

Hepatitis B Virus/HIV Coinfection

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Panel's Recommendations
<ul style="list-style-type: none"> • Triple panel (hepatitis B surface antigen [HBsAg], hepatitis B core antibody [HBcAb], and hepatitis B surface antibody [HBsAb]) screening is recommended for pregnant women who do not have a documented triple screen that indicates vaccine-induced immunity (HBsAb ≥ 10 mIU/mL with negative HBsAg and HBcAb) or presence of hepatitis B virus (HBV) infection (i.e., HBsAg positive) after age 18 years (AIII). Everyone should be tested for HBsAg in every pregnancy (AIII). • A negative screening for HBV infection and lack of HBV immunity (i.e., HBsAg negative, HBcAb negative, and HBsAb negative [e.g., HBsAb < 10 mIU/mL]) warrants administration of a HBV vaccines series (AI). • Because tenofovir disoproxil fumarate (TDF), tenofovir alafenamide (TAF), lamivudine (3TC) and emtricitabine (FTC) are active against both HIV and HBV, an antiretroviral (ARV) regimen for people with both HIV and HBV should include (TAF or TDF) plus (3TC or FTC) as the nucleoside reverse transcriptase inhibitor backbone of a fully suppressive ARV regimen (AI). • In people with HBV/HIV coinfection, using 3TC or FTC as the only drug with HBV activity in a regimen is not recommended (AII) because HBV resistance to these drugs can emerge. All people with HBV/HIV coinfection should be counseled and encouraged to continue ARV regimens that also include drugs with anti-HBV activity before, during, and after pregnancy (AII). Adefovir, entecavir, telbivudine, and interferon alfa drugs are not recommended (AIII) in the setting of HBV/HIV coinfection during pregnancy. • If medications with anti-HBV activity are discontinued during pregnancy with HBV/HIV coinfection, frequent monitoring of liver function tests for potential exacerbation of HBV infection is recommended, with prompt reinitiation of treatment for HBV when a flare is suspected (BIII). • When antiretroviral therapy (ART) is received during pregnancy in the setting of HBV/HIV coinfection, counseling about signs and symptoms of liver toxicity should be provided, and liver transaminases should be assessed 1 month after initiating ART and at least every 3 months thereafter during pregnancy (BIII). • HBV/HIV coinfection is not an independent indication for cesarean birth (see Intrapartum HIV Care) (AIII). • Infants with perinatal HBV exposure 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). • Infant feeding recommendations for people with HIV/HBV do not differ from recommendations for people with HIV but without HBV (AIII).
<p>Rating of Recommendations: A = Strong; B = Moderate; C = Optional</p> <p>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</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](#), [Centers for Disease Control and Prevention \(CDC\) Hepatitis B Guidelines](#) and [Hepatitis B Virus](#) in the [Pediatric Opportunistic Infection Guidelines](#).

Screening

Everyone with HIV should be screened for hepatitis A virus (HAV), HBV, and hepatitis C virus (HCV) at entry into general HIV care.¹ For guidance on screening for HCV in the context of pregnancy with HIV, see [Hepatitis C Virus/HIV Coinfection](#). For guidance on screening for HAV and HAV immunization in pregnancy with HIV, see [Antepartum Care](#).

Triple panel (hepatitis B surface antigen [HBsAg], hepatitis B core antibody [HBcAb], and hepatitis B surface antibody [HBsAb]) screening is recommended for pregnant women who do not have a documented triple screen that indicates vaccine-induced immunity (i.e., HBsAb ≥ 10 mIU/mL, HBcAb negative, HBsAg negative) or presence of HBV infection (HBsAg positive) after age 18 years.^{2,3} All women, including all women with HIV, should be tested for HBsAg in every pregnancy.^{2,3} The recommendation for HBsAg screening in every pregnancy applies even to women with known HBV infection to facilitate timely prophylaxis for the newborn. 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, hepatitis B e antibody and hepatitis D virus (HDV) immunoglobulin G antibodies (if positive, then HDV RNA).¹

Vaccination

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 an HBV vaccine series. For more information specifically about preventing HIV and HBV transmission, see the [CDC guidelines on pre-exposure prophylaxis](#), the [Hepatitis B Virus Infection](#) section of the [Adult and Adolescent Opportunistic Infection Guidelines](#), and the [Let's Stop HIV Together](#) resources from the CDC.^{4,5}

A negative screening for HBV infection and lack of HBV immunity (i.e., HBsAg negative, HBcAb negative, and HBsAb negative [HBsAb < 10 mIU/mL]) warrants prompt administration of the HBV vaccine series⁶; see [Hepatitis B Virus Infection](#) in the [Adult and Adolescent Opportunistic Infection Guidelines](#).

Available adult single-antigen HepB vaccines in the United States that have been studied in people with HIV include two recombinant HBsAg vaccines (Engerix-B and Recombivax HB) and a recombinant HBsAg vaccine conjugated to a cytosine phosphoguanine oligonucleotide adjuvant (HepBCpG), which is a toll-like receptor 9 agonist (Heplisav-B) (see the [Hepatitis B Vaccine](#) subsection of the [Immunizations for Preventable Diseases in Adults and Adolescents With HIV](#) section in the [Adult and Adolescent Opportunistic Infection Guidelines](#)). The preferred vaccine in previously unvaccinated adults with HIV, including during pregnancy, is Heplisav-B given intramuscularly at 0 and 4 weeks. If a prior vaccine series with Engerix-B or Recombivax HB failed, Heplisav-B at 0 and 4 weeks is recommended, and a third dose at 24 weeks can be considered because three doses results in higher HBsAb titers⁷ (see the [Hepatitis B Vaccine](#) subsection of [Immunizations for Preventable Diseases in Adults and Adolescents With HIV](#) in the [Adult and Adolescent Opportunistic Infection Guidelines](#)). Response to HepB vaccination, defined as HBsAb ≥ 10 mIU/mL, should be documented 4 weeks after the last dose of vaccine. No evidence exists that any of the HBV vaccines causes adverse effects in developing fetuses or newborns; current vaccines contain noninfectious HBsAg and all are recommended for use in pregnancy for people with HIV^{1,6,8,9} (see [Hepatitis B Virus Infection](#) in the [Adult and Adolescent Opportunistic Infection Guidelines](#)).

Special Circumstances

Isolated Detection of Hepatitis B Core Antibody

Isolated hepatitis B core (HBc) antibody (HBcAb), defined as testing positive for HBcAb but negative for HBsAg and HBsAb, can be the result of a false positive HBc antibody test, loss of HBsAb after past resolved infection, occult infection (HBsAg is negative and HBV DNA is positive), being in the window period before appearance of HBsAb, or an HBsAg mutant infection (HBsAg mutant not detected by some HBsAg tests).² Although detection of HBV DNA can confirm occult HBV infection, the other causes can be difficult to distinguish. The incidence of HBV viremia in people with HIV and isolated HBc antibody ranges from 1% to 36%, depending on the population sampled.^{1,10,11}

Guidelines for nonpregnant adults with HIV do not recommend routine HBV DNA testing for isolated HBc antibody and instead recommend proceeding to vaccination (see Vaccination for People With Isolated Hepatitis B Core Antibody below), as most people with isolated HBc antibody are not protected from HBV and would likely benefit from vaccination (see [Hepatitis B Virus Infection](#) in the [Adult and Adolescent Opportunistic Infection Guidelines](#)). The [CDC Hepatitis B Guidelines](#) recommend HBV DNA testing for isolated HBc antibody in the context of immunosuppression.² The Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission (the Panel) advises that providers consider HBV DNA testing in pregnant women with HIV with isolated HBc antibody, because the result may influence management during pregnancy and at delivery.² If HBV DNA testing is negative, then proceed with HBV vaccination (see Vaccination for Individuals With Isolated Hepatitis B Core Antibody below). If HBV DNA testing is positive (occult HBV infection), the antiretroviral therapy (ART) regimen should be adjusted to include two drugs that are active against HBV and monitoring HBV DNA during pregnancy should be considered. In the setting of HIV and pregnancy, occult HBV infection is typically associated with very low levels of HBV DNA and therefore low risk of transmitting HBV perinatally.^{1,12} However, many experts would manage infants as potentially exposed to HIV and administer both the HBV vaccine and hepatitis B immune globulin (HBIG) within 12 hours of birth (see Evaluating and Managing Infants Who Were Exposed to HBV below).¹³

Vaccination for People With Isolated Hepatitis B Core Antibody

People with HIV and isolated HBc antibody due to remote infection may have lost immunity to HBV and should be vaccinated with one standard dose of HepB vaccine (one dose of Heplisav-B, or Engerix-B, or Recombivax HB), and HBsAb titers should be checked 1 to 2 months after vaccination. If the HBsAb titer is >100 mIU/mL, no further vaccination is needed and the person is considered HBV immune; if the titer is ≤100 mIU/mL, a complete series of the same HepB vaccine should be completed and followed by HBsAb testing¹; see the [Hepatitis B Vaccine](#) subsection of [Immunizations for Preventable Diseases in Adults and Adolescents With HIV](#) section in the [Adult and Adolescent Opportunistic Infection Guidelines](#).

Management of Previously Vaccinated Women With Hepatitis B Surface Antibody Titer <10 mIU/mL

In pregnant women with HIV who have already received a full and appropriately timed HBV vaccine series with documented HBsAb titer ≥10 mIU/mL (titers are recommended following vaccination for people with HIV infection), recommended HBV screening during pregnancy would only include HBsAg screening. However, if HBsAb is measured and has declined to <10 mIU/mL, the person can be offered a single booster dose of any HBV vaccine (approved for use in pregnancy) without follow-up HBsAb testing.

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.¹³ Although variable by geographic region, HBV infection is diagnosed in approximately 8% of all people with HIV and 3% to 12% of pregnant women with HIV infection worldwide.¹⁴ HBV/HIV coinfection was not associated with preterm birth, lower CD4 T lymphocyte (CD4) cell counts, or detectable HIV viral load in this cohort.¹³ In a retrospective multivariable analysis of response to 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.¹⁵ 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 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 during pregnancy (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 people with high HBV DNA levels and severe liver disease.^{1,16}

The use of an ART regimen with anti-HBV activity during pregnancy in the context of HBV mono-infection lowers HBV viremia and lowers the risk of HBV transmission to the infant. For HIV/HBV coinfection during pregnancy, an ART regimen that includes tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF), and either lamivudine (3TC) or emtricitabine (FTC) should be administered, which will reduce HBV viremia and thus lower the risk of HBV transmission to the infant.^{1,17} 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 When Antiretroviral Therapy Has Never Been Received](#)). 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 antiretrovirals (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 birth 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.^{1,18-21}

When providing care during pregnancy with HBV/HIV coinfection, consultation with an expert in HIV and HBV is strongly recommended for those 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** in the setting of HBV/HIV coinfection during pregnancy (see the [Antiretroviral Pregnancy Registry interim report](#)).

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.²²

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 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 during pregnancy 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. Counseling about signs and symptoms of liver toxicity should be given when ART is administered during pregnancy with HBV/HIV coinfection, 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 at risk of perinatal HBV/HIV acquisition 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 birth to prevent perinatal transmission of HBV.^{23,24}

Infant Feeding

Maternal HBV infection is not a contraindication to breastfeeding. Infant feeding recommendations for people with HIV/HBV do not differ from recommendations for people with HIV who do not have HBV as long as the infant has received immunoprophylaxis at birth.³ For detailed guidance on HBV vaccination and testing of infants, see [Hepatitis B Virus](#) in the [Pediatric Opportunistic Infection Guidelines](#).

Evaluating and Managing Infants Who Were Exposed to HBV

All infants **at risk of perinatal HBV acquisition** (e.g., HBsAg positive), including those with HBV/HIV coinfection, should receive 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. **The Panel suggests managing infants of women with HIV and occult HBV infection in the same way.**

Please see current [infant HBV vaccination recommendations](#) in the [Pediatric Opportunistic Infection Guidelines](#).

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