Revised ACIP Hepatitis B (HepB) Vaccine Recommendations

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Advisory Committee on Immunization Practices
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Outline

- Overview
- Hepatitis B Virus (HBV) background, epidemiology, and prevention
- Existing HepB recommendations
- Revisions deliberated by Work Group
Overview

- Hepatitis B Virus (HBV) background, epidemiology, and prevention
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Revised Statement

- Single document with guidance for:
  - HepB vaccination of infants, children, adolescents, and adults
  - Testing pregnant women for hepatitis B surface antigen (HBsAg), and, if positive, HBV DNA
  - HepB pre-vaccination and postvaccination serologic testing
  - HBV post-exposure prophylaxis (occupational and non-occupational exposures)
Revised Statement, cont.

- Incorporates previously-published recommendations from:
  - ACIP
  - CDC

- Augmented with American Association for the Study of Liver Diseases (AASLD) recommendation 8A: *The AASLD suggests antiviral therapy to reduce the risk of perinatal transmission of hepatitis B in HBsAg-positive pregnant women with an HBV DNA level >200,000 IU/mL*

Existing HepB Statements

A Comprehensive Immunization Strategy to Eliminate Transmission of HBV Infection in the U.S.: Recommendations of ACIP

Infants, Children, Adolescents (2005)  
Adults (2006)
Existing HepB Statements, cont.

- Diabetes (ACIP, 2011)
- Health-care personnel (CDC, 2013)
- Testing interval for infants (CDC, 2015)
Overview

- Hepatitis B Virus (HBV) background, epidemiology, and prevention
- Existing HepB recommendations
- Revisions deliberated by Work Group
Hepatitis B Virus

- Transmitted through percutaneous or mucosal exposure to infectious blood or body fluids
- Highly infectious; remains viable on environmental surfaces for at least 7 days
  - Can be transmitted in the absence of visible blood

Epidemiology of HBV in the U.S.

- Nearly 3,000 cases of acute HBV infection reported to CDC in 2014
  - Estimated 19,200 new cases considering under-ascertainment and underreporting
  - Estimated 952 perinatal infections annually
- ~850,000 persons with HBV infection
  - Persons with chronic infection serve as the main reservoir for transmission
  - Imported chronic HBV infection accounts for ~95% of new U.S. cases

Reported Acute Hepatitis B

- Rate of reported acute HBV infections declined by 90.6% since recommendations for HepB vaccine first issued in 1982.
- Rate fairly stable from 2010-2014, although increases occurred in some populations (e.g., whites aged 30-39 years reporting injection drug use in Kentucky, Tennessee, and West Virginia).

National Notifiable Diseases Surveillance System (NNDSS); Harris et al. MMWR 2016.
Chronic Hepatitis B

- Chronic HBV infection develops in approximately:
  - 90% of infected infants
  - 30% of infected children aged <5 years
  - <5% of infected persons aged ≥5 years

- Risk of premature death from cirrhosis/liver cancer with chronic HBV infection
  - ~25% if infected during childhood
  - ~15% if infected after childhood

Perinatal HBV Infection

- Primarily from mucosal exposure to infected blood and other body fluids during delivery
- Without post-exposure prophylaxis, perinatal HBV infection develops in:
  - ~90% of infants born to mothers who are HBsAg-positive/ hepatitis B e antigen (HBeAg)-positive
  - 5-20% of infants born to mothers who are HBsAg-positive/HBeAg-negative

WHO recommends all infants receive their first dose of HepB vaccine as soon as possible after birth, preferably within 24 hours.

Efficacy of Post-exposure Prophylaxis for Preventing Perinatal HBV Transmission

- HepB vaccine alone is 75% effective in preventing perinatal HBV transmission
  - Hepatitis B immune globulin (HBIG) alone 71% effective

- Combined efficacy 94%

Assessment of Serologic Evidence of Protection

- Antibody to hepatitis B surface antigen (anti-HBs) ≥10mIU/mL measured 1-2 months after HepB vaccine series corresponds to vaccine-induced protection

- Protection lasts 30 years or longer among immunocompetent vaccine responders

Leuridan et al. CID 2011; Bruce et al. JID 2016.
HepB Vaccine Seroprotection

- 3-dose vaccine series results in protective anti-HBs (≥10 mIU/mL) in 98% of healthy infants and 90-95% of healthy children and adults aged <40 years

- Lower seroprotection associated with prematurity, advanced age, diabetes, obesity, chronic illness, smoking

Testing for Anti-HBs and Protection

- Anti-HBs after HepB vaccine series wanes over time
  - Measurable anti-HBs can drop to <10 mIU/mL
- Even when anti-HBs decreases to <10 mIU/mL, breakthrough HBV infection uncommon in immunocompetent vaccine responders

Overview

Hepatitis B Virus (HBV) background, epidemiology, and prevention

Existing HepB recommendations

Revisions deliberated by Work Group
Strategy to Eliminate HBV Transmission in the U.S.

- Screen all pregnant women for HBsAg
  - Prophylaxis (HepB vaccine and HBIG) within 12 hours of birth for all infants born to HBsAg-positive women

- Universal vaccination of all infants beginning at birth (before hospital discharge) as a safety net

- Routine vaccination of previously unvaccinated children and adolescents aged <19 years

- Vaccination of adults at risk for HBV infection, including those requesting protection from HBV without acknowledgment of a specific risk factor

Mast et al. MMWR 2005; Mast et al. MMWR 2006.
Identification of HBV-infected Pregnant Women

- All pregnant women should be tested routinely for HBsAg during an early prenatal visit
  - Testing should occur in each pregnancy, even if the woman has been previously vaccinated or tested
# HepB Vaccine and HBIG Schedule for Newborn Infants

<table>
<thead>
<tr>
<th>Maternal HBsAg status</th>
<th>Infant birth weight</th>
<th>≥2,000 grams</th>
<th>&lt;2,000 grams</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>HepB vaccine and HBIG within 12 hrs of birth</td>
<td>HepB vaccine and HBIG within 12 hrs of birth; birth dose not counted as part of vaccine series</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>HepB vaccine within 12 hrs of birth</td>
<td>HepB vaccine and HBIG within 12 hrs of birth; birth dose not counted as part of vaccine series</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>HepB vaccine before hospital discharge</td>
<td>Delay first dose of HepB vaccine until age 1 month or hospital discharge</td>
<td></td>
</tr>
</tbody>
</table>
Permissive Language to Delay Birth Dose

- “On a case-by-case basis and only in rare circumstances, the first dose may be delayed until after hospital discharge for an infant who weighs ≥2,000 grams and whose mother is HBsAg-negative”
  - Physician’s order to withhold birth dose
  - Copy of the original maternal HBsAg-negative laboratory report on chart
  - Administer by age 2 months
  - Do not delay if high risk situation
Vaccine Series Completion and Postvaccination Serologic Testing

- HepB vaccine series completed at age 6 months for infants born to HBsAg-positive/unknown mothers, age 6-18 months for infants born to HBsAg-negative mothers.

- Postvaccination serologic testing (anti-HBs and HBsAg) at age 9-12 month, or 1-2 months after the final dose of the vaccine series if delayed, for infants born to HBsAg-positive mothers.
  - Revaccination (3-dose), followed by repeat postvaccination serologic testing, for infants with anti-HBs <10mIU/mL.
Children and Adolescents not Previously Vaccinated

- HepB vaccination recommended for all children and adolescents aged <19 years
  - Those not previously vaccinated should be vaccinated routinely at any age with an appropriate dose and schedule
Adults Recommended for HepB Vaccination

- **Persons at risk for infection by sexual exposure**
  - e.g., sex partners of HBsAg-positive persons, men who have sex with men

- **Persons at risk for infection by percutaneous or mucosal exposure to blood**
  - e.g., injection-drug users, health-care and public safety workers, persons with end-stage renal disease, adults with diabetes

- **Others**
  - e.g., international travelers to regions with high or intermediate HBV endemicity, persons with chronic liver disease, persons with HIV infection

- **All persons seeking protection from HBV infection**
Settings in Which all Adults Recommended for HepB Vaccination

- Sexually transmitted disease treatment facilities
- HIV testing and treatment facilities
- Facilities providing drug-abuse treatment and prevention services
- Health-care settings targeting services to injection-drug users
- Correctional facilities
- Health-care settings targeting services to men who have sex with men
- Chronic-hemodialysis facilities and end-stage renal disease programs
- Institutions and nonresidential day care facilities for developmentally disabled persons
Pre-vaccination Serologic Testing

- Vaccination of persons who are immune to HBV infection (due to past infection or vaccination) does not increase risk for adverse events
  - Pre-vaccination serologic testing might reduce costs by avoiding vaccination of persons who are already immune
Pre-vaccination Serologic Testing, cont.

- Pre-vaccination serologic testing recommended for household, needle-sharing, or sex contacts of HBsAg-positive persons; persons born in regions of high HBV endemicity; and HIV-positive persons
  - Pre-vaccination serologic testing might be cost effective for injection drug users, incarcerated persons, men who have sex with men, and persons born in regions of intermediate HBV endemicity

- First vaccine dose should typically be administered immediately after collection of blood for serologic testing
Postvaccination Serologic Testing

- Serologic testing for immunity not recommended after routine vaccination of infants, children, adolescents, and adults

- Postvaccination serologic testing recommended for:
  - Infants born to HBsAg-positive mothers
  - Health-care personnel
  - Chronic hemodialysis patients
  - HIV-infected and other immunocompromised persons
  - Sex partners of HBsAg-positive persons

- Testing recommended 1-2 months after the final dose of the vaccine series (at age 9-12 months for infants)
  - Revaccination recommended if anti-HBs <10 mIU/mL
<table>
<thead>
<tr>
<th>Source patient HBsAg status</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HCP vaccination and response status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>HBIG x1, initiate vaccination</td>
<td>Initiate vaccination</td>
</tr>
<tr>
<td>Previously vaccinated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Known responder</td>
<td>No prophylaxis</td>
<td>No prophylaxis</td>
</tr>
<tr>
<td>Known non-responder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 3 doses</td>
<td>HBIG x1, initiate revaccination</td>
<td>Initiate revaccination</td>
</tr>
<tr>
<td>After 6 doses</td>
<td>HBIG x2 (separated by 1 month)</td>
<td>No prophylaxis</td>
</tr>
</tbody>
</table>
## Post-Exposure Prophylaxis for HBV: Non-Occupational Exposures

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Unvaccinated person</th>
<th>Vaccinated person</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg-positive source</td>
<td>HepB vaccine series</td>
<td>HepB dose</td>
</tr>
<tr>
<td></td>
<td>and HBIG</td>
<td></td>
</tr>
<tr>
<td>Source with unknown HBsAg status</td>
<td>HepB vaccine series</td>
<td>No prophylaxis</td>
</tr>
</tbody>
</table>

**Management**
Overview

- Hepatitis B Virus (HBV) background, epidemiology, and prevention
- Existing HepB recommendations
- Revisions deliberated by Work Group
Work Group Supports Testing HBsAg-Positive Pregnant Women for HBV DNA

- Identifies infants at greatest risk for perinatal HBV infection
  - AASLD suggests maternal antiviral therapy to reduce the risk of *perinatal* transmission when maternal HBV DNA >200,000 IU/mL

- Prioritizes women for referral for HBV management and therapy
Work Group Supports Postvaccination Serologic Testing for Infants whose Mother’s HBsAg Status Remains Unknown Indefinitely

- For example, when infant surrendered confidentially and anonymously shortly after birth
  - All 50 states have some form of safe-haven law to reduce risk of infant abandonment
  - Medical data on infants safely-surrendered lacking
**Work Group Deliberated over Removal of Permissive Language for Birth Dose after Hospital Discharge**

**Existing language**
For all medically stable infants weighing ≥2,000 grams at birth and born to HBsAg-negative mothers, the first dose of vaccine should be administered before hospital discharge. Only single-antigen HepB vaccine should be used for the birth dose.

On a case-by-case basis and only in rare circumstances, the first dose may be delayed until after hospital discharge for an infant who weighs ≥2,000 grams and whose mother is HBsAg-negative.

**Revised language (proposed)**
For all medically stable infants weighing ≥2,000 grams at birth and born to HBsAg-negative mothers, the first dose of vaccine should be administered within 24 hours of birth. Only single-antigen HepB vaccine should be used for the birth dose.
## Removal of Permissive Language for Delaying Birth Dose

- **Infants born to HBsAg-positive mothers in British Columbia, 1984-1989 (n=770)**

<table>
<thead>
<tr>
<th>Age at first dose (days)</th>
<th>Proportion of participants (%)</th>
<th>Infection rate per 1,000</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>96</td>
<td>47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4-7</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>8-61</td>
<td>1</td>
<td>222</td>
<td></td>
</tr>
<tr>
<td>≥62</td>
<td>1</td>
<td>333</td>
<td></td>
</tr>
</tbody>
</table>

- **aOR for increase in infection with increasing age at 1\textsuperscript{st} dose: 4.3 (95\% CI, 2.2-8.4)**


*One dose by 3 days
Universal birth dose prior to hospital discharge serves as a safety net to prevent HBV transmission for infants not identified due to errors in:

- Maternal HBsAg testing
- Transcription of maternal HBsAg test results
- Reporting maternal HBsAg test results

Work Group consensus not reached
Work Group Supports Providing Examples of Chronic Liver Disease

- Examples include, but are not limited to, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and liver function tests >2 times the upper limit of normal
  - ≥3-dose HepB vaccine coverage among adults aged ≥19 years with chronic liver conditions (2014): 29.8% (95% CI, 23.9-36.5)

Williams et al. MMWR 2016.
CDC Program Supports Explicit Recommendation for HepB Vaccine for Persons with HCV Infection

- Increasing incidence of HBV and HCV infections
  - Young, non-urban adults who inject drugs
  - East of Mississippi River (e.g., Kentucky, Tennessee, West Virginia)

- Risk for liver disease progression
  - Multiplicative risk for hepatocellular carcinoma with HBV/HCV co-infection

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Acknowledgements

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Discussion & Vote

Does ACIP approve removing the permissive language for the HepB vaccine birth dose to be administered after hospital discharge?

Does ACIP recommend HepB birth dose within 24 hours of birth for infants weighing ≥2,000 grams born to HBsAg-negative mothers?

Does ACIP approve the revised HepB statement?