

# Preventing HBV Perinatal Transmission

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Module 3: [Prevention of HBV](#)

Lesson 2: [Preventing HBV Perinatal Transmission](#)

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## Universal Screening for HBV Infection During Pregnancy

Universal screening for hepatitis B virus (HBV) infection is recommended at the first prenatal visit for all pregnant women, regardless of prior hepatitis B vaccination status.[1,2,3,4] Screening is done through the serologic detection of hepatitis B surface antigen (HBsAg), which has a sensitivity and specificity greater than 98% for detecting HBV infection.[4] Some experts also recommend screening for antibody to hepatitis B surface antigen (anti-HBs) and antibody to hepatitis B core antigen (anti-HBc) to identify pregnant women who are susceptible to HBV and thus candidates for vaccination, as well as those with prior HBV infection who should be counseled on HBV reactivation risk. In order to ensure postexposure prophylaxis is appropriately given to infants born to HBsAg-positive mothers, a copy of the mother's hepatitis B test results should be provided to her and the hospital or care facility where she intends to deliver.[2]

- **Pregnant Women with Positive HBsAg Screening Test:** Expectant mothers who screen positive for HBsAg should undergo additional laboratory testing for a hepatic alanine aminotransferase (ALT) level and a plasma quantitative HBV DNA level to evaluate if HBV treatment is indicated.[2,3]
- **Pregnant Women with Negative HBsAg Screening Test:** Women who screen negative for HBsAg, anti-HBs, and anti-HBc upon enrollment into prenatal care should be offered vaccination against HBV.[2,3,5] Pregnant women can receive hepatitis B immunization during pregnancy, but the Heplisav-B and PreHevbrio hepatitis B vaccines should not be used during pregnancy due to lack of safety and efficacy data in pregnancy.[2,6,7]
- **Screening for HBV at the Time of Labor and Delivery:** Women who were not screened earlier in pregnancy, those with clinical or laboratory evidence of hepatitis, and those with ongoing risk factors for HBV acquisition should have screening for HBV performed at the time of labor and delivery.[2]

## Risk of Perinatal HBV Transmission

In the United States, during the year 2021, there were an estimated 17,827 infants born to HBsAg-positive mothers.[8] Although there were only 13 cases of perinatal HBV transmission reported to the CDC in 2022, earlier modeling studies suggest there are approximately 950 cases of perinatally-acquired chronic HBV infection in the United States annually.[8,9,10,11] In the absence of HBV postexposure immunoprophylaxis or maternal receipt of antiviral medications, the estimated rate of HBV transmission from an HBsAg-positive mother to her neonate is approximately 40% (range 5 to 90%).[12,13,14,15,16] For HBsAg-positive mothers, three factors prominently impact the risk of perinatal HBV transmission: maternal HBV DNA levels, maternal hepatitis B e antigen (HBeAg) status, and use of hepatitis B immunoprophylaxis for the infant.

- **Risk Related to Maternal HBV DNA Levels:** The risk of perinatal HBV transmission is significantly higher among mothers who have plasma HBV DNA levels greater than 2,000 IU/mL and/or are HBeAg positive.[17,18] In a United States-based study of 17,951 mother-infant pairs (involving 9,252 HBsAg-positive mothers), 2.1% of infants born to HBsAg-positive mothers who had an HBV DNA level greater than 2,000 IU/mL became infected with HBV versus 0% of those born to mothers with HBV DNA less than 2,000 IU/mL, despite all infants receiving birth dose vaccination and hepatitis B immune globulin (HBIG).[18] A similar study in Taiwan, which was conducted from 1972 through 1980 and prior to the widespread use of immunoprophylaxis for infants, found the risk for persistent neonatal infection increased from 3.2% with maternal plasma HBV DNA levels less than 0.005 ng/mL (150,000 IU/mL) to 97.2% with HBV DNA levels greater than 1.4 ng/mL (45,000,000 IU/mL) among 773 HBsAg-positive mothers (Figure 1).[19]
- **Risk Related to HBeAg Status:** HBeAg positivity also appears to affect risk for perinatal transmission, and in the absence of hepatitis B infant immunoprophylaxis or maternal antiviral therapy, an estimated 70 to 90% of infants born to mothers with a positive HBeAg will become infected with HBV, which is markedly higher than the less than 10% of infants born to HBeAg-negative mothers.[13,14,20] Similarly, in the Taiwanese study mentioned above, the odds ratio of having an infant with persistent (chronic) HBV infection was 17.6 for HBeAg-positive mothers in comparison to HBeAg-negative mothers.[19]
- **Impact of HBV Immunoprophylaxis for the Infant:** The risk of perinatal HBV transmission is markedly impacted by the provision of birth dose hepatitis B vaccination and HBIG. In a 2006 Cochrane review, hepatitis B vaccination decreased the risk of perinatal transmission by 72% when compared to placebo or no intervention (relative risk [RR] 0.28 based on four trials).[21] Similarly, the use of HBIG alone reduced the risk of perinatal transmission by 48% when compared to placebo or no intervention (RR 0.52 based on 11 trials). When combined, the use of plasma-derived HBV vaccine and HBIG reduced the occurrence of perinatal HBV infection by 92% (RR 0.08 based on three trials).[21] These results are highlighted in a prospective review of five United States-funded Perinatal Hepatitis B Prevention Programs from 2007 through 2013. In this study, 17,951 infants born to HBsAg-positive mothers were evaluated and information on HBsAg status was available for 9,252 (51.5%) of the infants. Overall, 1.1% (100 of the 9,252) infants acquired perinatal HBV. In this cohort, 95% had received birth dose hepatitis B vaccine and HBIG within 12 hours of birth.[18]

## Route and Timing of Perinatal HBV Transmission

The exact mechanism and timing of perinatal HBV transmission remain unclear. It is believed that most infections occur intrapartum, but in utero transmission and postpartum horizontal transmission can also occur.[22] Although HBV DNA and HBsAg have been detected in amniotic fluid, placental cells, and cord blood, the exact timing and mechanisms for transplacental HBV transmission, when it occurs, remain uncertain.[23,24,25,26]

- **Intrauterine Transmission:** The exact timing and mechanism of intrauterine transmission is not clearly known, but the risk would be enhanced with a breach of the placental barrier and mixing of maternal and fetal blood, such as with threatened abortion early in pregnancy or preterm labor.[27,28,29] In a study of 402 infants born to 402 HBsAg-positive mothers in China, 15 (3.7%) were found to be HBsAg positive within 24 hours of birth, which authors defined as intrauterine transmission.[24] In this study, the main risk factors for intrauterine infection were maternal HBeAg positivity, threatened preterm labor, and the presence of HBV in the placenta, particularly if located in the villous capillary endothelial cells.[24]
- **Transmission During Amniocentesis:** Perinatal HBV transmission following amniocentesis has been described, but the risk appears to be low. Data indicate that the risk is highest among mothers with plasma HBV DNA levels greater than 10 million copies/mL and more likely among those who are HBeAg-positive.[30,31,32] There are few data on the risk for perinatal HBV transmission with other intrauterine procedures.
- **Intrapartum/Peripartum Transmission:** The greater than 90% efficacy of birth dose vaccination and HBIG in preventing perinatal HBV infection supports the hypothesis that most perinatal infections occur intrapartum.[16,27,33,34] Nevertheless, data on the use of elective cesarean section to reduce mother-to-child transmission are mixed.[27,35,36,37] Similarly, there are limited data on the risk of perinatal transmission in the setting of premature rupture of membranes. In one nested case-control study of 141 infant pairs in China, mothers with HBsAg-positive infants were more likely to have experienced premature rupture of membranes prior to birth than those with HBsAg-negative infants.[38] In contrast to these findings, a Korean study of 144 children born to HBsAg-positive mothers reported no correlation between premature rupture of membranes and increased risk for perinatal transmission.[39]
- **Transmission Via Breast Milk:** Transmission of HBV through breast milk is not a major concern, as several studies have suggested very low rates of transmission via breastfeeding, despite HBV being present in colostrum.[40,41,42] Although this limited risk of transmission may be due in part to the efficacy of birth dose vaccination and appropriate use of HBIG, studies performed before the routine use of neonatal prophylaxis similarly suggested limited risk of vertical transmission among breastfeeding mothers.[41,42]

## Management of Women with Chronic HBV in Pregnancy

Antiviral therapy to treat HBV in pregnant women can have two potential benefits: (1) prevent perinatal transmission of HBV, and (2) treat chronic HBV in the mother, if indicated.[43] The use of the nucleotide reverse transcriptase inhibitor tenofovir DF is the preferred antiviral agent to treat HBV in pregnant women.[3,44] The following summary outlines the general approach for the potential use of antiviral therapy in HBsAg-positive pregnant women (Figure 2).

### Recommended Antiviral to Treat HBV During Pregnancy

Of the preferred antiviral options to treat hepatitis B, only tenofovir DF has been adequately studied in pregnancy. In addition, tenofovir DF has multiple features that make it the preferred drug for treatment of HBV during pregnancy, including excellent potency, high barrier to resistance, a known good safety profile in pregnancy, and proven efficacy in preventing perinatal transmission in mothers with HBV DNA levels greater than 200,000 IU/mL (Figure 3).[3,44,45] The recommended dose of tenofovir DF is 300 mg daily; the dose of tenofovir DF must be adjusted and reduced in persons who have a creatinine clearance less than 50 mL/min. Prior to starting tenofovir DF, the following baseline laboratory studies should be performed: serum creatinine, estimated creatinine clearance, urine glucose, and urine protein. Although there is growing evidence to support the safety and efficacy of tenofovir alafenamide during pregnancy, its use is not currently recommended during pregnancy.[46,47]

### HBsAg-Positive Women Not on Antiviral Therapy at the Time of Pregnancy

- **Indications for HBV Therapy to Prevent Perinatal HBV Transmission:** For HBsAg-positive women who are not on HBV therapy at the time they become pregnant, the main indication for initiating HBV to prevent perinatal HBV transmission is a maternal HBV DNA level greater than 200,000 IU/mL.[2,3] This recommendation is based on data that suggest (1) perinatal HBV infections can occur even when infants receive appropriate doses of hepatitis B vaccination and HBIG, with most of these cases involving mothers with high plasma HBV DNA levels, and (2) the use of antiviral therapy in the third trimester can significantly reduce perinatal HBV transmission.[1,3,44,45,48] The optimal timing for initiating HBV therapy during pregnancy to prevent perinatal transmission is not clear, but most experts recommend initiating therapy at some time during weeks 28 to 32 of gestation since this was the time frame when antiviral therapy was started in most of the studies that showed reduction in perinatal HBV transmission.
- **Indications for HBV Therapy for Maternal Benefit:** All HBsAg-positive women who are not on HBV therapy at the time they become pregnant should undergo evaluation to determine if they have an indication to start therapy based on treatment guidelines for persons with chronic HBV.[3,49,50] We recommend initiating HBV for the purposes of maternal benefit for pregnant women who have (1) cirrhosis and/or (2) the presence of elevated HBV DNA (2,000 IU/mL or greater) and elevated ALT (greater than 25 U/mL).[3] In addition, as noted above, women in the third trimester who have an HBV DNA level of 200,000 IU/mL or greater should initiate antiviral treatment regardless of ALT levels.[2,3]
- **Monitoring Women Who Do Not Meet Criteria for Treatment:** For pregnant women who do not meet criteria for antiviral therapy, some experts recommend monitoring ALT levels every 3 months during pregnancy and for 6 months postpartum, primarily because of possible hepatic flares that can occur as a result of pregnancy-associated immunologic changes. In addition, HBV DNA should be checked at 26 to 28 weeks of gestation (and concurrent with any elevation of ALT) to determine the need for antiviral initiation in the third trimester.[2,3,44]
- **Duration of Antiviral Therapy for Pregnant Women:** Antiviral therapy with tenofovir DF, initiated purely for the prevention of mother-to-child transmission, can be discontinued at delivery. In this situation, however, women should undergo postpartum lab monitoring at least every 3 months and for up to 6 months to assess for hepatitis flares and seroconversion; some experts recommend more intensive monitoring with ALT and HBV DNA at 1, 3, and 6 months postpartum.[3,44] Postpartum HBV flares are common, especially among those who are HBeAg-positive and stop tenofovir DF, but there

are no formal recommendations to extend antiviral therapy in women who do not otherwise meet treatment criteria.[51,52] Women who have an indication for HBV treatment other than for preventing perinatal HBV transmission should continue on therapy indefinitely and follow the same treatment guidelines for monitoring and potentially discontinuing therapy as for all individuals receiving chronic treatment for HBV.[3] The safety of tenofovir DF is well established in the setting of lactation. Thus, if treatment is continued in the postpartum period and the mother is breastfeeding, tenofovir DF is the preferred agent. When the mother stops breastfeeding, consideration can be given to switching tenofovir DF to either tenofovir alafenamide or entecavir if indicated or preferred.

## **HBsAg-Positive Women on Antiviral Therapy at the Time of Pregnancy**

Women who are HBsAg positive and become pregnant while taking antiviral therapy to treat HBV should discuss the pros and cons of continuing therapy with their health care provider. Most experts would recommend continuing antiviral HBV treatment in this situation, both for the mother's benefit (reducing the risk of a hepatitis flare during pregnancy) and for decreasing the risk of perinatal HBV transmission. Tenofovir DF is the drug of choice for HBV treatment during pregnancy, and available data suggest it is safe for use during pregnancy and for breastfeeding.[53,54] For pregnant women who are going to continue receiving HBV treatment but are taking a regimen other than tenofovir DF, it is important they promptly switch the antiviral therapy to tenofovir DF, owing to its favorable safety profile in pregnancy, high barrier to resistance, and established efficacy in preventing perinatal HBV transmission.[45] Women and providers who choose to remain on entecavir or tenofovir alafenamide should consider enrolling in the [Antiviral Pregnancy Registry](#), which collects de-identified data on drug safety and pregnancy outcomes. Similar treatment endpoints should also be used for pregnant women as for nonpregnant women with chronic HBV. Noncirrhotic patients who seroconvert their HBeAg to anti-HBe can discontinue therapy after a period of treatment consolidation, which is typically defined as normal ALT and undetectable HBV DNA for 12 months following seroconversion. Conversely, cirrhotic patients should continue antiviral therapy indefinitely regardless of HBeAg seroconversion, HBV DNA values, or ALT levels.[3]

## **Considerations at the Time of Labor and Delivery**

There is no clear evidence of reduced perinatal HBV transmission among women who deliver via cesarean section, and as such, the American Association for the Study of Liver Diseases (AASLD) guidelines recommend against the routine use of elective cesarean section in HBsAg-positive mothers.[3] Similarly, owing to limited data on the risk of perinatal transmission in the setting of premature rupture of membranes, there are no recommendations to manage HBsAg-positive women who have premature rupture of membranes different than HBsAg-negative women who have premature rupture of membranes. In addition, there are no recommendations to give extra doses or additional antiviral medications to mothers during labor and delivery.

## **Considerations Regarding Amniocentesis**

Although perinatal HBV transmission following amniocentesis has been described, particularly among mothers with high plasma HBV DNA levels, the overall risk appears to be very low. The 2018 AASLD HBV guidance recommends considering the risk of perinatal HBV transmission when weighing the risks and benefits of performing amniocentesis in women with high plasma HBV DNA levels.[3]

## Management of Acute HBV in Pregnancy

Acute hepatitis B infection during pregnancy is typically mild (for the mother) and nonteratogenic, but it may confer a higher risk for low birth weight and prematurity.[[55,56](#)] Similarly, mothers with acute HBV during pregnancy may be more likely to progress to chronic infection, with one study from China suggesting that pregnant women with acute HBV had a relative risk of 4.6 for the development of chronic infection when compared with nonpregnant women controls.[[57](#)] Acquisition of acute HBV near the time of delivery poses the highest risk for perinatal transmission, and therefore women with ongoing risk factors for HBV acquisition should undergo repeat HBV screening near the time of delivery.[[2,55,56](#)]

Treatment of acute hepatitis B infection during pregnancy should be considered in the following situations: (1) the mother has a plasma HBV DNA level of 200,000 IU/mL or greater at any time during the third trimester, (2) the mother has severe, protracted hepatitis (increase in international normalized ratio [INR] and jaundice persisting for greater than 4 weeks), and (3) the mother has acute fulminant liver failure.[[3,58](#)] In these cases, the use of the nucleotide reverse transcriptase inhibitor tenofovir DF is preferred due to excellent potency, a high barrier to resistance, proven efficacy in preventing perinatal HBV transmission, and experience in pregnancy.[[3,44,45](#)] Management of women with protracted hepatitis during pregnancy or with fulminant liver failure should include involvement of experts, ideally both a hepatologist and an obstetrician who have experience with this complicated issue.

## Safety of Antivirals During Pregnancy

No antiviral medications have been FDA-approved for the treatment of chronic hepatitis B during pregnancy, owing to a lack of large-scale studies evaluating antiviral safety in pregnant women with HBV monoinfection. There are, however, large-scale studies with tenofovir DF in pregnant women with HIV that suggest it is safe for use during pregnancy.[59,60] In addition, smaller studies evaluating these drugs for the prevention of mother-to-child transmission in HBV have shown no evidence of adverse effects on the fetus.[33,45,48,54] The [Antiretroviral Pregnancy Registry](#) includes self-reported adverse effects of antivirals used during pregnancy for the treatment of HIV and/or HBV.[61] The following summarizes pregnancy-related information for the three preferred oral antiviral agents to treat HBV. Interferon and peginterferon are contraindicated for use during pregnancy and thus will not be discussed further here.

- **Entecavir:** The nucleoside analogue entecavir is highly active against HBV. It is not used in the treatment of HIV, and therefore, limited data exist on its use during pregnancy. Although animal studies in rats and rabbits revealed no signs of embryo-fetal toxicity, no well-controlled studies have been done in pregnant women. As such, the use of entecavir is not recommended during pregnancy.
- **Tenofovir alafenamide:** Tenofovir alafenamide is a nucleotide analogue that has been used to treat HBV and, in combination with other antiretroviral medications, to treat HIV. Although there is growing evidence to support the safety and efficacy of tenofovir alafenamide in pregnant women, at present, HBV guidelines do not recommend its routine use for treatment of HBV during pregnancy.[46,47,62] The HIV Perinatal guidelines now recommend tenofovir alafenamide (in combination with emtricitabine) as a preferred component of a three-drug antiretroviral regimen for pregnant women with HIV, including those with HBV coinfection.[63]
- **Tenofovir DF:** With the nucleotide analogue tenofovir DF, longitudinal human data have not shown an increased risk for teratogenicity among babies born to mothers who took tenofovir DF during pregnancy, although most of these women were taking tenofovir DF for HIV therapy.[64,65] In comparison to an estimated 3% rate of birth defects in the general United States population, the Antiretroviral Pregnancy Registry has found a 2.4% risk of birth defects in babies born to mothers who took any tenofovir DF-containing regimen during the first trimester and a 2.3% risk of birth defects when mothers took a tenofovir DF-containing regimen during the second and third trimester.[61] Despite some concern regarding the effect of in utero tenofovir DF exposure on bone health, a recent study of children born to mothers with HIV found no difference in length of head circumference at 2 years of age for children exposed to tenofovir DF in utero compared to children not exposed to tenofovir DF.[66,67]



## Hepatitis B Flares During Pregnancy and in the Postpartum Period

Although women with chronic HBV infection typically tolerate the infection well during pregnancy, the relative immunosuppressant state of pregnancy often causes hepatitis flares, with even greater risk in the postpartum period.[\[51,68\]](#) In a prospective study of predominantly untreated, pregnant women with chronic HBV in Australia, 25% (108 of 126) of the women for whom postpartum labs were available had evidence of a postpartum hepatitis flare based on increases in ALT levels.[\[68\]](#) By comparison, only 1.6% (2 of 126) women experienced a hepatitis flare during pregnancy in this cohort.[\[68\]](#) Flares during pregnancy and in the postpartum period are often mild, but rare cases of fulminant liver failure have been described.[\[69,70\]](#) In women with chronic hepatitis B, the risk for postpartum HBV flares is common regardless of receipt of antiviral therapy during pregnancy and even when treatment is extended for at least 4 weeks after birth.[\[52\]](#)



## Management of Neonates Born to HBsAg-Positive Mothers

Recommendations for neonatal immunoprophylaxis to prevent perinatal transmission of HBV differ depending on the HBsAg status of the mother and the birth weight of the infant. When giving the birth dose hepatitis B vaccination and any doses before age 6 weeks, the single-antigen (monovalent) hepatitis B vaccine should be used. For infants 6 weeks of age and older, the combined vaccine (Pediatrix) can be substituted for the single-antigen hepatitis B vaccines (Engerix-B or Recombivax-HB). If, however, Pediatrix is used, the full three-shot series of Pediatrix must be completed, regardless of receipt of birth dose vaccination or maternal HBsAg status.<sup>[2]</sup> The following reflect recommendations from the CDC Advisory Committee on Immunization Practices (ACIP).<sup>[2]</sup>

### Infants Born to HBsAg-Positive Mothers

All infants born to HBsAg-positive women, or women with other evidence of chronic HBV infection (e.g., positive HBV DNA, positive HBeAg, or known history of chronic HBV infection) should receive an intramuscular dose of single-antigen hepatitis B vaccine and one dose of intramuscular HBIG (0.5 mL), both within 12 hours of birth. The hepatitis B vaccine and HBIG should be given regardless of birth weight or maternal antiviral therapy, and the injections should be at different sites on the body.

- **Infants Weighing at Least 2,000 Grams:** Infants weighing at least 2,000 grams (4.4 pounds) should receive a second hepatitis B vaccine dose at 1 to 2 months of age and a third dose at 6 to 12 months of age.
- **Infants Weighing Less than 2,000 Grams:** For infants weighing less than 2,000 grams (4.4 pounds) at birth, the birth dose vaccine should not be counted towards their three-shot series due to possible decreased immunogenicity in these low-weight infants. As such, they should receive an additional 3 doses of vaccine, given at 1, 2 to 3, and 6 to 12 months of age (for a total of 4 doses). For all infants, regardless of birth weight, it is important that the final dose in the series not be administered earlier than 24 weeks of age.<sup>[2]</sup>
- **Follow-Up Serologic Testing:** After completion of the HBV vaccine series, all infants born to HBsAg-positive mothers should receive HBV serologic testing at approximately 9 to 12 months of age (making sure this is done at least 1 month after the final hepatitis B vaccine series dose and at least 9 months after HBIG has been given). Testing for anti-HBc is not recommended since passive transfer of maternal anti-HBc may persist for 24 months. Infants who test HBsAg negative and have an anti-HBs level of 10 mIU/mL or greater are considered immune to HBV.
  - The preferred approach for HBsAg-negative infants who have an anti-HBs level less than 10 mIU/mL is to first give one additional dose of HBV vaccine, followed by repeat serologic testing in 1 to 2 months after this dose ([Figure 4](#)).<sup>[2]</sup> If anti-HBs levels remain below 10 mIU/mL after a single repeat dose, infants should receive an additional two doses of vaccine to complete another three-dose series. This should again be followed by repeat serologic testing in 1 to 2 months, but if the child has not obtained immunity to HBV at this point, subsequent doses of vaccine are unlikely to provide additional benefit; these children are considered at risk of acquiring HBV and prevention measures should be used.<sup>[2]</sup>
  - The alternative approach for infants with an anti-HBs level less than 10 mIU/mL at 9 to 12 months of age is to revaccinate with 3 doses of the HBV vaccine and then repeat serologic testing 1 to 2 months after the last vaccine dose ([Figure 5](#)).<sup>[2]</sup>

### Infants Born to Mothers of Unknown HBsAg Status

Women without documentation of prior HBsAg testing should be screened at the time of delivery. The management in this situation is stratified based on the birth weight of the infant and the results of the mother's HBsAg test.

- **Infants Weighing at Least 2,000 Grams:** While maternal HBsAg test results are pending, infants

weighing 2,000 grams or more should receive the single-antigen hepatitis B vaccine within 12 hours of birth; administration of HBIG is not recommended in this situation. If the mother's HBsAg test result is positive, then HBIG should be administered as soon as possible, but no later than 7 days after birth. Regardless of the mother's test result, the infant should complete a standard three-dose hepatitis B vaccination series, with the remaining additional doses at 1 to 2 months and 6 to 18 months. If the mother's HBsAg test result is negative, the infant should not receive HBIG. If the HBsAg status of the mother remains unknown (e.g., in the case of confidential adoption), the infant should complete the standard three-shot hepatitis B vaccine series according to the recommended schedule for infants born to HBsAg-positive mothers; in this scenario, HBIG is not indicated.[2]

- **Infants Weighing Less than 2,000 Grams:** Due to decreased immunogenicity of the hepatitis B vaccine among infants with low birth weight, those infants weighing less than 2,000 grams should receive the single-antigen vaccine in addition to HBIG (administered at different sites on the body) if the mother's HBsAg status cannot be determined within 12 hours of birth. If the mother's HBsAg test is positive, or if the mother's HBsAg status remains unknown, low-birth-weight infants should complete a four-shot vaccination series as described in the section above on infants born to HBsAg-positive mothers. If the mother is ultimately found to be HBsAg negative, then infants less than 2,000 grams need only complete three doses of hepatitis B vaccine at the time of birth and subsequently at 2 months and 6 to 18 months.[2]
- **Follow-Up Serologic Testing:** If the mother's HBsAg test is negative, then postvaccination serologic testing for the infant is not recommended. If the mother's HBsAg testing is positive, or the mother's HBsAg status remains unknown, the infant should receive HBV serologic testing at 9 to 12 months of age (making sure this is done at least 1 month after the final hepatitis B vaccine series dose and at least 9 months after HBIG has been given). Infants who test HBsAg negative and have an anti-HBs level of 10 mIU/mL or greater are considered immune to HBV. Infants with an anti-HBs less than 10 mIU/mL are not immune and need further immunizations as outlined above for infants born to HBsAg-positive mothers.

## Infants Born to HBsAg-Negative Mothers

All infants weighing 2,000 grams or more born to HBsAg-negative mothers should receive their first HBV vaccine within 24 hours of birth. They should subsequently complete their hepatitis B vaccine series, with the second dose at 1 to 2 months of age and third dose at 6 to 18 months of age. Infants weighing less than 2,000 grams at birth should receive their first hepatitis B vaccine dose at the time of hospital discharge or at chronological age 1 month, whichever comes first, even if they still weigh less than 2,000 grams. These infants should complete the remaining doses of hepatitis B vaccine, with the second dose at age 2 months (making sure the second dose is given at least 1 month after the first dose) and the third dose at age 6 to 18 months (making sure the third dose is given at least 8 weeks after the second dose and at least 16 weeks after the first dose). There are no recommendations to perform routine follow-up serologic testing in infants born to HBsAg-negative mothers.[2]

## Efficacy of Immunoprophylaxis

Several studies and meta-analyses support the efficacy of birth dose HBV vaccination and HBIG in preventing vertical transmission of hepatitis B. When compared to no intervention, a 2006 Cochrane review found that HBV vaccine plus HBIG dramatically decreased the risk of perinatal transmission, with a relative risk of 0.08.[21] Similarly, several prospective studies have shown high efficacy rates for immunoprophylaxis in infants born to HBsAg-positive mothers, with less than 2% of exposed infants developing HBV infection when receiving both the HBIG and hepatitis B vaccine.[18,71] The same Cochrane review found that HBIG plus hepatitis B vaccine significantly decreased the rate of perinatal transmission when compared to hepatitis B vaccination alone (relative risk, 0.54).[21]

## Other Impacts of Maternal HBV on Infants

The effect of chronic maternal HBV infection on other noninfectious neonatal outcomes is uncertain. In a large study comparing 824 HBsAg-positive pregnant women with 6,281 HBsAg-negative pregnant women, the investigators found no difference in incidence of preterm birth, premature rupture of membranes, low birth weight, neonatal jaundice, fetal distress, perinatal asphyxia, congenital abnormalities, gastrointestinal tract abnormalities, or perinatal mortality.[[72](#)] A similar study from Germany found no difference in adverse pregnancy outcomes among 39 HBsAg-positive women when compared to 8,154 HBsAg-negative women.[[73](#)] Several other reports, however, have cited higher rates of preterm birth, lower birth weight, congenital malformations, and lower Apgar scores among infants born to HBsAg-positive mothers.[[74,75,76,77](#)]

## **Breastfeeding in HBsAg-Positive Mothers**

### **Risk of HBV Transmission via Breastfeeding**

Transmission of HBV through breast milk is not a significant source of perinatal HBV transmission, and there is no contraindication to breastfeeding in HBV-monoinfected mothers.[[3](#),[40](#),[41](#),[42](#)] In the United States, however, women who have HBV and HIV coinfection should not breastfeed, due to the substantial risk of HIV transmission during breastfeeding.

### **Safety of Antiviral Medications During Breastfeeding**

There are insufficient long-term safety data on breastfeeding among mothers receiving antiviral therapy for HBV treatment. Although drug labels recommend against breastfeeding while taking tenofovir DF, this antiviral medication, which is the preferred agent to treat hepatitis B in breastfeeding women, is unlikely to pose significant harm to breastfeeding infants.[[3](#),[44](#)] Although limited data are available in women with HBV monoinfection, studies done in women with HIV living in resource-limited settings support the safety of tenofovir DF during breastfeeding and suggest that drug concentrations in breast milk are quite low.[[44](#),[78](#),[79](#),[80](#)]

### **Recommendation for Breastfeeding in Women Taking Tenofovir DF**

Given the relative safety of the recommended antiviral agent tenofovir DF during breastfeeding, the 2018 AASLD Hepatitis B Guidance states that breastfeeding is not contraindicated in HBsAg-positive mothers on (and off) antiviral therapy.[[3](#)]

## Summary Points

- All pregnant women should undergo serologic screening for hepatitis B infection at their first prenatal visit, regardless of prior hepatitis B vaccination status.
- The overall rate of HBV transmission from an HBsAg-positive mother to her neonate is approximately 40% in the absence of HBV postexposure immunoprophylaxis or maternal receipt of antiviral medication.
- Increased risk of perinatal HBV transmission is associated with high maternal plasma HBV DNA levels, maternal HBeAg-positive status, and lack of appropriate immunoprophylaxis for babies.
- The exact mechanisms and timing of perinatal HBV transmission are unclear, but given the greater than 90% efficacy of birth dose vaccination and HBIG, most infections are believed to occur intrapartum.
- Indications for initiation of HBV treatment are generally the same in pregnant and nonpregnant women, except that pregnant women with an HBV DNA level of greater than 200,000 IU/mL should initiate antiviral treatment, ideally during weeks 28 to 32 of gestation, to prevent perinatal transmission.
- When antiviral therapy for hepatitis B is indicated in pregnancy, tenofovir DF is preferred due to its potency, high barrier to resistance, known safety profile in pregnancy, and proven efficacy in preventing perinatal transmission of HBV in pregnant women who have an HBV DNA level greater than 200,000 IU/mL.
- In general, HBsAg-positive women who become pregnant while on therapy should continue antiviral HBV treatment. If they are on a drug other than tenofovir DF, they should promptly switch to tenofovir DF, given its known safety profile in pregnancy.
- Acute HBV infection during pregnancy is typically mild and nonteratogenic, but it may confer a higher risk for low birth weight and prematurity. Treatment is only indicated if the mother's HBV DNA level is 200,000 IU/mL or greater during the third trimester or in the setting of protracted and/or fulminant hepatitis.
- All infants born to HBsAg-positive women should receive an intramuscular dose of single-antigen hepatitis B vaccine and one dose of intramuscular HBIG (0.5 mL), both within 12 hours of birth. These should be given regardless of birth weight or maternal antiviral therapy.
- After completion of the HBV vaccine series, all infants born to HBsAg-positive mothers should receive HBV serologic testing at approximately 9 to 12 months of age, making sure this is done at least 1 month after the final hepatitis B vaccine series dose and at least 9 months after HBIG has been given.

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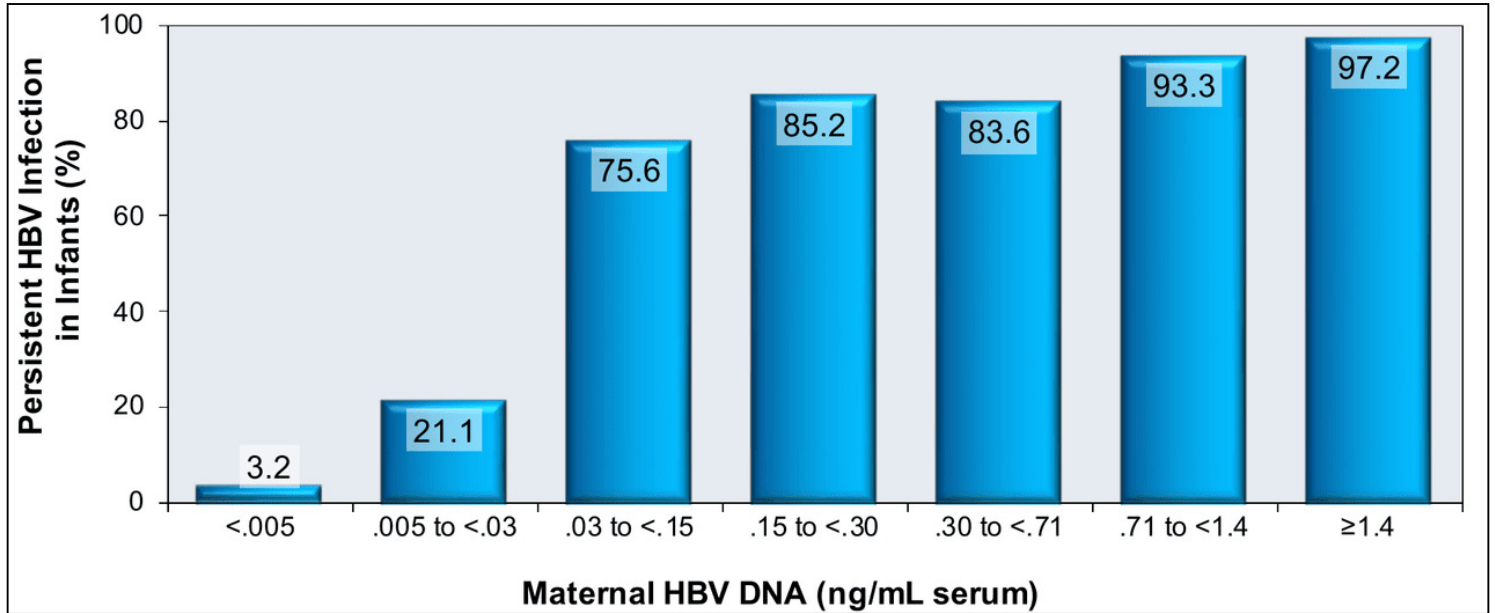
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## Figures

**Figure 1 Maternal HBV DNA Level and Risk of Transmission to Infants**

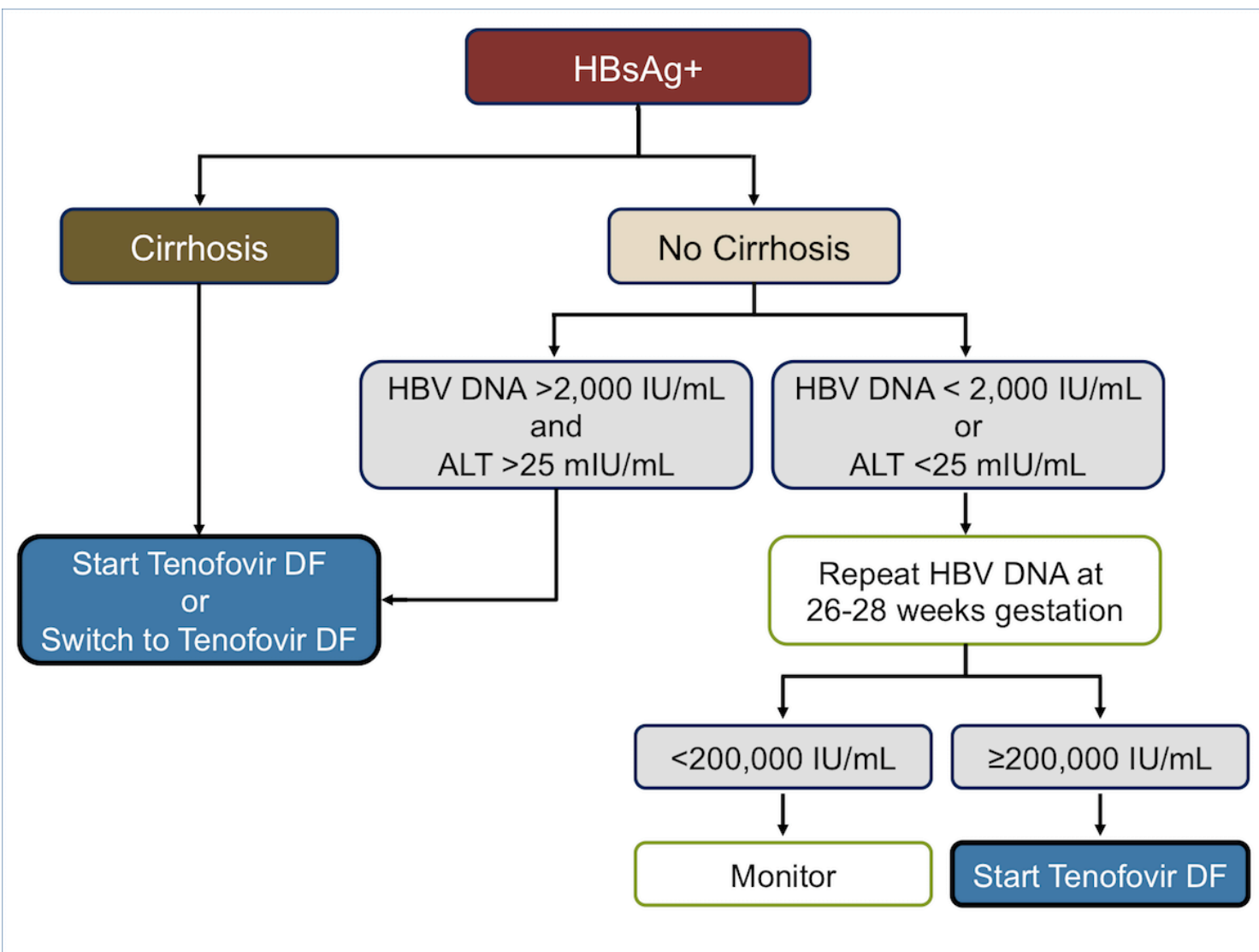
Source: Burk RD, Hwang LY, Ho GY, Shafritz DA, Beasley RP. Outcome of perinatal hepatitis B virus exposure is dependent on maternal virus load. J Infect Dis. 1994;170:1418-23.



## Figure 2 Treatment Approach to HBsAg-Positive Mothers During Pregnancy

This algorithm outlines a general approach for use of antiviral therapy in HBsAg-positive women during pregnancy. This recommended approach is based on recommendations in the 2020 HBV Primary Care Workgroup: Hepatitis B Management: Guidance for the Primary Care Provider.

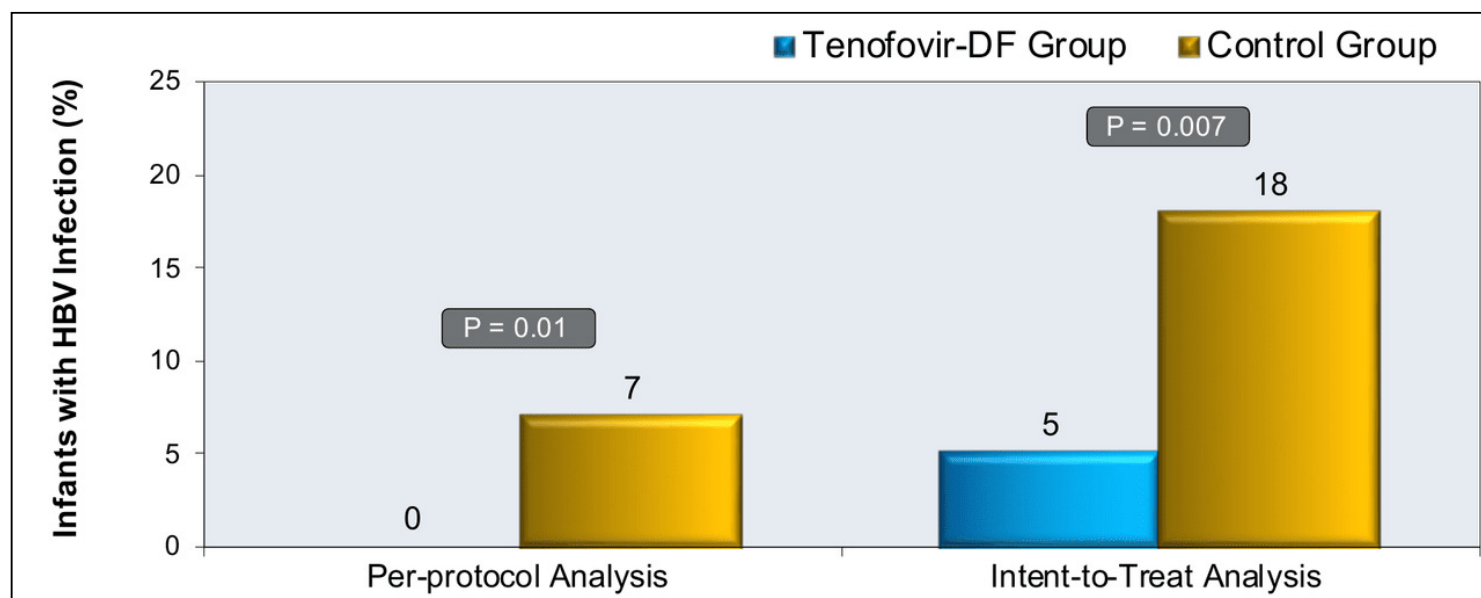
Source: 2020 HBV Primary Care Workgroup: Hepatitis B Management: Guidance for the Primary Care Provider



**Figure 3 Risk of Maternal HBV Transmission in Mothers Randomized to Tenofovir DF or Control**

This trial shows data from 200 pregnant, HBsAg-positive women with HBV DNA levels greater than 200,000 IU/mL who were randomized to receive tenofovir DF or placebo at week 28 of gestation. This graph shows the rate of HBV infection among infants in the control and tenofovir DF groups, with data shown for per-protocol analysis and intent-to-treat analysis.

Source: Pan CQ, Duan Z, Dai E, et al. Tenofovir to prevent hepatitis B transmission in mothers with high viral load. N Engl J Med. 2016;374:2324-34.



# Figure 4 Recommended Approach to Infants (Born to HBsAg-Positive Mothers) Who Do Not Respond to HBV Vaccine

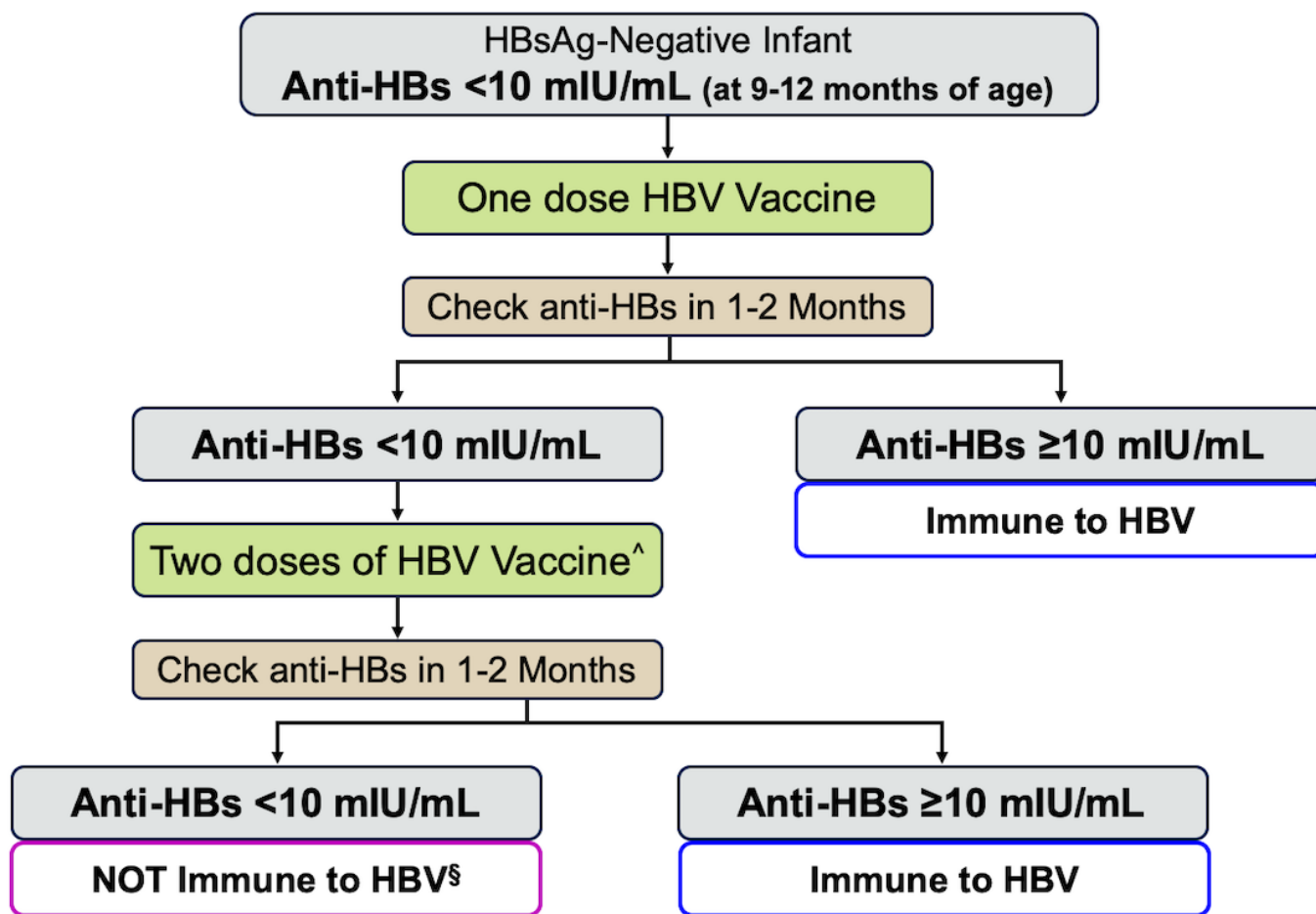
^The two additional doses should be given on regular vaccine schedule to complete the second HBV vaccine series.

§If anti-HBs remains <10 mIU/mL after repeat vaccination, there is no evidence for benefit of giving additional vaccine doses.

Source: Schillie S, Vellozzi C, Reingold A, et al. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep. 2018;67:1-31.

## Preferred Approach

Infants Born to HBsAg+ Mothers, Received ≥3 Hepatitis B Vaccine Doses



## Figure 5 Alternative Approach to Infants (Born to HBsAg-Positive Mothers) Who Do Not Respond to HBV Vaccine

<sup>§</sup>If anti-HBs remains <10 mIU/mL after repeat vaccination, there is no evidence for benefit of giving additional vaccine doses.

Source: Schillie S, Vellozzi C, Reingold A, et al. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep. 2018;67:1-31.

### Alternative Approach

Infants Born to HBsAg+ Mothers, Received ≥3 Hepatitis B Vaccine Doses

