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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Antepartum Care  (Last updated November 14, 2017; last reviewed November 14, 2017)

General Principles Regarding Use of Antiretroviral Drugs during Pregnancy

<table>
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<th>Panel's Recommendations</th>
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<tr>
<td>• Initial evaluation of pregnant women living with HIV should include assessment of HIV disease status and plans to initiate, continue, or modify antiretroviral therapy (ART) (AI). The National Perinatal HIV Hotline (888-448-8765) provides free clinical consultation on all aspects of perinatal HIV care.</td>
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<tr>
<td>• All pregnant women living with HIV 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 (AI). Maintenance of a viral load below the limit of detection throughout pregnancy and lifetime of the individual living with HIV is recommended (AII).</td>
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<td>• To minimize the risk of perinatal transmission, antiretroviral (ARV) drugs should be administered at all time points, including antepartum and intrapartum to the woman as well as postnatally to the neonate (AI).</td>
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<td>• The known benefits and potential risks of all medication use, including ARV drug use during pregnancy and postpartum, should be discussed with all women living with HIV (AII).</td>
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<td>• The importance of adherence to ARV drug regimens should be emphasized in patient counseling (AII).</td>
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<td>• 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., &gt;500 to 1,000 copies/mL) (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) (AIII).</td>
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<td>• 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 (BIII).</td>
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<td>• 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 women living with HIV adhere to their ARV drug regimens (AII).</td>
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<td>• Providers should also initiate counseling during pregnancy about key intrapartum and postpartum considerations, including mode of delivery, maternal lifelong HIV therapy, family planning and contraceptive options, infant feeding, infant ARV prophylaxis, timing of infant diagnostic testing, and neonatal circumcision (AIII).</td>
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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 women living with HIV 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;
• Screening for and treatment of sexually transmitted infections such as syphilis. Chlamydia trachomatis and Neisseria gonorrhoea and trichomonas;12
• 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{3,4}

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

• HLA-B*5701 testing if abacavir use is anticipated (see Table 9);

• 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 antiretroviral therapy (ART);

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

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

• Referral of children for HIV testing.

**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 women living with HIV and their infants.

**How Antiretrovirals Prevent Perinatal Transmission**

ARV drugs reduce the risk of perinatal transmission of HIV in 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{5-7} Low-level cervicovaginal HIV RNA and DNA shedding has been detected even in women treated with ART who have undetectable plasma viral load.\textsuperscript{8-10} Penetration of ARV drugs into the female genital tract varies by drug.\textsuperscript{11-13} Because maternal viremia is not the only risk factor for HIV transmission, another important mechanism of protection is infant pre-exposure prophylaxis achieved by maternal administration of 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 to the infant 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{15-21} Therefore, combined preconception ART, confirmation of antepartum plasma viral load suppression, scheduled surgical delivery (if indicated, based on most recent maternal plasma viral load), intrapartum continuation of current regimen with addition of intravenous zidovudine (if indicated, based on the most recent maternal plasma viral load), and infant ARV prophylaxis are all 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 in regimen selection 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 9 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 for reducing the risk of transmission of HIV to infants. Counseling of pregnant women about ARV use should be directive and non-coercive, and providers should help women 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;
- Benefit of ART for preventing perinatal transmission of HIV;\(^6\)
- Benefits of therapy for reducing sexual transmission to partners who do not have HIV when viral suppression is maintained;\(^22\)
- 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 after in utero drug exposure, especially for new antiretrovirals.

Transplacental passage of ARV drugs is thought to be 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 9).\(^23-27\)

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.\(^28\) The ART regimen can be modified, if necessary, based on resistance assay results\(^29\) (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 pregnant women living with HIV should initiate or continue ART during pregnancy to minimize the risk of transmission of HIV to their infants and partners. Providers should begin to counsel women living with HIV about what they can expect during labor and delivery and the postnatal period. This includes discussions about the mode of delivery, possible intrapartum zidovudine, as well as family planning and contraceptive options in the postpartum period. Providers should also discuss possible changes to the pregnant woman’s ART regimen post-delivery, because lifelong ART is recommended for all individuals living with HIV. In addition, discussions regarding prevention of postnatal transmission to the neonate should include recommendations about infant feeding, neonatal ARV prophylaxis, infant diagnostic HIV testing, and the avoidance of premastication of food.

Medical care of pregnant women living with HIV 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, and genital tract infections. Besides improving maternal health, cessation of cigarette smoking and drug use, treatment of sexually transmitted and other genital tract infections may reduce risk of perinatal transmission. Women should be assessed for mental health concerns and the risk of intimate partner violence and referred to appropriate services (i.e., depending on a woman’s 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 women living with HIV adhere to their ARV drug regimens.

References


