

HIV/Hepatitis C Virus Coinfection (Last updated October 26, 2016; last reviewed October 26, 2016)

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 coinfecting (see [HIV/Hepatitis B Virus Coinfection](#) section) (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 none of the approved HCV oral medications have been evaluated in pregnant women, and the use of ribavirin is contraindicated in pregnancy (AIII). If considering treatment of HCV in an HIV-coinfecting pregnant woman, consultation with an expert in HIV and HCV is strongly recommended (AIII).
- Recommendations for antiretroviral (ARV) 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 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; 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).

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 virus (HCV) and HIV, see [Hepatitis C Virus](#) in the [Pediatric Opportunistic Infections Guidelines](#), [HIV/Hepatitis C Coinfection](#) in the [Adult and Adolescent Antiretroviral Guidelines](#) and [Hepatitis C Virus Infection](#) in the [Adult and Adolescent Opportunistic Infections Guidelines](#). The American Association for the Study of Liver Diseases, the Infectious Diseases Society of America, and International Antiviral Society-USA recently updated their HCV treatment guidelines to add newly approved interferon-free direct-acting antiviral regimens and to provide more information about treating patients with HIV/HCV coinfection and decompensated liver disease. The guidelines are available online at HCVguidelines.org. The management of HIV/HCV coinfection in pregnancy is complex and consultation with an expert in HIV and HCV infection is strongly recommended, particularly if treatment of HCV infection during pregnancy is being considered.

Screening and Vaccination

All HIV-infected women should be screened for hepatitis B virus (HBV) and HCV at entry into general HIV care unless they are known to be previously infected. HIV-infected women should be rescreened for HBV and HCV during each pregnancy, unless they are known to be infected by one or both of these viruses. HCV coinfection is not uncommon in HIV-infected women, particularly those infected via parenteral use of drugs; among HIV-infected pregnant women in a European cohort, the observed HCV seroprevalence rate was 12%.¹ The male partners of all HIV/HCV-coinfecting patients should be referred for both HIV and hepatitis counseling and testing to prevent horizontal transmission of HIV as well as HCV from women to their male partners. All HIV-uninfected partners of HIV/HCV-coinfecting women should be counseled about the potential benefits and risks of starting oral pre-exposure prophylaxis to prevent HIV acquisition.

Current HCV treatment guidelines recommend therapy for all HCV-infected patients with estimated life expectancies >12 months. However, the management of HIV/HCV coinfection in pregnancy is complex because none of the approved HCV oral medications have been evaluated in pregnant women, and the use of ribavirin is contraindicated in pregnancy. If considering treatment of HCV in an HIV-coinfected pregnant woman, consultation with an expert in HIV and HCV is strongly recommended. In addition, the risks of perinatal HCV transmission are much lower than of perinatal HIV transmission, and many infected children will clear HCV infection spontaneously, making the balance of risks and benefits for treating HCV in pregnancy different from treating HIV.

The primary reasons for HCV testing during pregnancy, therefore, are:

- To identify HCV-infected women at a time when they are engaged with the health system, so that HCV treatment can be offered after delivery (ideally before a subsequent pregnancy);
- To be aware of the increased risk of HCV-related hepatotoxicity related to antiretroviral (ARV) use and potential for increased risk of preterm birth with HCV infection² in coinfecting women;
- To ensure vaccination against other viral hepatitis (hepatitis A virus [HAV] and HBV) if needed; and
- To ensure appropriate follow-up and evaluation of HCV-exposed infants.

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, but it is uncommon with the more sensitive immunoassays. If HCV infection is suspected despite a negative HCV antibody screen, a quantitative HCV RNA assay can be performed. 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 during pregnancy 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 injection drug use.³

Because of the added risk of hepatic decompensation from acute infection with any viral hepatitis, women with HCV infection should also be screened for both HAV and HBV. Using HAV antibody testing for immunoglobulin G (IgG), if HAV IgG is negative, HIV/HCV-coinfecting women should receive the HAV vaccine series. Although the safety of HAV vaccination during pregnancy has not been determined, HAV vaccine is produced from inactivated HAV and the theoretical risk to the developing fetus is expected to be low.⁴ HIV/HCV-coinfecting women who screen negative for HBV (i.e., hepatitis B surface antigen [HBsAg]-negative, hepatitis B core antibody-negative, and hepatitis B surface antibody-negative) should receive the HBV vaccine series. HIV-infected women who are HBsAb negative despite having received the HBV vaccine series may benefit from revaccination.⁵ Data indicate no apparent risk to developing fetuses from hepatitis B vaccination, as current vaccines contain noninfectious HBsAg.⁴

Impact of Hepatitis C Virus on HIV Management

Few data exist on the optimal management of HIV-infected pregnant women with HCV coinfection. Recommendations for ARV drug use during pregnancy for treatment of HIV and prevention of perinatal transmission are the same for women who have HIV/HCV coinfection as for those infected only with HIV (see [HIV/Hepatitis C Coinfection](#) in the [Adult and Adolescent Antiretroviral Guidelines](#)).

Hepatitis C Virus-Specific Therapy in Pregnancy

All currently available oral anti-HCV treatments lack sufficient safety data to be recommended during pregnancy. Until recently, most anti-HCV therapy included both interferon and ribavirin. Interferons are not recommended for use in pregnancy because they are abortifacient at high doses in monkeys and have direct antigrowth and antiproliferative effects.⁶ Ribavirin is contraindicated (Food and Drug

Administration 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.⁷ Pregnancies that occur in women taking ribavirin should be reported to the Ribavirin Pregnancy Registry (800-593-2214 or <http://www.ribavirinpregnancyregistry.com>).

Newer interferon-free and ribavirin-free agents approved for treatment of HCV include the protease inhibitor (PI) simeprevir (Pregnancy Category C), the nucleotide analogue NS5B polymerase inhibitor sofosbuvir (Pregnancy Category B), NS5A inhibitors ledipasvir (Pregnancy Category B) and daclatasvir (no concerning animal data and no human data to inform risk in pregnancy), and three fixed-dose combinations: ledipasvir/sofosbuvir, paritaprevir (NS3/4A PI)/ritonavir/ombitasvir (NS5A inhibitor) plus twice-daily dasabuvir (NS5B polymerase inhibitor), given with ribavirin except for genotype 1b, and elbasivir (NS5A inhibitor) and grazoprevir (NS3/4 PI).⁸ However, these medications are not yet recommended for use in pregnancy because of the lack of pharmacokinetic and safety data. In addition, potential drug interactions between these newer anti-HCV drugs and ARV drugs, particularly certain HIV PI regimens and non-nucleoside reverse transcriptase inhibitors, may reduce the effectiveness of HCV medications if used together or increase exposure to tenofovir disoproxil fumarate if it is included in the regimen. For more detailed information on drug interactions and newly approved medications, see Adult and Adolescent Antiretroviral Guidelines, Adult Opportunistic Infections Guidelines and the HCV treatment guidelines (<http://www.hcvguidelines.org>).

Although the HCV viral load appears to peak in the third trimester, pregnancy does not appear to influence the course of HCV infection. Women with chronic HCV generally do quite well during pregnancy, provided that they have not progressed to decompensated cirrhosis.^{9,10}

In a majority of studies of women with untreated HIV/HCV coinfection, the incidence of perinatal HCV transmission approximately doubles if the mother is coinfecting with HIV, with transmission rates between 10% and 20% reported primarily among women not treated with antiretroviral therapy (ART).¹¹⁻¹⁴ These higher transmission rates are likely related to an increase in HCV viremia and/or other HIV-related impact on HCV disease activity.¹⁵ However, early and sustained control of HIV viremia with ART may reduce HCV transmission to infants.^{10,16,17} A European study of perinatal transmission of HCV found that use of effective ART for HIV was associated with a strong trend toward reduction in HCV transmission (odds ratio 0.26, 95% confidence interval, 0.07–1.01).¹⁶

Maternal HIV/HCV coinfection also may increase the risk of perinatal transmission of HIV.¹⁸ Perinatal HIV transmission may be reduced in HIV/HCV-coinfecting pregnant women by following standard recommendations for ART for all women with HIV infection, regardless of CD4 T-lymphocyte (CD4) cell count or HIV viral load.

Monitoring of HIV/HCV-Coinfecting Women during Pregnancy

An elevation in hepatic enzymes following initiation of ART can occur in HIV/HCV-coinfecting 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 ART. 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 of 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.

Mode of Delivery

The majority of studies of elective cesarean delivery in HCV-infected women with or without HIV coinfection have found that the procedure does not reduce the risk of perinatal transmission of HCV.^{16,19-21} Thus, the general recommendations for **mode of delivery** are the same in women with HIV/HCV coinfection as in those with HIV infection alone (see [Intrapartum Care](#)).

Evaluation of HCV-Exposed Infants

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 after age 2 months, if earlier diagnosis is indicated or desirable.^{22,23} 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. Children are considered to be HCV-infected if they have two or more positive HCV RNA polymerase chain reaction results at any age, or are HCV antibody-positive beyond age 18 months.

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