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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Special Situations — Acute HIV Infection (Last updated July 31, 2012; last reviewed July 31, 2012)

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 an HIV antibody test (see Identifying, Diagnosing, and Managing Acute HIV-1 Infection in the Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents) **(AII)**.
- Repeat HIV antibody testing in the third trimester is recommended for pregnant women with initial negative HIV antibody tests who are known to be at risk of HIV, are receiving care in facilities that have an HIV incidence in pregnant women of at least 1 per 1,000 per year, 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) **(AII)**.
- All pregnant women with acute or recent HIV infection should start a combination antiretroviral (ARV) drug regimen as soon as possible to prevent mother-to-child 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 the combination ARV regimen, and the ARV regimen should be adjusted, if necessary, to optimize virologic response **(AIII)**.
- Because clinically significant resistance to protease inhibitors (PIs) is less common than resistance to non-nucleoside reverse transcriptase inhibitors in ARV-naive individuals in general, a ritonavir-boosted PI-based regimen 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 mother-to-child transmission (MTCT) in the United States.

In North Carolina from 2002 to 2005, 5 of 15 women found to have acute HIV infection on nucleic acid amplification testing of pooled HIV antibody-negative specimens were pregnant at the time of testing.[1] All 5 women received antiretroviral (ARV) drugs and delivered HIV-uninfected infants.

From 2002 to 2006, 3,396 HIV-exposed neonates were 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 (odds ratio 15.19; 95% confidence interval, 3.98–56.30). Maternal acquisition of HIV during pregnancy was documented in only 1.3% of perinatal HIV exposures, but it was associated with 9 (13.8%) of the 65 MTCT cases.[2] A case series from China reported a perinatal transmission rate of 35.8% in 106 breastfeeding infants of mothers who acquired HIV postnatally through blood transfusion.[3] 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[4, 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%–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.[4, 6-11] 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, a plasma HIV RNA test typically is used in conjunction with an HIV antibody test to diagnose acute infection. A low-positive HIV RNA level (<10,000 copies/mL) may represent a false-positive test because values in acute infection generally are very high (>100,000 copies/mL).[4, 10] In individuals infected with non-B HIV-1 subtypes, however, HIV RNA levels may be lower, even with acute infection, because those subtypes may not amplify as well as subtype B. In that situation, consultation with an HIV treatment specialist is recommended. Confirmatory serologic testing should be performed within 3 months on patients whose acute HIV infection is diagnosed with virologic testing but who are antibody negative or whose antibody levels cannot be determined.

Recent HIV infection also can be detected by repeat HIV antibody testing later in pregnancy in women whose initial HIV antibody testing earlier in pregnancy was negative. 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.[12] 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).[13]

Whether treatment of acute or recent HIV infection results in long-term virologic, immunologic, or clinical benefit is unknown, and in non-pregnant adults, therapy currently is considered optional.[14] In pregnant or breastfeeding women, however, acute or recent HIV infection is associated with a high risk of perinatal transmission of HIV. All HIV-infected pregnant women with acute or recent infection should start a combination ARV regimen 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%–16% of patients, transmitted virus may be resistant to at least one ARV drug.[15-17] 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 the combination ARV regimen should not be delayed. Because clinically significant resistance to protease inhibitors (PIs) is less common than resistance to non-nucleoside reverse transcriptase inhibitors in ARV-naive persons, a PI-based ARV drug regimen generally should be initiated. Choice of regimen should be based on recommendations for use of ARV drugs in pregnancy (see Table 5). Following delivery, considerations regarding continuation of the ARV regimen for treatment are the same for mothers as for other non-pregnant individuals.

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 definitively confirmed (see Breastfeeding Infants of Mothers Diagnosed with HIV Infection in Infant Antiretroviral Prophylaxis). In such a situation, consultation with a pediatric HIV specialist regarding appropriate infant management is recommended.

All women who are pregnant or breastfeeding should be counseled about prevention of acquisition of HIV (*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[18-21], 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 no reliable data on HIV serodiscordance rates in the United States exist, data on women from sub-Saharan Africa show that women in serodiscordant relationships may be particularly vulnerable to acquisition of HIV.[22, 23] HIV testing of the sexual partners of pregnant women should be encouraged. 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.

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