Perinatal Human Immunodeficiency Virus Testing

Provisional Committee on Pediatric AIDS

Continuing technologic and medical advances in the detection, treatment, and prevention of pediatric human immunodeficiency virus (HIV) infection require an ongoing assessment and review of recommendations relating to pediatric HIV infection, including issues that involve prenatal and perinatal HIV counseling and testing.

Changes in the epidemiology of HIV infection in women require that prenatal testing recommendations based on risk group and geographic prevalence be reconsidered. The following factors support the importance of the evaluation of HIV infection status in reproductive-age women and newborns: the recent finding that administration of zidovudine to some HIV-infected pregnant women and their newborns significantly reduced perinatal transmission of HIV, the requirement that prophylaxis to prevent Pneumocystis carinii pneumonia be initiated in the first few months of life for maximal efficacy, improvements in diagnostic confirmation of pediatric HIV infection in early infancy, and the recommendation that HIV-infected women should not breast-feed their infants if safe alternatives are available.

CHANGING EPIDEMIOLOGY OF HIV INFECTION IN WOMEN OF CHILDBEARING AGE

The annual proportionate increase in cases of acquired immunodeficiency syndrome (AIDS) in women currently exceeds that observed among men. Although in 1982 only 6% of newly diagnosed AIDS cases involved women, in 1993 12.6% of new cases were diagnosed in women. Currently, more than 80% of women with AIDS are of childbearing age, and the increasing rate of AIDS among adolescents females portends a further increase among women of childbearing age. The increase in the rate of AIDS in women has been reflected by a similar increase in children; more than 95% of AIDS cases in children from birth to 4 years old are caused by perinatal infection.

In addition to the increasing incidence of AIDS in women, cases are no longer confined to urban areas of the United States; currently, more than 25% of women with AIDS are from smaller cities and rural areas of the United States. Furthermore, behavioral risk factors for HIV infection in women are shifting. Since 1992, heterosexual contact has exceeded intravenous drug use as the primary exposure category in women with AIDS. A significant proportion of HIV-infected women are not aware of their own or partner's risk for HIV infection. Evaluation of national data from publicly funded HIV counseling and testing services from 1989 to 1990 indicates that 35% of women found to be HIV-infected do not report risk factors that have been commonly associated with HIV acquisition, such as intravenous drug use or having sex with a partner at known high risk for HIV infection; 44% of black seropositive women did not report these behaviors. Unprotected sexual intercourse may be the only high risk factor for HIV acquisition for these women.

In geographic areas with low HIV seroprevalence among childbearing women, the ethnic distribution of HIV infection in women may differ substantially from that observed in areas of the country with high HIV seroprevalence. A recent report from San Diego County indicated that 34% of mothers with perinatally infected infants were Caucasian. Similar to the data cited above, heterosexual contact was the only risk factor for HIV infection in 43% of mothers.

Because surveillance of AIDS cases detects only infected individuals who have progressed to end-stage disease, use of AIDS case surveillance reports to detect population trends in HIV infection will reflect the scope of the HIV epidemic 7 to 10 years ago. However, anonymous HIV antibody seroprevalence surveys provide estimates of HIV infection trends that are independent of disease stage, and depict more recent patterns of HIV infection in women. Serosurveys indicate that HIV infection, like AIDS, has become widespread among women of childbearing age in nonurban areas of the country.

It is evident that HIV infection in women has spread beyond previously defined risk groups and geographic areas.

USE OF ZIDOVUDINE TO REDUCE PERINATAL HIV TRANSMISSION

The risk of perinatal HIV transmission can be reduced through the administration of zidovudine to HIV-infected pregnant women and their infants. Interim results have recently been reported from a randomized, double-blind, placebo-controlled clinical trial, AIDS Clinical Trial Group (ACTG) Protocol 076, that evaluated the use of zidovudine administered during pregnancy, labor, and to the newborn to reduce perinatal HIV transmission. This trial enrolled HIV-infected pregnant women with early stage HIV disease (CD4 count of 200 cells/mm³ or above at the time of entry into the study, who had...
received no antiretroviral therapy during their current pregnancy and had no clinical indications for antiretroviral therapy. Oral zidovudine was administered beginning between 14 and 34 weeks of gestation and was continued for the remainder of the pregnancy. During labor, a continuous intravenous infusion of zidovudine was administered, followed by the administration of oral zidovudine to the newborn for 6 weeks. Analysis of data available through December 1993 demonstrated a two-thirds reduction in the estimated rates of HIV transmission at 18 months of age, from 25.5% in placebo recipients to 8.3% in those who received zidovudine; the difference between the two groups was highly statistically significant ($P = 0.0006$). No significant short-term side effects were observed from zidovudine use other than mild, reversible anemia in the infants. Although the short-term safety concerns appear minimal for the mother and child, the study has not yet provided information about the long-term risks for mothers and infants (both infected and uninfected) treated with the ACTG 076 zidovudine regimen.

Although the ACTG 076 zidovudine regimen may not yield the same results in HIV-infected women who are severely ill with low CD4 counts, those who have been receiving zidovudine for an extended period before pregnancy, or those who present very late for prenatal care, it is possible that zidovudine may be associated with some reduction in transmission in such situations. A variety of other therapeutic interventions to interrupt perinatal transmission of HIV are currently or soon to be under evaluation. The US Public Health Service recently published recommendations regarding the use of zidovudine to prevent perinatal HIV transmission. These recommendations cover a variety of clinical situations that commonly occur in clinical practice, and highlight the factors to be considered by the woman and her health care provider when making decisions regarding use of zidovudine to prevent perinatal transmission. The health care provider and mother need to discuss the potential benefits, unknown long-term effects, and gaps in knowledge relating to the woman’s specific clinical situation to ensure that the woman can make informed decisions about her treatment.

**DIAGNOSIS AND MANAGEMENT OF PEDIATRIC HIV INFECTION**

Early identification of infected infants is essential for adequate medical management. *Pneumocystis carinii* pneumonia (PCP) is the most frequent opportunistic infection associated with pediatric HIV infection, occurs most commonly between 3 to 6 months of age, is the most common initial disease to occur in infants and children with previously unrecognized HIV infection, and is associated with high mortality. Effective prophylaxis is available to prevent PCP, and in March 1991, the US Public Health Service issued guidelines for PCP prophylaxis in pediatric HIV infection.

Because of the age distribution of infants with PCP, PCP prophylaxis should begin in the first months of life, which requires recognition of the infant's HIV serostatus. PCP, however, continues to be the presenting manifestation of previously unrecognized HIV infection in nearly half of reported PCP cases. In these children, HIV status was unknown until the child developed PCP; this suggests that early identification of patients requiring prophylaxis is incomplete. To adequately prevent the complications of HIV disease, identification of an infected child must be followed by the provision of appropriate medical care. In addition, education of the parents and other guardians regarding the need for close follow-up of these infants and instruction in administration of necessary medications is also crucial for the prevention of PCP and other complications of HIV infection.

Early identification of HIV-infected infants enables appropriate modifications and additions to the routine schedule of pediatric immunizations; early monitoring of nutritional status and implementation of aggressive nutritional supplementation at early stages of growth failure; initiation of antiretroviral therapy; careful monitoring of immunologic and neurologic/psychologic function to evaluate the need for change in antiretroviral therapy and the need for special educational interventions; consideration of other adjunctive therapies, such as intravenous immunoglobulin for the prevention of bacterial infections; screening and treatment for tuberculosis; appropriate management of communicable disease exposures; and the provision of other needed services.

With virologic diagnostic techniques such as HIV culture, polymerase chain reaction, and immune complex-dissociated p24 antigen, diagnosis of HIV infection can be made in almost 50% of infected infants at birth and in more than 95% of infected infants by 1 to 3 months of age. Unfortunately, identification of HIV-infected infants at early stages of disease in the United States appears to be relatively poor; data from a population-based study in Massachusetts indicate that only 35% to 65% of perinatally infected infants have been identified by the health care system by 3 to 4 years of age.

**BENEFITS OF HIV TESTING IN THE PRENATAL AND NEWBORN PERIODS**

There are now clear medical benefits for pregnant women to know their HIV serostatus. In addition to the importance HIV testing has for early diagnosis and treatment of women, the availability of a treatment capable of significantly reducing perinatal transmission of HIV clearly provides an important impetus for all pregnant women to know their HIV serostatus during early pregnancy.

Knowledge of HIV serostatus permits infected mothers to be counseled about the risk of HIV transmission through breast-feeding. Because of the risk of HIV transmission via breast milk, women in the United States who are known to be HIV-infected are advised not to breast-feed, since safe alternatives to breast milk are available.

While evaluation for HIV infection during pregnancy offers potential preventive as well as therapeutic benefits, when maternal serostatus is
unknown, HIV antibody testing of the newborn remains important for therapeutic reasons. Knowledge of neonatal HIV serostatus permits early evaluation of the infant for HIV infection and immunologic monitoring to evaluate the need for initiation of PCP prophylaxis, antiretroviral, and other therapies.

Human immunodeficiency virus infection in women and children is often accompanied by HIV infection in other family members. Family members should be offered the opportunity to undergo evaluation to determine whether they are HIV-infected and provided appropriate medical care and follow-up if found to be infected.

**RISKS OF HIV TESTING IN THE PRENATAL AND NEWBORN PERIODS**

Risks of prenatal/perinatal HIV testing include those inherent to the identification of HIV infection in any individual. Detection of HIV infection may be associated with anxiety and depression. Other risks include potential social stigmatization and discrimination. Also, because illicit intravenous drug use is associated with HIV infection and may be used as a basis to remove an infant from the mother’s care, women who use illicit drugs may fear HIV testing. It is possible if the benefits of HIV testing are not made known to pregnant women, fear of the potential negative consequences may deter some women from seeking prenatal care, particularly if testing is perceived as involuntary. However, in several settings in which HIV counseling and voluntary testing have been routinely offered to all prenatal patients, no measurable decrease in women seeking prenatal care has been observed.

Human immunodeficiency virus seropositivity in a newborn measures maternally derived HIV IgG antibodies that, while not diagnostic of infection in the infant, provide unequivocal evidence of infection in the mother. Human immunodeficiency virus antibody screening of the newborn indirectly evaluates maternal HIV infection status, and therefore has the same intrinsic risks as prenatal HIV testing.

**THE ISSUE OF CONSENT FOR HIV TESTING**

A relationship of respect and trust between women and the health care system is critically important to the identification of women who are HIV-infected and their subsequent care and treatment. Therefore, provision of education concerning the benefits and possible risks of HIV testing is an important part of the process of HIV testing.

Documentation that information about HIV infection has been provided and that consent for testing was obtained has generally been accomplished by individual counseling followed by written or oral consent. Alternative, less resource intensive, acceptable options to individualized counseling include routine provision of education about HIV in written or video form or in group settings.

Some states have legal requirements for counseling followed by written consent for HIV testing. Routinely used methods in medical practice to document consent or refusal for medical procedures other than HIV testing include: 1) individualized counseling followed by a signature that affirms consent to testing; 2) provision of education followed by a signature that either explicitly consents to or explicitly refuses testing; or 3) education followed by a signature only to explicitly refuse the test. Each of these methods is an ethically acceptable way to respect the individual’s decision whether or not to be tested. Each method, however, has different associated dimensions.

Individualized counseling in conjunction with obtaining a signature on an informed consent form requires significant health care resources. Patient education in written form or group settings followed by a signature of consent or refusal may require less intensive resources. In both of these methods of consent, the provider may directly recommend the test. Routine patient education accompanied by a signature only to reject the test (right of refusal) implies that the test is recommended by the health care professional and therefore will be performed unless the patient signs the form, and may also result in the largest number of women being tested. Although some believe that right of refusal consent is inherently coercive, documentation of appropriate patient education and confidentiality reduce the likelihood of such concern.

Because the results of ACTG 076 indicate that zidovudine has the potential to reduce perinatal transmission of HIV, there is now a compelling reason for universal antepartum HIV education and routine testing with consent. Whichever method of obtaining consent is chosen, it is critically important that appropriate education regarding HIV infection is provided to the individual before a decision regarding testing.

Currently, the percentage of pregnant women being evaluated for HIV infection is regrettablly small. Therefore, testing programs for HIV infection should undergo periodic evaluation regarding the proportion of women being tested. Those programs in which a proportionately low number of women consent to receive HIV testing should examine the reasons for poor acceptance. Appropriate program modifications may need to be made to ensure that women understand the benefits of testing and feel comfortable undergoing testing.

Because infant testing provides information important to the well-being of the infant and also information regarding the infection status of the mother, the health care provider is obligated to educate the mother about HIV infection and to obtain consent using one of the methods described above when HIV testing of the infant is contemplated.

The purpose of HIV testing is to engage a woman in continuing care for herself and her baby, not to label a woman as being infected. Compliance with medical care is likely to be greatest when the patient feels she has made an informed judgment regarding HIV testing for herself or her infant. Routine HIV education accompanied by offering HIV testing to all pregnant women appears most likely to achieve this goal. Women need to be given sufficient information in a clear and understandable manner to appreciate the benefits and risks of the proposed HIV test and
the consequences of accepting or rejecting testing for herself and her infant. This process is best performed within the context of a professional relationship between the woman and her health care provider.

CONCLUSION

Human immunodeficiency virus infection continues to spread among women of childbearing age in the United States, and is occurring in rural as well as urban areas. With the increasing heterosexual spread of HIV, previously defined risk behaviors for HIV infection incompletely identify women found to be infected. The predominant risk behavior for HIV infection in many women is unprotected sexual intercourse. Perinatal HIV infection has mirrored the increases in HIV infection in women. With the availability of an intervention to reduce perinatal transmission of HIV, there is clear rationale for universal education and routine HIV testing of all women entering prenatal care. The persisting occurrence of PCP in young infants despite the availability of effective prophylactic regimens indicates that the identification and treatment of HIV infection in infants at an early age remains inadequate. Testing programs for HIV antibody must be confidential, voluntary, and accompanied by cultural and ethnically appropriate information regarding HIV infection. Such programs should be universally available.

RECOMMENDATIONS

1. On the basis of recent advances in therapy to reduce the rate of perinatal HIV transmission and the continued occurrence of life-threatening illness in young infants with unrecognized HIV infection, the AAP recommends documented, routine HIV education, and routine testing with consent, for all pregnant women in the United States. Documented consent for maternal and/or newborn HIV testing may be obtained in a variety of ways, including by right of refusal (documented patient education, with testing to take place unless rejected in writing by the patient). The Academy supports utilization of consent procedures that facilitate rapid incorporation of HIV education and testing into the routine medical care setting.

2. Routine education about HIV infection and testing needs to be a part of a comprehensive program of health care for women, particularly for women of child-bearing age.

3. All testing programs for the detection of HIV infection should periodically evaluate the proportion of women who refuse HIV testing following HIV education. Those programs in which a proportionately low number of women receive HIV testing should examine the reasons for poor acceptance, with appropriate program modifications made as needed.

4. For women who are seen by a health care professional for the first time in labor and who have either not received prenatal care or have previously tested negative, but have not been tested for HIV infection during the current pregnancy, education about HIV infection and maternal HIV testing are recommended during the perinatal period.

5. For newborns whose mother’s HIV serostatus was not determined during the recent pregnancy or the postpartum period, the infant’s health care provider should educate the mother concerning the potential benefits of HIV testing for her infant and the possible risks and benefits to herself of knowing the child’s serostatus and recommend HIV testing for the newborn.

6. In the absence of parental availability for consent to test the newborn for HIV antibody, procedures need to be established to facilitate the rapid evaluation and testing of the infant.

7. The health care provider for the infant needs to be informed of maternal HIV serostatus so that appropriate care and testing of the infant can be accomplished. Similarly, if the infant is found to be seropositive when maternal serostatus is unknown, the health care provider for the child should ensure that information about the serostatus and its significance be provided to the mother and, with her consent, to her health care provider. The mother should receive appropriate referral to adult HIV-related services.

8. Comprehensive, HIV-related medical services should be accessible to all infected mothers, their infants, and other family members.


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