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

Panel's Recommendations

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

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

For additional information on hepatitis C and HIV, see *Hepatitis C Virus Infection* of the *Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-infected Adults and Adolescents, Recommendations from the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the HIV Medicine Association of the Infectious Diseases Society of America* at *http://www.cdc.gov/mmwr/pdf/rr/rr5804.pdf*.[1]

Coinfection with hepatitis C virus (HCV) is not uncommon in HIV-infected women, particularly those infected via parenteral use of drugs; among HIV-infected pregnant women, the HCV seroprevalence rate ranges from 17% to 54%.[2] Screening for chronic HCV infection using a sensitive immunoassay for HCV antibody is recommended for all HIV-infected individuals, including pregnant women. False-negative anti-HCV immunoassay results can occur in HIV-infected individuals, particularly those with very low CD4 T-lymphocyte (CD4-cell) counts, but it is uncommon with the most sensitive immunoassays. Individuals who have a positive HCV antibody test should undergo confirmatory testing for plasma HCV RNA using a commercially available quantitative diagnostic assay. Testing for HCV RNA also should be performed on individuals whose serologic test results are indeterminate or negative but in whom HCV infection is suspected because of elevated aminotransaminase levels or risk factors such as a history of intravenous drug use.

Few data exist on the optimal management of HIV-infected pregnant women with HCV coinfection. Recommendations for antiretroviral (ARV) drug use during pregnancy for treatment of HIV and/or prevention of mother-to-child transmission (MTCT) are the same for women who have HCV coinfection as for those with HIV alone (see HIV/Hepatitis C [HCV] Coinfection in Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, http://AIDSinfo.nih.gov). However, currently available anti-HCV treatments are not recommended during pregnancy. Interferons are not recommended for use in pregnancy because they are abortifacient at high doses in monkeys and have direct antigrowth and antiproliferative effects,[3] and ribavirin is contraindicated (Food and Drug Administration [FDA] Pregnancy Category X) because of teratogenicity at low doses in multiple animal species. Ribavirin-associated defects in animals include limb abnormalities, craniofacial defects, anencephaly, and anophthalmia. Concerns have been raised about potential mutagenic effects of ribavirin in the offspring of men taking ribavirin before conception because of possible accumulation of ribavirin in spermatozoa. However, in a small number of inadvertent pregnancies occurring in partners of men receiving ribavirin therapy, no adverse outcomes were reported.[4] Pregnancies that occur in women taking ribavirin should be reported to the Ribavirin Pregnancy Registry (800-593-2214 or http://www.ribavirinpregnancyregistry.com). There are no data in pregnancy on telaprevir or boceprevir, both recently approved by the FDA for treatment of HCV. Telaprevir and boceprevir are Pregnancy Category B agents; however, these agents must be used in combination with pegylated inteferon and ribavirin, which should not be used in pregnancy. In addition, recent data demonstrated potential drug interactions between boceprevir and certain ritonavir-boosted protease inhibitor (PI) regimens that may reduce the effectiveness of these medications if used together (for more detailed information see Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents).[5] Pregnancy does not appear to influence the course of HCV infection and women with chronic HCV generally do quite well during pregnancy, provided that their infections have not progressed to decompensated cirrhosis.[6]

Because of the added risk of acute infection with hepatitis A virus (HAV) and hepatitis B virus (HBV) in individuals with chronic HCV, women who are found to have chronic HCV infection should also be screened for HAV and HBV. Women with chronic HCV infection who are hepatitis A immunoglobulin G negative should receive the HAV vaccine series, and if they are not infected with HBV (that is, hepatitis B surface antigen negative, hepatitis B core antibody negative, and hepatitis B surface antibody negative), they should receive the HBV vaccine series.

In a majority of studies, the incidence of HCV transmission from mother to infant increases if the mother is coinfected with HIV, with transmission rates between 10% and 20%.[7-10] These higher transmission rates are likely related to an increase in HCV viremia and/or other HIV-related impact on HCV disease activity.[11] A European study of perinatal transmission of HCV found that use of effective combination therapy for HIV was associated with a strong trend toward reduction in HCV transmission (odds ratio 0.26, 95% confidence interval, 0.07–1.01).[12] Maternal HIV/HCV coinfection also may increase the risk of perinatal transmission of HIV.[13] Therefore, potent antiretroviral therapy (ART) with at least three drugs is recommended for all HIV/HCV-coinfected pregnant women, regardless of CD4-cell count or HIV viral load.

As with chronic HBV infection, an elevation in hepatic enzymes following initiation of ART can occur in HIV/HCV-coinfected women—particularly in those with low CD4-cell counts at treatment initiation—as a result of an immune-mediated flare in HCV disease triggered by immune reconstitution with effective ART. Like HBV, HCV infection may increase the hepatotoxic risk of certain ARV agents, specifically PIs and nevirapine. Pregnant women with HIV/HCV coinfection should be counseled about signs and symptoms of liver toxicity, and transaminase levels should be assessed 1 month after initiation of ARV drugs and then every 3 months thereafter. If hepatic toxicity occurs, consideration may need to be given to substituting a less hepatotoxic drug regimen, and if clinical symptoms or significant elevations of transaminases occur, drugs may need to be temporarily discontinued. Differentiating between a flare in HCV disease associated with

immune reconstitution and drug toxicity often can be difficult; therefore, consultation with an expert in HIV and HCV coinfection is strongly recommended.

As with transmission of HIV, risk of MTCT of HCV may be increased by use of internal fetal monitoring, amniocentesis, and rupture of membranes for more than 6 hours.[9, 14] The majority of studies of elective cesarean delivery that have included HIV-infected women have found that the procedure does not reduce the risk of perinatal transmission of HCV.[12, 15-17] The general recommendations for intrapartum management are the same in women with HIV/HCV coinfection as in those with HIV infection alone (see Intrapartum Care).

Infants born to women with HIV/HCV coinfection should be assessed for HCV infection with anti-HCV antibody testing after age 18 months. Infants who screen positive should undergo confirmatory HCV RNA testing. HCV RNA virologic testing can be done between ages 3 and 6 months, if earlier diagnosis is indicated or desirable.[18, 19] Because HCV viremia can be intermittent, at least two negative tests are needed to exclude HCV infection. Children are considered to be HCV infected if they have two or more positive HCV RNA polymerase chain reaction results or are HCV antibody positive beyond age 18 months.

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