Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States

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Maternal HIV Testing and Identification of Perinatal HIV Exposure
(Last updated December 7, 2018; last reviewed December 7, 2018)

Panel’s Recommendations

- HIV testing is recommended as standard of care for all sexually active women and should be a routine component of preconception care (AII).
- All pregnant women should be tested as early as possible during each pregnancy (see Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations and Recommended Laboratory HIV Testing Algorithm) (AII).
- Partners of pregnant women should be encouraged to undergo HIV testing when their status is unknown (AIII).
- Repeat HIV testing in the third trimester is recommended for pregnant women with negative initial HIV antibody tests who are at increased risk of acquiring HIV, including those who are receiving care in facilities that have an HIV incidence of ≥1 case per 1,000 pregnant women per year, those who are incarcerated, those who reside in jurisdictions with elevated HIV incidence, or those who reside in states that require third-trimester testing (see Prenatal and Perinatal Human Immunodeficiency Virus Testing and Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings) (AII).
- Expedited HIV testing at the time of labor or delivery should be performed for any woman with undocumented HIV status; testing should be available 24 hours a day, and results should be available within 1 hour (AII). If results are positive, intrapartum antiretroviral (ARV) prophylaxis should be initiated immediately (AII) and infants should receive an ARV regimen that is appropriate for infants at higher risk of perinatal HIV transmission as soon as possible, pending results of supplemental HIV testing (AII). See Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV for guidance.
- Women who have not been tested for HIV before or during labor should undergo expedited HIV antibody testing during the immediate postpartum period (or their newborns should undergo expedited HIV antibody testing) (AII). If the results for the mother or infant are positive, an appropriate infant ARV drug regimen should be initiated immediately, and the mother should not breastfeed unless supplemental HIV testing is negative (AII). Infants with initial positive HIV viral tests (RNA, DNA) should have their ARV regimen modified, if necessary, to a three-drug combination of ARV drugs at treatment dosages (antiretroviral therapy) (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV) (AII).
- Results of maternal HIV testing should be documented in the newborn’s medical record and communicated to the newborn’s primary care provider (AIII).
- HIV testing to determine HIV status is recommended for infants and children in foster care and adoptees for whom maternal HIV status is unknown (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials in children† with clinical outcomes and/or validated endpoints; † = One or more randomized trials in adults with clinical outcomes and/or validated laboratory endpoints with accompanying data in children† from one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; II = One or more well-designed, nonrandomized trials or observational cohort studies in children† with long-term outcomes; II* = One or more well-designed, nonrandomized trials or observational studies in adults with long-term clinical outcomes with accompanying data in children† from one or more similar nonrandomized trials or cohort studies with clinical outcome data; III = Expert opinion

† Studies that include children or children and adolescents, but not studies limited to post-pubertal adolescents

HIV Testing in Pregnancy

HIV infection should be identified prior to pregnancy (see Preconception Counseling and Care) 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 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 (the Panel), 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 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 care unless they choose not to be tested for HIV. The “opt-out” approach during pregnancy is allowed in...
every jurisdiction. The “opt-in” approach involves obtaining specific consent before testing, and it has been associated with lower testing rates.\textsuperscript{6,7} 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. This will facilitate linkage to care if they are found to have HIV infection and will prompt special attention to preventive interventions if the pregnant woman does not have HIV, given the possible increased risk of HIV acquisition during pregnancy and the postpartum period.\textsuperscript{8} The mandatory newborn HIV testing approach, adopted by several states, involves testing newborns for perinatal HIV exposure with or without maternal consent, when prenatal or intrapartum maternal testing is not performed.

Providers should be aware that gaps in maternal HIV testing do occur and can contribute to missed opportunities for preventing perinatal HIV transmission.\textsuperscript{9-12} 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 at increased risk of acquiring HIV. Women with unknown or undocumented HIV status should be tested during labor or after delivery.\textsuperscript{8,12} Determining antenatal maternal HIV status enables:

- Women living with HIV to receive appropriate antiretroviral therapy (ART) and prophylaxis against opportunistic infections for their own health;
- Initiation of treatment in the identified women, which may also decrease the risk of transmission to their partners;\textsuperscript{2,13,14}
- 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 perinatal transmission of HIV;\textsuperscript{15-17}
- 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);\textsuperscript{18} and
- 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 in individuals with HIV.\textsuperscript{1,19-21}

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 Panel now incorporates CDC’s 2014 Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations.\textsuperscript{22} The guidelines recommend that HIV testing begin with an immunoassay 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 assay 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 (see the CDC’s Recommended Laboratory HIV Testing Algorithm).

The antigen/antibody combination immunoassay is the test of choice and can be done quickly (referred to as expedited), 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, testing for confirmation of HIV should be done as soon as possible (as with all initial positive assays). 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*) for pregnant women with initial negative HIV antibody tests who:  

- 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 >1 sex partner during the current pregnancy, or those who have been diagnosed with a new sexually transmitted disease during pregnancy); or

- Are receiving health care in facilities in which prenatal screening identifies ≥1 pregnant woman with HIV per 1,000 women screened, or are incarcerated, or reside in a jurisdiction that has a high incidence of HIV or AIDS in women between ages 15 and 45 (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 reside in states that require third-trimester testing; or

- Have signs or symptoms of acute HIV (e.g., fever, lymphadenopathy, skin rash, myalgia, headaches, oral ulcers, leukopenia, thrombocytopenia, or transaminase elevation).

Women who decline testing earlier in pregnancy should be offered testing again during the third trimester, using an antigen/antibody combination immunoassay, as these tests have a higher sensitivity in the setting of acute HIV-1 than older antibody tests. When acute HIV is suspected during pregnancy, during the intrapartum period, or while breastfeeding, a plasma HIV RNA test should be obtained 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. A study of data from 2007 to 2014 on Florida children with perinatal HIV exposure found that the risk of perinatal HIV transmission was increased with late diagnosis of maternal HIV during labor and delivery (relative risk [RR] 5.66; 95% CI, 2.31–13.91) or after birth (RR 26.50; 95% CI, 15.44–45.49) when compared with maternal HIV diagnosis before or during pregnancy. The authors concluded that late diagnosis appeared to be primarily the result of acute HIV infection during pregnancy and inadequate prenatal care.

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

HIV testing is recommended to screen women in labor whose HIV status is undocumented and to identify 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 ARV prophylaxis (see *Intrapartum Antiretroviral Therapy/Prophylaxis*) and an appropriate ARV regimen for infants at high risk of perinatal transmission (see Table A-8).

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. Immediate initiation of ARV drug prophylaxis (including intravenous intrapartum zidovudine) to prevent perinatal transmission of HIV is recommended pending the supplemental result after an initial positive expedited HIV test (see Intrapartum Antiretroviral Therapy/Prophylaxis). No further testing is required for specimens that are nonreactive (negative) on the initial immunoassay, unless acute HIV infection is suspected.

**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 combination antigen/antibody immunoassay. Maternal testing should be done using the combination antigen/antibody immunoassay to screen for established and acute HIV-1; results should be obtained in <1 hour. If acute HIV-1 is a possibility, then a plasma HIV NAT test should be sent as well. Use of expedited HIV assays for prompt identification of infants exposed to HIV is essential because postnatal ARV drugs should be initiated as soon as possible—ideally ≤6 hours after birth—to be effective for the prevention of perinatal transmission. When an initial HIV test is positive in mother or infant, initiating an ARV regimen that is appropriate for infants who are at higher risk of perinatal HIV transmission and counseling against breastfeeding are strongly recommended, pending the results of supplemental maternal HIV tests to confirm and/or differentiate between HIV-1 and HIV-2 (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 tests 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 adopted from a country where results are not reported in English), HIV testing is indicated to identify HIV in those infants or children. 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**

There may be an increased susceptibility to acquiring HIV during pregnancy and the early postpartum period. 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). The risk of perinatal transmission of HIV is increased in infants born to women who have acute HIV during pregnancy or lactation. The antigen/antibody combination immunoassay will detect acute infection more readily than other immunoassays, within approximately 10 days. When acute HIV is suspected, a plasma HIV RNA test should be sent as well; this will be positive a few days before the antigen/antibody combination immunoassay. Women with possible acute HIV who are breastfeeding should cease breastfeeding immediately until HIV is confirmed or excluded. 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.
Other Issues

Clinicians should be aware of public health surveillance systems and regulations that may exist in their jurisdictions for reporting infants 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 for appropriate public health functions to be accomplished.

References


