



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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Preconception Counseling and Care for HIV-Infected Women of Childbearing Age (Last updated March 28, 2014; last reviewed March 28, 2014)

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).
- All HIV-infected women contemplating pregnancy should be on a maximally suppressive antiretroviral regimen (AII).
- When selecting or evaluating combination antiretroviral therapy (cART) for HIV-infected women of childbearing age, consider a regimen's effectiveness, a woman's hepatitis B virus disease status, teratogenic potential of the drugs in the cART regimen, should pregnancy occur, and possible adverse outcomes for the 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 March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

For Couples who Want to Conceive

For Both Concordant (Both Partners are HIV-Infected)/Discordant Couples:

- Expert consultation is recommended so that approaches can be tailored to specific needs, which may vary from couple to couple (AIII).
- Partners should be screened and treated for genital tract infections before attempting to conceive (AII).
- The HIV-infected partner should attain maximum viral suppression before attempting conception (AIII).

For Discordant Couples:

- Combination antiretroviral therapy (cART) for the infected partner may not be fully protective against sexual transmission of HIV.
- 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 cART and has a suppressed viral load has not been studied.

Discordant Couples with HIV-Infected Female:

- The safest conception option is artificial insemination, including the option of self-insemination with a partner's sperm during the peri-ovulatory period (AIII).

Discordant Couples with HIV-Infected Male:

- The use of donor sperm from an HIV-uninfected male with artificial insemination is the safest option.
- When the use of donor sperm is unacceptable, the use of sperm preparation techniques coupled with either intrauterine insemination or *in vitro* fertilization should be considered (AII).
- Semen analysis is recommended for HIV-infected males before conception is attempted to prevent unnecessary exposure to infectious genital fluid when the likelihood of getting pregnant is low because of semen abnormalities (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

Antepartum Care (Last updated March 28, 2014; last reviewed March 28, 2014)

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 combination antiretroviral therapy (cART) or the need for any modification if currently receiving cART (**AIII**). The National Perinatal HIV Hotline (1-888-448-8765) provides free clinical consultation on all aspects of perinatal HIV care.
- All pregnant HIV-infected women should receive cART to prevent perinatal transmission regardless of plasma HIV RNA copy number or CD4 T lymphocyte count (**AI**).
- Combined antepartum, intrapartum, and infant antiretroviral (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 (**AI**).
- The known benefits and potential risks of ARV use during pregnancy should be discussed with all **HIV-infected** women (**AIII**).
- In counseling patients, the importance of adherence to their ARV regimens should be emphasized (**AI**).
- 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**). When HIV is diagnosed later in pregnancy, cART should be initiated promptly without waiting for results of resistance testing (**BIII**).
- Coordination of services among prenatal care providers, primary care and HIV specialty care providers, **and when appropriate**, 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

Teratogenicity (Last updated March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- All cases of antiretroviral (ARV) drug exposure during pregnancy should be reported to the Antiretroviral Pregnancy Registry (see <http://www.APRegistry.com>) (**AIII**).
- Nonpregnant 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**).
 - Alternate ARV regimens that do not include efavirenz should be strongly considered in women who are planning to become pregnant or are 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

Nevirapine and Hepatic/Rash Toxicity (Last updated March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- Nevirapine-based regimens should be initiated in women with CD4 T lymphocyte (CD4) cell counts >250 cells/mm³ 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 March 28, 2014; last reviewed March 28, 2014)

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

Combination Antiretroviral Drug Regimens and Pregnancy Outcome

(Last updated March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

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

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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

Recommendations for Use of Antiretroviral Drugs during Pregnancy (Last updated March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- In general, the same regimens as recommended for treatment of non-pregnant adults should be used in pregnant women unless there are known adverse effects for women, fetuses or infants that outweigh benefits **(AII)**.
- Multiple factors must be considered when choosing a regimen for a pregnant woman including comorbidities, convenience, adverse effects, drug interactions, resistance testing results, pharmacokinetics (PK), and experience with use in pregnancy **(AIII)**.
- PK changes in pregnancy may lead to lower plasma levels of drugs and necessitate increased dosages, more frequent dosing, or boosting, especially of protease inhibitors **(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 Have Never Received Antiretroviral Drugs (Antiretroviral Naive) (Last updated March 28, 2014; last reviewed March 28, 2014)

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 (see [Table 6](#) and [Table 7](#)).
- 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 count, HIV RNA levels, and maternal conditions (e.g., 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.
- ARV drug-resistance studies should be performed before starting the ARV regimen if HIV RNA is above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL) unless drug-resistance studies have already been performed (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)**.
- If there is no evidence of resistance, combination ARV regimens that are preferred for the treatment of antiretroviral-naive HIV-infected pregnant women include: a dual nucleoside reverse transcriptase inhibitor combination (abacavir/lamivudine, tenofovir/emtricitabine or lamivudine, or zidovudine/lamivudine) and either a ritonavir-boosted protease inhibitor (ritonavir-boosted atazanavir or ritonavir-boosted lopinavir) or a non-nucleoside reverse transcriptase inhibitor (efavirenz initiated after 8 weeks of pregnancy) (see [Table 6](#)) **(AIII)**.

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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 March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- In general, HIV-infected **pregnant** women receiving combination antiretroviral therapy (cART) who present for care during the first trimester should continue treatment during pregnancy, assuming the regimen is tolerated and effective in suppressing viral replication (**HIV-1 viral load less than lower limits of detection of the assay**) (**AII**).
- The Panel recommends that efavirenz be continued in pregnant women receiving efavirenz-based cART who present for antenatal care in the first trimester provided the regimen is **achieving** virologic suppression (see text below) (**CIII**).
- HIV antiretroviral drug-resistance testing is recommended for pregnant women who have detectable viremia (i.e., >500 to 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 March 28, 2014; last reviewed March 28, 2014)

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 (i.e., >500 to 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 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

Monitoring of the Woman and Fetus During Pregnancy (Last updated March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- Plasma HIV RNA levels should be monitored at the initial visit (**A1**); 2 to 4 weeks after initiating (or changing) antiretroviral (ARV) drug regimens (**B1**); 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 (**A1**) and at least every 3 months during pregnancy (**BIII**). Monitoring of CD4 cell count can be performed every 6 months in patients on combination ARV therapy (cART) with consistently suppressed viral load who have immune reconstitution (CD4 count increase well above threshold for opportunistic infection risk) related to use of the regimen (**CIII**).
- Genotypic ARV drug-resistance testing should be performed at baseline in all HIV-infected pregnant women with HIV RNA levels above the threshold for resistance testing (that is, >500 to 1,000 copies/mL), whether they are ARV-naive or currently on therapy (**AIII**). However, it is not necessary to repeat a genotype in pregnancy if the woman already had a genotype prior to pregnancy and was ARV-naive. Repeat testing is indicated following initiation of an ARV regimen in women who have suboptimal viral suppression or who have persistent 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**).
- HIV-infected women taking cART 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**).
- Early 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 cART, 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 cART 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

Antiretroviral Drug Resistance and Resistance Testing in Pregnancy (Last updated March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- HIV drug-resistance studies should be performed before starting antiretroviral (ARV) regimens in all ARV-naïve pregnant women whose HIV RNA levels are above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL) unless they have already been tested for ARV resistance (AIII).
- HIV drug-resistance studies should be performed before modifying ARV regimens for those entering pregnancy with detectable HIV RNA levels that are above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL) while receiving ARV drugs or who have suboptimal viral suppression after starting ARV drugs 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 >1,000 copies/mL near delivery (see [Intrapartum Antiretroviral Therapy/ Prophylaxis](#)), unless a history of hypersensitivity is documented (AII).
- The optimal prophylactic regimen for newborns of women with ARV resistance is unknown. 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 therapy (cART) 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 inhibitor 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 Drugs 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

Failure of Viral Suppression (Last updated March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- If an ultrasensitive HIV RNA assay indicates failure of viral suppression (that is, persistent HIV viral load >20 to 75 copies/mL, depending on the assay used) after an adequate period of treatment:
 - Assess resistance and adherence (**AII**).
 - 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

Stopping Antiretroviral Drugs during Pregnancy (Last updated March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- HIV-infected women receiving combination antiretroviral therapy 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 for non-life-threatening reasons and the patient is receiving a non-nucleoside reverse transcriptase inhibitor (NNRTI), consideration should be given to either:
 - Stopping the NNRTI first and continuing the other ARV drugs for a period of time; or
 - 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 2 other agents for up to 30 days after stopping the NNRTI drug (**CIII**).
- If nevirapine is stopped and more than 7 days 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

HIV/Hepatitis B Virus Coinfection (Last updated March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- All HIV-infected pregnant women should be screened during pregnancy for hepatitis B virus (HBV) and hepatitis C virus (HCV), unless they are known to be coinfecting or have already been screened during the current pregnancy (see [HIV/Hepatitis C Virus Coinfection](#)) (AIII).
- All pregnant women who screen negative for HBV (i.e., HBV surface antigen [HBsAg]-negative, HBV core antibody-negative, and HBV surface antibody [anti-HBs]-negative) should receive the HBV vaccine series (AII).
- Women with chronic HBV infection should also be screened for hepatitis A virus (HAV) because they are at increased risk of complications from coinfection with other viral hepatitis infections (AIII).
- Women with chronic HBV infection who are negative for hepatitis A immunoglobulin G should receive the HAV vaccine series (AII).
- The management of HIV/HBV coinfection in pregnancy is complex and consultation with an expert in HIV and HBV is strongly recommended (AIII).
- Interferon alfa and pegylated interferon alfa are not recommended during pregnancy (AII).
- All pregnant women with HIV/HBV coinfection should receive combination antiretroviral therapy (cART), 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 NtRTI/NRTI backbone of antepartum cART in HIV/HBV-coinfecting pregnant women (AI).
- Pregnant women with HIV/HBV coinfection receiving antiretroviral (ARV) drugs should be counseled about 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 during pregnancy (BIII).
- If 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).
- Decisions concerning mode of delivery in HIV/HBV-coinfecting pregnant women should be based on standard obstetric and HIV-related indications alone (see [Intrapartum Care](#)) (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). Post-vaccination testing for anti-HBs and HBsAg should be performed after completion of the vaccine series, at age 9 months to 18 months.

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/Hepatitis C Virus Coinfection (Last updated March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- All HIV-infected pregnant women should be screened during pregnancy for hepatitis B virus (HBV) and hepatitis C virus (HCV), unless they are known to be coinfecting or have already been screened during the current pregnancy (see [HIV/Hepatitis B Virus Coinfection section](#)) (AIII).
- Screening for HCV infection should use the most sensitive immunoassays licensed for detection of antibody to HCV (anti-HCV) in blood (AIII).
- All pregnant women who screen negative for HBV (i.e., HBV surface antigen negative, HBV core antibody negative, and HBV surface antibody negative) should receive the HBV vaccine series (AII).
- Women with chronic HCV infection should also be screened for hepatitis A virus (HAV) because they are at increased risk of complications from coinfection with other viral hepatitis infections (AIII).
- Women with chronic HCV who are negative for hepatitis A immunoglobulin G should receive the HAV vaccine series (AII).
- The management of HIV/HCV coinfection in pregnancy is complex, given currently approved medications for HCV. If considering treatment of HCV in an HIV coinfecting pregnant woman, consultation with an expert in HIV and HCV is strongly recommended (AIII).
- Interferon alfa and pegylated interferon alfa are not recommended and ribavirin is contraindicated during pregnancy (AII).
- Recommendations for antiretroviral (ARV) drug use during pregnancy are the same for HIV-infected 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 liver transaminases should be assessed 1 month following initiation of ARV drugs and at least every 3 months thereafter during pregnancy (BIII).
- Decisions concerning mode of delivery in HIV/HCV-coinfecting 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 screen positive should undergo confirmatory HCV RNA testing. HCV RNA virologic testing can be done after age 2 months, if earlier diagnosis is indicated (AIII). Because HCV viremia can be intermittent, two negative HCV RNA tests at or after age 2 months, including one at or after age 12 months, are needed to definitively exclude HCV infection (BIII). Children are considered to be HCV-infected if they have two or more positive HCV RNA results or are HCV antibody-positive beyond age 18 months (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-2 Infection and Pregnancy (Last updated March 28, 2014; last reviewed March 28, 2014)

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/mm³ **(AIII)**.
- Lopinavir/ritonavir plus zidovudine/lamivudine or abacavir/lamivudine or tenofovir/emtricitabine is the preferred ART regimen for HIV-2-infected pregnant women who require treatment, based on safety data on use of these drugs in HIV-1-infected pregnant women **(AIII)**.
- Optimal prophylactic regimens have not been defined for HIV-2-infected pregnant women who do not require treatment for their own health (i.e., CD4 cell counts >500 cells/mm³ and no significant clinical disease). Experts have recommended the following approaches:
 - A boosted PI-based regimen (two NRTIs plus ritonavir-boosted lopinavir) 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, where safe infant formula is readily available, 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

Acute HIV Infection (Last updated March 28, 2014; last reviewed March 28, 2014)

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 [Adult and Adolescent Antiretroviral Guidelines](#)) (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 **acquiring** 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 perinatal 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

Intrapartum Care (Last updated March 28, 2014; last reviewed March 28, 2014)

Intrapartum Antiretroviral Therapy/Prophylaxis

Panel's Recommendations

- Women should continue their antepartum combination antiretroviral (ARV) drug 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 **>1,000** copies/mL (or unknown HIV RNA) near delivery (AI), but is not required for HIV-infected women receiving combination ARV regimens who have HIV RNA **≤1,000** copies/mL **consistently during late pregnancy and near delivery and no concerns regarding adherence to the regimen** (BII).
- For women who have suboptimal viral suppression near delivery (i.e., HIV RNA >1,000 copies/mL), scheduled cesarean delivery is recommended (see [Transmission and 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 **confirmatory HIV** 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 March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- Scheduled cesarean delivery at 38 weeks' gestation to minimize perinatal transmission of HIV is recommended for women with HIV RNA levels >1000 copies/mL or unknown HIV levels near the time of delivery, irrespective of administration of antepartum antiretroviral drugs (**AII**). Data are insufficient to evaluate the potential benefit of cesarean delivery used solely for prevention of perinatal transmission in women receiving combination antiretroviral therapy with HIV RNA levels ≤1000 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 (**BIII**). In women with HIV RNA levels ≤1000 copies/mL, cesarean delivery performed for standard obstetrical indications should be scheduled at 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 antiretroviral 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 March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- The following should generally be avoided because of a potential increased risk of transmission, unless there are clear obstetric indications:
 - Artificial rupture of membranes (**BIII**)
 - Routine use of fetal scalp electrodes for fetal monitoring (**BIII**)
 - 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 (Last updated March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- Decisions regarding continuing combination antiretroviral therapy (cART) after delivery should be made in consultation with the woman and her HIV provider, ideally before delivery (**AIII**). cART is currently recommended for all HIV-infected individuals to reduce the risk of disease progression and to prevent HIV sexual transmission, although the strength and evidence for this recommendation varies by pre-treatment CD4 T lymphocyte (CD4) count. Decisions should take into account current recommendations for initiation of cART in adults, pre-treatment CD4 cell counts and trajectory, HIV RNA levels, adherence issues, whether a woman has an HIV-uninfected sexual partner, and patient preference.
- For women continuing cART 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**).
- Contraceptive counseling should be a critical aspect of postpartum care (**AIII**).
- 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 cART and opportunistic infection prophylaxis (**AII**).
- Breastfeeding is not recommended for HIV-infected women in the United States, including those receiving cART (**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

Infant Antiretroviral Prophylaxis (Last Updated March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- The 6-week neonatal component of the zidovudine chemoprophylaxis regimen is generally recommended for all HIV-exposed neonates to reduce perinatal transmission of HIV (AI). However, a 4-week neonatal chemoprophylaxis regimen can be considered when the mother has received standard combination antiretroviral therapy (cART) during pregnancy with consistent viral suppression and there are no concerns related to maternal adherence (BII).
- 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 (AI).
- Infants born to HIV-infected women who have not received cART should receive prophylaxis with zidovudine given for 6 weeks combined with three doses of nevirapine in the first week of life (i.e., 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 maternal counseling on the potential risks and benefits of this approach (BIII).
- For infants born to mothers with unknown HIV status, expedited (rapid) HIV testing of mothers and/or infants is recommended as soon as possible, either during labor or after birth, with immediate initiation of infant antiretroviral (ARV) prophylaxis if the initial expedited test is positive (AI). If supplemental testing is negative, ARV prophylaxis can be discontinued.
- In the United States, the use of ARV drugs other than zidovudine and nevirapine cannot be recommended in premature infants as prophylaxis to prevent transmission 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 March 28, 2014; last reviewed March 28, 2014)

Panel's Recommendations

- A complete blood count and differential should be performed on newborns as a baseline evaluation (**BIII**).
- 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**).
- 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 therapy (**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 (**A**).
- 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 aged <18 months and should be performed within the first 14 to 21 days of life and at age 1 to 2 months and age 4 to 6 months (**AII**).
- To prevent *Pneumocystis jirovecii* pneumonia (PCP), all infants born to HIV-infected women 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 the [Pediatric Opportunistic Infections Guidelines](#)) (**AII**).
- Health care providers should routinely inquire about premastication, 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 March 28, 2014; last reviewed March 28, 2014)

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