Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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HIV Testing in Pregnancy

HIV infection should be identified prior to pregnancy (see Preconception Counseling and Care for Women of Childbearing Age Living with HIV) or as early in pregnancy as possible. This provides the best opportunity to improve maternal health and pregnancy outcomes, to prevent infant acquisition of HIV, and to identify HIV infection and start therapy as soon as possible in infants who acquire HIV. Universal voluntary HIV testing is recommended as the standard of care for all pregnant women in the United States by the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV and the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission (the Panels), the Centers for Disease Control and Prevention (CDC), the American Academy of Pediatrics, the American College of Obstetricians and Gynecologists, and the U.S. Preventive Services Task Force.1-5 All HIV testing should be performed in a manner that is consistent with state and local laws. The CDC recommends the “opt-out” approach, which involves notifying pregnant women that HIV testing will be performed as part of routine health care. 

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care unless they choose not to be tested for HIV. The “opt-out” approach during pregnancy is allowed in some jurisdictions. The “opt-in” approach involves obtaining specific consent before testing, and this approach has been associated with lower testing rates. The mandatory newborn HIV testing approach, adopted by several states, involves testing newborns for perinatal HIV exposure with or without maternal consent if the mother has declined prenatal or intrapartum testing.

Partners of pregnant women should also be encouraged to undergo HIV testing when their status is unknown, consistent with the 2006 CDC recommendations for HIV testing of all individuals in the United States. Testing will facilitate linkage to care if a partner is found to have HIV infection. Because women are more susceptible to HIV acquisition during pregnancy and the postpartum period, clinicians can also initiate a discussion about preventative interventions, including pre-exposure prophylaxis, if the pregnant woman is uninfected. In addition, clinicians should assess the risk of acute HIV infection, particularly in late in pregnancy, because a pregnant woman may receive a negative result by expedited or rapid HIV testing when she is in the window period. However, during this period she would be viremic with high risk of perinatal transmission to her newborn. See Acute HIV Infection for more information.

Providers should be aware that gaps in maternal HIV testing do occur and can contribute to missed opportunities for preventing perinatal HIV transmission. As discussed in the following sections, maternal HIV testing should be performed as early as possible during pregnancy, with repeat HIV testing in the third trimester for women who are at increased risk of acquiring HIV or who are living in areas of high HIV incidence. Women with unknown or undocumented HIV status should be tested during labor or after delivery. Determining antenatal maternal HIV status enables:

- Women living with HIV to receive appropriate antiretroviral therapy (ART) and prophylaxis against opportunistic infections;
- Initiation of treatment in the identified women, which may also decrease the risk of transmission to their partners;
- Referral of partners without HIV for preventative interventions;
- Provision of ART to the mother during pregnancy and labor, and provision of antiretroviral (ARV) drug prophylaxis to the newborn to reduce the risk of perinatal transmission;
- Counseling of women living with HIV about the indications for (and potential benefits of) scheduled elective cesarean delivery to reduce the risk of perinatal transmission of HIV;
- Counseling of women living with HIV about the risks of HIV transmission through breast milk (breastfeeding is not recommended for women with HIV living in the United States);
- Early diagnostic evaluation of infants exposed to HIV (see Diagnosis of HIV Infection in Infants and Children), as well as testing of partners and other children, to permit prompt initiation of ART and any indicated prophylaxis.

Technological improvements have resulted in an increased ability to detect early HIV infection and reduced performance time for laboratory-based assays; assays can now be completed in <1 hour. Accordingly, the Panels now incorporate CDC’s 2014 Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations. The guidelines recommend that clinicians initiate HIV testing with an immunoassay that is capable of detecting HIV-1 antibodies, HIV-2 antibodies, and HIV-1 p24 antigen (referred to as an antigen/antibody combination immunoassay). Individuals with a reactive antigen/antibody combination immunoassay should be tested further with an HIV-1/HIV-2 antibody differentiation assay (referred to as supplemental testing). Individuals with a reactive antigen/antibody combination immunoassay and a nonreactive differentiation test should be tested with a Food and Drug Administration-approved HIV nucleic acid test (NAT) to establish diagnosis of acute HIV infection (see the CDC’s Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens).
The antigen/antibody combination immunoassay is the test of choice and can be done quickly (referred to as an expedited test), but it requires trained laboratory staff and therefore may not be available in some hospitals 24 hours a day. When this test is unavailable, then initial testing should be performed by the most sensitive expedited or rapid test available. Every delivery unit needs to have access to an HIV test that can be done rapidly (i.e., in <1 hour) 24 hours a day. If the test result is positive, the test to confirm HIV infection should be done as soon as possible (as with all initial assays with positive results). Older antibody tests have lower sensitivity in the context of recent acquisition of HIV than antigen/antibody combination immunoassays. Therefore, testing that follows the 2014 CDC algorithm should be considered if HIV risk cannot be ruled out. Results of maternal HIV testing should be documented in the newborn’s medical record and communicated to the newborn’s primary care provider.

**Repeat HIV Testing in the Third Trimester**

Repeat HIV testing during the third trimester, before 36 weeks’ gestation, is recommended (see Acute HIV Infection)\(^24\) for pregnant women with negative results on their initial HIV antibody tests who:\(^5\)

- Are known to be at high risk of acquiring HIV (e.g., those who are injection drug users or partners of injection drug users, those who exchange sex for money or drugs, those who are sex partners of individuals with HIV, those who have had a new sex partner or more than one sex partner during the current pregnancy, or those who have been diagnosed with a new sexually transmitted disease during pregnancy. Additionally, an analysis of 2013 National HIV Behavioral Surveillance data found that the prevalence of risk-related sexual behaviors was higher in recently incarcerated women than in those who were never incarcerated)\(^25\) or
- Are receiving health care in facilities in which prenatal screening identifies one or more pregnant women with HIV per 1,000 women screened, or who reside in a jurisdiction that has a high incidence of HIV or AIDS in women between the ages of 15 and 45 years (a list of jurisdictions where such screening is recommended is found in the 2006 CDC recommendations; a more up-to-date list is forthcoming), or who reside in states that require third-trimester testing;
- Have signs or symptoms of acute HIV (e.g., fever, lymphadenopathy, skin rash, myalgia, headaches, oral ulcers, leukopenia, thrombocytopenia, elevated transaminase levels).\(^2,26-28\)

Women who decline testing earlier in pregnancy should be offered testing again during the third trimester. In these cases, an antigen/antibody combination immunoassay should be used, as these tests have a higher sensitivity in the setting of acute HIV infection than older antibody tests.\(^2,29\) When acute HIV infection is suspected during pregnancy, during the intrapartum period, or while breastfeeding, a plasma HIV RNA test result should be performed in conjunction with an antigen/antibody combination immunoassay (see Acute and Recent [Early] HIV Infection in the Adult and Adolescent Antiretroviral Guidelines).

Providers should be proactive in assessing a woman’s HIV acquisition risk and implementing third-trimester HIV retesting in areas where it is not routine, when indicated. A recent study in Baltimore found that only 28% of women were retested for HIV despite the high incidence of HIV in Maryland and a high frequency of clinical risk factors.\(^13,30\) A study of data from 2007 to 2014 on Florida children with perinatal HIV exposure found that perinatal HIV transmission was associated with poor or late prenatal care, diagnosis of maternal HIV during labor and delivery or after birth, and, in some, acute maternal infection (as indicated by negative results for initial tests). In addition, the study noted that third-trimester HIV tests were not performed in a portion of the patients.\(^30\)

**HIV Testing During Labor in Women with Unknown HIV Status**

Women in labor whose HIV status is undocumented should undergo HIV testing in order to identify HIV infection in the mothers and HIV exposure in their infants. HIV testing during labor has been found to be feasible, accurate, timely, and useful both in ensuring prompt initiation of intrapartum maternal ARV
prophylaxis (see Intrapartum Antiretroviral Therapy/Prophylaxis) and in developing an appropriate ARV regimen for infants who are at high risk of perinatal transmission (see Table 11).1,3,20,27,31,32

Policies and procedures must be in place to ensure that staff are prepared to provide patient education and expedited HIV testing, that appropriate ARV drugs are available whenever needed, and that follow-up procedures are in place for women who receive an HIV diagnosis and their infants.

If the antigen/antibody combination immunoassay is not available, initial testing should be performed by the most sensitive expedited test available.

A positive expedited HIV test result must be followed by a supplemental test.23 Immediate initiation of maternal intravenous intrapartum zidovudine is recommended to prevent perinatal transmission of HIV pending the supplemental result after an initial positive expedited HIV test result (see Intrapartum Antiretroviral Therapy/Prophylaxis).1-4,20,27 Pending results of supplemental maternal testing, infants should receive an ARV regimen that is appropriate for infants who are at higher risk of perinatal HIV transmission as soon as possible. (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV). No further testing is required for specimens that are nonreactive (negative) on the initial immunoassay, unless acute HIV infection is suspected.23

**HIV Testing During the Postpartum Period**

Women who have not been tested for HIV before or during labor should be offered expedited testing during the immediate postpartum period. When mothers are unavailable for testing, their newborns should undergo expedited HIV testing, using the antigen/antibody combination immunoassay.1,20,27 Maternal testing should be done using the antigen/antibody combination immunoassay to screen for established and acute HIV; results should be obtained in <1 hour. If acute HIV infection is a possibility, then a plasma HIV NAT test should be sent as well. Expedited HIV assays should be used to identify infants who have been exposed to HIV, because postnatal ARV drugs need to be initiated as soon as possible—ideally ≤6 hours after birth—to be effective in preventing perinatal transmission. When an initial HIV test is positive in mother or infant, it is strongly recommended that clinicians initiate an ARV regimen that is appropriate for infants who are at higher risk of perinatal HIV transmission and counsel the mother against breastfeeding. Both actions can be taken before the results of supplemental maternal HIV tests have confirmed the presence of HIV (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV). Breast milk can be expressed while supplemental HIV diagnostic testing is being completed, but it should not be given to the infant until testing confirms that the mother is HIV negative. If supplemental test results are negative and acute HIV is excluded, infant ARV drugs can be discontinued. In the absence of ongoing maternal HIV exposure, breastfeeding can be initiated.

**Infant HIV Testing when Maternal HIV Test Results are Unavailable**

When maternal HIV test results are unavailable (e.g., for infants and children who are in foster care) or their accuracy cannot be evaluated (e.g., for infants and children who were adopted from countries where results are not reported in English), HIV testing is indicated to identify HIV in those infants or children.1 Mechanisms should be developed to facilitate prompt HIV screening for infants who have been abandoned and are in the custody of the state. The choice of test will vary based on the age of the child (see Diagnosis of HIV Infection in Infants and Children).

**Acute Maternal HIV Infection During Pregnancy or Breastfeeding**

Women are more susceptible to HIV infection during pregnancy and the early postpartum period.9 Risk of HIV exposure should be assessed in all women who are considering becoming pregnant, as well as in all pregnant women who previously tested HIV negative. Women with risk factors for HIV acquisition should receive prevention counseling and appropriate interventions, including pre-exposure prophylaxis if indicated (see Preconception Counseling and Care for Women of Childbearing Age Living with HIV). The risk of
perinatal transmission of HIV is increased in infants born to women who have acute HIV during pregnancy or lactation.24,33-36 The antigen/antibody combination immunoassay will detect acute infection more quickly than other immunoassays, within approximately 10 days. When acute HIV infection is suspected, a plasma HIV RNA test should be sent as well, because virologic tests can detect the presence of HIV earlier than the antigen/antibody combination immunoassay. Women with possible acute HIV infection who are breastfeeding should cease breastfeeding immediately until HIV infection is confirmed or excluded.19

Expressing breast milk can be recommended while HIV diagnostic testing is completed. Breastfeeding can resume if HIV infection is excluded and there is no ongoing maternal exposure to HIV. Care of pregnant or breastfeeding women with acute or early HIV and their infants should follow the recommendations in the Perinatal Guidelines (see Acute HIV Infection and Guidance for Counseling and Managing Women Living with HIV in the United States Who Desire to Breastfeed).

Other Issues

Clinicians should be aware of public health surveillance systems and regulations that may exist in their jurisdictions for reporting infants who have been exposed to HIV; this is in addition to mandatory reporting of persons with HIV, including infants. Reporting infants who have been exposed to HIV allows the appropriate public health functions to be accomplished.

References


27. American College of Obstetrics: Gynecology Committee on Obstetric Practice. ACOG committee opinion no.


