Screening for Hepatitis B Virus Infection in Pregnant Women: US Preventive Services Task Force Reaffirmation Recommendation Statement

US Preventive Services Task Force

Et al.

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Screening for Hepatitis B Virus Infection in Pregnant Women
US Preventive Services Task Force Reaffirmation Recommendation Statement

US Preventive Services Task Force

**IMPORTANCE** Screening for hepatitis B virus (HBV) infection during pregnancy identifies women whose infants are at risk of perinatal transmission. Data from a nationally representative sample showed a prevalence of maternal HBV infection of 85.8 cases per 100,000 deliveries from 1998 to 2011 (0.09% of live-born singleton deliveries in the United States). Although there are guidelines for universal infant HBV vaccination, rates of maternal HBV infection have increased annually by 5.5% since 1998. Children infected with HBV during infancy or childhood are more likely to develop chronic infection. Chronic HBV infection increases long-term morbidity and mortality by predisposing infected persons to cirrhosis of the liver and liver cancer.

**OBJECTIVE** To update the 2009 US Preventive Services Task Force (USPSTF) recommendation on screening for HBV infection in pregnant women.

**EVIDENCE REVIEW** The USPSTF commissioned a reaffirmation evidence update to identify substantial new evidence sufficient enough to change the prior recommendation. The USPSTF targeted its evidence review on the effectiveness and potential harms of screening and the effectiveness and harms of case management to prevent perinatal transmission.

**FINDINGS** The USPSTF previously found adequate evidence that serologic testing for hepatitis B surface antigen accurately identifies HBV infection. Interventions are effective for preventing perinatal transmission, based on foundational evidence and observational studies of US case management programs. In addition, there is evidence that over time, perinatal transmission has decreased among women and infants enrolled in case management, providing an overall substantial health benefit. Therefore, the USPSTF reaffirms its previous conclusion that there is convincing evidence that screening for HBV infection in pregnant women provides substantial benefit.

**CONCLUSIONS AND RECOMMENDATION** The USPSTF recommends screening for HBV infection in pregnant women at their first prenatal visit. (A recommendation)

Corrected on September 17, 2019.
HBV infection of 85.8 cases per 100,000 deliveries from 1998 to 2011 (0.09% of live-born singleton deliveries in the United States). Although there are guidelines for universal infant HBV vaccination, rates of maternal HBV infection have increased annually by 5.5% since 1998. Persons infected with HBV during infancy or childhood are more likely to develop chronic infection. Chronic HBV infection increases long-term morbidity and mortality by predisposing infected persons to cirrhosis of the liver and liver cancer.

Reaffirmation
In 2009, the USPSTF reviewed the evidence for screening for HBV infection in pregnant women and issued an A recommendation. The USPSTF has decided to use a reaffirmation deliberation process to update this recommendation. The USPSTF uses the reaffirmation process for well-established, evidence-based standards of practice in current primary care practice for which only a very high level of evidence would justify a change in the grade of the recommendation. In its deliberation of the evidence, the USPSTF...
The USPSTF previously reviewed the evidence on serologic testing for HBV (hepatitis B surface antigen [HBsAg]) in pregnancy and found adequate evidence of its accuracy (sensitivity and specificity both >98%).

### Benefits of Early Detection and Interventions
The USPSTF found convincing evidence that universal prenatal screening for HBV infection substantially reduces perinatal transmission of HBV and the subsequent development of chronic HBV infection. For HBV-positive mothers, case management during pregnancy includes HBV DNA viral load testing and referral to specialty care for counseling and medical management of HBV infection. For infants born to mothers who test positive for HBsAg, current guidelines for case management include HBV vaccination and hepatitis B immune globulin (HBIG) prophylaxis within 12 hours of birth and completing the vaccine series and serologic testing for infection and immunity at age 9 to 12 months. For infants born to mothers with unknown HBsAg status, current guidelines for case management include HBV vaccination within 12 hours of birth, followed by HBIG prophylaxis.

### Harms of Screening and Interventions
The USPSTF found limited evidence on the harms of screening for HBV infection in pregnant women but bounded the potential harms of screening as no greater than small based on the high accuracy of screening and the low likelihood of harms from preventive interventions.

### USPSTF Assessment
Using a reaffirmation process, the USPSTF concludes with high certainty that the net benefit of screening for HBV infection in pregnant women is substantial.

### Clinical Considerations

#### Patient Population Under Consideration
This recommendation applies to all pregnant persons (Figure 2).

#### Screening Tests
The principal screening test for detecting maternal HBV infection is the serologic identification of hepatitis B surface antigen (HBsAg). Screening should be performed in each pregnancy, regardless of previous HBV vaccination or previous negative HBsAg test results.

#### Screening Interval
A test for HBsAg should be ordered at the first prenatal visit. Women with unknown HBsAg status or with new or continuing risk factors for HBV infection (eg, injection drug use or a sexually transmitted infection) should be screened at the time of admission to a hospital or other delivery setting.

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**Figure 2. Clinical Summary: Screening for Hepatitis B Virus Infection in Pregnant Women**

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant persons</td>
<td>Screen for hepatitis B virus (HBV) infection.</td>
</tr>
</tbody>
</table>

**Risk Assessment**
In the United States, new cases of HBV among adults are largely transmitted through injection drug use or sexual intercourse, but most prevalent cases of HBV infection are chronic infections from exposure occurring in infancy or childhood. Another major risk factor for HBV infection is country of origin. In the United States, adults with HBV born in high-prevalence countries were commonly infected during childhood. In children, the primary source of infection is perinatal transmission at birth.

**Screening Tests**
The principal screening test for detecting maternal HBV infection is the serologic identification of HBsAg. Screening should be performed in each pregnancy, regardless of previous HBV vaccination or previous negative HBsAg test results.

**Screening Intervals**
A test for HBsAg should be ordered at the first prenatal visit. Women with unknown HBsAg status or with new or continuing risk factors for HBV infection (eg, injection drug use or a sexually transmitted infection) should be screened at the time of admission to a hospital or other delivery setting.

**Treatment and Interventions**
Interventions to prevent perinatal transmission of HBV infection include screening all pregnant women for HBV, vaccinating infants born to HBV-negative mothers within 24 hours of birth, and completing the HBV vaccination series in infants by age 18 months. For HBV-positive mothers, case management during pregnancy includes HBV DNA viral load testing and referral to specialty care for counseling and medical management of HBV infection. For infants born to mothers who test positive for HBsAg, current guidelines for case management include HBV vaccination and hepatitis B immune globulin (HBIG) prophylaxis within 12 hours of birth and completing the vaccine series and serologic testing for infection and immunity at age 9 to 12 months. For infants born to mothers with unknown HBsAg status, current guidelines for case management include HBV vaccination within 12 hours of birth, followed by HBIG prophylaxis.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to [https://www.uspreventiveservicestaskforce.org](https://www.uspreventiveservicestaskforce.org).

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Treatment
Interventions to prevent perinatal transmission of HBV infection include screening all pregnant women for HBV followed by treatment, vaccinating infants born to HBV-negative mothers within 24 hours of birth, and completing the HBV vaccination series in infants by age 18 months. For HBV-positive mothers, case management during pregnancy includes HBV DNA viral load testing and referral to specialty care for counseling and medical management of HBV infection. For infants born to mothers who test positive for HBsAg, current guidelines for case management include HBV vaccination and HBIG prophylaxis within 12 hours of birth and completing the vaccine series and serologic testing for infection and immunity at age 9 to 12 months. For infants born to mothers with unknown HBsAg status, current guidelines for case management include HBV vaccination within 12 hours of birth, followed by HBIG prophylaxis.5

Emerging evidence has demonstrated that administering tenofovir to HBV-positive women with acute infection significantly reduces the risk of HBsAg seropositivity in infants when combined with HBIG prophylaxis at birth and HBV vaccination.6,7 As a result, recent guidelines recommend testing for viral load, antiviral treatment, and HBV vaccination and HBIG prophylaxis.5

Useful Resources
The USPSTF has made recommendations on screening for other infections, including chlamydia and gonorrhea,8 HBV in nonpregnant adults and adolescents,9 genital herpes,10 HIV,11 and syphilis in pregnant women.12

The Centers for Disease Control and Prevention (CDC) provides more information about HBV infection, including perinatal transmission.13,14

Discussion

Burden of Disease
Hepatitis B is a viral infection of the liver transmitted through contact with the bodily fluids or blood of an infected individual. In the United States, prevalence estimates of chronic HBV infection range from approximately 850,000 to more than 2 million cases.18,19 In the United States, new cases of HBV among adults are largely transmitted through injection drug use or sexual intercourse, but most prevalent cases of HBV infection are chronic infections from exposure occurring in infancy or childhood. Another major risk factor for HBV infection is country of origin. In the United States, adults with HBV born in high-prevalence countries were commonly infected during birth.19 In US-born children, the primary source of infection is vertical transmission at birth.21 According to the CDC, 800 to 1000 cases of perinatal transmission (3.8% of infants born to HBV-positive women) occurred yearly from 2000 to 2009.22

Since 1998, rates of maternal HBV infection have increased annually by 5.5%.2,12 Older maternal age, race/ethnicity (non-Hispanic black and Asian populations), lower education, higher poverty levels, and lack of insurance coverage are risk factors for HBV infection among women.2,23

Persons infected with HBV during infancy or childhood are more likely to develop chronic HBV infection and have poor long-term health outcomes (eg, chronic hepatitis, cirrhosis, or hepatocellular carcinoma) compared with persons infected later in life.3 Acute HBV infections progress to chronic disease in 80% to 90% of infected infants, 30% of acute infections progress before age 6 years, and less than 1% to 12% of acute infections progress in older children or adults. Approximately 25% of persons who become chronically infected during childhood and 15% of those infected as adults will die of cirrhosis or hepatocellular carcinoma.1,5,24

Scope of Review
To reaffirm its 2009 recommendation on screening for HBV infection in pregnant women, the USPSTF commissioned a reaffirmation evidence update. The aim of this update is to identify substantial new evidence sufficient enough to change the prior recommendation. Case management is the standard intervention in the United States for all HBV-positive pregnant women. As a result, the USPSTF targeted its evidence review to focus on the effectiveness and potential harms of screening and the effectiveness and harms of case management to prevent perinatal transmission.25

Accuracy of Screening Tests
The primary screening test for detecting maternal HBV infection is the serologic detection of HBsAg. Serologic immunoassays for detecting HBsAg have a reported sensitivity and specificity greater than 98%.26,27

Effectiveness of Early Detection and Treatment
No studies were identified that directly assessed the benefits or harms of universal HBV screening during pregnancy. Two fair-quality observational studies reported perinatal transmission rates (primary outcome) over time.1,28,29

Research Needs and Gaps
The USPSTF has identified areas of needed research. Continued research on effective implementation of case management in vulnerable populations most at risk for perinatal transmission of HBV infection is needed. Additional studies on the effectiveness of prenatal antiviral medication to reduce perinatal transmission are needed. Analyses of recent data from existing case management programs, such as the Perinatal Hepatitis B Prevention Program (PHBPP), would be helpful in understanding program performance and research needs.1 There is emerging evidence on the use of antiviral therapy during pregnancy.16,7 Further research is needed to examine the prevention of perinatal transmission.
One study reported outcomes of case management from 1994 to 2008 for 155,081 infants born to HBV-positive women in the national PHBPP, administered by the CDC. From 1994 to 2008, the estimated number of infants born to HBV-positive women increased in the United States from 19,208 to 25,600 (P < .001). The proportion of infants born to HBV-positive women enrolled in the PHBPP for case management also increased during this period, from 42.1% to 47.9% (P = .002). The number of infants receiving case management increased from 7,415 in 1994 to 12,033 in 2008 (P < .001).

Perinatal transmission outcomes were reported for infants born from 1999 to 2008 who received serologic testing (n = 55,362). There was a statistically significant decrease in the perinatal transmission rate (P = .001). In 1999, 1.9% of infants who received serologic testing were infected with HBV; by 2008, the rate had decreased to 0.8% (P = .001).

The second observational study was conducted in a large regional health care system in the United States (Kaiser Permanente Northern California). The case management program reported on 44,446 infants born to HBV-positive women from 1997 to 2010. More than 97% of the infants received HBV vaccination and HBIG prophylaxis within 12 hours of birth. Overall rates of perinatal transmission were very low (0.75%), and a decreasing trend in perinatal transmission was reported (incidence rate ratio, 0.90 [95% CI, 0.82-1.00]).

The results on historical trends from the observational studies are at risk of bias because of changes in case management program implementation, other interventions (eg, antiviral medication), cultural or secular changes (eg, universal vaccination), changes in reporting methods, and differences in data collection procedures.

Potential Harms of Screening and Treatment
No studies identified that reported the potential harms of universal HBV screening during pregnancy or case management. Screening has a low false-positive rate, and treatment is rarely harmful.

Estimate of Magnitude of Net Benefit
The USPSTF considered the evidence using a reaffirmation process. The USPSTF previously found adequate evidence that serologic testing for HBsAg accurately identifies HBV infection. Interventions are effective for preventing perinatal transmission, based on foundational evidence and observational studies of US case management programs. In addition, there is evidence that over time, perinatal transmission has decreased among women and infants enrolled in case management, providing an overall substantial health benefit. Therefore, the USPSTF reaffirms its previous conclusion that there is convincing evidence that screening for HBV infection in pregnant women provides substantial benefit.

Response to Public Comment
A draft version of this recommendation statement was posted for public comment on the USPSTF website from January 8, 2019, to February 4, 2019. A majority of the comments wanted more information about treatment with antiviral therapy. In response, the USPSTF added information about emerging evidence that treatment with antiviral therapy works and that more research is needed in the Clinical Considerations and Research Needs and Gaps sections.

Reaffirmation of Previous USPSTF Recommendation
This recommendation is a reaffirmation of the USPSTF 2009 recommendation statement. In 2009, the USPSTF reviewed the evidence for screening for HBV infection in pregnant women and found that the benefits of screening substantially outweighed the harms.

For the current recommendation, the USPSTF commissioned a targeted review to look for new and substantial evidence on the benefits and harms of screening and determined that the net benefit of screening for HBV infection in pregnant women continues to be well established. The USPSTF found no new substantial evidence that would change its recommendation and, therefore, reaffirms its recommendation to screen for HBV infection in pregnant women.

Recommendations of Others
The American College of Obstetricians and Gynecologists recommends screening for HBV with serologic testing for HBsAg in every pregnant patient at the earliest prenatal visit. These tests should be designated as “prenatal.” Pregnant women who test positive for HBsAg should then be tested for HBV DNA. The CDC Advisory Committee on Immunization Practices similarly recommends testing for HBsAg in all pregnant women during an early prenatal visit (eg, in the first trimester) and HBV DNA testing for pregnant women who test positive for HBsAg.

The American Academy of Family Physicians recommends screening for HBV infection in pregnant women at their first prenatal visit. The American Association for the Study of Liver Diseases recommends screening in all pregnant women by testing for HBsAg and the hepatitis B surface antibody (anti-HBs).
USPSTF Recommendation: Screening for Hepatitis B Virus Infection in Pregnant Women

Clinical Review & Education

US Preventive Services Task Force


