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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Mechanisms of Action of Antiretroviral Prophylaxis in Reducing Perinatal Transmission of HIV (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendation
• Antiretroviral (ARV) drugs reduce perinatal transmission by several mechanisms, including lowering maternal antepartum viral load and providing infant pre- and post-exposure prophylaxis. Therefore, combined antepartum, intrapartum, and infant ARV prophylaxis is recommended to prevent perinatal transmission of HIV **(AI)**.
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*

Perinatal Transmission of HIV and Maternal HIV RNA Copy Number (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendation
• All HIV-infected pregnant women should be counseled about and administered antiretroviral drugs during pregnancy for prevention of perinatal transmission, regardless of their HIV RNA levels **(AI)**.
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*

Preconception Counseling and Care for HIV-Infected Women of Childbearing Age

Overview (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• Discuss childbearing intentions with all women of childbearing age on an ongoing basis throughout the course of their care **(AIII)**. • Include information about effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy **(AI)**. • During preconception counseling, include information on safer sexual practices and elimination of alcohol, illicit drugs, and smoking, which are important for the health of all women as well as for fetal/infant health, should pregnancy occur **(AII)**. • When evaluating HIV-infected women, include assessment of HIV disease status and need for antiretroviral therapy (ART) for their own health **(AII)**. • Choose an ART regimen for HIV-infected women of childbearing age based on consideration of effectiveness for treatment of maternal disease, hepatitis B virus disease status, teratogenic potential of the drugs in the regimen should pregnancy occur, and possible adverse outcomes for mother and fetus **(AII)**.
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*

Reproductive Options for HIV-Concordant and Serodiscordant Couples (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• For serodiscordant couples who want to conceive, expert consultation is recommended so that approaches can be tailored to specific needs, which may vary from couple to couple **(AIII)**. It is important to recognize that treatment of the infected partner may not be fully protective against sexual transmission of HIV. • Partners should be screened and treated for genital tract infections before attempting to conceive **(AII)**. • For HIV-infected females with HIV-uninfected male partners, the safest conception option is artificial insemination, including the option of self-insemination with a partner's sperm during the peri-ovulatory period **(AIII)**. • For HIV-infected men with HIV-uninfected female partners, the use of sperm preparation techniques coupled with either intrauterine insemination or *in vitro* fertilization should be considered if using donor sperm from an HIV-uninfected male is unacceptable **(AII)**. • For serodiscordant couples who want to conceive, initiation of antiretroviral therapy (ART) for the HIV-infected partner is recommended (**AI** for CD4 T-lymphocyte (CD4-cell) count ≤550 cells/mm^3, **BIII** for CD4-cell count >550 cells/mm^3). If therapy is initiated, maximal viral suppression is recommended before conception is attempted **(AIII)**. • Periconception administration of antiretroviral pre-exposure prophylaxis (PrEP) for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission **(CIII)**. The utility of PrEP of the uninfected partner when the infected partner is receiving ART has not been studied.
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*

Antepartum Care (Last updated July 31, 2012; last reviewed July 31, 2012)

General Principles Regarding Use of Antiretroviral Drugs during Pregnancy

Panel's Recommendations

- Initial evaluation of infected pregnant women should include assessment of HIV disease status and recommendations regarding initiation of antiretroviral (ARV) drugs or the need for any modification if currently receiving antiretroviral therapy (ART) **(AIII)**. The National Perinatal HIV Hotline (1-888-448-8765) provides free clinical consultation on all aspects of perinatal HIV care.
- Regardless of plasma HIV RNA copy number or CD4 T-lymphocyte count, all pregnant HIV-infected women should receive a combination ARV drug regimen antepartum to prevent perinatal transmission **(AI)**. A combination regimen is recommended both for women who require therapy for their own health **(AI)** and for prevention of perinatal transmission in those who do not yet require therapy **(AII)**.
- The known benefits and potential risks of ARV use during pregnancy should be discussed with all women **(AIII)**.
- 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 (that is, >500 to 1,000 copies/mL) (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) **(AIII)**. When HIV is diagnosed later in pregnancy, ART or combination ARV prophylaxis should be initiated promptly without waiting for results of resistance testing **(BIII)**.
- In counseling patients, the importance of adherence to their ARV regimens should be emphasized **(AII)**.
- Considerations regarding continuing the ARV regimen for maternal treatment after delivery are the same as in non-pregnant individuals. The pros and cons of continuing versus discontinuing ARV drugs postpartum should be discussed with women so they can make educated decisions about postpartum ARV use before delivery **(AIII)**. Those decisions should be made in consultation with the provider who will assume responsibility for the women's HIV care after delivery.
- 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 **(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*

HIV-Infected Pregnant Women Who Have Never Received Antiretroviral Drugs (Antiretroviral Naive) (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations

- All HIV-infected pregnant women should receive a potent combination antiretroviral (ARV) regimen to reduce the risk of perinatal transmission of HIV **(AI)**. The choice of regimen should take into account current adult treatment guidelines, what is known about the use of specific drugs in pregnancy, and the risk of teratogenicity (Table 5).
- The decision as to whether to start the regimen in the first trimester or delay until 12 weeks' gestation will depend on CD4 T-lymphocyte (CD4-cell) count, HIV RNA levels, and maternal conditions such as nausea and vomiting **(AIII)**. Earlier initiation of a combination ARV regimen may be more effective in reducing transmission, but benefits must be weighed against potential fetal effects of first-trimester drug exposure.
- Combination ARV regimens should include a dual nucleoside reverse transcriptase inhibitor (NRTI) backbone that includes one or more NRTIs with high levels of transplacental passage (zidovudine, lamivudine, emtricitabine, tenofovir, or abacavir) **(AIII)**.
- ARV drug-resistance studies should be performed before starting the ARV regimen if HIV RNA is above the threshold for resistance testing (that is, >500–1,000 copies/mL) (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) **(AI)**. If HIV is diagnosed later in pregnancy the ARV regimen should be initiated promptly without waiting for the results of resistance testing **(BIII)**.
- Nevirapine can be used as a component of the ARV regimen in pregnant women with CD4 cell counts ≤250 cells/mm^3. In pregnant women with CD4 cell counts >250 cells/mm^3, however, nevirapine should be used only if the benefit clearly outweighs the risk because the drug is associated with an increased risk of hepatic toxicity **(AII)**.

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*

HIV-Infected Pregnant Women Who Are Currently Receiving Antiretroviral Therapy (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations

- In general, HIV-infected women receiving antiretroviral therapy (ART) who present for care during the first trimester should continue treatment during pregnancy, assuming the regimen is tolerated and effective in suppressing viral replication **(AII)**.
- The Panel recommends that efavirenz be continued in pregnant women receiving efavirenz-based ART who present for antenatal care in the first trimester provided the regimen is resulting in virologic suppression (see text) **(CIII)**.
- Pregnant women receiving and tolerating nevirapine-containing regimens who are virologically suppressed should continue the regimen, regardless of CD4 count **(AIII)**.
- HIV antiretroviral drug-resistance testing is recommended for pregnant women who have detectable viremia (that is, >500–1,000 copies/mL) on therapy (see Failure of Viral Suppression) **(AI)**.

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*

HIV-Infected Pregnant Women Who Have Previously Received Antiretroviral Treatment or Prophylaxis but Are Not Currently Receiving Any Antiretroviral Medications (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• Obtain an accurate history of all prior antiretroviral (ARV) regimens used for treatment of HIV disease or prevention of transmission, including virologic efficacy, tolerance to the medications, results of prior resistance testing, and any adherence issues **(AIII)**. • If HIV RNA is above the threshold for resistance testing (that is, >500–1,000 copies/mL), ARV drug-resistance studies should be performed before starting an ARV drug regimen (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) **(AIII)**. In women who present late in pregnancy, therapy or prophylaxis should be initiated promptly without waiting for the results of resistance testing **(BIII)**. • Choose and initiate a combination ARV drug regimen based on results of resistance testing and prior history of antiretroviral therapy while avoiding drugs with teratogenic potential or with known adverse potential for the mother **(AII)**. • Consult specialists in treatment of HIV infection about the choice of a combination ARV regimen in women who previously received ARV drugs for their own health **(AIII)**. • Perform repeat ARV drug-resistance testing **(AI)**, assess adherence, and consult with an HIV treatment specialist to guide changes in ARV drugs in women who do not achieve virologic suppression on their ARV regimens (see Monitoring of the Woman and Fetus During Pregnancy).
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*

Special Situations — HIV/Hepatitis B Virus Coinfection (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations

- Screening for hepatitis B virus (HBV) infection with hepatitis B surface antigen (HBsAg), hepatitis B core antibody (anti-HBc), and hepatitis B surface antibody (anti-HBs) is recommended for all pregnant women who have not been screened during the current pregnancy **(AII)**.
- The HBV vaccine series should be administered to pregnant women who screen negative for hepatitis B (that is, HBsAg negative, anti-HBc negative, and anti-HBs negative) **(AII)**.
- Pregnant women with chronic HBV infection should be screened for antibodies to hepatitis A virus (HAV), and those who screen negative should receive the HAV vaccine series **(AII)**.
- Interferon alfa and pegylated interferon alfa are not recommended during pregnancy **(AIII)**.
- The management of HIV/HBV coinfection in pregnancy is complex and consultation with an expert in HIV and HBV is strongly recommended **(AIII)**.
- All pregnant women with HIV/HBV coinfection should receive antiretroviral therapy (ART), including a dual nucleoside reverse transcriptase inhibitor (NRTI)/nucleotide analogue reverse transcriptase inhibitor (NtRTI) backbone with two drugs active against both HIV and HBV **(AII)**. Tenofovir plus lamivudine or emtricitabine is the preferred dual NRTI/NtRTI backbone of antepartum ART in HIV/HBV-coinfected pregnant women **(AI)**.
- If antiretroviral (ARV) drugs are discontinued postpartum in women with HIV/HBV coinfection, frequent monitoring of liver function tests for potential exacerbation of HBV infection is recommended, with prompt reinitiation of treatment for both HIV and HBV if a flare is suspected **(BIII)**.
- Pregnant women with HIV/HBV coinfection receiving ARV drugs should be counseled about the signs and symptoms of liver toxicity, and liver transaminases should be assessed 1 month following initiation of ARV drugs and at least every 3 months thereafter **(BIII)**.
- Within 12 hours of birth, infants born to women with HBV infection should receive hepatitis B immune globulin and the first dose of the HBV vaccine series. The second and third doses of vaccine should be administered at ages 1 and 6 months, respectively **(AI)**.

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*

Special Situations — HIV/Hepatitis C Virus Coinfection (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations

- Screening for hepatitis C virus (HCV) infection is recommended for all HIV-infected pregnant women who have not been screened during the current pregnancy **(AIII)**.
- Interferon alfa and pegylated interferon alfa are not recommended and ribavirin is contraindicated during pregnancy **(AIII)**.
- Recommendations for antiretroviral (ARV) drug use during pregnancy are the same for women who have chronic HCV as for those without HCV coinfection **(BIII)**.
- Pregnant women with HIV/HCV coinfection receiving ARV drugs should be counseled about signs and symptoms of liver toxicity, and transaminases should be assessed 1 month following initiation of ARV drugs and then every 3 months thereafter **(BIII)**.
- Decisions concerning mode of delivery in HIV/HCV-coinfected pregnant women should be based on standard obstetric and HIV-related indications alone (see Intrapartum Care) **(BIII)**.
- Infants born to women with HIV/HCV coinfection should be evaluated for HCV infection with anti-HCV antibody testing after age 18 months **(AII)**. Infants who test positive for anti-HCV antibodies should undergo confirmatory HCV RNA testing. If earlier diagnosis is indicated or desired, HCV RNA virologic testing can be performed between ages 3 and 6 months **(AIII)**.
- Women who are found to have chronic HCV infection should also be screened for hepatitis A virus (HAV) and hepatitis B virus (HBV) because they are at increased risk of complications from those two infections. Women with chronic HCV who are negative for hepatitis A immunoglobulin G should receive the HAV vaccine series **(AIII)**. If they are not infected with HBV (that is, hepatitis B surface antigen negative, hepatitis B core antibody negative, and hepatitis B surface antibody negative), they should receive the HBV vaccine series **(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*

Special Situations — HIV-2 Infection and Pregnancy (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations

- HIV-2 infection should be suspected in pregnant women who are from—or have partners from—countries in which the disease is endemic, who are HIV antibody positive on an initial enzyme-linked immunoassay screening test, and who have repeatedly indeterminate results on HIV-1 Western blot along with HIV-1 RNA viral loads at or below the limit of detection **(BII)**.
- A regimen with two nucleoside reverse transcriptase inhibitors (NRTIs) and a boosted protease inhibitor (PI) currently is recommended for HIV-2-infected pregnant women who require treatment for their own health because they have significant clinical disease or CD4 T-lymphocyte (CD4-cell) counts <500 cells/mm^3 **(AIII)**.
    - Based on available data on safety in pregnancy, zidovudine/lamivudine plus lopinavir/ritonavir would be preferred **(AIII)**. Tenofovir plus lamivudine or emtricitabine plus lopinavir/ritonavir can be considered as an alternative **(BIII)**.
- Optimal prophylactic regimens have not been defined for HIV-2-infected pregnant women who do not require treatment for their own health (that is, CD4-cell counts >500 cells/mm^3 and no significant clinical disease). Experts have recommended the following approaches:
    - A boosted PI-based regimen (two NRTIs plus lopinavir/ritonavir) for prophylaxis, with the drugs stopped postpartum **(BIII)**; or
    - Zidovudine prophylaxis alone during pregnancy and intrapartum **(BIII)**.
- Non-nucleoside reverse transcriptase inhibitors and enfuvirtide are not active against HIV-2 and should not be used for treatment or prophylaxis **(AIII)**.
- All infants born to HIV-2-infected mothers should receive the standard 6-week zidovudine prophylactic regimen **(BIII)**.
- In the United States, breastfeeding is not recommended for infants of HIV-2-infected mothers **(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*

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*

Special Situations — Stopping Antiretroviral Drugs During Pregnancy (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• HIV-infected women receiving antiretroviral therapy (ART) who present for care during the first trimester should continue treatment during pregnancy **(AII)**. If an antiretroviral (ARV) drug regimen is stopped acutely for severe or life-threatening toxicity, severe pregnancy-induced hyperemesis unresponsive to antiemetics, or other acute illnesses that preclude oral intake, all ARV drugs should be stopped and reinitiated at the same time **(AIII)**.
• If an ARV drug regimen is being stopped electively and the patient is receiving a non-nucleoside reverse transcriptase inhibitor (NNRTI) drug, consideration should be given to either: (1) stopping the NNRTI first and continuing the other ARV drugs for a period of time or (2) switching from an NNRTI to a protease inhibitor (PI) before interruption and continuing the PI with the other ARV drugs for a period of time before electively stopping. The optimal interval between stopping an NNRTI and the other ARV drugs is unknown; at least 7 days is recommended. Given the potential for prolonged detectable efavirenz concentrations for >3 weeks in patients receiving efavirenz-based therapy, some experts recommend continuing the other ARV agents or substituting a PI plus two other agents for up to 30 days **(CIII)**.
• If nevirapine is stopped and more than 2 weeks have passed before restarting therapy, nevirapine should be restarted with the 2-week half-dose escalation period **(AII)**.
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*

Special Situations — Failure of Viral Suppression (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• If an ultrasensitive HIV RNA assay indicates failure of viral suppression (that is, detectable virus) after an adequate period of treatment: o Assess resistance and adherence **(AII)**. o Consult an HIV treatment expert **(AIII)**.
• Scheduled cesarean delivery is recommended for HIV-infected pregnant women who have HIV RNA levels >1,000 copies/mL near the time of delivery **(AII)**.
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*

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*

Pharmacokinetic Changes (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendation
• Altered dosing during pregnancy may be required for some protease inhibitors, such as lopinavir/ritonavir (see Table 5) **(AII)**
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*

Teratogenicity (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• All cases of antiretroviral (ARV) drug exposure during pregnancy should be reported to the Antiretroviral Pregnancy Registry (see details at http://www.APRegistry.com) **(AIII)**.
• Non-pregnant women of childbearing potential should undergo pregnancy testing before initiation of efavirenz and receive counseling about the potential risk to the fetus and desirability of avoiding pregnancy while on efavirenz-containing regimens **(AIII)**. o Alternate ARV regimens that do not include efavirenz should be strongly considered in women who are (1) planning to become pregnant or (2) sexually active and not using effective contraception, assuming these alternative regimens are acceptable to the provider and are not thought to compromise the woman's health **(BIII)**.
• Because the risk of neural tube defects is restricted to the first 5 to 6 weeks of pregnancy and pregnancy is rarely recognized before 4 to 6 weeks of pregnancy, and unnecessary changes in ARV drugs during pregnancy may be associated with loss of viral control and increased risk of perinatal transmission, efavirenz can be continued in pregnant women receiving an efavirenz-based regimen who present for antenatal care in the first trimester, provided the regimen produces virologic suppression (see HIV-Infected Pregnant Women Who are Currently Receiving Antiretroviral Treatment) **(CIII)**.
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*

Combination Antiretroviral Drug Regimens and Pregnancy Outcome (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendation
• Clinicians should be aware of a possible small increased risk of preterm birth in pregnant women receiving protease inhibitor (PI)-based combination antiretroviral regimens; however, given the clear benefits of such regimens for both a woman's health and prevention of mother-to-child transmission, PIs should not be withheld for fear of altering pregnancy outcome **(AII)**.
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*

Nevirapine and Hepatic/Rash Toxicity (Last updated September 14, 2011; last reviewed July 31, 2012)

Panel's Recommendations
• Nevirapine-based regimens should be initiated in women with CD4 T-lymphocyte (CD4-cell) counts >250 cells/mm^3 only if the benefits clearly outweigh the risks because of the drug's potential for causing hepatic toxicity/hypersensitivity reaction **(AII)**. • Women who become pregnant while receiving nevirapine-containing regimens and who are tolerating the regimen well can continue on the therapy regardless of CD4-cell count **(AII)**.
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*

Nucleoside Reverse Transcriptase Inhibitor Drugs and Mitochondrial Toxicity (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• The combination of stavudine and didanosine should not be prescribed during pregnancy because of reports of lactic acidosis and maternal/neonatal mortality with prolonged use in pregnancy **(AII)**. • Mitochondrial dysfunction should be considered in uninfected children with perinatal exposure to antiretroviral (ARV) drugs who present with severe clinical findings of unknown etiology, particularly neurologic findings **(AII)**. • Long-term clinical follow-up is recommended for any child with *in utero* exposure to ARV drugs **(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*

Protease Inhibitor Therapy and Hyperglycemia (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendation
• HIV-infected women taking antiretroviral drug regimens during pregnancy should undergo standard glucose screening at 24 to 28 weeks' gestation **(AIII)**. Some experts would perform earlier glucose screening in women receiving ongoing protease inhibitor-based regimens initiated before pregnancy, similar to recommendations for women with high risk factors for glucose intolerance **(BIII)**.
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*

Antiretroviral Drug Resistance and Resistance Testing in Pregnancy (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• HIV drug-resistance studies should be performed before starting or modifying antiretroviral (ARV) regimens in all pregnant women whose HIV RNA levels are above the threshold for resistance testing (that is >500–1,000 copies/mL) before initiation of ARVs **(AIII)** and for those entering pregnancy with detectable HIV RNA levels while receiving antiretroviral therapy or who have suboptimal viral suppression after starting ARVs during pregnancy **(AII)**.
• In women who present late in pregnancy, an empiric ARV regimen should be initiated promptly without waiting for the results of resistance testing, with adjustment as needed after test results are available, for optimal prevention of perinatal transmission and maternal health **(BIII)**.
• Women who have documented zidovudine resistance and are on regimens that do not include zidovudine for their own health should still receive intravenous zidovudine during labor along with their established ARV regimens if they have HIV RNA levels >400 copies/mL near delivery (see Intrapartum Antiretroviral Prophylaxis/Therapy), unless a history of hypersensitivity is documented **(AII)**.
• The optimal prophylactic regimen for newborns of women with ARV resistance is unknown (see Infant Antiretroviral Prophylaxis). Therefore, ARV prophylaxis for an infant born to a woman with known or suspected drug resistance should be determined in consultation with a pediatric HIV specialist, preferably before delivery (see Infant Antiretroviral Prophylaxis) **(AIII)**.
• HIV-infected pregnant women should be given combination ARV drug regimens to maximally suppress viral replication, which is the most effective strategy for preventing development of resistance and minimizing risk of perinatal transmission **(AII)**.
• All pregnant and postpartum women should be counseled about the importance of adherence to prescribed ARV medications to reduce the potential for development of resistance **(AII)**.
• To minimize development of resistance, pregnant women who receive a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based combination ARV regimen that is discontinued after delivery should receive either dual nucleoside analogue reverse transcriptase agents alone **(AI)** or with a protease inhibitor **(BII)** for 7 to 30 days **(AII)** after stopping the NNRTI drug. The optimal interval between stopping an NNRTI and the other ARV drugs is unknown (see Stopping Antiretroviral Therapy during Pregnancy and Postpartum Follow-Up of HIV-Infected Women).
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*

Intrapartum Care

Intrapartum Antiretroviral Therapy/Prophylaxis (Last updated July 31, 2012; last reviewed July 31, 2012

Panel's Recommendations
• Women who are receiving an antepartum combination antiretroviral (ARV) drug regimen should continue this regimen on schedule as much as possible during labor and before scheduled cesarean delivery **(AIII)**.
• Intravenous (IV) zidovudine should be administered to HIV-infected women with HIV RNA ≥400 copies/mL (or unknown HIV RNA) near delivery, regardless of antepartum regimen or mode of delivery **(AI)**. • IV zidovudine is not required for HIV-infected women receiving combination ARV regimens who have HIV RNA <400 copies/mL near delivery **(BII)**.
• For women who have received antepartum ARV drugs but have suboptimal viral suppression near delivery (that is, HIV RNA >1,000 copies/mL), scheduled cesarean delivery is recommended (see Mode of Delivery) **(AI)**. • Women whose HIV status is unknown who present in labor should undergo rapid HIV antibody testing **(AII)**. If the results are positive, a confirmatory HIV test should be done as soon as possible and maternal (IV zidovudine)/infant (combination ARV prophylaxis) ARV drugs should be initiated pending results of the confirmatory test **(AII)**. If the confirmatory HIV test is positive, infant ARV drugs should be continued for 6 weeks (see Infant Antiretroviral Prophylaxis) **(AI)**; if the test is negative, the infant ARV drugs should be stopped.
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*

Transmission and Mode of Delivery (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations

- Scheduled cesarean delivery at 38 weeks' gestation to minimize perinatal transmission of HIV is recommended for women with HIV RNA levels >1,000 copies/mL or unknown HIV levels near the time of delivery, irrespective of administration of antepartum antiretroviral (ARV) drugs **(AII)**. Scheduled cesarean delivery is not recommended for prevention of perinatal transmission in pregnant women receiving combination ARV drugs with plasma HIV RNA levels <1,000 copies/mL near the time of delivery **(BIII)**. Data are insufficient to evaluate the potential benefit of cesarean delivery used solely for prevention of perinatal transmission in women with HIV RNA levels <1,000 copies/mL, and given the low rate of transmission in these patients, it is unclear whether scheduled cesarean delivery would confer additional benefit in reducing transmission. In women with HIV RNA levels <1,000 copies/mL, cesarean delivery performed for standard obstetrical indications should be scheduled for 39 weeks' gestation.
- It is not clear whether cesarean delivery after rupture of membranes or onset of labor provides benefit in preventing perinatal transmission. Management of women originally scheduled for cesarean delivery who present with ruptured membranes or in labor must be individualized at the time of presentation based on duration of rupture and/or labor, plasma HIV RNA level, and current ARV regimen **(BII)**.
- Women should be informed of the risks associated with cesarean delivery. If the indication for cesarean delivery is prevention of perinatal transmission of HIV, the risks to a woman should be balanced with potential benefits expected for the neonate **(AII)**.

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*

Other Intrapartum Management Considerations (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• The following should generally be avoided unless there are clear obstetric indications because of a potential increased risk of transmission: o Artificial rupture of membranes **(BIII)** o Routine use of fetal scalp electrodes for fetal monitoring **(BIII)** o Operative delivery with forceps or a vacuum extractor and/or episiotomy **(BIII)**
• The antiretroviral drug regimen a woman is receiving should be taken into consideration when treating excessive postpartum bleeding resulting from uterine atony: • In women who are receiving a cytochrome P (CYP) 3A4 enzyme inhibitor such as a protease inhibitor, methergine should be used only if no alternative treatments for postpartum hemorrhage are available and the need for pharmacologic treatment outweighs the risks. If methergine is used, it should be administered in the lowest effective dose for the shortest possible duration **(BIII)**. • In women who are receiving a CYP3A4 enzyme inducer such as nevirapine, efavirenz, or etravirine, additional uterotonic agents may be needed because of the potential for decreased methergine levels and inadequate treatment effect.
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*

Postpartum Care

Postpartum Follow-Up of HIV-Infected Women (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• Contraceptive counseling should be included in the prenatal period as well as immediately postpartum as a critical aspect of postpartum care **(AIII)**.
• Decisions about continuing antiretroviral (ARV) drugs after delivery should take into account current recommendations for initiation of antiretroviral therapy (ART), current and nadir CD4 T-lymphocyte counts and trajectory, HIV RNA levels, adherence issues, whether a woman has an HIV-uninfected sexual partner, and patient preference **(AIII)**.
• For women continuing ARV drugs postpartum, arrangements for new or continued supportive services should be made before hospital discharge because the immediate postpartum period poses unique challenges to adherence **(AII)**.
• Women with a positive rapid HIV antibody test during labor require immediate linkage to HIV care and comprehensive follow-up, including confirmation of HIV infection. If infection is confirmed, a full health assessment is warranted, including evaluation for associated medical conditions, counseling related to newly diagnosed HIV infection, and assessment of need for ART and opportunistic infection prophylaxis **(AII)**.
• Breastfeeding is not recommended for HIV-infected women in the United States, including those receiving ART **(AII)**.
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*

Infants Born to Mothers with Unknown HIV Infection Status (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• For infants born to mothers with unknown HIV status, rapid HIV antibody testing of mothers and/or infants is recommended as soon as possible after birth, with immediate initiation of infant antiretroviral (ARV) prophylaxis (see Infant Antiretroviral Prophylaxis) if the rapid test is positive **(AII)**.
• In the setting of a positive test, standard antibody confirmatory testing such as a Western blot also should be performed on mothers (or their infants) as soon as possible. Clinicians should not wait for the results of the confirmatory test before initiating postnatal prophylaxis. If the confirmatory test is negative, ARV prophylaxis can be discontinued **(AIII)**.
• If the HIV antibody confirmatory test is positive, a newborn HIV DNA polymerase chain reaction (PCR) assay should be performed **(AIII)**.
• If the newborn HIV DNA PCR is positive, ARV prophylaxis should be discontinued and the infant promptly referred to a pediatric HIV specialist for confirmation of the diagnosis and treatment of HIV infection with standard combination antiretroviral therapy **(AI)**.
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*

Infant Antiretroviral Prophylaxis (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• The 6-week neonatal component of the zidovudine chemoprophylaxis regimen is recommended for all HIV-exposed neonates to reduce perinatal transmission of HIV **(AI)**.
• Zidovudine, at gestational age-appropriate doses, should be initiated as close to the time of birth as possible, preferably within 6 to 12 hours of delivery **(AII)**.
• Infants born to HIV-infected women who have not received antepartum antiretroviral (ARV) drugs should receive prophylaxis with zidovudine given for 6 weeks combined with three doses of nevirapine in the first week of life (at birth, 48 hours later, and 96 hours after the second dose), begun as soon after birth as possible **(AI)**.
• In other scenarios, the decision to combine other drugs with the 6-week zidovudine regimen should be made in consultation with a pediatric HIV specialist, preferably before delivery, and should be accompanied by counseling of the mother on the potential risks and benefits of this approach **(BIII)**.
• In the United States, the use of ARV drugs other than zidovudine and nevirapine cannot be recommended in premature infants because of lack of dosing and safety data **(BIII)**.
• The National Perinatal HIV Hotline (1-888-448-8765) provides free clinical consultation on all aspects of perinatal HIV, including infant care.
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*

Initial Postnatal Management of the HIV-Exposed Neonate (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• A complete blood count and differential should be performed on newborns as a baseline evaluation **(BIII)**.
• Decisions about the timing of subsequent monitoring of hematologic parameters in infants depend on baseline hematologic values, gestational age at birth, clinical condition of the infants, the zidovudine dose being administered, receipt of other ARV drugs and concomitant medications, and maternal antepartum ARV therapy **(CIII)**.
• If hematologic abnormalities are identified in infants receiving prophylaxis, decisions on whether to continue infant antiretroviral (ARV) prophylaxis need to be individualized. Consultation with an expert in pediatric HIV infection is advised if early discontinuation of prophylaxis is considered **(CIII)**.
• Some experts recommend more intensive monitoring of hematologic and serum chemistry and liver function assays at birth and when diagnostic HIV polymerase chain reaction tests are obtained in infants exposed to combination ARV drug regimens *in utero* or during the neonatal period **(CIII)**.
• A recheck of hemoglobin and neutrophil counts is recommended 4 weeks after initiation of prophylaxis for infants who receive combination zidovudine/lamivudine-containing ARV prophylaxis regimens **(AI)**.
• Routine measurement of serum lactate is not recommended. However, measurement can be considered if an infant develops severe clinical symptoms of unknown etiology (particularly neurologic symptoms) **(CIII)**.
• Virologic tests are required to diagnose HIV infection in infants <18 months of age and should be performed within the first 14 to 21 days of life, at 1 to 2 months, and at 4 to 6 months of age **(AII)**.
• To prevent *Pneumocystis jirovecii* pneumonia (PCP), all infants born to women with HIV infection should begin PCP prophylaxis at ages 4 to 6 weeks, after completing their ARV prophylaxis regimen, unless there is adequate test information to presumptively exclude HIV infection (see USPHS/IDSA Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Exposed and Infected Children) **(AII)**.
• Health care providers should routinely inquire about premastication of foods fed to infants, instruct HIV-infected caregivers to avoid this practice, and advise on safer feeding options **(AII)**.
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*

Long-Term Follow-Up of Antiretroviral Drug-Exposed Infants (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• Children with *in utero*/neonatal exposure to antiretroviral (ARV) drugs who develop significant organ system abnormalities of unknown etiology, particularly of the nervous system or heart, should be evaluated for potential mitochondrial dysfunction **(CIII)**. • Follow-up of children with exposure to ARVs should continue into adulthood because of the theoretical concerns regarding the potential for carcinogenicity of nucleoside analogue ARV drugs **(CIII)**.
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*