

Special Populations: Hepatitis B Virus/HIV Coinfection

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Panel's Recommendations
<ul style="list-style-type: none">• All pregnant people with HIV should be screened during each pregnancy for hepatitis B virus (HBV) infection unless they are already known to have HBV/HIV coinfection or have serologic documentation of HBV immunity (AIII).• All pregnant people with HIV who screen negative for HBV infection and lack HBV immunity (i.e., HBV surface antigen negative, HBV core antibody negative, and HBV surface antibody negative) should promptly receive the HBV vaccine series (AII).• All pregnant people with chronic HBV infection who have not already received the hepatitis A virus (HAV) vaccine series should be screened for immunity to HAV. If they screen negative for HAV antibodies (either immunoglobulin G [IgG] or total antibody [IgG and immunoglobulin M]), they should receive the HAV vaccine series (AIII).• After delivery, people with HBV/HIV coinfection should continue antiretroviral regimens that include drugs with anti-HBV activity: tenofovir disoproxil fumarate or tenofovir alafenamide plus lamivudine or emtricitabine (AII).• Pregnant people with HBV/HIV coinfection who are receiving antiretroviral therapy (ART) should be counseled about signs and symptoms of liver toxicity, and liver transaminases should be assessed 1 month after initiating ART and at least every 3 months thereafter during pregnancy (BIII).• For pregnant people with HBV/HIV coinfection who discontinue medications with anti-HBV activity, frequent monitoring of liver function tests for potential exacerbation of HBV infection is recommended, with prompt reinstitution of treatment for HBV when a flare is suspected (BIII).• HBV/HIV coinfection is not an independent indication for cesarean delivery (see Intrapartum Care for People with HIV) (AIII).• Infants born to people with HBV should receive hepatitis B immune globulin and the first dose of the HBV vaccine series as soon as possible and within 12 hours of birth (AI).
<p><i>Rating of Recommendations: A = Strong; B = Moderate; C = Optional</i></p> <p><i>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</i></p>

The management of hepatitis B virus (HBV)/HIV coinfection in pregnancy is complex, and consultation with an expert in HIV and HBV coinfection is strongly recommended. For additional information on HBV and HIV, see [Hepatitis B Virus/HIV Coinfection](#) in the [Adult and Adolescent Antiretroviral Guidelines](#), [Hepatitis B Virus Infection](#) in the [Adult and Adolescent Opportunistic Infection Guidelines](#), and [Hepatitis B Virus](#) in [Guidelines for the Prevention and Treatment of Opportunistic Infections in Children with and Exposed to HIV](#).

Screening and Vaccination

Everyone with HIV should be screened for HBV at entry into general HIV care. For guidance on screening for hepatitis C virus (HCV), see [Hepatitis C Virus/HIV Coinfection](#). All pregnant people with HIV should be screened for HBV during each pregnancy unless they are known to have HBV/HIV coinfection or to have serologic documentation of HBV immunity. Screening for HBV should include hepatitis B surface antigen (HBsAg), hepatitis B core antibody (anti-HBc or HBcAb), and hepatitis B surface antibody (anti-HBs or HBsAb). People who test positive for HBsAg should

have follow-up testing to evaluate liver function; prothrombin time; and levels of HBV DNA, hepatitis B e antigen (HBeAg), and hepatitis B e antibody (HBeAb).¹

To prevent transmission of HIV and HBV from people with HBV/HIV coinfection to their sex partners, their sexual contacts should be counseled and tested for HIV and HBV. All HBV-susceptible contacts should then receive the HBV vaccine series; all sex partners who do not have HIV infection should be counseled about the benefits of condom use, pre-exposure prophylaxis, and having a sex partner with undetectable HIV (**Undetectable = Untransmittable or U=U**) in preventing HIV transmission. For information on testing and prevention of HIV transmission to sex partners, see [Reproductive Options for Couples When One or Both Partners Have HIV](#) and the [Let's Stop HIV Together](#) resources from the Centers for Disease Control and Prevention (CDC).^{2,3} For more information specifically about preventing HIV and HBV transmission, see the [CDC guidelines on pre-exposure prophylaxis](#) and the [Hepatitis B Virus Infection](#) section of the [Adult and Adolescent Opportunistic Infection Guidelines](#).

Pregnant people with HIV who screen negative for HBV (i.e., HBsAg negative, anti-HBc negative, and anti-HBs negative) or who lack HBV immunity (i.e., anti-HBs negative) should promptly receive the HBV vaccine series.⁴ People with HIV who have remote HBV infection and who have only anti-HBc antibody detected (i.e., they test negative for HBV DNA, HBsAg, and anti-HBs) may have lost immunity to HBV and should be vaccinated.¹ Assessment of anti-HBs titers 1 to 2 months after the vaccine series and management of nonresponders should be conducted in pregnant people with HIV/HBV coinfection in the same way as recommended for nonpregnant people with HIV/HBV coinfection; see [Hepatitis B Virus Infection](#) in the [Adult and Adolescent Opportunistic Infection Guidelines](#).¹ No evidence exists that the HBV vaccine causes adverse effects in developing fetuses or newborns; current vaccines contain noninfectious HBsAg and are recommended for use in pregnancy for people with HIV.^{4,6} **Although the two-dose Heplisav-B is an alternative vaccine for nonpregnant people to prevent HBV, available data on its use in pregnancy are insufficient to inform vaccine-associated risks in pregnancy.**^{7,8}

A positive test for anti-HBc alone can be a false positive, especially in regions of low HBV prevalence; alternatively, it may signify remote infection with subsequent loss of anti-HBs antibodies or longstanding chronic HBV infection with loss of surface antigen (this is known as “occult” HBV infection, which can be confirmed by detection of HBV DNA) (see the [Hepatitis B Virus Infection](#) section of the [Adult and Adolescent Opportunistic Infection Guidelines](#)).^{9,10} Incidence of HBV viremia with the isolated anti-HBc pattern ranges from 1% to **36%** in patients with HIV, depending on the population sampled.^{1,11,12} The clinical significance of isolated anti-HBc is unknown. **Most people with HIV with isolated anti-HBc are HBV DNA–negative and not immune to HBV infection; therefore, they would benefit from HBV vaccination (see below).** While routinely checking HBV DNA is currently not recommended in non-pregnant adults with isolated anti-HBc (see the [Hepatitis B Virus Infection](#) section of the [Adult and Adolescent Opportunistic Infection Guidelines](#)), it may be considered in pregnancy.¹³ **If pregnant people with isolated anti-HBc are found to have HBV viremia, their ART should be adjusted to assure control of both HBV and HIV.** Pregnant people with HIV who have isolated anti-HBc and occult HBV infection typically have very low levels of HBV DNA and are thought to be at extremely low risk of transmitting HBV to their infants.^{1,15} **However, people with isolated anti-HBc and negative or unknown HBV DNA should be vaccinated with one standard dose of HBV vaccine, and anti-HBs titers should be checked 1 to 2 months after vaccination.** If the anti-HBs titer is >100 IU/mL, no further vaccination is needed. If the titer is <100 IU/mL, the patient should receive a complete HBV vaccine series, followed by anti-HBs testing¹⁴ (See the [Hepatitis B Virus Infection](#) section of the [Adult and Adolescent Opportunistic Infection Guidelines](#)).¹

Pregnant people who have HBV infection and who have not already received the hepatitis A virus (HAV) vaccine series also should be screened for HAV using antibody testing for immunoglobulin G (IgG) (note that some laboratories provide only a combined IgG and immunoglobulin M [IgM] HAV titer, which is acceptable). Individuals with chronic HBV have an added risk of hepatic decompensation from acute infection with HAV. Pregnant people with chronic HBV infection who have not already received the HAV vaccine series and who are not immune to HAV should receive the HAV vaccine series. Responses to the HAV vaccine are reduced in persons with HIV who have CD4 **T lymphocyte (CD4) cell** counts <200 cells/mm³. Antibody response should be assessed in such persons 1 month after the HAV vaccine series is complete. If HAV antibody immunoglobulin (HAV Ab IgG) is negative,¹ these persons should be revaccinated when the CD4 count is >200 cells/mm³. Pregnant people who received the HAV vaccine series when their CD4 count was ≥ 200 cells/mm³ do not need to be revaccinated for HAV because they are likely protected (even if their HAV IgG levels are undetectable using commercially available assays). Although the safety of HAV vaccination during pregnancy has not been directly evaluated, the HAV vaccine contains inactivated HAV, and the theoretical risk to the developing fetus is expected to be low.¹⁶

HBV/HIV Coinfection in Pregnancy

A study of 4,236 pregnant women with HIV in France who were followed between 2005 and 2013 found that the prevalence of HBV (HBsAg positive) was 6.2%; HBV/HIV coinfection was six times more frequent in pregnant women who were born in sub-Saharan Africa than in those who were born in France.¹⁷ HBV/HIV coinfection was not associated with preterm delivery, lower CD4 counts, or detectable HIV viral load in this cohort.¹⁷ In a retrospective multivariable analysis of response to antiretroviral therapy (ART) in 1,462 pregnancies among Italian women with HIV in which 12% of the women had HBV/HIV coinfection, women with only HIV had better CD4 responses on ART during pregnancy than women with HBV/HIV coinfection.¹⁸ However, no differences in maternal and infant outcomes were observed between women with HBV/HIV coinfection and women with only HIV.

Therapy for HIV and HBV in Pregnancy

An antiretroviral (ARV) regimen that includes drugs that are active against both HIV and HBV is recommended and should be offered to all individuals with HBV/HIV coinfection, including all pregnant people (see [Hepatitis B Virus Infection in the Adult and Adolescent Opportunistic Infection Guidelines](#)). Initiation of ART may be associated with activation of HBV and development of immune reconstitution inflammatory syndrome, particularly in persons with high HBV DNA levels and severe liver disease.^{1,19}

The use of **an ART regimen** with anti-HBV activity during pregnancy in people with HBV mono-infection lowers HBV viremia and lowers the risk of HBV transmission to the infant. All pregnant people with HIV/HBV coinfection should be receiving an ART regimen that includes tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF), and either lamivudine (3TC) or emtricitabine (FTC), which will reduce HBV viremia and thus lower the risk of HBV transmission to the infant.^{1,20} **All these drugs are Preferred nucleoside and nucleotide reverse transcriptase inhibitors for use during pregnancy (see [Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naive](#)).** Please see individual drug sections for **TDF, TAF, FTC, and 3TC** for detailed reviews of safety, pharmacologic properties, and other clinical data informing use in pregnancy.

In addition to treatment with an ART regimen containing two ARVs that have anti-HBV activity, treatment of symptomatic acute HBV infection during pregnancy should be supportive, with special attention given to maintaining blood glucose levels and normal clotting status. Risk of preterm labor and delivery may increase with acute HBV infection. High maternal HBV DNA levels are strongly correlated with perinatal HBV transmission and with failures of HBV passive-active immunoprophylaxis.^{1,21-24}

Consultation with an expert in HIV and HBV is strongly recommended when providing care for pregnant people with HBV/HIV coinfection who continue to have detectable HBV DNA viremia despite receiving an ARV regimen that includes two anti-HBV nucleotide or nucleoside analogues.

Several other antiviral agents have activity against HBV, including entecavir, adefovir, and telbivudine; however, these drugs have not been well evaluated in pregnancy, with too few exposures to assess overall risk. They **are currently not recommended** for pregnant people with HBV/HIV coinfection.²⁵

Interferon alfa and pegylated interferon alfa are also **not recommended** for use during pregnancy, and they should be used only if the potential benefits outweigh the potential risks. Although interferons are not teratogenic, they are abortifacient at high doses in monkeys and should not be used in pregnancy because of their direct antigrowth and antiproliferative effects.²⁶

Cases of exposure during pregnancy to any of the ARV drugs and HBV drugs listed above should be reported to the [Antiretroviral Pregnancy Registry](#) online or by telephone at 1-800-258-4263.

Monitoring People with HBV/HIV Coinfection During Pregnancy

Prior to initiating ARV drugs that are active against HBV, a baseline HBV DNA level should be measured. After initiating therapy, HBV DNA should be monitored every 12 weeks to ensure adequate response to therapy (see [Hepatitis B Virus Infection](#) in the [Adult and Adolescent Opportunistic Infection Guidelines](#)).

Following initiation of ART, an elevation in hepatic enzymes can occur in pregnant people with HBV/HIV coinfection—particularly those with low CD4 counts at the time of treatment initiation—as a result of an immune-mediated flare in HBV disease triggered by immune reconstitution with effective HIV therapy. HBV infection can also increase the hepatotoxic risk of certain ARV drugs, specifically protease inhibitors. Pregnant people with HBV/HIV coinfection should be counseled about the signs and symptoms of liver toxicity, and transaminase levels should be assessed 1 month after initiating ARV drugs and at least every 3 months thereafter. If hepatotoxicity occurs, it may be necessary to consider substituting a less hepatotoxic regimen or, if clinical symptoms or significant elevations of transaminases occur, drugs may need to be temporarily discontinued. Differentiating between the effects of drug toxicity and a flare in HBV disease caused by immune reconstitution often can be difficult, and consultation with an expert in HIV and HBV coinfection is strongly recommended.

Discontinuing anti-HBV agents may lead to reactivation of HBV, resulting in hepatocellular damage. If anti-HBV drugs are discontinued, serum transaminase levels should be monitored every 6 weeks for 3 months, and then every 3 to 6 months thereafter, with prompt reinitiation of HBV treatment if a flare is suspected.¹

Mode of Delivery

Decisions concerning mode of delivery of the infant in a pregnant person with HBV/HIV coinfection should be based on standard obstetric and HIV-related indications alone (see [Intrapartum Care for People with HIV](#)). Currently, the guidelines for **management of pregnancy** with HBV mono-infection do not recommend performing a cesarean delivery to prevent perinatal transmission of HBV.²⁷⁻²⁹

Evaluating and Managing Infants Who Were Exposed to HBV

All infants born to people with HBV infection, including those with HBV/HIV coinfection, should receive hepatitis B immune globulin (HBIG) and the first dose of the HBV vaccination series to prevent perinatal transmission of HBV **as soon as possible and within 12 hours of birth.** For infants weighing ≥ 2 kg at birth, the second and final doses of the vaccine series should be administered at age 1 to 2 months and 6 months, respectively. For infants with birth weights < 2 kg, do not count the birth dose as part of the vaccine series, and administer three additional doses at ages 1 month, 2 to 3 months, and 6 months.^{30,31} This regimen is $>95\%$ effective in preventing HBV infection in these infants. Maternal ART that includes nucleoside analogues with anti-HBV activity will result in low or suppressed HBV viral loads near delivery, which should further reduce the risk of perinatal HBV transmission in people with HBV/HIV coinfection.^{32,33}

Infant post-vaccination testing for anti-HBs and HBsAg should be performed after completing the vaccine series, between the ages of 9 months and 18 months. Serologic testing should not be performed before age 9 months; this delay helps avoid detecting anti-HBs from HBIG that was administered during infancy and maximizes the likelihood of detecting late HBV infection. Anti-HBc testing of infants is not recommended because passively acquired maternal anti-HBc might be detected in infants aged ≤ 24 months who were born to mothers with HBV. HBsAg-negative infants with anti-HBs levels >10 mIU/mL are protected and need no further medical management. HBsAg-negative infants with anti-HBs levels <10 mIU/mL should be revaccinated with a single dose of HBV vaccine and receive postvaccination serologic testing 1 to 2 months later. Infants whose anti-HBs levels remain <10 mIU/mL following single-dose revaccination should receive two additional doses of HBV vaccine to complete the second series, followed by postvaccination serologic testing at 1 to 2 months after the final dose.³⁴

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