Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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Acute HIV Infection (Last updated October 26, 2016; last reviewed October 26, 2016)

Panel's Recommendations
• When acute retroviral syndrome is suspected in pregnancy or during breastfeeding, a plasma HIV RNA test should be obtained in conjunction with a routine HIV antibody screening test or an antigen/antibody immunoassay test (see Acute and Recent (Early) HIV Infection in the Adult and Adolescent Antiretroviral Guidelines and http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf) **(AII)**.
• Repeat HIV testing in the third trimester is recommended for pregnant women with initial negative HIV antibody tests who are known to be at risk of acquiring HIV, who are receiving care in facilities that have an HIV incidence in pregnant women of at least 1 per 1,000 per year, who are incarcerated, or who reside in jurisdictions with elevated HIV incidence (see Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings and http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf) **(AII)**.
• All pregnant women with acute or recent HIV infection should start an antiretroviral therapy as soon as possible to prevent perinatal transmission, with the goal of suppressing plasma HIV RNA to below detectable levels **(AI)**.
• In women with acute HIV infection, baseline genotypic resistance testing should be performed simultaneously with initiation of antiretroviral therapy, and the regimen should be adjusted, if necessary, to optimize virologic response **(AIII)**. A ritonavir-boosted-protease-inhibitor-based regimen with tenofovir disoproxil fumarate/emtricitabine should be initiated **(AIII)**.
Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*
Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Primary or acute HIV infection in pregnancy or during breastfeeding is associated with an increased risk of perinatal transmission of HIV and may represent a significant proportion of residual perinatal transmission in the United States.[1]

In North Carolina, from 2002 to 2005, of 15 women found to have acute HIV infection on nucleic acid amplification testing of pooled HIV antibody-negative specimens, 5 were pregnant at the time of testing.[2] All five women received antiretroviral (ARV) drugs and delivered HIV-uninfected infants. From 2002 to 2006, of 3,396 HIV-exposed neonates born in New York State, 22% (9 of 41) of infants born to mothers who acquired HIV during pregnancy became infected with HIV, compared with 1.8% of those born to mothers who did not acquire HIV during pregnancy (OR 15.19; 95% CI, 3.98–56.30).[3] In the United States, of 10,308 HIV-infected pregnant women who delivered live infants from 2005 to 2010 in 15 areas conducting Enhanced Perinatal Surveillance, 124 (1.2%) were identified as seroconverting during pregnancy. The rate of perinatal transmission was 8 times higher among women who seroconverted during pregnancy (12.9%) than in those who became infected prior to pregnancy (1.6%) ($P < 0.0001$).[4] The high rate of transmission associated with acute infection likely is related to the combination of the high viral load in plasma, breast milk, and the genital tract associated with acute infection[5] and the fact that the diagnosis is easy to miss, which results in lost opportunities for implementation of prevention interventions.

Health care providers should maintain a high level of suspicion of acute HIV infection in women who are pregnant or breastfeeding and have a compatible clinical syndrome, even when they do not report high-risk behaviors, because it is possible that their sexual partners are practicing high-risk behaviors of which the women are unaware. An estimated 40% to 90% of patients with acute HIV infection will experience symptoms of acute retroviral syndrome, characterized by fever, lymphadenopathy, pharyngitis, skin rash, myalgias/arthralgias, and other symptoms.[6,7] Providers often do not recognize acute HIV infection, however, because the symptoms are similar to those of other common illnesses and individuals with the condition also can be asymptomatic. Antiretroviral therapy (ART) is currently recommended for all adults and adolescents with HIV infection, including those with acute or recent infection.[8] Whether treatment of acute or recent HIV infection results in long-term virologic, immunologic, or clinical benefit is unknown.

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When acute retroviral syndrome is suspected in pregnancy or during breastfeeding, a plasma HIV RNA test should be obtained in conjunction with a routine HIV antibody screening test or an antigen/antibody immunoassay test. Updated guidance for HIV testing recommends initial testing for HIV with a Food and Drug Administration-approved antigen/antibody combination (fourth generation) immunoassay that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen. These tests are used to screen for established infection with HIV-1 or HIV-2 and for acute HIV-1 infection. These fourth-generation tests have the advantage of a shorter window to detect infection (2 weeks compared with 4 weeks by Western Blot testing).[9] The fourth-generation tests are becoming increasingly available and will likely result in improved detection of acute and early HIV infection (see Acute and Recent (Early) HIV Infection in the Adult and Adolescent Antiretroviral Guidelines and http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf). Positive fourth-generation tests are followed by a type-specific antibody differentiation assay. Negative antibody differentiation assays are followed by HIV nucleic acid testing, which (if positive) confirms acute HIV infection. Serologic testing should be performed within 3 months on patients whose acute HIV infection is diagnosed with virologic testing but who are antibody-negative.

Recent HIV infection also can be detected by repeat HIV testing later in pregnancy in women whose initial HIV test earlier in pregnancy was negative.[10] A report from the Mother-Infant Rapid Intervention at Delivery study found that 6 (11%) of 54 women whose HIV was identified with rapid HIV testing during labor had primary infection.[10,11] Repeat HIV testing in the third trimester is recommended for pregnant women known to be at risk of HIV, who receive care in facilities with an HIV incidence of at least 1 case per 1,000 pregnant women per year, who are incarcerated, or who reside in jurisdictions with elevated HIV incidence (see Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings and http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf).[12]

Acute or recent HIV infection during pregnancy and breastfeeding is associated with a high risk of perinatal transmission of HIV. Therefore, all HIV-infected pregnant women with acute or recent infection should start ART as soon as possible, with the goal of preventing perinatal transmission by optimal suppression of plasma HIV RNA below detectable levels.[13] Data from the United States and Europe demonstrate that in 6% to 16% of patients, transmitted virus may be resistant to at least one ARV drug.[14,15] Therefore, baseline genotypic resistance testing should be performed to guide selection or adjustment of an optimal ARV drug regimen. If results of resistance testing or the source virus's resistance pattern are known, that information should be used to guide selection of the drug regimen, but initiation of ART should not be delayed. A protease inhibitor (PI)-based ARV drug regimen generally should be initiated because clinically significant resistance to PIs is uncommon. Choice of regimen should be based on recommendations for use of ARV drugs in pregnancy (see Table 6 and Table 8).[16] Dolutegravir plus tenofovir disoproxil fumarate (TDF)/emtricitabine is considered a reasonable treatment option for treatment of acute infection in non-pregnant adults but data are limited regarding efficacy of this regimen in treatment of early infection and until safety and dosing are determined, it is not recommended during pregnancy (see Acute or Recent (Early) HIV Infection in the Adult Guidelines). Due to the lower resistance barrier raltegravir should not be used in this situation as viral loads are expected to be high.[17] Some clinicians would consider combining raltegravir with a boosted PI for treatment of acute infection during pregnancy. Abacavir is not recommended for empiric treatment of acute infection unless the patient is known to be HLA-B*5701 negative so TDF/emtricitabine is the preferred nucleoside reverse transcriptase inhibitor backbone for treatment of acute infection.

When acute HIV infection is diagnosed during pregnancy, and particularly if it is documented in late pregnancy, cesarean delivery is likely to be necessary because there may be insufficient time to fully suppress a patient's viral load. In nursing mothers in whom seroconversion is suspected, breastfeeding should be interrupted and it should not resume if infection is confirmed (see Breastfeeding in Infants of Mothers Diagnosed with HIV Infection in Infant Antiretroviral Prophylaxis). Women can continue to express and store breast milk while awaiting confirmation of infection status. In such a situation, given the high risk of transmission to the infant with acute maternal infection, consultation with a pediatric HIV specialist regarding appropriate infant management is strongly recommended.

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All women who are pregnant or breastfeeding should be counseled about prevention of acquisition of HIV (see Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis and Antiretroviral Postexposure Prophylaxis After Sexual, Injection-Drug Use, or Other Nonoccupational Exposure to HIV in the United States). Several studies suggest that pregnancy may be a time of increased risk of transmission of HIV[18-23] even when controlling for sexual risk behaviors.[18] It is hypothesized that the heightened risk may be attributable to hormonal changes that affect the genital tract mucosa or immune responses.[18] Although only limited data exist on HIV serodiscordance rates in the United States, data on women from sub-Saharan Africa show that women in serodiscordant relationships may be particularly vulnerable to acquisition of HIV.[24-26] All women should be asked if they know the HIV status of their partner. HIV testing of the sexual partners of pregnant women should be encouraged; initiation of ART is recommended for partners who are identified to be HIV-infected to reduce the risk of HIV acquisition by the woman.[27] Furthermore, the importance of using condoms should be reinforced in pregnant and breastfeeding women who may be at risk of acquisition of HIV, including those whose partners are HIV-infected, and the potential use of pre- or post-exposure ARV prophylaxis also should be emphasized (see Reproductive Options for HIV-Concordant and Serodiscordant Couples).

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