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 August 6, 2015; last reviewed August 6, 2015)

Panel's Recommendations
• Discuss childbearing intentions with all women of childbearing age on an ongoing basis throughout the course of their care **(AIII)**.
• Provide 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 **(AII)**.
• All HIV-infected women contemplating pregnancy should be receiving combination antiretroviral therapy (cART) and have a plasma viral load below the limit of detection prior to conception **(AII)**.
• When selecting or evaluating cART for HIV-infected women of childbearing age, consider a regimen's effectiveness, a woman's hepatitis B status, teratogenic potential of the drugs in the cART regimen, and possible adverse outcomes for the mother and fetus **(AII)**.
• HIV infection does not preclude the use of any contraceptive method **(AII)**. However, drug-drug interactions between hormonal contraceptives and cART should be taken into account.
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 August 6, 2015; last reviewed August 6, 2015)

Panel's Recommendations
For Couples Who Want to Conceive *For Concordant (Both Partners are HIV-Infected) and Discordant Couples:* • Expert consultation is recommended so that approaches can be tailored to couples' specific needs **(AIII)**. • Partners should be screened and treated for genital tract infections before attempting to conceive **(AII)**. • The HIV-infected partner(s) should attain maximum viral suppression before attempting conception **(AIII)**. *For Discordant Couples:* • The HIV-infected partner should be receiving combination antiretroviral therapy and demonstrate sustained suppression of plasma viral load below the limits of detection **(AI)**. • Periconception administration of antiretroviral pre-exposure prophylaxis for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission **(CIII)**. The utility of pre-exposure prophylaxis for the uninfected partner when the infected partner is receiving combination antiretroviral therapy with maximal viral suppression has not been studied. *Discordant Couples with HIV-Infected Women:* • 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 Men:* • The use of donor sperm from an HIV-uninfected man with artificial insemination is the safest option **(AIII)**. • 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 men before conception is attempted to prevent unnecessary exposure to infectious genital fluid when the likelihood of conception 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 August 6, 2015; last reviewed August 6, 2015)

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 (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)**. The goal of cART is to maintain a viral load below the limit of detection throughout pregnancy.
- Combined antepartum, intrapartum, and infant antiretroviral prophylaxis is recommended because antiretroviral 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 all medication use, including antiretroviral use, during pregnancy should be discussed with all HIV-infected women **(AIII)**.
- The importance of adherence to antiretroviral regimens should be emphasized in patient counseling **(AII)**.
- Antiretroviral drug-resistance studies should be performed before starting or modifying ARV drug regimens in women whose HIV RNA levels are above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL) (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) **(AIII)**. In pregnant women not already receiving cART, consideration should be given to initiating cART before results of drug-resistance testing are available because earlier viral suppression has been associated with lower risk of transmission. If cART is initiated before results are available, the regimen should be modified, if necessary, based on resistance assay results **(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 antiretroviral 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 August 6, 2015; last reviewed August 6, 2015)

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)**.
- 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)**.
  - Alternate ARV regimens that do not include efavirenz should be considered in women who are planning to become pregnant or are sexually active and not using effective contraception, assuming these alternative regimens are not thought to compromise a woman's health **(BIII)**.
- Efavirenz can be continued in women receiving an efavirenz-based regimen who present for antenatal care in the first trimester, because the risk of neural tube defects is restricted to the first 5 to 6 weeks of pregnancy. Pregnancy is rarely recognized before 5 to 6 weeks, and unnecessary changes in ARV drugs during pregnancy may be associated with loss of viral control and increased risk of perinatal transmission. In such situations, fetal ultrasound is recommended at 18 to 20 weeks to assess anatomy (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 August 6, 2015; last reviewed August 6, 2015)

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 the prevention of perinatal 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*

Recommendations for Use of Antiretroviral Drugs during Pregnancy (Last updated August 6, 2015; last reviewed August 6, 2015)

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, and experience with use in pregnancy **(AIII)**.
• Pharmacokinetic 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 August 6, 2015; last reviewed August 6, 2015)

Panel's Recommendations
• All HIV-infected pregnant women should receive combination antiretroviral therapy (cART) 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).
• Consideration should be given to initiating cART as soon as HIV is diagnosed during pregnancy; earlier viral suppression is associated with lower risk of transmission. This decision may be influenced by CD4 T lymphocyte count, HIV RNA levels, and maternal conditions (e.g., nausea and vomiting) **(AIII)**. The benefits of early cART must be weighed against potential fetal effects of drug exposure.
• Antiretroviral drug-resistance studies should be performed to guide selection of antiretroviral regimens in women whose HIV RNA levels are 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 cART is initiated before the results of the drug-resistance assays are available, the antiretroviral regimen should be modified, if necessary, based on the resistance assay results **(BIII)**.
• If there is no evidence of resistance, cART 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 disoproxil fumarate/emtricitabine or lamivudine, or zidovudine/lamivudine) and either a ritonavir-boosted protease inhibitor (atazanavir/ritonavir or darunavir/ritonavir), a non-nucleoside reverse transcriptase inhibitor (efavirenz initiated after 8 weeks of pregnancy), or an integrase inhibitor (raltegravir) (see Table 6) **(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 Are Currently Receiving Antiretroviral Therapy (Last updated August 6, 2015; last reviewed August 6, 2015)

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 **(CIII)**.
• HIV antiretroviral drug-resistance testing should be performed to assist in the selection of active drugs when changing antiretroviral regimens in pregnant women on therapy with virologic failure and HIV RNA levels >1,000 copies/mL **(AI)**. In individuals with HIV RNA levels >500 but <1,000 copies/mL, testing may be unsuccessful but should still be considered **(BII)** (see Lack of Viral Suppression).
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 August 6, 2015; last reviewed August 6, 2015)

Panel's Recommendations
• Obtain an accurate history of all prior antiretroviral 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 copies/mL), antiretroviral drug-resistance studies should be performed before starting an antiretroviral drug regimen (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) **(AI)**.
• Consideration should be given to initiating combination antiretroviral therapy (cART) prior to receiving results of antiretroviral drug-resistance studies in light of data demonstrating an association between earlier viral suppression and lower risk of HIV transmission. The antiretroviral regimen should be modified based on the results of the resistance assay, if necessary **(BIII)**.
• Choose and initiate a cART regimen based on results of resistance testing if available and prior history of cART while avoiding drugs with known adverse potential for the mother or fetus/infant **(AII)**.
• Consider obtaining a consultation with specialists in treatment of HIV infection about the choice of a cART regimen in women who previously received antiretroviral drugs **(BIII)**.
• Perform repeat antiretroviral 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 antiretroviral regimens **(AIII)** (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 August 6, 2015; last reviewed August 6, 2015)

Panel's Recommendations
• Plasma HIV RNA levels should be monitored at the initial visit **(AI)**; 2 to 4 weeks after initiating (or changing) antiretroviral 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) and to inform decisions about optimal treatment of the newborn (see Infant ARV Prophylaxis) **(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 combination antiretroviral therapy (cART) with consistently suppressed viral load who have CD4 counts well above the threshold for opportunistic infection risk) **(CIII)**.
• Genotypic antiretroviral drug-resistance testing should be performed at baseline in all HIV-infected pregnant women with HIV RNA levels >1,000 copies/mL **(AI)**. In individuals with HIV RNA levels >500 but <1,000 copies/mL, testing may be unsuccessful but should still be considered **(BII)**. Tests should be performed whether the women are antiretroviral-naive or currently on therapy **(AIII)**.
• HIV drug-resistance studies should be performed before modifying antiretroviral 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 antiretroviral drugs. They should also be performed on women who have suboptimal viral suppression after starting ARV drugs during pregnancy **(AII)**.
• Monitoring for complications of antiretroviral 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 risk factors for glucose intolerance **(BIII)**. For further information on protease inhibitors see Combination Antiretroviral Drug Regimens and Pregnancy Outcome.
• 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. Amniocentesis should be performed on HIV-infected women only after initiation of an effective cART regimen and, ideally, 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 **(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 August 6, 2015; last reviewed August 6, 2015)

Panel's Recommendations
• HIV drug-resistance studies should be performed before starting antiretroviral (ARV) regimens in all ARV-naive 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 virologic response to ARV drugs started during pregnancy **(AII)**.
• Combination antiretroviral therapy (cART) should be initiated in pregnant women prior to receiving results of ARV-resistance studies. The ARV regimen should be modified, if necessary, based on the results of the resistance assay **(BIII)**.
• Documented zidovudine resistance does not affect the indications for use of intrapartum zidovudine **(BIII)**.
• 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 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 cART 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*

Lack of Viral Suppression (Last updated August 6, 2015; last reviewed August 6, 2015)

Panel's Recommendations
• Because maternal antenatal viral load correlates with risk of perinatal transmission of HIV, suppression of HIV RNA to undetectable levels should be achieved as rapidly as possible **(AII)**.
• If an ultrasensitive HIV RNA assay indicates failure of viral suppression (after an adequate period of treatment):
◦ Assess adherence and resistance (if HIV RNA level is high enough for resistance testing) **(AII)**.
◦ Consult an HIV treatment expert and consider possible antiretroviral regimen modification **(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 August 6, 2015; last reviewed August 6, 2015)

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 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 antiretroviral drugs should be stopped simultaneously and ARV therapy should be reinitiated as soon as possible **(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/Hepatitis B Virus Coinfection (Last updated August 6, 2015; last reviewed August 6, 2015)

Panel's Recommendations
• All HIV-infected pregnant women should be screened during the current pregnancy for hepatitis B virus (HBV) and hepatitis C virus, unless they are known to be coinfected (see HIV/Hepatitis C Virus Coinfection) **(AIII)**.
• All HIV-infected 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 HBV infection who have not already received the hepatitis A virus (HAV) vaccine series should be screened for immunity to HAV because they are at increased risk of complications from coinfection with other viral hepatitis infections **(AIII)**.
• Women with chronic HBV infection who are hepatitis A immunoglobulin G antibody-negative should receive the HAV vaccine series if they have never received it **(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). Antepartum cART in HIV/HBV-coinfected pregnant women should include tenofovir disoproxil fumarate plus lamivudine or emtricitabine **(AI)**.
• Pregnant women with HIV/HBV coinfection receiving antiretroviral drugs should be counseled about signs and symptoms of liver toxicity, and liver transaminases should be assessed 1 month following initiation of antiretroviral drugs and at least every 3 months thereafter during pregnancy **(BIII)**.
• If antiretroviral 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 re-initiation of treatment for both HIV and HBV if a flare is suspected **(BIII)**.
• Decisions concerning mode of delivery in HIV/HBV-coinfected pregnant women should be based on standard obstetric and HIV-related indications alone; HBV coinfection does not necessitate cesarean delivery, if not otherwise indicated (see Intrapartum Care) **(AIII)**.
• Within 12 hours of birth, infants born to women with HBV infection should receive hepatitis B immune globulin and should initiate the HBV vaccine series **(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/Hepatitis C Virus Coinfection (Last updated August 6, 2015; last reviewed August 6, 2015)

Panel's Recommendations

- All HIV-infected pregnant women should be screened during the current pregnancy for hepatitis B virus (HBV) and hepatitis C virus (HCV), unless they are known to be coinfected (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 HIV-infected 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 HBV or 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 if they have never received it **(AII)**.
- The management of HIV/HCV coinfection in pregnancy is complex because currently approved medications for HCV are not recommended during pregnancy, and no safety data exist for use of the recently approved HCV oral medications in pregnant women **(AIII)**. If considering treatment of HCV in an HIV-coinfected 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 drug use during pregnancy are the same for HIV-infected women whether or not they have chronic HCV **(BIII)**.
- Pregnant women with HIV/HCV coinfection receiving antiretroviral drugs should be counseled about signs and symptoms of liver toxicity, and liver transaminases should be assessed 1 month following initiation of antiretroviral drugs and at least every 3 months thereafter during pregnancy **(BIII)**.
- Decisions concerning mode of delivery in HIV/HCV-coinfected pregnant women should be based on standard obstetric and HIV-related indications alone; HCV coinfection does not necessitate cesarean delivery, if not otherwise indicated (see Intrapartum Care) **(AIII)**.
- 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. If earlier diagnosis is desired, HCV RNA virologic testing can be done after age 2 months **(AIII)**. Because HCV viremia can be intermittent, 2 negative HCV RNA tests at or after age 2 months, including 1 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 at any age, 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 August 6, 2015; last reviewed August 6, 2015)

Panel's Recommendations
• HIV-2 infection should be considered in pregnant women who are from—or have partners from—countries in which the disease is endemic and who have positive results on an HIV-1/HIV-2 antibody or HIV-1/HIV-2 antigen/antibody immunoassay. They should be tested with a supplemental HIV-1/HIV-2 antibody differentiation assay. If they are indeed HIV-2 infected it would show negative HIV-1 antibodies and positive HIV-2 antibodies **(AII)**.
• A regimen with two nucleoside reverse transcriptase inhibitors and a boosted protease inhibitor 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 cell (CD4) counts <500 cells/mm^3 **(AIII)**.
• Lopinavir/ritonavir plus zidovudine/lamivudine or abacavir/lamivudine or tenofovir disoproxil fumarate/emtricitabine is the preferred combination antiretroviral therapy regimen for HIV-2-infected pregnant women who require treatment **(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 counts >500 cells/mm^3 and no significant clinical disease). Experts have recommended the following approaches:
  • A boosted protease inhibitor-based regimen (two nucleoside reverse transcriptase inhibitors 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, 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 August 6, 2015; last reviewed August 6, 2015)

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 a routine HIV antibody screening test or an antigen/antibody immunoassay test (see Identifying, Diagnosing, and Managing Acute HIV-1 Infection in the Adult and Adolescent Antiretroviral Guidelines, http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf) **(AII)**.
• Repeat HIV 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 and http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf) **(AII)**.
• All pregnant women with acute or recent HIV infection should start a combination antiretroviral 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 antiretroviral regimen, and the antiretroviral 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 antiretroviral-naive individuals, 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 August 6, 2015; last reviewed August 6, 2015)

Intrapartum Antiretroviral Therapy/Prophylaxis

Panel's Recommendations
• Women should continue their antepartum combination antiretroviral therapy (cART) 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 cART regimens who have HIV RNA ≤1,000 copies/mL during late pregnancy and near delivery and no concerns regarding adherence to the cART regimen **(BII)**. Scheduled cesarean delivery at 38 weeks' gestation (compared to 39 weeks for most indications) is recommended for women who have HIV RNA >1,000 copies/mL near delivery (see Transmission and Mode of Delivery) **(AI)**.
• Women who present in labor with unknown HIV status should undergo expedited HIV testing **(AII)**. If the results are positive, a confirmatory HIV test should be done as soon as possible and maternal (IV zidovudine)/infant (combination antiretroviral [ARV] prophylaxis) ARV drugs should be initiated pending results of the confirmatory test **(AII)**. If the maternal confirmatory HIV test is positive, infant ARV drugs should be managed as discussed in the Infant Antiretroviral Prophylaxis section **(AI)**; if the maternal confirmatory HIV test is negative, the maternal and 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 August 6, 2015; last reviewed August 6, 2015)

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)**. Scheduled cesarean delivery performed solely for prevention of perinatal transmission in women receiving combination antiretroviral therapy with HIV RNA ≤1000 copies/mL is not routinely recommended due to the low rate of perinatal transmission in this group and the potential for increased complications following cesarean delivery in HIV-infected women **(AII)**. In women with HIV RNA levels ≤1000 copies/mL, cesarean delivery performed for standard obstetrical indications should be scheduled at 39 weeks' gestation **(AII)**.
• Because there is insufficient evidence to determine whether cesarean delivery after rupture of membranes or onset of labor reduces the risk of perinatal HIV 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 **(BII)**. In these circumstances, consultation with an expert in perinatal HIV (e.g., telephone consultation with the National Perinatal HIV/AIDS Clinical Consultation Center at (888) 448-8765) may be helpful in rapidly developing an individualized plan.
• Women with HIV infection should be counseled that HIV infection may put them at higher risk of surgical complications of cesarean 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*

Other Intrapartum Management Considerations (Last updated August 6, 2015; last reviewed August 6, 2015)

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 P450 (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 **(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*

Postpartum Care (Last updated August 6, 2015; last reviewed August 6, 2015)

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 **(AI)**. Decisions should take into account current recommendations for initiation of cART in adults, HIV RNA levels, adherence issues, whether a woman has an HIV-uninfected sexual partner, and patient preferences.
• Because the immediate postpartum period poses unique challenges to antiretroviral adherence, arrangements for new or continued supportive services should be made before hospital discharge for women continuing cART **(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 **(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 August 6, 2015; last reviewed August 6, 2015)

Panel's Recommendations
• A 6-week neonatal zidovudine prophylaxis regimen is generally recommended for all HIV-exposed neonates to reduce perinatal transmission of HIV **(AI)**. However, a 4-week neonatal zidovudine prophylaxis regimen can be considered for full-term infants when the mother has received standard combination antiretroviral therapy 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 **(AII)**.
• Infants at higher risk of HIV acquisition, including those born to HIV-infected women who have received only intrapartum antiretroviral drugs **(AI)** **or** have not received antepartum or intrapartum antiretroviral drugs **(AI)** **or** have received antepartum antiretroviral drugs but have had suboptimal viral suppression (>1000 copies/mL) near delivery **(BIII)**, 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.
• Some experts recommend triple-antiretroviral prophylaxis for infants at higher risk of acquisition (as described above) although there are no data demonstrating improved efficacy for a three-drug regimen over a two-drug regimen in prevention of transmission. A decision to administer triple-antiretroviral prophylaxis should be made only in consultation with a pediatric HIV specialist, preferably before delivery, and should be accompanied by parental counseling on the potential risks (e.g., neonatal toxicity), and benefits (e.g., prevention of perinatal transmission) of this approach **(BIII)**.
• For infants born to mothers with unknown HIV status, expedited 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 prophylaxis if the initial expedited test is positive **(AII)**. If supplemental testing is negative, antiretroviral prophylaxis can be discontinued.
• In the United States, the use of antiretroviral 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 August 6, 2015; last reviewed August 6, 2015)

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 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 antiretroviral drugs and concomitant medications, and maternal antepartum therapy **(CIII)**. • Hemoglobin and neutrophil counts should be remeasured 4 weeks after initiation of prophylaxis for infants who receive combination zidovudine/lamivudine-containing antiretroviral 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 aged <18 months and should be performed at 14 to 21 days of life and at ages 1 to 2 months and 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 antiretroviral 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 August 6, 2015; last reviewed August 6, 2015)

Panel's Recommendation
• Children with *in utero*/neonatal exposure to antiretroviral 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)**.
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*