



## **Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection**

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## Identification of Perinatal HIV Exposure (Last updated March 1, 2016; last reviewed March 1, 2016)

### Panel's Recommendations

- HIV testing early in pregnancy is recommended as standard of care for all pregnant women in the United States (**AII**).
- Repeat HIV testing in the third trimester, before 36 weeks' gestation, should be considered for all HIV-seronegative pregnant women and is recommended for pregnant women who are at high risk of HIV infection (**AIII**).
- 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 available within 1 hour**. If results are positive, intrapartum and infant postnatal antiretroviral (ARV) drug prophylaxis should be initiated immediately, pending results of supplemental HIV testing (**AII**).
- 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. If results in mother or infant are positive, infant ARV drug prophylaxis should be initiated immediately, and the mothers should not breastfeed unless supplemental HIV testing is negative (**AII**). In infants with initial positive HIV viral tests (RNA, DNA), prophylaxis should be stopped and antiretroviral therapy initiated.
- **When acute HIV infection is suspected during pregnancy, in the intrapartum period, or while breastfeeding, initial testing should be performed with an antigen/antibody combination immunoassay; if the initial testing was performed with an HIV antibody test or supplemental testing is negative, an additional virologic test (RNA, DNA) may be necessary to diagnose HIV infection (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**).
- Infant HIV antibody testing to determine HIV exposure should be considered for infants in foster care and adoptees for whom maternal HIV infection status is unknown (**AIII**).

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

**Rating of Evidence:** I = One or more randomized trials in children<sup>†</sup> with clinical outcomes and/or validated endpoints; I\* = One or more randomized trials in adults with clinical outcomes and/or validated laboratory endpoints with accompanying data in children<sup>†</sup> 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<sup>†</sup> 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<sup>†</sup> from one or more similar nonrandomized trials or cohort studies with clinical outcome data; III = Expert opinion

<sup>†</sup> Studies that include children or children/adolescents, but not studies limited to post-pubertal adolescents

### HIV Testing in Pregnancy

HIV infection should be identified prior to pregnancy or as early in pregnancy as possible. This provides the best opportunity to prevent infant HIV infection and to identify and start therapy as soon as possible in infants who become infected. 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 HIV-Infected Children (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.<sup>1-6</sup> All HIV testing should be performed in a manner consistent with state and local laws (<http://nccc.ucsf.edu/clinical-resources/hiv-aids-resources/state-hiv-testing-laws/>). 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 has been associated with lower testing rates.<sup>7,8</sup> The mandatory newborn HIV testing approach, adopted by several states, involves testing of newborns for perinatal HIV exposure with or without maternal consent, if prenatal or intrapartum maternal testing is not performed.

Knowledge of antenatal maternal HIV infection enables:

- HIV-infected women to receive appropriate antiretroviral therapy (ART) and prophylaxis against opportunistic infections for their own health, which may also decrease risk of transmission to their partners.<sup>2,9,10</sup>

- Provision of ART to the mother during pregnancy and labor, and antiretroviral (ARV) drug prophylaxis to the newborn to reduce the risk of perinatal transmission of HIV;<sup>4</sup>
- Counseling of HIV-infected women about the indications for (and potential benefits of) scheduled elective cesarean delivery to reduce perinatal transmission of HIV;<sup>4,11-13</sup>
- Counseling of HIV-infected women about the risks of HIV transmission through breast milk (breastfeeding is not recommended for HIV-infected women living in the United States and other countries where safe alternatives to breast milk are available);<sup>14</sup>
- Initiation of prophylaxis against *Pneumocystis jirovecii* pneumonia beginning at age 4 to 6 weeks in all HIV-infected infants and in those HIV-exposed infants whose HIV infection status remains indeterminate;<sup>15</sup> and
- Early diagnostic evaluation of HIV-exposed infants, as well as testing of partners and other children, to permit prompt initiation of ART in infected individuals.<sup>1,16,17</sup>

Technological improvements have resulted in increased sensitivity for early infection and reduced performance time for laboratory-based assays, allowing completion in less than 1 hour. Accordingly, the Panel now incorporates CDC's 2014 HIV Laboratory Testing Recommendations.<sup>18</sup> The guidelines recommend that HIV testing begin with a fourth-generation immunoassay capable of detecting HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen (called an antigen/antibody combination assay). Individuals with a reactive antigen/antibody combination assay should be tested further with an HIV-1/HIV-2 antibody differentiation assay (supplemental testing). Individuals with a reactive antigen/antibody combination assay and a nonreactive differentiation test should be tested with a Food and Drug Administration-approved HIV nucleic acid test to establish diagnosis of acute HIV infection (<http://www.cdc.gov/hiv/pdf/hivtestingalgorithmrecommendation-final.pdf#page=11>).

The fourth-generation immunoassay testing for both antigen and antibody is the test of choice and can be done quickly (referred to as expedited), but requires trained laboratory staff and therefore may not be available in some hospitals 24 hours a day. If 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 (<1 hour) 24 hours a day. If positive, testing for confirmation of infection should be done as soon as possible (as with all initial positive assays). Because older tests have lower sensitivity in the context of recent infection, testing following the 2014 CDC algorithm should be considered as soon as feasible 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 should be considered for all HIV-seronegative pregnant women. A second HIV test during the third trimester, before 36 weeks' gestation, is recommended<sup>4,19</sup> for women who:

- Are receiving health care in a jurisdiction that has a high incidence of HIV or AIDS in women between ages 15 and 45, or who are receiving health care in facilities in which prenatal screening identifies at least 1 HIV-infected pregnant woman per 1,000 women screened (a list of areas where such screening is recommended is found in the 2006 CDC recommendations; a more up-to-date list is forthcoming);
- Are known to be at high risk of acquiring HIV (e.g., those who are injection drug users or partners of injection drug users, exchange sex for money or drugs, are sex partners of HIV-infected individuals, have had a new or more than one sex partner during the current pregnancy, or have been diagnosed with a new sexually transmitted disease during pregnancy); or
- Have signs or symptoms of acute HIV infection.<sup>2,3,20,21</sup>

Women who decline testing earlier in pregnancy should be offered testing again during the third trimester, using a fourth-generation antigen/antibody combination immunoassay, as these tests have a higher sensitivity in the setting of acute infection, compared to older antibody tests.<sup>18,22</sup> When acute retroviral syndrome is a

possibility, a plasma RNA test should be used in conjunction with the fourth-generation test to diagnose acute HIV infection.

## 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 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 and neonatal ARV prophylaxis and in reducing perinatal transmission of HIV.<sup>1-3,5,16</sup>

Every hospital offering intrapartum care and every delivery unit must have access to an HIV test that can be performed rapidly (that is, in an expedited fashion with results available within 1 hour) and is available 24 hours a day. 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 found to be HIV-infected and their infants.

The test of choice is the fourth-generation antigen/antibody combination immunoassay. Because it can be done quickly it is sometimes referred to as “expedited,” but it requires trained lab staff and may not yet be available in hospitals 24 hours a day. If the fourth-generation antigen/antibody combination immunoassay is not available, initial testing should be performed by the most sensitive expedited or rapid test available.

A positive expedited HIV test result must be followed by a supplemental test.<sup>18</sup> However, immediate initiation of ARV drug prophylaxis for prevention of perinatal transmission of HIV is recommended pending the supplemental result after an initial positive expedited HIV test.<sup>1-6,16</sup> No further testing is required for specimens that are nonreactive (negative) on the initial immunoassay.<sup>18</sup>

## HIV Testing During the Postnatal Period

Women who have not been tested for HIV before or during labor should be offered expedited testing during the immediate postpartum period or their newborns should undergo expedited HIV testing with maternal consent (unless state law allows testing without consent).<sup>1,3,4,16</sup> Testing should be done using the fourth-generation antigen/antibody combination immunoassay to screen for established infection and for acute HIV-1 infection; results should be obtained in less than 1 hour. If acute HIV-1 infection is a possibility, then a plasma HIV RNA test should be sent as well. Use of expedited HIV assays for prompt identification of HIV-exposed infants is essential because neonatal ARV prophylaxis should be initiated as soon as possible after birth—ideally no more than 6 to 12 hours after birth—to be effective for the prevention of perinatal transmission. When an initial HIV test is positive in mother or infant, initiation of infant ARV drug prophylaxis and counseling against initiation of breastfeeding is strongly recommended pending results of supplemental HIV tests to confirm and/or differentiate between HIV-1 and HIV-2 infection.<sup>4</sup> If supplemental tests are negative and acute HIV infection is excluded, infant ARV drug prophylaxis can be discontinued. In the absence of ongoing maternal HIV exposure, breastfeeding can be initiated. Mechanisms should be developed to facilitate HIV screening for infants who have been abandoned and are in the custody of the state.

### *Infant HIV Testing when Maternal HIV Test Results Are Unavailable*

When maternal HIV test results are unavailable (e.g., for infants who are in foster care) or their accuracy cannot be evaluated (e.g., for infants adopted from a country where results are not reported in English), HIV antibody testing is indicated to identify HIV exposure in those infants.<sup>1</sup> If antibody testing is positive, further testing is needed to diagnose HIV infection, or in the case of infants older than 18 months, to confirm HIV infection (see [Diagnosis of HIV Infection in Infants](#)).

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

The risk of perinatal transmission of HIV is increased in infants born to women who have acute HIV infection during pregnancy or lactation.<sup>19,23-26</sup> The fourth-generation antigen/antibody combination

immunoassay will detect acute infection more readily than other immunoassays. If acute HIV infection is suspected, and the supplemental test is negative, a plasma HIV RNA test should be sent as well. Women with possible acute HIV infection who are breastfeeding should cease breastfeeding immediately until HIV infection is confirmed or excluded.<sup>14</sup> Pumping and temporarily discarding breast milk can be recommended and (if HIV infection is excluded), in the absence of ongoing maternal exposure to HIV, breastfeeding can resume. Care of pregnant or breastfeeding women identified with acute or early HIV infection, and their infants, should follow the recommendations in the [Perinatal Guidelines](#).<sup>4</sup>

## Other Issues

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

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