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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General Principles Regarding Use of Antiretroviral Drugs during Pregnancy

Panel’s Recommendations

- Initial evaluation of HIV-infected pregnant women should include assessment of HIV disease status, and recommendations regarding initiation of antiretroviral therapy (ART) or the need for any modification if currently receiving ART (AIII). The National Perinatal HIV Hotline (888-448-8765) provides free clinical consultation on all aspects of perinatal HIV care.

- All pregnant HIV-infected women should receive ART, initiated as early in pregnancy as possible, to prevent perinatal transmission regardless of plasma HIV RNA copy number or CD4 T lymphocyte count (AII). Maintenance of a viral load below the limit of detection throughout pregnancy and lifetime of the HIV-infected individual is recommended.

- Combined maternal antepartum and intrapartum (ARV) treatment/prophylaxis as well as infant ARV prophylaxis is recommended because ARV drugs reduce perinatal transmission by several mechanisms, including lowering maternal antepartum viral load and providing infant pre- and post-exposure prophylaxis (AII).

- The known benefits and potential risks of all medication use, including ARV drug use during pregnancy, should be discussed with all HIV-infected women (AIII).

- The importance of adherence to ARV drug regimens should be emphasized in patient counseling (AII).

- ARV drug-resistance studies should be performed before starting or modifying ARV drug regimens in women whose HIV RNA levels are above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL) (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) (AIII). In pregnant women not already receiving ART, ART should be initiated before results of drug-resistance testing are available because earlier viral suppression has been associated with lower risk of transmission. If ART is initiated before results are available, the regimen should be modified, if necessary, based on resistance assay results (BII).

- Coordination of services among prenatal care providers, primary care and HIV specialty care providers, and when appropriate, mental health and drug abuse treatment services, intimate partner violence support services, and public assistance programs, is essential to help ensure that infected women adhere to their ARV drug regimens (AII).

- Providers should also initiate counseling during pregnancy about key intrapartum and postpartum considerations, including mode of delivery, maternal lifelong HIV therapy, postpartum contraception, infant feeding, infant ARV prophylaxis and timing of infant diagnostic testing and neonatal circumcision (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

In addition to the standard antenatal assessments for all pregnant women, the initial evaluation of those who are HIV infected should include assessment of HIV disease status, and recommendations for HIV-related medical care. This initial assessment should include the following:

- Review of prior HIV-related illnesses and past CD4 T lymphocyte (CD4) cell counts and plasma HIV RNA levels;

- Current CD4 cell count;

- Current plasma HIV RNA level;

- Assessment of the need for prophylaxis against opportunistic infections such as *Pneumocystis jirovecii* pneumonia and *Mycobacterium avium* complex (see Adult and Adolescent Opportunistic Infections Guidelines);

- Screening for hepatitis A virus (HAV), hepatitis C virus, and tuberculosis in addition to standard screening for hepatitis B virus (HBV) infection;
• Assessment of the need for immunizations per guidelines from the American College of Obstetricians and Gynecologists, the Centers for Disease Control and Prevention (CDC), and the Infectious Diseases Society of America with particular attention to HAV, HBV, influenza, pneumococcus, and Tdap immunizations;\textsuperscript{1,2}

• Complete blood cell count and renal and liver function testing;

• HLA-B*5701 testing if abacavir use is anticipated (see Table 8);

• History of prior and current antiretroviral (ARV) drug use, including prior ARV use for prevention of perinatal transmission or treatment of HIV and history of adherence problems;

• Results of prior and current ARV drug-resistance studies;

• History of adverse effects or toxicities from prior ARV regimens;

• Assessment of supportive care needs (e.g., mental health services, substance abuse treatment, smoking cessation) as well as support to help ensure lifelong ART;

• Intimate partner violence-related screening and supportive care needs; and

• Referral of sexual partner(s) for HIV testing and ARV prophylaxis

The National Perinatal HIV Hotline
The National Perinatal HIV Hotline (888-448-8765) is a federally funded service providing free clinical consultation to providers caring for HIV-infected women and their infants.

How Antiretrovirals Prevent Perinatal Transmission
ARV drugs for prevention of perinatal transmission of HIV are recommended for all pregnant women, regardless of CD4 cell counts and HIV RNA levels. ARV drugs can reduce perinatal transmission through a number of mechanisms. Antenatal drug administration decreases maternal viral load in blood and genital secretions. Although the risk of perinatal transmission in women with undetectable plasma HIV RNA levels appears to be extremely low, it has been reported even among women on antiretroviral therapy (ART).\textsuperscript{3-5} Low-level cervicovaginal HIV RNA and DNA shedding has been detected even in women treated with ART who have undetectable plasma viral load.\textsuperscript{6-8} Penetration of ARV drugs into the female genital tract has been shown to vary between drugs.\textsuperscript{9-11} Because maternal viremia is not the only risk factor for HIV transmission, another important mechanism of protection is infant pre-exposure prophylaxis achieved by administering ARV drugs that cross the placenta and produce adequate systemic drug levels in the fetus. In addition, infant post-exposure prophylaxis is achieved by administering drugs after birth, providing protection from cell-free or cell-associated virus that may have entered the fetal/infant systemic circulation during labor and delivery. The importance of the pre- and post-exposure components of prophylaxis in reducing perinatal transmission is demonstrated by the reduced efficacy of interventions that involve administration of ARVs only during labor and/or to the newborns.\textsuperscript{12-18} Therefore, combined preconception ART, confirmation of antepartum viral load suppression, intrapartum continuation of current regimen with intravenous zidovudine added if the plasma viral load is >1,000 copies/mL, and infant ARV prophylaxis are recommended to prevent perinatal transmission of HIV.

General Principles of Drug Selection
In general, guidelines for the use of ART for the benefit of maternal health during pregnancy are the same as for women who are not pregnant, with some modifications based on concerns about specific drugs or limited experience with newer drugs during pregnancy, where the perinatal guidelines may differ from the adult guidelines.
The known benefits and known and unknown risks of ARV drug use during pregnancy should be considered and discussed with women (see Table 8 and Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy). Potential risks of these drugs should be placed into perspective by reviewing the substantial benefits of ARV drugs for maternal health and in reducing the risk of transmission of HIV to infants. Counseling of pregnant women about ARV use should be directive but non-coercive, and providers should help them make informed decisions regarding use of ARV drugs.

Discussions with women about initiation of ART regimens should include information about:

- Maternal risk of disease progression and benefits and risks of initiation of therapy for maternal health and lifelong treatment and viral suppression with ART;
- Benefit of ART for preventing perinatal transmission of HIV;\(^4\)
- Benefits of therapy for reducing sexual transmission to discordant partners when viral suppression is maintained;\(^19\)
- The need for strict adherence to the prescribed drug regimen to avoid resistance;
- Potential adverse effects of ARV drugs for mothers, fetuses, and infants, including potential interactions with other medications the women may already be receiving (see Recommendations for use of ARVs during pregnancy); and
- The limited long-term outcome data for infants after in utero drug exposure.

Transplacental passage of ARV drugs is an important mechanism of infant pre-exposure prophylaxis. Thus, when selecting an ARV regimen for a pregnant woman, at least one nucleoside/nucleotide reverse transcriptase inhibitor agent with high placental transfer should be included as a component of the ART regimen (see Table 8).\(^20-24\)

In women with plasma HIV RNA levels above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL), ARV drug-resistance studies should be performed before starting ART. However, in pregnant women not already receiving ART, ART should be initiated while awaiting results of genotype resistance testing because earlier viral suppression is associated with lower risk of perinatal transmission.\(^25\) The ART regimen can be modified, if necessary, based on resistance assay results (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy). Counseling should emphasize the importance of adherence to the ARV drug regimen to minimize the development of resistance.

All HIV-infected pregnant women should initiate or continue on ART during pregnancy to minimize the risk of transmission of HIV to their infant and partner(s). Providers should begin to counsel HIV-infected women about what they can expect during labor and delivery and the postnatal period. This includes discussions about the mode of delivery and possible intrapartum zidovudine, lifelong ART recommendation for all HIV-infected individuals and therefore continuing ART postpartum and possible changes in maternal ARV therapy postpartum and beyond, and discussion of family planning and available contraception. In addition, recommendations regarding the avoidance of both breastfeeding and premastication of food to prevent postnatal HIV transmission and the importance of neonatal ARV prophylaxis and infant diagnostic HIV testing should be discussed.

Medical care of HIV-infected pregnant women requires coordination and communication between HIV specialists and obstetric providers. General counseling should include current knowledge about risk factors for perinatal transmission. Risk of perinatal transmission of HIV has been associated with potentially modifiable factors, including cigarette smoking, illicit drug use, genital tract infections, and unprotected sexual intercourse with multiple partners during pregnancy. Besides improving maternal health, cessation of cigarette smoking and drug use, treatment of genital tract infections, and use of condoms with sexual intercourse during pregnancy may reduce risk of perinatal transmission. Additional support services such as mental health services and intimate partner violence assessment may be required, depending on a woman’s condition and risk factors.
individual circumstances. Coordination of services among prenatal care providers, primary care and HIV specialty care providers, mental health and drug abuse treatment services, and public assistance programs is essential to ensure that infected women adhere to their ARV drug regimens.

References


