Revaccination for Infants Born to Hepatitis B Virus (HBV)-Infected Mothers

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Revaccination for Infants Born to HBV-Infected Mothers

Current recommendation:

- Providers should order postvaccination serologic testing (PVST), consisting of hepatitis B surface antigen [HBsAg] and antibody to HBsAg [anti-HBs], for infants born to HBsAg-positive mothers at age 9–12 months (or 1–2 months after the final dose of the vaccine series, if the series is delayed)\(^1\)
- HBsAg-negative infants with anti-HBs levels $\geq 10$ mIU/ml* are protected and need no further medical management\(^2\)
- HBsAg-negative infants with anti-HBs levels $< 10$ mIU/mL* should be revaccinated with a second 3-dose series and retested 1–2 months after the final dose of vaccine\(^2\)


*Anti-HBs $\geq 10$ mIU/mL, when following a complete Hepatitis B vaccine series, is serologic correlate of protection (Jack et al., J Infect Dis 1999)

Note: Available data do not suggest a benefit from administering additional hepatitis B vaccine doses to infants who have not attained anti-HBs $\geq 10$ mIU/mL following receipt of two complete hepatitis B vaccine series.
Revaccination for Infants Born to HBV-Infected Mothers, cont.

- **Considerations**
  - Some infants may need only a single dose to achieve protective anti-HBs levels
  - Single dose revaccination may conserve public health resources by shortening the duration of case management
    - For some infants, providing case management services through completion of a 2nd hepatitis B (HepB) vaccine series is difficult (e.g., infant moves out of the country)
Permissive Single Dose Revaccination

- **Existing Language**
  - HBsAg-negative infants with anti-HBs levels <10 mIU/mL should be revaccinated with a second 3-dose series and retested 1–2 months after the final dose of vaccine.¹ ²

- **Revised Language (Proposed)**
  - HBsAg-negative infants with anti-HBs levels <10 mIU/mL should be revaccinated with a second three-dose HepB series and **postvaccination serologic testing (PVST)** performed 1-2 months after the final dose of vaccine.
  - Alternatively, these infants may be re-vaccinated with a single dose of HepB vaccine and retested 1-2 months later. Infants whose anti-HBs remains <10 mIU/mL following single dose revaccination should receive two additional doses of HepB vaccine, followed by testing 1-2 months later.
  - Available data do not suggest a benefit from administering additional HepB vaccine doses to infants who have not attained anti-HBs ≥10 mIU/mL following receipt of two complete HepB vaccine series.

Options for Revaccination of Infants Born to HBV-Infected Mothers

**Strategy 1**

- Born to HBV-infected mother
- After 3 doses of hepatitis B (HepB) vaccine:
  - HBsAg = negative
  - Anti-HBs < 10 mIU/mL

1. 1 dose HepB vaccine; post-vaccination serologic testing
2. 3 doses Hep B vaccine, post-vaccination serologic testing
3. Anti-HBs ≥ 10 mIU/mL → Protected
4. Anti-HBs < 10 mIU/mL → Non-responder

**Strategy 2**

1. 1 dose HepB vaccine; post-vaccination serologic testing
2. 2 doses HepB vaccine; post-vaccination serologic testing
3. Anti-HBs < 10 mIU/mL → Non-responder
4. Anti-HBs ≥ 10 mIU/mL → Protected
Perinatal Hepatitis B Prevention Program: Background

- Established in 1990
- Funded in CDC Immunization Cooperative Agreements (Section 317 funding)
- Programs in 64 jurisdictions (50 states, 6 cities, 5 territories & 3 freely associated island nations)
- Program works collaboratively with other CDC centers (NCHHSTP/DVH)
- Program Required Objectives are based upon selected ACIP recommendations
Outcomes from Perinatal Hepatitis B Prevention Program, 2014

- Number of infants enrolled: 11,157 (expected: LL 18,807, PE 26,236)
- Percent of infants with PEP within 1 calendar day of birth: 97%
- Percent with HBIG and series complete by 8 months: 74%
- Percent of all enrolled infants with PVST results: 64%
- Percent of all enrolled infants with HBsAg-positive results: 0.4%
- Percent of all enrolled infants with protective levels: 95%
- Percent of all enrolled infants that need revaccination: 2%
- Percent of infants with indeterminate results: 2%
Background

What proportion of infants are protected after the initial vaccination series?

- Seroprotection and vaccine response for infants born to HBsAg-positive mothers*:
  - Ko et al., Hepatitis B vaccine response using data from the Enhanced Perinatal B Prevention Hepatitis B Prevention Program (EPHBPP)
    - 94.7%\(^1\) response rate among infants who completed a 3- or 4-dose hepatitis B vaccine series
  - Barbosa et al., Efficacy of vaccine and HBIG by time of administration and completion of vaccination series
    - 92.0% (83.0-97.0)\(^2,3\) efficacy for infants who received HBIG + Hep1Vacc ≤ 24 hours and remaining doses on time
  - Schillie et al., EPHBPP data, factors associated with infection status among infants born to HBsAg-positive mothers
    - 99.0%\(^4\) of infants were HBsAg-negative after receipt of ≥3 vaccine doses

\(^{*}\)HBIG = hepatitis B immune globulin; Hep1Vacc = hepatitis B vaccine birth dose
Background, cont.

What proportion of individuals who do not respond to the initial hepatitis B vaccine series are seroprotected after one additional dose?

- Lolekha et al., healthy newborn infants (birth weight ≥2000g) born to HBsAg-positive/hepatitis B e-antigen (HBeAg)-positive mothers, no HBIG, open, randomized to schedule, HBsAg and anti-HBs evaluated at 4 time points
  - Schedule A: birth, 1, 6 months
    - 91.9% response at 9 months, 88.6% response at 13 months*
  - Schedule B: birth, 1, 2, 12 months
    - 86.5% response* at 9 months, 94.4% response at 13 months*

*Anti-HBs responses (≥ 10 mIU/mL) in uninfected infants

What proportion of individuals who do not respond to the initial hepatitis B vaccine series are seroprotected after one additional dose?

- Assateerawatt et al., Healthy newborn infants (birth weight ≥2500g) born to HBsAg-positive/hepatitis B e-antigen (HBeAg)-positive mothers, randomized to 2 groups; tested for HBsAg, anti-HBs, and anti-HBc at 5 time points
  - Group A: HBIG + vaccine at 0; vaccine at 1, 2 and 12 months
    - 96% seroconversion rate at 12 months; 100% at 13 months
  - Group B: vaccine at 0, 1, 2 and 12 months
    - 95.2% seroconversion rate at 12 months; 95.7% at 13 months

What percent of infants who do not respond to the initial hepatitis B vaccine series are protected after a complete second vaccine series?

- Ko et al., Hepatitis B vaccine response using data from the EPHBPP
  - Of non-responder infants who completed a second vaccination series at the time of analysis 94.8% demonstrated a response after the second series

Ko et al., *Vaccine* 2014; 32(18): 2127-33
Data Limitations

- Studies not designed specifically to evaluate response to single dose revaccination in initial infant non-responders

- Variability among the studies with regard to maternal HBsAg status, HBIG administration, schedule, HBeAg status, infant birth weight (<2000g vs. ≥2000g)

- Limited data are available
Response to Single-dose Vaccination Among Infants Enrolled in Perinatal Hepatitis B Prevention Program

- Infants born to HBsAg-positive mothers from 2012-2016* in Georgia, Michigan, and New York City
- Received 3 doses hepatitis B vaccine and PVST with anti-HBs <10mIU/mL, followed by single dose revaccination with anti-HBs measurement
  - 14/15 (93.3%) with anti-HBs ≥10 mIU/mL after single dose revaccination

*Initial year of range 2011 for one jurisdiction; final year of range 2015 for one jurisdiction