Acute HIV Infection

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Panel's Recommendations
• When acute HIV infection is suspected in pregnancy or during breastfeeding, a plasma HIV RNA test should be obtained in conjunction an antigen/antibody immunoassay test (see Acute and Recent [Early] HIV Infection in the Adult and Adolescent Antiretroviral Guidelines and the Centers for Disease Control and Prevention HIV testing algorithm for more information) **(AII)**. • Repeat HIV testing in the third trimester is recommended for pregnant women with initial negative HIV test results who are known to be at risk of acquiring HIV, who are receiving care in facilities that have an HIV incidence of ≥1 case per 1,000 pregnant women per year, who reside in jurisdictions with elevated HIV incidence, or who reside in states that require third-trimester testing (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 antiretroviral therapy (ART) as soon as possible to prevent perinatal transmission, with the goal of rapidly suppressing plasma HIV RNA below detectable levels **(AI)**. • In women with acute HIV infection, baseline genotypic resistance testing should be performed simultaneously with initiation of ART **(AII)**, and the regimen should be adjusted, if necessary, to optimize virologic response **(BIII)**. • Dolutegravir plus tenofovir disoproxil fumarate (TDF) plus emtricitabine (FTC) is the *Preferred* ART regimen for pregnant women, irrespective of trimester, and for breastfeeding women with acute HIV (see Table 4, Table 5, Recommendations for Use of Antiretroviral Drugs During Pregnancy, and Appendix C: Antiretroviral Counseling Guide) **(AII)**.   • Raltegravir plus TDF plus FTC or a ritonavir-boosted protease inhibitor (either atazanavir ATV/r or darunavir/r) plus TDF plus FTC are *Alternative* ART regimens for pregnant and breastfeeding women with acute HIV **(AIII).** See Table 4, Table 5, and Recommendations for Use of Antiretroviral Drugs During Pregnancy for more information. • The Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission emphasizes the importance of counseling and informed decision making regarding all antiretroviral (ARV) regimens for people with HIV **(AIII)**. • Providers should inform individuals starting ART of the importance of strict adherence to rapidly achieve and maintain viral suppression **(AIII)**. • Lactating women who receive a diagnosis of acute HIV infection should be counseled to discontinue breastfeeding. • Infants born to women who received a diagnosis of acute HIV infection during pregnancy or breastfeeding are at high risk of acquiring HIV infection and should receive an ARV regimen that is appropriate for this elevated risk (see Table 6 in Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection) **(AII)**. Consulting a pediatric HIV specialist regarding appropriate infant management is strongly recommended (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection).
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

Women may have an increased risk of HIV infection during pregnancy and breastfeeding.[1,2] Women who are at risk for acquiring HIV during pregnancy and the postpartum period should consider using interventions that prevent HIV acquisition, such as oral daily pre-exposure prophylaxis (PrEP).[3] For more information, see Pre-exposure Prophylaxis (PrEP) to Reduce the Risk of Acquiring HIV During Periconception, Antepartum, and Postpartum Periods.

Risk of perinatal transmission after maternal acute HIV infection

Acute or recent HIV infection during pregnancy or breastfeeding is associated with an increased risk of perinatal HIV transmission, and a significant proportion of pediatric infections can be attributed to maternal acute infection.[4] Among 10,308 pregnant women with HIV who delivered live infants from 2005 to 2010 in 15 areas of the United States that conducted Enhanced Perinatal Surveillance, 124 women (1.2%) seroconverted during pregnancy. The rate of perinatal transmission was eight times higher among women who seroconverted during pregnancy (12.9%) than among those who seroconverted prior to pregnancy (1.6%) ($P < 0.0001$).[5] Similarly, among 108 new perinatal HIV infections that were identified between 2006 and 2013 in the United

Kingdom, 23 were associated with a concurrent maternal seroconversion.[6] The high rate of transmission in people with acute infection is likely related to the high viral loads in plasma, breast milk, and the genital tract that are present during acute infection[7]; in addition, acute HIV infection symptoms can be nonspecific, which results in missed opportunities to diagnose and implement interventions that can reduce the risk of perinatal transmission.

Diagnosis of acute HIV infection in pregnant women

Health care providers should maintain a high level of suspicion of acute HIV infection in women who are pregnant or breastfeeding and have clinical signs and symptoms that are compatible with acute infection. Even when women do not report high-risk behaviors, it still is possible that their sexual partners are practicing high-risk behaviors without their knowledge. An estimated 40% to 90% of patients with acute HIV infection will experience symptoms of acute retroviral syndrome, which is characterized by fever, lymphadenopathy, pharyngitis, skin rash, myalgias/arthralgias, headache, diarrhea, oral ulcers, and other symptoms.[8–10] Providers often do not recognize acute HIV infection because the symptoms are similar to those of other common illnesses, and individuals with acute HIV infection may be asymptomatic.

When acute retroviral syndrome is suspected during pregnancy or breastfeeding, a plasma HIV RNA test should be obtained in conjunction with an antigen/antibody immunoassay test. Guidance for HIV testing recommends using a Food and Drug Administration (FDA)-approved antigen/antibody combination (fourth-generation) immunoassay that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen for initial testing. 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 Infection section of the Adult and Adolescent Antiretroviral Guidelines, the Centers for Disease Control and Prevention (CDC) HIV testing algorithm, and the Maternal HIV Testing and Identification of Perinatal HIV Exposure.

Recent HIV infection also can be detected by repeat HIV testing later in pregnancy in women whose initial HIV test was negative.[11] A report from the Mother-Infant Rapid Intervention at Delivery (MIRIAD) study found that six of 54 women (11%) whose HIV was identified with rapid HIV testing during labor had acute or recent infection.[12] Repeat HIV testing during the third trimester is recommended for pregnant women who are known to be at risk of HIV infection, who receive care in facilities with an HIV incidence of ≥1 case per 1,000 pregnant women per year, or who reside in jurisdictions with elevated HIV incidence (see Prenatal and Perinatal Human Immunodeficiency Virus Testing, Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings, the CDC HIV testing algorithm, and Maternal HIV Testing and Identification of Perinatal HIV Exposure).[13] Implementation of the recommendation for repeat HIV testing later in pregnancy has varied. 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.[14] At a large, urban tertiary hospital in Florida, 82% of women were retested in the third trimester.[15]

Antiretroviral therapy for women with acute or recent HIV infection during pregnancy

Acute or recent HIV infection during pregnancy and breastfeeding is associated with a high risk of vertical transmission of HIV.[1,4] 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 rapid suppression of plasma HIV RNA below detectable levels. Baseline genotypic resistance testing should be performed to guide adjustment of an optimal antiretroviral (ARV) drug regimen. Data from the United States and Europe demonstrate that in 6% to 16% of patients, transmitted virus may be resistant to ≥1 ARV drugs.[16,17] If results of resistance testing are already available or the source virus's resistance pattern is known, that information can be used to guide the selection of the drug regimen.

A regimen that includes dolutegravir (DTG) plus tenofovir disoproxil fumarate (TDF) plus emtricitabine (FTC) should be initiated in pregnant women and breastfeeding women with acute HIV infection (see

Recommendations for Use of Antiretroviral Drugs During Pregnancy, Table 4, Table 5, and Appendix C: Antiretroviral Counseling Guide for Health Care Providers). DTG is associated with higher rates of virologic suppression, faster rates of viral load decline, and a higher genetic barrier to drug resistance than other *Preferred* and *Alternative* agents. DTG plus TDF (or tenofovir alafenamide) plus FTC (or lamivudine) is one of the recommended ARV regimens for treatment of acute and early infection in nonpregnant adults. *Alternative* regimens for treatment of acute infection during pregnancy and breastfeeding include raltegravir (RAL) plus TDF plus FTC or a regimen that includes a ritonavir-boosted protease inhibitor (either atazanavir/r or darunavir/r) plus TDF plus FTC (see Table 4 and Table 5). TDF plus FTC is the *Preferred* nucleoside reverse transcriptase inhibitor (NRTI) backbone for treatment of acute infection. Abacavir **is not recommended** for empiric treatment of acute infection unless the patient previously tested negative for the HLA-B*5701 gene variant; this will avoid delays in ART initiation while awaiting HLA-B*5701 test results.

Several studies have demonstrated that the use of integrase strand transfer inhibitor (INSTI)-based regimens is associated with shorter time to viral suppression compared with other ARV regimens.[18–20] Although no data are available to inform the treatment of acute HIV during pregnancy, two recent studies in women who presented to care late in pregnancy demonstrated more rapid viral decline on INSTI-based regimens than on efavirenz (EFV)-based ART. In the DolPHIN 2 study, 268 ART-naive pregnant women in Uganda and South Africa with a median gestational age of 31 weeks were randomized to receive either DTG plus two NRTIs or EFV plus two NRTIs. At delivery, women in the DTG arm were significantly more likely to have achieved HIV RNA <50 copies/mL than those in the EFV arm (74% vs. 43%, respectively; adjusted risk ratio 1.66 [95% CI, 1.3–2.1], $P < 0.0001$).[21] Similarly, in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development P1081 trial, 408 ART-naive, late-presenting pregnant women in South America, Africa, Thailand, and the United States were randomized to receive RAL plus two NRTIs or EFV plus two NRTIs. Fifty percent of these women presented to care at 20 weeks to <28 weeks gestation, and 50% presented at 28 weeks to <37 weeks gestation. Overall, 144 women (94%) in the RAL group and 129 (84%) in the EFV group achieved a viral load of < 200 copies/mL at delivery. Furthermore, 131 of 153 women (86%) on RAL-based ART versus 90 of 154 (58%) in the EFV group achieved a viral load below the limit of detection.[22]

Obstetrical and neonatal considerations

When acute HIV infection is diagnosed during pregnancy, and particularly when it is documented in late pregnancy, cesarean delivery may be necessary when there is insufficient time to fully suppress a patient's viral load. When acute HIV infection is diagnosed during breastfeeding, breastfeeding should be discontinued. In nursing mothers with suspected seroconversion, breastfeeding should be interrupted, and it should not resume if infection is confirmed (see Counseling and Managing Women with HIV in the United States Who Desire to Breastfeed). Women can continue to express and store breast milk while awaiting confirmation of infection status.

Given the high risk of transmission to the infant with acute maternal infection, an infant should receive an ARV regimen that is appropriate for this elevated risk when acute HIV infection is diagnosed during pregnancy or breastfeeding (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection). Consulting a pediatric HIV specialist regarding appropriate infant management is strongly recommended. All women who receive a diagnosis of acute infection should be asked whether they know the HIV status of their partner. HIV testing of the sexual partners of all pregnant women who test HIV positive should be encouraged, and PrEP should be offered to partners who test HIV negative.

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