
Lynne M. Mofenson, MD, and the Committee on Pediatric AIDS

ABSTRACT. In 1994, the US Public Health Service published guidelines for the use of zidovudine to decrease the risk of perinatal transmission of human immunodeficiency virus (HIV). In 1995, the American Academy of Pediatrics and the US Public Health Service recommended documented, routine HIV education and testing with consent for all pregnant women in the United States. Widespread incorporation of these guidelines into clinical practice has resulted in a dramatic decrease in the rate of perinatal HIV transmission and has contributed to more than a 75% decrease in reported cases of pediatric acquired immunodeficiency syndrome (AIDS) since 1992. Substantial advances have been made in the treatment and monitoring of HIV infection; combination antiretroviral regimens that maximally suppress virus replication are now available. These regimens are recommended for pregnant and nonpregnant individuals who require treatment. Risk factors associated with perinatal HIV transmission are now better understood, and recent results from trials to decrease the rate of mother-to-child HIV transmission have contributed new strategies with established efficacy. However, perinatal HIV transmission still occurs; the Centers for Disease Control and Prevention estimates that 300 to 400 infected infants are born annually. Full implementation of recommendations for universal, routine prenatal HIV testing and evaluation of missed prevention opportunities will be critical to further decrease the incidence of pediatric HIV infection in the United States. This technical report summarizes recent advances in the prevention of perinatal transmission of HIV relevant to screening of pregnant women and their infants. Pediatrics 2000;106:666. URL: http://www.pediatrics.org/cgi/content/full/106/6/e88; perinatal transmission, human immunodeficiency virus, prenatal testing, antiretroviral prophylaxis.

ABBREVIATIONS. HIV, human immunodeficiency virus; ZDV, zidovudine; AAP, American Academy of Pediatrics; AIDS, acquired immunodeficiency syndrome; CDC, Centers for Disease Control and Prevention; PACTG, Pediatric AIDS Clinical Trials Group; 3TC, lamivudine; EIA, enzyme immunoassay; PCR, polymerase chain reaction.

Marked changes in the epidemiology of pediatric human immunodeficiency virus (HIV) infection have occurred since 1994, when administration of zidovudine (ZDV) to the HIV-infected woman during pregnancy and labor and to the newborn was shown to decrease the risk of perinatal HIV transmission.1,2 The American Academy of Pediatrics (AAP) recommended documented HIV education and routine testing with consent (which included consent obtained with patient notification, or “right of refusal” consent) for all pregnant women in the United States in 1995; the US Public Health Service also recommended universal prenatal HIV counseling and testing in 1995.3,4 Since then, a significant decrease in new cases of pediatric HIV infection and reported cases of pediatric acquired immunodeficiency syndrome (AIDS) has been observed, raising the possibility that perinatal HIV infection could be eliminated in the United States. The Centers for Disease Control and Prevention (CDC) estimates that the rate of new cases of perinatal HIV infection has decreased from approximately 1500 to between 300 and 400 per year.5,6 The persistence of perinatal transmission reflects a continued incidence of new HIV infections among women, rare prophylaxis failures, and a series of missed prevention opportunities in pregnant women, the most important of which are lack of prenatal HIV counseling and testing and absence of prenatal care.

EPIDEMIOLOGY OF HIV INFECTION IN WOMEN OF CHILDBEARING AGE

Among women of childbearing age, the rate of HIV infection has continued to increase in the United States. Of reported AIDS cases in adults, women accounted for 7% in 1985, 13% in 1993, and 23% in 1999.7 Young women are at particular risk; 41% of young adults 13 to 24 years old reported in 1999 as having AIDS were females. During 1999 alone, AIDS was newly diagnosed in nearly 11,000 women, an incidence of 9.3 per 100,000 women.7

The incidence of AIDS was 21 times higher among black women (49.0 per 100,000) and 7 times higher among Hispanic women (14.9 per 100,000) than white women (2.3 per 100,000). Disproportionately high AIDS rates among women of color may be markers for socioeconomic factors, such as the relationship of race or ethnicity with poverty and the association of poverty with substance abuse, prostitution, and sexually transmitted diseases.8,9 Additionally, decreased access to health care associated with disadvantaged socioeconomic status and cultural and language barriers may limit access of women of color to HIV prevention information.

Heterosexual contact surpassed injection drug use as the predominant mode of HIV transmission for women with AIDS in 1992.7,10 Among young adults 13 to 24 years old in whom AIDS was diagnosed...
in 1999, only 11% of males acquired HIV infection via heterosexual contact, compared with 69% of females. Women with HIV infection acquired via heterosexual contact are often unaware of their partner’s risk of HIV infection.\textsuperscript{8,10} In 1999, 32% of young women with AIDS had no risk reported or identified; many of these women were likely infected through heterosexual contact with a partner who was not known to be infected with HIV.\textsuperscript{7} Although AIDS cases in women continue to be concentrated in the northeast and large metropolitan areas, the epidemic now affects all regions, particularly the southeast, as well as rural areas.\textsuperscript{12,13} During 1999, the annual incidence of AIDS in women in Florida was the third highest in the United States, with only New York and the District of Columbia having higher rates.\textsuperscript{7}

Surveillance of AIDS does not accurately reflect the incidence and prevalence of HIV infection among women. In 1994, the CDC estimated that only 15% of HIV-infected women had developed AIDS. Because of improvements in therapy, many HIV-infected individuals are living for prolonged periods without developing clinical AIDS. Data from states that report cases of HIV infection indicate that women accounted for 32% of adults and 42% of youth 13 to 24 years old reported to have HIV infection during 1999.\textsuperscript{7}

Data on HIV seroprevalence among childbearing women are available from the Survey of Childbearing Women, which was conducted at 45 sites between 1989 and 1995.\textsuperscript{5,14} During this time, an estimated 6000 to 7000 HIV-infected women gave birth annually. HIV seroprevalence among childbearing women remained stable nationwide, ranging from 1.5 to 1.7 per 1000 women, although trends differed regionally. HIV seroprevalence decreased in the northeastern states (from 4.1 to 3.2 per 1000), whereas seroprevalence increased in the southern states through 1991 (from 1.6 to 2.0 per 1000) and then stabilized. Seroprevalence among black women in some southern states continued to increase significantly. Rates in the Midwest and western states remained stable at approximately 0.6 per 1000. The highest seroprevalence rates were observed in urban areas, particularly on the East Coast, but high rates were also observed in some rural areas, particularly in the south. Rates among black women were 3 to 35 times higher than those among white women regardless of geographic area of residence.

**CHANGES IN THE EPIDEMIOLOGY OF PERINATAL HIV INFECTION**

Remarkable changes in pediatric HIV infection have been observed in the United States since 1994, when the results of Pediatric AIDS Clinical Trials Group (PACTG) protocol 076 showed that administration of ZDV to the woman during pregnancy and labor and to the newborn decreased the risk of mother-to-child transmission by nearly 70%.\textsuperscript{2} Epidemiologic studies demonstrated decreases in the risk of perinatal transmission temporally associated with increased prenatal HIV testing and use of ZDV prophylaxis as early as 1995.\textsuperscript{5,15,16} In a study of 18 states that report HIV status, the percentage of HIV-exposed infants whose mothers were tested for HIV before giving birth increased from 70% to 94% between 1993 and 1997, and the percentage of HIV-infected pregnant women receiving ZDV increased from 7% to 91% during this same time period.\textsuperscript{5}

The widespread incorporation of ZDV prophylaxis into clinical practice and decrease in the risk of perinatal HIV transmission has already contributed to a substantial decrease in reported perinatal AIDS cases in the United States, which peaked in 1992 and then decreased by 75% from 1992 through 1998.\textsuperscript{17} This decrease was most dramatic in the youngest age groups; AIDS cases in infants younger than 1 year decreased by 86%, cases in children 1 to 5 years old decreased by 78%, while in children older than 5 years (who would have been born before 1994), there was little decrease. The number of perinatal AIDS cases has decreased in all regions of the country and among all racial and ethnic groups.

**ADVANCES IN PREVENTION OF PERINATAL HIV TRANSMISSION**

Prenatal HIV RNA Copy Number and Risk of Perinatal Transmission

A number of studies have shown that maternal viral load is a critical determinant of the risk of perinatal transmission of HIV.\textsuperscript{18,19} In the late 1990s, highly active combination antiretroviral therapy became available that could decrease viral load below the level of quantitation and is now standard treatment for HIV-infected individuals, including pregnant women.\textsuperscript{20,21} Preliminary data indicate that use of such regimens by pregnant HIV-infected women may be associated with a further decrease in risk of perinatal transmission to 2% or less.\textsuperscript{22,23}

Although the risk of perinatal transmission in women with HIV RNA below the level of quantitation appears very low, there is no HIV RNA threshold below which there is no risk of transmission. Studies evaluating the relationship between prenatal HIV RNA and risk of transmission have used a variety of assays for RNA quantification; these tests vary in the HIV RNA copy number that constitutes the lower limit of assay detection. This complicates the ability to compare transmission rates across studies among women with low RNA.

In PACTG 185, no transmission was observed in 84 women receiving ZDV who had baseline HIV RNA below the level of quantitation (<500 copies/mL), but the upper 95% confidence interval for transmission was 3.5%.\textsuperscript{18} Rate of transmission was 2% among 51 women receiving ZDV with HIV RNA of 500 to 1000 copies/mL but increased to 7% among the 344 remaining women with HIV RNA >1000 copies/mL. In the Women and Infants Transmission Study, although no transmission was observed among 57 women with baseline HIV RNA <1000 copies/mL, the upper 95% confidence interval was 5.1%.\textsuperscript{19}

In PACTG 076, ZDV had a protective effect even among women with HIV RNA below the level of quantitation.\textsuperscript{24} A multivariate analysis of data from 1482 women followed between 1990 and 1999 in the Women and Infants Transmission Study found that...
the protective effect of antiretroviral prophylaxis was independent of viral load at the time of delivery.

These data suggest that the mechanism of protection provided by antiretroviral prophylaxis is more than just a decrease in viral load. It is likely that pre- and postexposure prophylaxis of the infant provided by transplacental passage of antiretroviral drugs administered to the mother during labor and continued administration to the infant for 6 weeks is also important.

Interventions to Decrease the Risk of Perinatal HIV Transmission

Elective (scheduled) cesarean delivery performed before the onset of labor and rupture of membranes has been shown to decrease the risk of perinatal transmission from infected women receiving no antiretroviral drugs or receiving only ZDV. However, these studies did not include data on maternal viral load or women receiving highly active antiretroviral therapy. Whether the benefit of elective cesarean delivery in decreasing the risk of perinatal HIV transmission outweighs the risks of operative delivery in women with HIV RNA below the level of quantitation, in whom the risk of transmission is extremely low, requires more evaluation. The American College of Obstetricians and Gynecologists recommends that HIV-infected pregnant women with HIV RNA of 1000 copies/mL or greater be counseled regarding the potential benefit of scheduled cesarean delivery in addition to ZDV prophylaxis to further decrease the risk of perinatal transmission, but states that data are insufficient to demonstrate a benefit for women with HIV RNA <1000 copies/mL.

Consistent with the perception that most fetal and newborn HIV infections are acquired near or during delivery, recent clinical trials have shown that abbreviated antiretroviral regimens focused on the peripartum period are also effective in decreasing the risk of perinatal transmission. In 1998, a short ZDV regimen started at 36 weeks’ gestation and administered orally to the mother during labor with no administration to the infant decreased the risk of perinatal HIV transmission by 50% in a study of nonbreastfeeding women in Thailand (Table 1). Data from a second Thailand study indicate that a longer 3-part ZDV regimen (ie, starting at 28 weeks’ gestation and administered to the infant for 6 weeks after birth) is more effective than a shorter 3-part ZDV regimen (ie, starting at 36 weeks’ gestation and administered to the infant for 3 days after birth). This may be because longer prenatal treatment was more effective in decreasing the risk of in utero transmission (in utero infection rate was 1.6% when ZDV was begun at 28 weeks’ gestation, compared with 5.1% when ZDV began at 36 weeks’ gestation). When maternal prenatal treatment began at 28 weeks’ gestation, there did not appear to be a significant difference in efficacy if infant prophylaxis was administered for 6 weeks or 3 days; however, when maternal treatment began at 36 weeks’ gestation, better efficacy was observed with more prolonged (eg, 6 weeks) infant prophylaxis.

Intrapartum and postpartum antiretroviral regimens in which prophylaxis is initiated as late as during labor have also been shown to be effective in decreasing the risk of perinatal transmission in clinical trials, although not as effective as regimens that include prenatal as well as intrapartum and postpartum treatment. A study in breastfeeding women in Uganda demonstrated that a single oral dose of nevirapine administered to the woman at the onset of labor followed by a single oral dose administered to the infant decreased the risk of infant HIV infection by 41% at 6 to 8 weeks of age, compared with a very short ZDV regimen administered orally to the woman during labor and to the infant for 1 week after birth (Table 1). Although HIV transmission via breast milk occurred in infants receiving both regimens in this breastfeeding population, the infant infection rate in the group receiving nevirapine remained significantly lower than in the group receiving a short regimen of ZDV even at 12 months of age. In another African trial in breastfeeding women (the PETRA trial), oral administration of ZDV and lamivudine (3TC) during labor followed by 1 week of oral administration to the mother and infant decreased the risk of infant infection by 48%, compared with placebo at 14 to 16 weeks of age (Table 1). However, in contrast to the nevirapine trial, efficacy of the ZDV-3TC regimen was not retained at 18 months of age in this breastfeeding population. A third trial in South Africa (the SAIN T trial) compared the efficacies of the nevirapine and ZDV-3TC regimens. An analysis of early efficacies showed that the risk of infant infection was similar between the 2 regimens when evaluated at 8 weeks of age (Table 1). Use of postpartum antiretroviral prophylaxis alone has not been evaluated in a randomized clinical trial. Although some observational data and studies of animals have suggested this may provide some measure of protection, other studies have not. The timing of antiretroviral administration after exposure and duration of treatment appear to be important. In studies of rhesus macaque monkeys, postexposure prophylaxis with an acyclic nucleoside phosphonate analog with a long half-life (9-[2-phosphonomethoxypropyl]adenine; PMPA), administered 24 hours after challenge and continued for 28 days, successfully protected against intravenous simian immunodeficiency virus challenge. However, prophylaxis initiated after 24 hours or with a decreased duration of treatment decreased the effectiveness in preventing establishment of persistent infection. In a study of neonatal macaque monkeys in which PMPA was administered immediately after oral challenge with simian immunodeficiency virus and continued for 2 weeks, 3 of 4 animals had transient viremia, suggesting abortive infection, but a fourth animal was not protected. In an observational study in humans in New York, administration of only ZDV for 6 weeks to newborns was associated with a significant decrease in transmission if the drug was initiated within 24 hours of birth (most infants started receiving ZDV within 12 hours). However, in an observational study from North Carolina, administration of ZDV only to the newborn
<table>
<thead>
<tr>
<th>Drug</th>
<th>Study Characteristics</th>
<th>Prepartum Maternal Regimen</th>
<th>Intrapartum Maternal Regimen</th>
<th>Postpartum Maternal Regimen</th>
<th>Postpartum Infant Regimen</th>
<th>Rate of HIV Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZDV</td>
<td>PACTG 076^2</td>
<td>100 mg, administered orally, 5 times/d starting at 14–34 wk of gestation</td>
<td>2.0 mg/kg of body weight, infused intravenously for 1 h, followed by continuous intravenous infusion of 1 mg/kg/h</td>
<td>—</td>
<td>2 mg/kg, administered orally, 4 times/d for 6 wk</td>
<td>Rate of transmission at 18 mo of age: 25.5% with placebo versus 8.3% with ZDV, a 68% decrease.</td>
</tr>
<tr>
<td>ZDV</td>
<td>Bangkok Trial^28</td>
<td>300 mg, administered orally, twice/d starting at 36 wk of gestation</td>
<td>300 mg, administered orally, every 3 h</td>
<td>—</td>
<td>—</td>
<td>Rate of transmission at 6 mo of age: 18.9% with placebo versus 9.4% with ZDV, a 50% decrease.</td>
</tr>
<tr>
<td>ZDV</td>
<td>Perinatal HIV Prevention Trial^29</td>
<td>300 mg, administered orally, twice/d starting at 28 or 36 wk of gestation</td>
<td>300 mg, administered orally, every 3 h</td>
<td>—</td>
<td>2 mg/kg, administered orally, 4 times/d for 6 wk or 3 d</td>
<td>Rate of transmission at 6 mo of age: Interim analysis—4.1% in long-long versus 10.5% in short-short arm (P = .004); enrollment in short-short arm stopped before final analysis. Final analysis—6.5% in long-long versus 47% in short-long versus 8.6% in short-short arms. In utero transmission—1.6% in combined long prepartum arms versus 5.1% in combined short prepartum arms (P &lt; .001).</td>
</tr>
<tr>
<td>ZDV</td>
<td>Ivory Coast Trial^37</td>
<td>300 mg, administered orally, twice/d starting at 36 wk of gestation</td>
<td>300 mg, administered orally, every 3 h</td>
<td>—</td>
<td>—</td>
<td>Rate of transmission at 4 wk of age: 21.7% with placebo versus 12.2% with ZDV, a 44% decrease. Rate of transmission at 3 mo of age: 24.9% with placebo versus 15.7% with ZDV, a 37% decrease.</td>
</tr>
<tr>
<td>ZDV</td>
<td>DITRAME ANRS 049^96,99</td>
<td>300 mg, administered orally, twice/d starting at 36–38 wk of gestation</td>
<td>600 mg, administered orally, at onset of labor</td>
<td>300 mg, administered orally, twice/d for 1 wk</td>
<td>—</td>
<td>Rate of transmission at 6 mo of age: 27.5% with placebo versus 18.0% with ZDV, a 38% decrease. Rate of transmission at 15 mo of age: 30.6% with placebo versus 21.5% with ZDV, a 30% decrease.</td>
</tr>
<tr>
<td>ZDV-3TC</td>
<td>PETRA^32,33</td>
<td>300 mg of ZDV and 150 mg of 3TC, administered orally, twice/d starting at 36 wk of gestation</td>
<td>300 mg of ZDV, administered orally, every 3 h and 150 mg of 3TC, administered orally, every 12 h</td>
<td>300 mg of ZDV and 150 mg of 3TC, administered orally, twice/d for 1 wk</td>
<td>4 mg/kg of ZDV and 2 mg/kg of 3TC, administered orally, twice/d for 1 wk</td>
<td>Rate of transmission at 6 wk of age: 19.2% with placebo versus 9.2% with the 3-part regimen (a decrease of 52%); versus 12.6% with the 2-part regimen (a decrease of 52%); versus 18.4% with the 1-part regimen (no efficacy). Rate of transmission at 18 mo of age: 26.6% with placebo versus 20.7% with the 3-part regimen (not significant); versus 24.4% with the 2-part regimen (not significant); versus 25.7% with the 1-part regimen (not significant).</td>
</tr>
</tbody>
</table>
was not associated with a decrease in the risk of transmission, although the time of prophylaxis initiation was not provided.15

These data emphasize the importance of early identification of HIV-infected pregnant women so that effective interventions may be offered to decrease the risk of mother-to-child transmission. In the United States, the 3-part PACTG 076 ZDV regimen, administered in combination with additional antiretroviral agents, is recommended for optimal prevention when treatment of maternal HIV infection is required; use of the 3-part ZDV regimen without additional drugs may be considered for prophylaxis of perinatal transmission in women with low viral loads (eg, <1000 copies/mL) who do not otherwise require treatment.21 However, initiation of antiretroviral prophylaxis even as late as labor and delivery may still diminish the risk of transmission. Thus, identification of HIV-infected women as late as delivery or HIV-exposed infants on the first day after birth may still provide potential benefit if antiretroviral prophylaxis can be rapidly initiated. Additionally, in the United States and other countries where a safe and sustainable source of infant formula is available, HIV-infected women should be advised not to breastfeed to avoid postnatal transmission of HIV through breast milk; this recommendation includes infected women who are receiving antiretroviral therapy.21,39

**BARRIERS TO PREVENTION OF PERINATAL HIV TRANSMISSION**

The estimated 300 to 400 HIV-infected infants born annually represent populations in which prevention efforts are impeded by poor prenatal care and lack of timely HIV testing and treatment of pregnant women. Of 329 children who acquired HIV infection perinatally who were born in 1995 and 1996, 34% had mothers who were not tested for HIV until after giving birth.5 Birth of an infected child is a sentinel health event signaling a chain of missed opportunities and barriers to prevention.40 These barriers often also result in failure to ensure that HIV-infected women have access to adequate health care. Implementation of interventions to decrease the risk of perinatal HIV transmission needs to be accompanied by improved access to comprehensive care and support services for the infected woman and her child during and after pregnancy to ensure optimal health for both.

Further progress in decreasing the risk of perinatal HIV transmission in the United States will require accurate national HIV surveillance data to track trends in perinatal transmission throughout time, determine risk factors for transmission, and guide HIV prevention programs. However, although national HIV reporting has been recommended by the AAP and the CDC, at present only 39 states, Puerto Rico, and the Virgin Islands have HIV reporting and surveillance systems in place.31,42

**HIV Infection in Women**

An important barrier to elimination of perinatal HIV transmission in the United States is the contin-
ueed increase in the number of women of childbear-
ing age infected with HIV, particularly adolescents of
minority race or ethnicity. Data from out-of-school
youth 16 to 21 years old participating in the US Jobs
Corps between 1990 and 1996 showed that HIV prev-
ance in young women (2.8 per 1000) was higher
than that for young men (2.0 per 1000). The preva-
ance of HIV was highest among black female youth
(4.9 per 1000) and highest in black women from the
south. In a study in which HIV incidence trends
among young adults 20 to 25 years old were esti-
mated with modeling, the rate of HIV infection ac-
quired from heterosexual contact increased between
1988 and 1993 while the rate of HIV infection ac-
quired from homosexual contact or injection drug
use decreased. The prevalence of HIV infection
among men decreased during this time period, while
prevalence increased among young women 18 to 22
years old by 36% and among those 23 to 27 years old
by 45%; HIV infection in young women was predom-
nantly acquired via heterosexual contact.

Unplanned Pregnancy in Women

The same women at risk of HIV infection are also
at high risk of becoming pregnant, often unintention-
ally. Although there has been a decrease in adoles-
cent pregnancy rates since 1991, pregnancy rates in
youth continue to be high. In 1995, the pregnancy
rate for the overall population of women 15 to 19
years old was 83.6 per 1000 but was 210.6 per 1000
for sexually active youth; this compares with a preg-
nancy rate of 66.0 per 1000 for all women 15 to 44
years old. Youth engaging in behaviors that place
them at high risk of HIV acquisition are at particular
risk of unplanned pregnancy. In a study of runaway
and homeless youth, the likelihood of an individual
having participated in “survival sex” (exchange of
sex for shelter, food, drugs, or money) was 2.4 times
more common among pregnant than nonpregnant
street youth. Programs for HIV prevention and
decreasing the rate of unplanned pregnancy targeted
to high-risk young women are important compo-
nents of a perinatal HIV prevention strategy.

Unplanned pregnancy is not uncommon among
HIV-infected women. In a study of 83 HIV-infected
pregnant women in Atlanta, most repeat pregnancies
(90%) were unplanned. In a survey of almost 4000
HIV-infected women of childbearing age receiving
care in 11 cities in the United States in the CDC Adult
and Adolescent Spectrum of Disease Project, 14%
were pregnant at the time of enrollment, and annu-
ally, an additional 5.8% became pregnant thereaft-
ero. Among women who were pregnant at enroll-
ment or during observation, 12% had more than 1
pregnancy.

Youth with HIV infection may be at higher risk
than older infected women of becoming pregnant
and continuing risky behaviors. In a study in Seattle,
36% of HIV-infected women younger than 25 years
followed between 1990 and 1998 became pregnant,
compared with 19% of HIV-infected women older
than 25 years. Similarly, in HIV-infected women
followed in the Adult and Adolescent Spectrum of
Disease Project between 1990 and 1997, pregnancy
rates were 11-fold higher among HIV-infected
women 15 to 24 years old than among those 35 to 44
years old and 1.5-fold higher among black infected
women than among white infected women. Provi-
sion of and improved access to family planning
counseling, services, and contraception to enable
HIV-infected women to make informed decisions
about childbearing and prevent unplanned preg-
nancy are additional components of perinatal HIV
prevention programs.

Delayed or Lack of Prenatal Care

Delayed or lack of prenatal care constitutes an-
other significant barrier to prevention of HIV trans-
mission. In the United States, the percentage of
women who delayed receiving prenatal care de-
creased from 22% to 16%, and those who received no
prenatal care decreased from 2% to 1% between 1989
and 1997. However, women who were more likely
to have delayed receiving or not received prenatal
care were those at higher risk of HIV infection—
women of minority race or ethnicity, women
younger than 20 years, and women with fewer than
12 years of education. The most common reasons
women gave for delaying or not receiving prenatal
care in the Pregnancy Risk Assessment Monitoring
System were not knowing they were pregnant, lack
of money or insurance coverage, and inability to get
an earlier appointment.

Women infected with HIV may be at particular
risk of delaying or not receiving prenatal care. In 1
study from 4 states, 14% of HIV-infected women
received no prenatal care, and 23% started receiving
prenatal care only in the third trimester. Lack of
prenatal care was more common among infected
women who used illicit drugs or in whom HIV in-
fec tion was not diagnosed until after they gave birth;
35% of women who did not receive prenatal care
were drug users, and in 50%, HIV infection was not
diagnosed until the postnatal period. In a study of
more than 2000 HIV-infected pregnant women from
New York, 20% had received no prenatal care; women
with shorter Medicaid enrollment during pregnancy
and those who used illicit drugs were more likely to
not receive prenatal care.

Lack of Prenatal HIV Testing

After starting to receive prenatal care, to take ad-
advantage of interventions to prevent mother-to-child
HIV transmission, an HIV-infected pregnant woman
must know her HIV status. Thus, she must be offered
and must accept HIV testing. In an assessment of
prenatal HIV counseling and testing practices in 14
states during 1996 and 1997, more than 70% of
women recalled discussing HIV testing during pre-
natal care, and at least 50% reported being tested for
HIV during pregnancy or delivery. However, de-
spite national recommendations for universal prena-
tal HIV counseling and testing, rates varied by state,
type of prenatal health care provider, health insur-
ance, and maternal demographic characteristics.
Higher rates of testing were reported for black
women, younger women, and those who sought care
from a public provider, received Medicaid benefits,
HIV counseling and testing is now recommended by Physicians need to be aware that because offering of testing into the routine medical care setting.3,62 It is important to educate and test for HIV during pregnancy, as it is a critical component of prenatal care and can help prevent transmission to the infant. The AAP recommends universal, routine provider counseling and testing for HIV.55 A number of studies have indicated the importance of provider counseling and recommendation for testing as a determinant of test acceptance.56,57

The Institute of Medicine issued a report in 1998 recommending perinatal HIV transmission in the United States.58,59 The Institute found that, when offered, acceptance of HIV testing by pregnant women was high, but that requirements for extensive prenatal counseling were deterring some providers from recommending testing. The report recommended that a national policy of HIV testing with patient notification as a routine component of prenatal care should be implemented in the United States. This means that HIV testing would be integrated into the standard battery of prenatal tests and the woman would be informed that the HIV test is being conducted and given the right to refuse the test. In studies in Scotland and the United Kingdom, this approach was found to be acceptable to women and to significantly increase prenatal HIV test acceptance.60,61

Because the purpose of HIV testing is to engage the mother in continuing care for herself and her infant, the mother’s knowledge of and consent for testing of herself or her infant is important. Compliance with medical care is likely to be greatest when the woman feels she has made an informed decision regarding HIV testing and has a relationship of respect and trust with her health care provider. Routine HIV testing with patient notification implies that the woman is provided with information about HIV infection, that the HIV test is recommended by the provider, and that the test will be performed unless the patient rejects the test. This differs from involuntary HIV testing without patient consent.

These recommendations are consistent with existing AAP recommendations for universal, routine prenatal HIV education and use of consent procedures (including right of refusal consent) that facilitate rapid incorporation of HIV education and testing into the routine medical care setting.5,62 Physicians need to be aware that because offering of HIV counseling and testing is now recommended by the AAP, the American College of Obstetricians and Gynecologists, and the US Public Health Service as a standard of care for pregnancy, lack of offering such testing has medicolegal implications if an infected infant is born to a woman who was not offered testing.63 Maternal HIV infection status needs to be communicated from the obstetrician to the pediatrician to ensure that antiretroviral prophylaxis is provided to HIV-exposed newborns, the mother is advised not to breastfeed to avoid postnatal transmission of HIV via breast milk, prophylaxis against Pneumocystis carinii pneumonia is initiated at 4 to 6 weeks of age, and ongoing evaluation to determine the infant’s infection status is performed.

In addition to allowing women to make choices related to interventions that could decrease the risk of HIV transmission to their infants, the diagnosis of HIV infection allows them to make informed decisions regarding treatment choices for themselves. Prolonging the health and survival of women is important for improving infant and child health and survival. The number of children orphaned by the death of an HIV-infected mother is increasing in the United States as well as the developing world, and HIV infection has come to rival or surpass other causes of death of mothers of young children.64 It is estimated that 45 600 children and adolescents in the US had lost their mothers to death resulting from HIV infection at the end of 1995; by the end of 2000, this number will have increased to more than 80 000.64

Interventions to Decrease the Risk of HIV Transmission

Women identified as HIV infected need to be counseled about ways to prevent HIV transmission to their infant, including avoidance of breastfeeding, use of ZDV prophylaxis (as well as other antiretroviral drugs as needed for treatment of maternal disease), and elective cesarean delivery. Several studies have shown that more than 90% of women identified during pregnancy as HIV infected in recent years have accepted ZDV prophylaxis.5,15 Acceptance of ZDV prophylaxis and appropriate prescription of the full 3-part ZDV regimen is more common in women receiving care from providers who are experienced in the care of HIV-infected pregnant women than those receiving care from primary care providers with less expertise in the care of HIV infection.65,66

Rapid HIV Testing During Labor

Women who receive inadequate or no prenatal care or who have not received prenatal HIV counseling and testing constitute a population denied the advantages of prevention and treatment. As described previously, recent perinatal trials indicate that short antiretroviral regimens can decrease the risk of perinatal transmission, including regimens administered only during labor and to the newborn. Thus, women identified as HIV seropositive during labor could be offered 1 of several antiretroviral regimens that could significantly decrease the risk of intrapartum transmission and could also be advised

http://www.pediatrics.org/cgi/content/full/106/6/e88
Downloaded from http://pediatrics.aappublications.org/ by guest on October 14, 2017
not to breastfeed to avoid postnatal transmission of HIV in breast milk.

To enable preventive interventions to be offered to women who lack prenatal care or who have not been tested during the current pregnancy, use of rapid HIV testing during labor has been proposed.\textsuperscript{67,68} In the United States, only 1 rapid test (Single Use Diagnostic System, Abbott Diagnostics, Abbott Park, IL) is approved by the US Food and Drug Administration. The sensitivity and specificity of rapid assays are similar to those of the standard antibody enzyme immunoassay (EIA). The negative predictive value of these assays is high; thus, a negative result from a rapid test would not require further confirmatory testing and indicates absence of HIV infection. However, the positive predictive value of the test (the probability that a positive test accurately predicts HIV infection in the individual tested) will vary depending on the prevalence of HIV in the population. Therefore, a positive result from a rapid test requires a confirmatory supplemental test to definitively diagnose infection. Expedited results from standard EIA or Western blot analysis of blood from the mother obtained during labor could be available within 24 hours, which would not permit intrapartum maternal drug administration but would permit initiation of postexposure prophylaxis for the infant. Presumptive prophylactic antiretroviral treatment could be administered to the woman and newborn with a single positive rapid test pending results of a confirmatory assay and discontinued if the mother is found to be uninfected. However, this would require discussion with and consent of the mother.

In studies outside of the United States, performance of 2 different rapid test assays in tandem have been shown to have sensitivity and specificity similar to the standard EIA and confirmatory Western blot analysis and could be used to provide rapid and definitive test results during labor.\textsuperscript{69} Although only the Single Use Diagnostic System is commercially available in the United States at present, several other rapid tests are currently under review by the US Food and Drug Administration. Two cost-effectiveness analyses of voluntary rapid intrapartum testing for women without adequate prenatal care showed such testing was cost-effective across a wide range of assumptions.\textsuperscript{68,70} However, logistic and ethical questions related to implementation of rapid testing programs remain, including the acceptability to women of rapid testing during labor and of antiretroviral prophylaxis. Preliminary data from a pilot program in New Orleans are promising; the sensitivity and specificity of the rapid test were 100% and 99.5%, respectively, and rapid screening was responsible for identifying 20% of HIV-seropositive women who gave birth at the pilot site.\textsuperscript{71} New York recently implemented a requirement that HIV testing be available within 48 hours for women with unknown HIV status who arrive at the hospital in labor.\textsuperscript{69} The CDC has initiated a multicenter study, Mother-Infant Rapid Intervention at Delivery, to assess the feasibility of this approach in communities with high HIV seroprevalence and increased rates of births to women who lack prenatal care.

**HIV TESTING OF THE NEWBORN**

When maternal HIV status has not been determined during pregnancy or labor, HIV testing of the newborn with maternal consent is recommended. However, delay in identification of infant HIV exposure until the newborn period is suboptimal in terms of prevention of transmission. In 1 New York City hospital with an aggressive prenatal HIV screening program, addition of newborn HIV screening had little incremental impact on identification of HIV-exposed infants.\textsuperscript{72} Therefore, programs to identify maternal HIV infection during pregnancy should be a priority. For infants born to mothers with unknown HIV status, identification of HIV exposure during the immediate newborn period can provide a potential benefit in terms of prevention of transmission and is important for infant management (such as initiation of prophylaxis against *Pneumocystis carinii* pneumonia and avoidance of breastfeeding).\textsuperscript{73} However, although 2 randomized clinical trials have identified regimens that effectively decrease the risk of HIV transmission even when administered only during labor and to the newborn, only observational data suggest that postpartum antiretroviral administration to the newborn alone may provide some protection from HIV transmission if initiated within 24 hours of birth.\textsuperscript{92,74} Thus, if decreasing the risk of perinatal transmission of HIV is a goal of newborn HIV screening programs, test results will need to be available soon after birth, optimally within 24 hours, to permit rapid initiation of prophylaxis.

**MANAGEMENT OF INFANTS WITH PERINATAL HIV EXPOSURE**

Because of the rapidly evolving nature and increasing complexity in the management of HIV infection, care of the HIV-infected infant should be directed by or in consultation with a specialist in pediatric HIV infection. Recommendations on the management of HIV-exposed infants have previously been published.\textsuperscript{72} During the immediate neonatal period, monitoring for potential toxicity of antiretroviral prophylaxis is necessary. A mild, transient anemia is the primary complication of the 6-week infant ZDV prophylaxis regimen,\textsuperscript{2} and a complete blood cell count is recommended at birth and 4 and 6 weeks of age. Data are very limited regarding potential toxicities in infants whose mothers have received combination antiretroviral therapy. More intensive monitoring during the first weeks after birth may be advisable.

In 1995, the CDC issued revised guidelines for prevention of *P carinii* pneumonia in HIV-exposed infants.\textsuperscript{74} Because the peak incidence of *P carinii* pneumonia in infected infants occurs at 3 to 6 months of age (often before definitive diagnosis of HIV infection) and may occur despite a normal CD4\textsuperscript{+} lymphocyte count, initiation of prophylaxis is recommended for all HIV-exposed infants at 4 to 6 weeks of age regardless of CD4\textsuperscript{+} count. Prophylaxis should be continued through the first year after birth in all
infected children and children in whom HIV status has not yet been confirmed. Children in whom HIV infection has been reasonably excluded (usually possible by 4 to 6 months of age) can discontinue prophylaxis before 12 months of age. For infected children older than 1 year, prophylaxis should be guided by age-related CD4+ count thresholds.

With use of current virologic assays, HIV infection may be diagnosed as early as the first day after birth in some infants and by 1 month of age in most infected infants. The HIV DNA polymerase chain reaction (PCR) assay is the preferred diagnostic tool. In a meta-analysis of data representing 271 HIV-infected children, the estimated sensitivity of the HIV DNA PCR assay was 38% at birth, increasing to 93% at 14 days of age, and 96% at 28 days of age. Some studies have suggested that HIV RNA assays may be useful for early diagnosis of perinatal infection, but data are limited, and these assays are not approved for diagnostic testing. Although ZDV prophylaxis does not appear to alter the diagnostic sensitivity of either the HIV DNA PCR or HIV RNA assays, the effect of combination antiretroviral maternal and infant treatment on the sensitivity of viral diagnostic testing is unknown; therefore, infants with negative results from virologic tests during the first 6 weeks after birth should have diagnostic evaluation repeated after completion of the neonatal antiretroviral prophylaxis regimen. Diagnostic testing for HIV is recommended within the first 48 hours after birth and at 14 days, 1 to 2 months, and 3 to 6 months of age. A positive result from a virologic test should be confirmed by a second assay on a separate blood specimen. Infection with HIV can be reasonably excluded among children with 2 or more negative results from virologic assays, at least 1 of which is performed after 1 month and 1 after 4 months of age.

Initiation of antiretroviral therapy should be considered for infants with HIV infection. Optimal antiretroviral treatment is not yet established but should be initiated as early as the diagnosis is confirmed, regardless of clinical, immunologic, or virologic status. Infants infected with HIV are at particularly high risk of disease progression, and the predictive value of immune and viral parameters is lower at a very young age. Combination antiretroviral therapy—generally 2 nucleoside analog drugs combined with a protease inhibitor or a nonnucleoside reverse transcriptase inhibitor—is recommended. Infants in whom HIV infection is diagnosed while they are receiving the 6-week ZDV prophylaxis regimen should be changed to a combination antiretroviral regimen.

In PACTG 076, ZDV resistance was not detected in infants who became infected with HIV despite maternal and infant ZDV prophylaxis, and disease progression did not differ from that observed in infected infants who received placebo, suggesting ZDV could be a component of the initial combination treatment regimen. However, in an Italian study, infants who became infected with HIV despite maternal ZDV monotherapy were observed to have more rapid disease progression than those born to mothers not receiving treatment.

LONG-TERM FOLLOW-UP OF CHILDREN WITH IN UTERO ANTIRETROVIRAL EXPOSURE

Strategies to enable detection of any potential short- or long-term adverse consequences of in utero and neonatal antiretroviral drug exposure on the infant are critical, particularly now that most infants will not be infected with HIV. Because combination antiretroviral therapy is now standard treatment for HIV-infected individuals, including pregnant women, the fetus may be exposed to multiple antiretroviral drugs. Some nucleoside analog drugs have been found to be mutagenic in some in vitro and rodent studies, and in rhesus macaque monkeys, incorporation of ZDV into DNA in some fetal organs has been demonstrated with in utero ZDV exposure. In humans, ZDV incorporation into cord blood leukocyte DNA has been found in some infants with in utero ZDV exposure, although persistence after discontinuation of prophylaxis and the clinical significance of this finding are unclear. Additionally, HIV-infected individuals receiving long-term antiretroviral treatment have developed toxicity related to mitochondrial dysfunction, although this generally resolves after treatment discontinuation, and a genetic susceptibility may be involved. Prophylaxis with ZDV appears safe in the short term for women and infants followed for as long as 6 years; however, long-term data are not yet available, and definitive information about safety will require many years of follow-up.

A report from France suggested possible mitochondrial dysfunction in 8 infants not infected with HIV with in utero or neonatal exposure to combination ZDV and 3TC or ZDV alone. Two infants with exposure to ZDV and 3TC developed severe neurologic disease and died before 2 years of age, 3 had mild to moderate symptoms, and 3 had no symptoms but transient laboratory abnormalities. The US Perinatal Safety Review Group has conducted an extensive review of 5 large perinatal cohorts in the United States, including all perinatal clinical trials; examination of 353 deaths in more than 20,000 HIV-exposed children with and without antiretroviral exposure revealed no deaths similar to those reported from France. Evaluation of living children in these cohorts for any milder symptoms of mitochondrial disease is underway. A prospective evaluation of echocardiograms in infants born to HIV-infected women with and without ZDV exposure revealed no association of ZDV exposure with acute or chronic abnormalities in cardiac structure or function.

Follow-up data from the international ZDV prophylaxis trials are also reassuring. In the PETRA clinical trial of ZDV and 3TC for prevention of perinatal transmission, no increase in neurologic adverse events was observed among children who received treatment, compared with those who received placebo, suggesting that if mitochondrial dysfunction is associated with in utero antiretroviral exposure, it is likely to be uncommon. In the short-course ZDV prophylaxis trial conducted in Thailand no signifi-


cant differences in growth, immunologic parameters, rates of hospitalization, seizures, or mortality were detected at 18 months of age between infants exposed and those unexposed to ZDV.92 Similarly, mortality rates at 12 months of age were no different between infants exposed and those unexposed to ZDV in the French short-course ZDV trial in Africa.93

Data available to date indicate that serious early toxicity, if it occurs, is likely to be rare. Given the fatal nature of HIV infection, the potential of toxicity is clearly outweighed by the proven benefit of decreasing the risk of mother-to-child transmission by nearly 70% with ZDV prophylaxis.94–96 However, careful follow-up into adulthood is recommended by the US Public Health Service for all children with in utero or neonatal exposure to antiretroviral drugs, regardless of HIV infection status.

CONCLUSIONS

Multiple effective strategies are now available to decrease the risk of perinatal HIV transmission. The continued incidence of perinatal HIV transmission underscores the need for strategies to prevent HIV infection among women and ensure that women receive adequate prenatal care and timely HIV counseling and voluntary testing. In addition, infected women need to have access to HIV-related care and services, receive chemoprophylaxis to decrease the risk of perinatal transmission, and be advised to avoid breastfeeding. In 1995, the AAP recommended that all pregnant women receive HIV education and routine prenatal HIV testing with consent (which may include right of refusal consent). This recommendation remains a critical component of pediatric HIV infection prevention. Rapid HIV testing with consent during labor for women with unknown HIV status deserves further evaluation given the new availability of proven effective antiretroviral prevention strategies for this population. Finally, newborn HIV antibody testing with maternal consent should be recommended for infants born to women who have not had their HIV status determined perinatally or during labor, which will hopefully become a diminishing number. Results of newborn HIV antibody testing, when performed, need to be rapidly available to permit initiation of antiretroviral prophylaxis.

REFERENCES


23. McGowan JP, Crane M, Wiznia AA, Blum S. Combination antiretroviral
27. American College of Obstetricians and Gynecologists, Committee on Obstetric Practice. Committee opinion: scheduled cesarean delivery and the prevention of vertical transmission of HIV infection. ACOG Coun Opin. 2000;234:1–3
43. Blair JM, Hanson DL, Jones JL, Dworkin MS. Have pregnancy rates in human immunodeficiency virus-infected women changed in the era of effective antiretroviral therapy to prevent perinatal transmission? Paper presented at: 48th Annual Epidemic Intelligence Service Conference; April 14–18, 1999; Atlanta, GA
54. Blott M, Yearwood J, Gervais M, Welch J, Zuckerman M. Routine antenatal HIV testing is acceptable to women. BMJ. 1999;319:1069–1070
60. Minkoff H, O’Sullivan MJ. The case for rapid HIV testing during labor. JAMA. 1999;280:1743–1744
63. Stringer JS, Rouse DJ. Rapid testing and zidovudine treatment to pre-
vent vertical transmission of human immunodeficiency virus in unreg-
istered parturients: a cost-effectiveness analysis. Obstet Gynecol. 1999;94:
34–40
71. Maupin R, Jones B, Friloux D. HIV rapid screening in an obstetric
72. Polaneczky M, Cadogan M, McGuinness K, Waterstone M. State-
mandated voluntary newborn human immunodeficiency virus screen-
73. American Academy of Pediatrics, Committee on Pediatric AIDS. Eval-
uation and treatment of the HIV-exposed infant. Pediatrics. 1997;99:
97–111
74. Centers for Disease Control and Prevention. Revised guidelines for
prophylaxis against Pneumocystis carinii pneumonia for children in-
fected with or perinatally exposed to human immunodeficiency virus.
75. Dunn DT, Brandt CD, Krivine A, et al. The sensitivity of HIV-1 DNA
polymerase chain reaction in the neonatal period and the relative con-
tributions of intra-uterine and intra-partum transmission. AIDS. 1995;
9:F7–F11
76. Cunningham CK, Charbonneau TT, Song K, et al. Comparison of hu-
man immunodeficiency virus 1 DNA polymerase chain reaction
and qualitative and quantitative RNA polymerase chain reaction in human
immunodeficiency virus 1-exposed infants. Pediatr Infect Dis J. 1999;18:
30–35
qualitative RNA detection assay to diagnose HIV infection in young
infants. AIDS. 1998;12:1545–1549
78. Mofenson L, Harris R, Stehme ER, et al. Performance characteristics of
HIV-1 culture, DNA PCR or quantitative RNA for early diagnosis of
perinatal HIV-1 infection [abstract 713]. Paper presented at: 7th Confer-
ence on Retroviruses and Opportunistic Infections; January 30-February
2, 2000; San Francisco, CA
79. Centers for Disease Control and Prevention. Guidelines for the use of
antiretroviral agents in pediatric infection. MMWR Morb Mortal Wkly Rep.
hivatis.org
80. McSherry GD, Shapiro DE, Coombs RW. The effects of zidovudine in the
1999;134:717–724
81. The Italian Register for HIV Infection in Children. Rapid disease pro-
gression in HIV-1 perinatally infected children born to mothers receiv-
ing zidovudine monotherapy during pregnancy. AIDS. 1999;13:927–933
82. Olivero OA, Anderson LM, Diwan BA, et al. Transplacental effect of 3-
azido-2,3′-dideoxythymidine (AZT): tumorigenicity in mice and
83. Poitier MC, Patterson TA, Slikker W, Olivero OA. Incorporation of 3-
azido-2,3′-dideoxythymidine (AZT) into fetal DNA and fetal tissue
distribution of drug after infusion of pregnant late-term rhesus ma-
ques with a human-equivalent AZT dose. J Acquir Immune Defic Syndr
84. Olivero OA, Shearer GM, Chougnet CA, et al. Incorporation of zidovu-
dine into leukocyte DNA from HIV-1-positive adults and pregnant
women and cord blood from infants exposed in utero. AIDS. 1999;13:
919–925
Adverse effects of reverse transcriptase inhibitors: mitochondrial tox-
icity as a common pathway. AIDS. 1998;12:1735–1744
86. Hanson IC, Antonelli TA, Sperling RS, et al. Lack of tumors in infants
with perinatal HIV-1 exposure and fetal/neonatal exposure to zidovu-
exposure to zidovudine among uninfected children born to HIV-
infected women. JAMA. 1999;281:151–157
88. Blanche S, Tardieu M, Rustin P, et al. Persistent mitochondrial dysfunc-
tion and perinatal exposure to antiretroviral nucleoside analogues. Lanc.
et. 1999;354:1084–1089
89. Perinatal Safety Review Working Group. Nucleoside exposure in the
offspring of HIV-infected women receiving antiretroviral drugs: ab-
sence of clear evidence for mitochondrial disease and children who died
before 5 years of age in 5 United States cohorts. J Acquir Immune Defic
Syndr Hum Retrovirology. In press
90. Lipshultz SE, Easley KA, Orav EJ, et al. Absence of cardiac toxicity of
events in relation to mitochondrial dysfunction in the prevention of
mother-to-child transmission of HIV: the PETRA study [abstract 250].
Paper presented at: 2nd Conference on Global Strategies for Prevention of
HIV Transmission from Mothers to Infants; September 1–6, 1999;
Montreal, Quebec, Canada
92. Chotpitayasunondh T, Chearskul S, Vanprapa N, et al. Safety of short-
course antenatal zidovudine for children born to HIV-infected women,
Bangkok, Thailand [abstract ThPec 5304]. Paper presented at: XIII In-
ternational AIDS Conference; July 9–14, 2000; Durban, Natal, South
Africa
exposure to zidovudine in Africa [abstract MoPpB 1024]. Paper pre-
presented at: XIII International AIDS Conference; July 9–14, 2000; Durban,
Natal, South Africa
94. Morris AA, Carr A. HIV nucleoside analogues: new adverse effects on
95. Rose D, Oyen J, Goldenberg RL, Vermund SH. Zidovudine for preven-
tion of vertical HIV transmission: a decision analytic approach. J
96. Mofenson LM. Perinatal exposure to zidovudine—benefits and risks.
97. Wiktor SZ, Ekpine E, Karon JM, et al. Short-course oral zidovudine for
prevention of mother-to-child transmission of HIV-1 in Abidjan, Cote
98. Dabis F, Msellati P, Meda N, et al. 6-month efficacy, tolerance, and
acceptability of a short regimen of oral zidovudine to reduce vertical
transmission of HIV in breastfed children in Cote d'Ivoire and Burkina
1999;353:786–792
99. DITRAME ANRS 049 Study Group. 15-month efficacy of maternal oral
zidovudine to decrease vertical transmission of HIV-1 in breastfed
Lynne M. Mofenson and the Committee on Pediatric AIDS
*Pediatrics* 2000;106:e88
DOI: 10.1542/peds.106.6.e88

<table>
<thead>
<tr>
<th>Updated Information &amp; Services</th>
<th>including high resolution figures, can be found at: <a href="http://pediatrics.aappublications.org/content/106/6/e88">http://pediatrics.aappublications.org/content/106/6/e88</a></th>
</tr>
</thead>
<tbody>
<tr>
<td>References</td>
<td>This article cites 79 articles, 8 of which you can access for free at: <a href="http://pediatrics.aappublications.org/content/106/6/e88.full#ref-list-1">http://pediatrics.aappublications.org/content/106/6/e88.full#ref-list-1</a></td>
</tr>
<tr>
<td>Subspecialty Collections</td>
<td>This article, along with others on similar topics, appears in the following collection(s):</td>
</tr>
<tr>
<td></td>
<td><strong>Infectious Disease</strong> <a href="http://classic.pediatrics.aappublications.org/cgi/collection/infectious_diseases_sub">http://classic.pediatrics.aappublications.org/cgi/collection/infectious_diseases_sub</a></td>
</tr>
<tr>
<td></td>
<td><strong>HIV/AIDS</strong> <a href="http://classic.pediatrics.aappublications.org/cgi/collection/hiv:aids_sub">http://classic.pediatrics.aappublications.org/cgi/collection/hiv:aids_sub</a></td>
</tr>
<tr>
<td>Permissions &amp; Licensing</td>
<td>Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: <a href="https://shop.aap.org/licensing-permissions/">https://shop.aap.org/licensing-permissions/</a></td>
</tr>
<tr>
<td>Reprints</td>
<td>Information about ordering reprints can be found online: <a href="http://classic.pediatrics.aappublications.org/content/reprints">http://classic.pediatrics.aappublications.org/content/reprints</a></td>
</tr>
</tbody>
</table>
Lynne M. Mofenson and the Committee on Pediatric AIDS

*Pediatrics* 2000;106;e88
DOI: 10.1542/peds.106.6.e88

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://pediatrics.aappublications.org/content/106/6/e88