Screening for Hepatitis B Virus Infection in Pregnant Women: Evidence for the U.S. Preventive Services Task Force Reaffirmation Recommendation Statement

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Background: Screening for hepatitis B virus (HBV) infection in pregnant women to identify newborns who will require prophylaxis against perinatal infection is a well-established, evidence-based standard of current medical practice. In 2004, the U.S. Preventive Services Task Force (USPSTF) recommended universal screening of pregnant women for HBV infection at the first prenatal visit.

Purpose: To search for large, high-quality studies related to hepatitis B screening in pregnancy that have been published since the 2004 USPSTF recommendation.

Data Sources: English-language studies indexed in PubMed and the Cochrane Database of Systematic Reviews and published between 1 January 2001 and 5 March 2008.

Study Selection: For benefits of screening and newborn prophylaxis, we included systematic reviews; meta-analyses; and randomized, controlled trials. For harms of screening, we included systematic reviews; meta-analyses; randomized, controlled trials; cohort studies; case–control studies; and case series of large, multisite databases. Abstracts and full articles were independently reviewed for inclusion by both reviewers.

Data Extraction: Data on the benefits of screening, including benefits of hepatitis B immune globulin and hepatitis B vaccine prophylaxis of newborns of hepatitis B surface antigen–positive mothers, were extracted by 1 reviewer.

Data Synthesis: No new studies met inclusion criteria. A 2006 systematic review of randomized, controlled trials found that newborn prophylaxis reduced perinatal transmission of HBV infection; all relevant trials were published in 1996 or earlier.

Limitation: The focused search strategy, which was restricted to English-language articles, may have missed some smaller studies or new research published in languages other than English.

Conclusion: No new evidence was found on the benefits or harms of screening for HBV infection in pregnant women. Previously published randomized trials support the 2004 USPSTF recommendation for screening.

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An estimated 24 000 infants are born each year in the United States to hepatitis B surface antigen (HBsAg)–positive mothers (1). In HBsAg-positive mothers who are also positive for hepatitis B e antigen, a marker of increased viral replication and infectivity, perinatal transmission rates have been noted to be as high as 85% to 90%.

Studies performed in the 1980s demonstrated that passive–active prophylaxis of newborns with hepatitis B immune globulin and hepatitis B vaccine dramatically reduced expected rates of perinatal transmission (2). In 1988, noting that risk factor–based screening did not identify between 35% and 65% of all HBsAg-positive mothers, the Centers for Disease Control and Prevention (CDC) recommended universal prenatal screening for hepatitis B virus (HBV) infection (3).

See also:

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In 2004, the U.S. Preventive Services Task Force (USPSTF) recommended screening for HBV infection in pregnant women at the first prenatal visit, on the basis of good evidence that universal prenatal screening using HBsAg, followed by prophylaxis of newborns of HBsAg-positive mothers, substantially reduces the risk for chronic HBV infection (4, 5). In 2008, the USPSTF decided to update the evidence to reaffirm its previous recommendation. The goal of this reaffirmation update was to search for large, high-quality studies related to HBV screening in pregnancy that have been published since the 2004 USPSTF recommendation.

The USPSTF requested that this update address 2 primary key questions:

1. What are the benefits of screening for HBV infection in pregnant women?

2. What are the harms of screening for HBV infection in pregnant women?

METHODS

Data Sources and Searches

We performed literature searches for the benefits and harms of screening for HBV infection in pregnant women, limited to the period from 1 January 2001 (the last year searched by the previous USPSTF review [5]) through 5 March 2008, using the search terms *hepatitis B*, *pregnancy*,

screening, and *mass screening*. We limited our initial searches to English-language articles indexed in the Cochrane Database of Systematic Reviews and the PubMed core clinical journal subset (previously known as the Abridged Index Medicus). When the initial searches revealed few articles, we expanded our searches to include noncore journals. We supplemented these searches by reviewing reference lists of recent reviews and clinical guidelines.

Study Selection

For benefits of prenatal screening for HBV infection, we included randomized, controlled trials; meta-analyses; and systematic reviews. For harms of screening, we included systematic reviews; meta-analyses; randomized, controlled trials; cohort studies; case–control studies; and large case series. We excluded editorials, case reports, narrative reviews, and guideline reports. We also excluded studies that were not generalizable to the United States. We determined generalizability of the study sample by consensus after discussing differences between the health care system and population characteristics of the study country and the United States with the USPSTF. Considerations about generalizability to the United States included the population prevalence of HBV infection and the availability of prenatal care and resources for passive and active prophylaxis against perinatal HBV transmission.

Because the most important benefits of screening for HBV infection in expectant mothers accrue to their offspring, we also searched for evidence of the benefits of prophylaxis in newborns whose mothers were identified through prenatal screening as having chronic HBV infection. The USPSTF determined that this update need not review evidence of the harms of hepatitis B vaccine or hepatitis B immune globulin, because the benefits of prophylaxis for newborns of HBsAg-positive mothers greatly outweigh the potential adverse effects.

Both reviewers evaluated all articles at the abstract and full-text article stage on the basis of predetermined exclusion criteria. Articles selected at the first stage by at least 1 reviewer were advanced to the next stage of review. At the full-text article stage, we resolved differences of opinion by a consensus process.

Data Extraction

One reviewer abstracted information on study design, sample size, entry criteria, demographic characteristics, treatment group allocation, and clinical outcomes of interest.

Quality Appraisal

We provided narrative descriptions of key limitations in quality and generalizability of retrieved evidence.

Data Synthesis and Analysis

We described and synthesized the data qualitatively in a narrative format.

RESULTS

We identified 90 potentially eligible articles and entered them into a reference database. After sequentially reviewing the abstracts and full articles (**Figure**), we found 1 systematic review that met inclusion criteria for this update.

Key Question 1

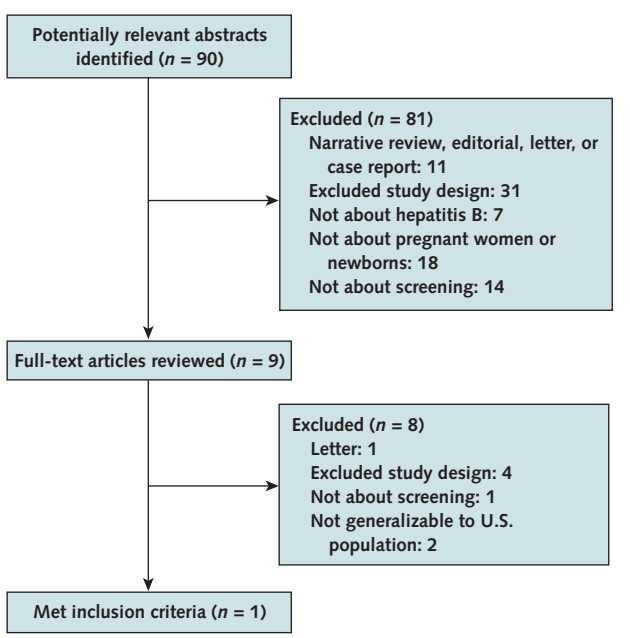
What are the benefits of screening for HBV infection in pregnant women?

We identified no new randomized, controlled trials of prenatal screening or newborn prophylaxis for HBV infection.

A 2006 Cochrane systematic review by Lee and colleagues (6) identified 4 randomized, controlled trials, published in 1996 or earlier, that compared newborn hepatitis B vaccination with placebo or no intervention. A meta-analysis of the 5 independent vaccination–placebo comparisons in these trials found that vaccination alone resulted in a statistically significant reduction in HBV transmission (relative risk, 0.28 [95% CI, 0.20 to 0.40]). In 4 other trials, efficacy did not differ between recombinant and plasma-derived vaccine (relative risk, 1.00 [CI, 0.71 to 1.42]). In addition, a meta-analysis of 10 trials that contained 12 independent comparisons found that the combination of hepatitis B vaccine and hepatitis B immune globulin given at birth was more efficacious than hepatitis B vaccine alone at preventing virus transmission (relative risk, 0.54 [CI, 0.41 to 0.73]).

Lee and colleagues rated most of the included trials as having low methodological quality because of limited in-

Figure. **Study flow diagram.**



formation regarding allocation concealment and the absence of blinding to the intervention (6). Few trials included newborns whose HBsAg-positive mothers were negative for hepatitis B e antigen (a disease state associated with a lower risk for perinatal HBV transmission). All of the trials were performed outside of the United States in countries with markedly higher prevalences of HBV infection.

Key Question 2

What are the harms of screening for HBV infection in pregnant women?

Potential harms of screening for HBV infection in pregnant women include false-positive test results, which may lead to psychological harms, increased costs, and inconvenience of subsequent testing, and adverse effects for the mother and newborn from unnecessary treatment. Previous reviews performed for the USPSTF (5, 7) identified no published data on these potential harms. We found no new studies that described false-positive screening rates or downstream events associated with false-positive test results.

Discussion

It is not surprising that we found no new studies meeting this update's restrictive inclusion criteria, which were designed to identify only types of evidence that would be necessary to alter the current USPSTF recommendation to screen for hepatitis B infection in pregnant women. Ethical considerations make it hard to imagine an institutional review board approving a contemporary randomized trial of prenatal screening versus no screening (or newborn prophylaxis versus no prophylaxis). Possible harms of screening for hepatitis B may include anxiety and false-positive results. Our inability to identify any published studies on harms—recognizing that Chinese-language articles would have been missed by our search strategy—after more than 2 decades of routine prenatal screening in the United States makes it likely that such harms are, at most, minimal.

It is important to note that the benefits of screening rest on the timely and accurate transfer of maternal test results to the labor, delivery, and newborn medical records. In 2005, deficiencies in such systems led to 6% of infants in the United States whose mothers were known to be HBsAg-positive not receiving prophylaxis with both hepatitis B immune globulin and hepatitis B vaccine at birth (1).

Current national recommendations to routinely provide hepatitis B vaccination to all infants starting at birth (since 1991) and to provide catch-up vaccination to children up to 18 years of age (since 1999) have the potential to eventually eliminate chronic hepatitis B infections among U.S.-born women of childbearing age (8). However, in areas of the United States with large immigrant populations, the yield of prenatal HBsAg screening has remained constant or has increased since the 1990s. In New York City, the overall rate of HBsAg-positive pregnancies increased from 612 to 800 per 100 000 pregnancies from 1995 to 2005 because of increased immigration of women from China (9).

In conclusion, we found no new evidence on the benefits or harms of screening for HBV infection in pregnant women. Future research will be needed to assess the effect of universal childhood hepatitis B vaccination on the benefits of prenatal screening for HBV infection in U.S.-born populations.

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