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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Monitoring of the Woman and Fetus During Pregnancy (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations

- Plasma HIV RNA levels should be monitored at the initial visit **(AI)**; 2 to 4 weeks after initiating (or changing) antiretroviral (ARV) drug regimens **(BI)**; monthly until RNA levels are undetectable **(BIII)**; and then at least every 3 months during pregnancy **(BIII)**. HIV RNA levels also should be assessed at approximately 34 to 36 weeks' gestation to inform decisions about mode of delivery (see Transmission and Mode of Delivery) **(AIII)**.
- CD4 T-lymphocyte (CD4-cell) count should be monitored at the initial antenatal visit **(AI)** and at least every 3 months during pregnancy **(BIII)**. Monitoring of CD4-cell count can be performed every 6 months in patients on antiretroviral therapy (ART) for more than 2 to 3 years who are adherent to therapy, clinically stable, and have sustained viral suppression **(CIII)**.
- Genotypic ARV drug-resistance testing should be performed at baseline in all HIV-infected pregnant women with HIV RNA levels >500 to 1,000 copies/mL, whether they are ARV naive or currently on therapy **(AIII)**. Repeat testing is indicated following initiation of an ARV regimen in women who have suboptimal viral suppression or who have persistant viral rebound to detectable levels after prior viral suppression on an ARV regimen **(AII)**.
- Monitoring for complications of ARV drugs during pregnancy should be based on what is known about the adverse effects of the drugs a woman is receiving **(AIII)**.
- First-trimester ultrasound is recommended to confirm gestational age and, if scheduled cesarean delivery is necessary, to guide timing of the procedure (see Transmission and Mode of Delivery) **(AII)**.
- In women on effective ART, no perinatal transmissions have been reported after amniocentesis, but a small risk of transmission cannot be ruled out. If amniocentesis is indicated in HIV-infected women, it should be done only after initiation of an effective ART regimen and, if possible, when HIV RNA levels are undetectable **(BIII)**. In women with detectable HIV RNA levels in whom amniocentesis is deemed necessary, consultation with an expert should be considered.

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*

Viral load should be monitored in HIV-infected pregnant women at the initial visit, 2 to 4 weeks after initiating or changing antiretroviral (ARV) regimens, monthly until undetectable, and at least every 3 months thereafter. If adherence is a concern, more frequent monitoring is recommended because of the potential increased risk of perinatal HIV infection associated with detectable HIV viremia during pregnancy. More frequent viral load monitoring is recommended in pregnant versus non-pregnant individuals because of the urgency to lower viral load as rapidly as possible to reduce the risk of perinatal transmission. Therefore, there is a need to identify pregnant women in whom the decline in viral load is slower than expected. Adult ARV guidelines note that patients should have a decrease in plasma HIV RNA level by at least one $\log_{10}$ copies/mL within 1 month after initiation of potent therapy.[1] Viral suppression generally is achieved in 16 to 24 weeks in ARV-naive treatment-adherent individuals who do not harbor resistance mutations to the drugs they are receiving but, in rare cases, it may take longer. Viral load also should be assessed at approximately 34 to 36 weeks' gestation to inform decisions about mode of delivery (see Transmission and Mode of Delivery).

In HIV-infected pregnant women, CD4 T-lymphocyte (CD4-cell) count should be monitored at the initial visit and at least every 3 months during pregnancy. CD4-cell counts can be performed every 6 months in

patients on antiretroviral therapy (ART) for more than 2 to 3 years who are adherent to therapy, clinically stable, and have sustained viral suppression. Because of physiologic changes such as hemodilution that are associated with pregnancy, CD4 percentage may be more stable than absolute CD4 count during pregnancy.[2-5] Nevertheless, most clinicians still rely on absolute CD4 count to evaluate immune status during pregnancy because parameters for initiating therapy are based on those values.

Whenever feasible, ARV drug-resistance testing should be performed in HIV-infected pregnant women before initiation of ARV drugs if HIV RNA levels are above the threshold for resistance testing (that is, >500–1,000 copies/mL) unless delay in getting results back would lead to delay in starting ARV for prevention of mother-to-child transmission. Testing also should be performed on women taking an ARV regimen who have suboptimal viral suppression or who have persistant viral rebound to detectable levels after prior viral suppression on an ARV regimen (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy). Drug-resistance testing in the setting of virologic failure should be performed while patients are receiving ARV drugs or within 4 weeks after discontinuation of drugs. Genotypic testing is preferable to phenotypic testing because it costs less, has a faster turnaround time, and is more sensitive for detection of mixtures of wild-type and resistant virus.

Monitoring for potential complications of ARV drugs during pregnancy should be based on what is known about the adverse effects of the drugs a woman is receiving. For example, routine hematologic monitoring is recommended for women receiving zidovudine-containing regimens and routine renal monitoring should be recommended for women on tenofovir. Liver function should be monitored in all women receiving ARV drugs. Hepatic dysfunction has been observed in pregnant women on protease inhibitors, and hepatic steatosis and lactic acidosis in pregnancy have been related to nucleoside reverse transcriptase inhibitor use. Women with CD4-cell counts >250 cells/mm^3 are thought to be at particular risk of developing symptomatic, rash-associated, nevirapine-associated hepatotoxicity within the first 18 weeks after initiation of therapy. However, recent data from an international study did not show the same association between nevirapine toxicity and CD4-cell counts among pregnant women.[6] Additional data from a 2010 study suggest that abnormal liver transaminase levels at baseline may be more predictive of risk than CD4-cell count.[7] Transaminase levels should be monitored more frequently and carefully in pregnant women initiating therapy with nevirapine, and they should also be watched for clinical symptoms of potential hepatotoxicity (see Nevirapine and Hepatic/Rash Toxicity). The drug can be used cautiously with careful monitoring in women with mildly abnormal liver function tests at the time of ARV drug initiation.

First-trimester ultrasound is recommended to confirm gestational age and, if scheduled cesarean delivery is necessary, to guide potential timing because such deliveries for prevention of perinatal transmission of HIV should be performed at 38 weeks' gestation (see Transmission and Mode of Delivery).[8, 9] In patients who are not seen until later in gestation, second-trimester ultrasound can be used for both anatomical scanning and determination of gestational age.

Although data are still somewhat limited, the risk of transmission does not appear to be increased with amniocentesis or other invasive diagnostic procedures in women receiving effective ART resulting in viral suppression. This is in contrast to the pre-ART era, during which invasive procedures such as amniocentesis and chorionic villus sampling (CVS) were associated with a two- to fourfold increased risk of perinatal transmission of HIV.[10-13] Although no transmissions have occurred among 159 cases reported to date of amniocentesis or other invasive diagnostic procedures among women on effective ART regimens, a small increase in risk of transmission cannot be ruled out.[14-17] HIV-infected women who have indications for invasive testing in pregnancy, such as abnormal ultrasound or aneuploidy screening, should be counseled about the potential risk of transmission of HIV along with other risks of the procedure and allowed to make an informed decision about testing. Some experts consider CVS and cordocentesis too risky to offer to HIV-infected women and they recommend limiting invasive procedures to amniocentesis,[15] but existing data on

transmission risk associated with these procedures are limited. At a minimum, HIV-infected pregnant women should receive effective ART before undergoing any invasive prenatal testing and, ideally, have an undetectable HIV RNA level at the time of the procedure. In women with detectable HIV RNA levels for whom amniocentesis is deemed necessary, consultation with an expert should be considered. These procedures should be done under continuous ultrasound guidance and, if possible, the placenta should be avoided.

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