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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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 antiretroviral therapy (ART) as soon as possible to prevent perinatal transmission, with the goal of suppressing plasma HIV RNA to below detectable levels (AII).

- In women with acute HIV infection, baseline genotypic resistance testing should be performed simultaneously with initiation of ART, and the regimen should be adjusted, if necessary, to optimize virologic response (AIII).

- In women with acute HIV infection, a ritonavir-boosted protease-inhibitor-based regimen or a dolutegravir-based regimen with tenofovir disoproxil fumarate/emtricitabine should be initiated (AII) (see Table 6).

- When acute HIV infection is diagnosed during pregnancy or breastfeeding, given the high risk of transmission to the infant, consultation with a pediatric HIV specialist regarding appropriate infant management and antiretroviral prophylaxis regimen is strongly recommended (see Infant Management section) (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 and 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. From 2002 to 2006, of 3,396 neonates exposed to HIV 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). Among 70 infants born with perinatal HIV infection in Florida during 2007 through 2014, 12 (17%) of their mothers had evidence of acute infection during pregnancy. In the United States, of 10,308 pregnant women with HIV 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 seroconverted prior to pregnancy (1.6%) \( (P < 0.0001). \)

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/arthritis, and other symptoms. 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.

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. More specific guidance on HIV testing can be found in the Acute and Recent (Early) HIV section of the Adult and Adolescent Antiretroviral Guidelines, the CDC HIV testing algorithm (http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf), and the Maternal HIV Testing and Identification of Perinatal HIV Exposure sections.

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. A report from the Mother-Infant Rapid Intervention at Delivery study found that 6 of 54 (11%) women whose HIV was identified with rapid HIV testing during labor had primary infection. 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, http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf, and Maternal HIV testing and Identification of Perinatal HIV Exposure). Despite this recommendation, a retrospective cohort study at a large metropolitan hospital in a high-prevalence jurisdiction reported that repeat prenatal HIV testing was performed in only 28.4% of women.

Acute or recent HIV infection during pregnancy and breastfeeding is associated with a high risk of perinatal transmission of HIV. Therefore, all pregnant women with acute or recent HIV infection should start antiretroviral therapy (ART) as soon as possible, with the goal of preventing perinatal transmission by optimal suppression of plasma HIV RNA below detectable levels. Data from the United States and Europe demonstrate that in 6% to 16% of patients, transmitted virus may be resistant to at least 1 antiretroviral (ARV) drug. 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. The choice of PI for treatment of acute infection during pregnancy should be based on recommendations for use of ARV drugs in pregnancy (see Table 6 and Table 9) and includes atazanavir/ritonavir and darunavir/ritonavir.

However, recent data suggest that integrase strand transfer inhibitor (INSTI)-based regimens may be associated with shorter time to viral suppression. An observational study evaluated time to viral suppression among 86 non-pregnant adults with newly-diagnosed HIV infection: 36 (42%) had acute, 27 (31%) early and 23 (27%) had established HIV infection. ART was initiated within 30 days of diagnosis and the median time to documented viral suppression was 12 weeks. Time to viral suppression was significantly shorter in those receiving an integrase inhibitor- versus a PI-based regimen (median weeks to viral suppression: 12 and IQR 4–24 weeks in those with INSTI vs. median weeks to viral suppression 24 and IQR 12–24 in those with protease inhibitors; \( P = 0.022 \); baseline viral loads did not differ between those 2 groups). Due to the lower resistance barrier raltegravir is not recommended in this situation as viral loads are expected to be high. Dolutegravir plus tenofovir disoproxil fumarate (TDF)/emtricitabine is considered a reasonable ARV regimen for treatment of acute infection in non-pregnant adults but data are limited regarding efficacy of this regimen in treatment of early infection. Although dolutegravir is not a preferred INSTI for ART initiation in pregnant women due to the limited data supporting safety and dosing of dolutegravir in pregnancy, dolutegravir may be considered for acute infection during pregnancy because of the high viral load in acute/early infection, higher barrier to resistance of dolutegravir (compared with raltegravir), once-a-day dosing and the goal of achieving maternal virologic suppression promptly with minimal risk of needing to adjust the treatment regimen. TDF/emtricitabine is the preferred nucleoside reverse transcriptase inhibitor backbone for treatment of acute
When acute HIV infection is diagnosed during pregnancy, and particularly if it is documented in late pregnancy, cesarean delivery may be necessary if there is 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). Women can continue to express and store breast milk while awaiting confirmation of infection status. When acute HIV infection is diagnosed during pregnancy or breastfeeding, given the high risk of transmission to the infant with acute maternal infection, consultation with a pediatric HIV specialist regarding appropriate infant management and ARV prophylaxis regimen is strongly recommended (see Infant Prophylaxis). All women diagnosed with acute infection should be asked whether they know the HIV status of their partner. HIV testing of the sexual partners of all pregnant women testing HIV positive should be encouraged.

References


