell profile¶			x			x			
Quantitative immunoglobulins								x	
Initiate prophylaxis for <i>Pneumocystis carinii</i> pneumonia				x					
Immunizations									
Hepatitis B	x		x						x
Diphtheria-pertussis-tetanus					x		x		x
<i>Haemophilus influenzae</i> #					x		x		x
Polio vaccine (IPV)					x		x		

\* ACTG-076 indicates AIDS (Acquired Immunodeficiency Syndrome) Clinical Trials Group Protocol-076; CBC, complete blood count; PCR, polymerase chain reaction; and HIV, human immunodeficiency virus.

† Test mother or neonate if maternal status for other infections has not been assessed (see text).

‡ Zidovudine therapy to decrease the risk of HIV infection in the infant is discontinued at 6 weeks of age.

§ CBC and differential leukocyte count should continue to be done monthly beyond 4 months of age in the infected child and the child whose infection status is unclear at 4 months.

|| Repeat PCR or viral culture immediately if positive to confirm infection. If initial test is negative, repeat test at 4 weeks to 2 months. If clinical status or other laboratory parameters suggest HIV infection, repeat testing earlier than 4 months. If at 4 months the tests are still negative for infection, ongoing serologic follow-up is indicated.

¶ T-cell profile should be repeated at 6 months in infected children and in those whose infection status is unclear at 6 months.

# *Haemophilus influenzae* vaccine schedule may vary depending on which type of vaccine is used.

who reside with HIV-infected individuals or are otherwise members of a high-risk group (Table 5) should have annual TB skin testing beginning at 1 year of age. Only the Mantoux (containing 5 tuberculin units of purified protein derivative [PPD]) skin test should be used. Multipuncture skin tests should not be used for screening in the United States. All skin tests should be interpreted by a qualified health care professional. The criteria for a positive Mantoux skin test are given in Table 5.

The criterion for a positive PPD is 5-mm induration for HIV-infected persons and for children in close contact with a person with infectious TB. A negative PPD never rules out tuberculous infection, and patients with symptoms or physical findings suggestive of TB require additional laboratory testing even if the PPD is negative. Administration of Bacille Calmette-Guérin (BCG) is not routinely recommended in the United States and BCG should not be given to HIV-infected individuals.

#### COUNSELING OF MOTHERS OR CARE GIVERS OF HIV-EXPOSED INFANTS

Pediatricians who counsel mothers of HIV-exposed infants must realize that infection may have been identified initially in the mother during this pregnancy or even after delivery. The diagnosis has profound implications for the future of the mother and family. If the mother is not already receiving health care for herself, she should be given a referral for her own health care. Testing for HIV should be recommended for the father and other children. During infancy, determination of HIV-infection status may take several months, which creates anxiety for the parents or care giver.

Some HIV-infected women are already seriously ill and may have partners or other children who are ill or have died because of complications of AIDS. Poverty, lack of health care coverage or fear of losing

existing coverage, substance abuse involving drugs or alcohol, difficulty finding housing, domestic violence, and depression are all factors that may require increased use of social services to enhance proper care of the infant.

The mother or care giver should be informed about the need for the following: frequent medical follow-up, the difficulties with obtaining an early diagnosis of HIV infection in infants, the testing necessary to determine infection status in infants, the administration of zidovudine to decrease the risk of infection in the infant, the need for prophylaxis for PCP, the modifications in recommendations for immunizations, recommendations for avoiding breastfeeding, and precautions to prevent the spread of HIV infection. Pediatricians should discuss the importance of prompt assessment of symptoms of illness, such as fever or respiratory distress. Parents (or care givers) should also be educated regarding the myriad of clinical presentations HIV infection may have (eg, recurrent infections, unusual infections, failure to thrive, hematologic manifestations, renal disease, and neurologic manifestations).

When a foster parent or other relative is the primary care giver, pediatricians must provide the care giver and personnel from the child protection agency sufficient information about the child's HIV status to ensure appropriate health care. The physician should also emphasize the importance of maintaining the family's confidentiality. It is estimated that 80 000 children in the United States will be orphaned as a result of AIDS by the year 2000.<sup>46</sup> Thus, when an infected mother is the primary care giver for her children, pediatricians should discuss the need for permanency planning for the children so that in the event the mother becomes too ill to provide care, alternative child care arrangements have been planned in advance.

## CHILD CARE ATTENDANCE

Infected children should not be denied access to child care based on HIV status alone. In making recommendations for child care attendance, the physician should consider the immunologic and neurologic status of the child, and the presence of open skin lesions.<sup>47</sup> In addition, the parent or care giver should be told that, even for healthy children, child care attendance is associated with an increased risk for acquisition of a variety of infections (eg, otitis media, gastroenteritis or *Cytomegalovirus*). Also, physicians should discuss the potential benefits and risks associated with disclosure of the child's status to the child care center. Such disclosure should occur only with the informed consent of the parent or care giver.

## CONCLUSION

These guidelines enable pediatricians to become increasingly involved in the care of HIV-exposed infants. However, because of the rapid advances in knowledge about HIV and AIDS, frequent changes in recommendations for evaluation and therapy, and opportunities for participation in clinical research trials, pediatricians providing care to HIV-exposed or infected infants should obtain periodic consultation from physicians with expertise in pediatric HIV infection.

## RECOMMENDATIONS

1. Physicians and other clinicians providing care for pregnant women should educate them about HIV and strongly recommend that they be tested. These clinicians should ensure that the physician who will be providing care for the infant is informed of the mother's HIV status. Pediatricians, family physicians, and obstetricians should counsel HIV-infected women about the means available to decrease the risk of transmission of HIV infection to the infant (ie, by using the ACTG-076 zidovudine regimen<sup>8</sup> and not breastfeeding).
2. All HIV-exposed infants should be assessed (by review of test results or recent testing of the mother or by testing the infant) for exposure to other infections that may be acquired in utero or at delivery.
3. Counseling and education of the parents or care givers about HIV infection should be provided by pediatricians caring for HIV-exposed infants.
4. All HIV-exposed infants should undergo testing for HIV (by PCR or virus culture) at birth (cord blood should not be used), at 1 to 2 months of age, and again at 4 months (in those whose initial tests were negative) to determine infection status. If the PCR or virus culture is positive for infection, the test should be repeated immediately for confirmation. If all of the above tests (PCR or virus cultures) are negative, the infant should have serologic testing to document disappearance of HIV antibody at 12 months of age or older.
5. Hematologic and immunologic parameters should be monitored periodically in all HIV-exposed infants while infection status is being determined. Monitoring should continue in children

who are infected and in those whose infection status has not been determined by 4 to 6 months of age.

6. Prophylaxis for PCP should be initiated for all HIV-exposed infants by 6 weeks of age. Prophylaxis beyond 4 to 6 months of age should be provided to those who are infected and those whose infection status is indeterminate.
7. Immunizations and tuberculosis screening should be provided for HIV-exposed infants in accordance with guidelines established by the American Academy of Pediatrics and the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention.
8. Table 6 summarizes the recommendations for laboratory monitoring and immunizations for HIV-exposed infants from birth to 6 months of age.
9. The pediatrician providing care to HIV-exposed or HIV-infected infants or children should obtain periodic consultation from a physician with expertise in pediatric HIV infection.

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