Perinatal Hepatitis B

Investigative Guidelines

June 2018

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To prevent new cases of hepatitis B (HBV).
2. To facilitate case management of infants born to hepatitis B positive mothers, as well as household and sexual contacts of the mother.
3. To recommend appropriate preventive measures, including screening of close contacts and immunization of all susceptible contacts.
4. To assess the burden of perinatal hepatitis B in Oregon.

1.2 Laboratory and Physician Reporting Requirements

Physicians are required to report suspected or confirmed cases of acute or chronic hepatitis B within one working day of identification/diagnosis. All positive test results indicating hepatitis B disease must be reported by licensed laboratories within one working day (OAR 333-018-0000; 333-018-0015).[1]

- Oregon Revised Statute (ORS) 433.071 requires individuals attending a pregnant woman to collect or order the collection of a blood specimen for submission to a licensed laboratory to test for hepatitis B and selected other infections, unless the pregnant woman declines testing (OAR 333-019-0036).[1,2]
- Hepatitis B surface antigen (HBsAg) testing may be conducted at the same time as other routine prenatal laboratory tests. All pregnant women should be tested early (at the first prenatal visit) in each pregnancy, even if they have been previously vaccinated or tested.

1.3 Local Public Health Authority Reporting and Follow-Up Responsibilities

1. At the time of initial report or upon receipt of a new lab result for a previously investigated case, verify the pregnancy status of all women of child-bearing age (15–44 years).
2. A pregnant woman positive for HBsAg, hepatitis B e antigen (HBeAg), or HBV DNA must be enrolled ***with each pregnancy*** into the Oregon Perinatal Hepatitis B Prevention Program (PHBPP). The case should be enrolled in the PHBPP within one week of receiving the laboratory report. This includes creating a pregnancy in the electronic communicable disease database (i.e. Orpheus).
3. Each pregnancy should be added to the individual's hepatitis B case report in Orpheus.

4. Every infant born to a hepatitis B case should be added to the case's disease report as a contact.
5. LPHAs are required to complete perinatal hepatitis B case management for every infant contact born to a hepatitis B case. See §5.2 for detailed case management activities.
6. Infants testing positive for hepatitis B following case management need to be reported to the Acute and Communicable Disease Prevention Section (ACDP) as soon as possible, but no later than the end of the calendar week of initial physician or laboratory report. HBsAg, HBeAg, or HBV DNA positive infants will become their own case in Orpheus. Refer to the chronic hepatitis B Investigative Guidelines for more information.

2. THE DISEASE AND ITS EPIDEMIOLOGY

This Investigative Guideline focuses on management of infants rather than on case investigation. Additional information on management of household and sexual contacts of pregnant hepatitis B cases is included where relevant to PHBPP case management. Please refer to the acute and chronic hepatitis B Investigative Guidelines for more information on hepatitis B and its epidemiology, including etiologic agents, reservoir, incubation period, period of communicability and treatment.

2.1 Description of Illness

Children who are exposed to HBV during infancy have an 80%–90% chance of becoming chronically infected. Up to 25% of those chronic carriers will die prematurely from cirrhosis or liver cancer. Hepatitis B infection can range from asymptomatic to fulminant hepatitis. As a rule, however, infants and young children (<10 years) typically have asymptomatic infections.[3]

2.2 Serologic Markers

Post-vaccination serologic testing (PVST), for children (<24 months of age) is done to screen for infection and immunity provided through vaccination. Infants can acquire passive immunity from their mothers, which is detectible up to 24 months of age. Therefore, the recommended serologic markers for testing infants are HBsAg, for infection, and hepatitis B surface antibody (anti-HBs), for immunity. HBeAg and HBV DNA can also serve as markers of infection. See §5.2.4 for more details.

2.3 Sources and Routes of Transmission

Perinatal hepatitis B infections result from vertical transmission of hepatitis B from a mother to her fetus or newborn, primarily occurring during delivery with rare instances of in utero transmission.[3] Breastfeeding is not a significant route of transmission.

3. CASE DEFINITIONS, DIAGNOSIS AND LABORATORY SERVICES

3.1 Confirmed Case Definition

A child:

1. Born to a HBV-infected mother; and
2. Positive for HBsAg at ≥1 month of age and ≤ 24 months of age; OR
3. Positive for HBeAg or HBV DNA ≥9 months of age and ≤24 months of age.[4]

3.2 Probable Case Definition

A child:

1. Born to a mother whose mother's hepatitis B status is unknown (i.e. epidemiologic linkage is not present); and
2. Positive for HBsAg at ≥1 month of age and ≤24 months of age; OR
3. Positive for HBeAg or HBV DNA ≥9 months of age and ≤24 months of age.[4]

3.3 Suspect Case Definition

There is no suspect case definition for perinatal hepatitis B.

3.4 Services Available at the Oregon State Public Health Laboratory (OSPHL)

OSPHL offers serologic testing for HBsAg, anti-HBs, hepatitis B core antibody (anti-HBc), and IgM anti-HBc. HBeAg testing is not routinely available, but may be arranged under special circumstances. Consult with ACDP. For more information, refer to OSPHL's Guide to Services. As of 2018, OSPHL does not yet do PCR testing for hepatitis B virus.

4. ROUTINE CASE INVESTIGATION

Please see the acute and chronic hepatitis B Investigative Guidelines for details on routine case investigation. With each pregnancy, it is recommended that the pregnant woman be interviewed to determine whether there are any new household or sexual contacts. If there are household or sexual contacts without a known disease status or vaccine history, refer to §5.3 for guidance regarding management of these contacts.

5. CONTROLLING FURTHER SPREAD

Through proper case management of pregnant women and their infants, perinatal infections can be prevented. The full passive+active post-exposure prophylaxis (PEP) course for an infant (Hepatitis B Immunoglobulin [HBIG] + 3 doses of vaccine) has been shown to be nearly 95% effective in preventing HBV infection.[3] Please see below for a detailed description of case management activities.

5.1 Case Management of Pregnant Women

All women should be screened for HBV infection during each pregnancy, regardless of vaccination history or previous test results. HBsAg is the preferred

test during hepatitis B prenatal screening. HBeAg and HBV DNA also indicate infection and should trigger enrollment in the PHBPP.

Susceptible (negative HBsAg test results and no history of vaccination) pregnant women at risk for HBV infection during pregnancy should be vaccinated. Refer to Table 1 for immunization dosage and spacing information. If a pregnant woman is not tested for HBsAg at a prenatal visit, partakes in high-risk behaviors during her pregnancy, or presents with clinical hepatitis, she should be tested at the time of admission to the hospital for delivery. Behaviors that place women at high risk of infection include:

- Personal injection drug use OR
- Having had:
  - more than one sex partner in the previous 6 months, or
  - an HBsAg-positive sex partner, or
  - a partner who has been evaluated or treated for a sexually transmitted disease (STD), or
  - a partner who is a recent or current injection drug user.

Pregnant women who are HBsAg-positive should be tested for HBV DNA. For pregnant women whose HBV DNA is >200,000 IU/mL, maternal antiviral therapy is recommended to reduce perinatal transmission.[3]

Along with connecting a pregnant woman with treatment, identifying HBsAg-positive women ensures their infants receive timely PEP and follow-up. The woman's healthcare provider should send a copy of the original laboratory report, if available, indicating the pregnant woman's HBsAg status to the hospital where delivery is planned.

In addition, women who are HBsAg-positive should be enrolled in the PHBPP with each pregnancy and provided with appropriate counseling and medical management, including:

- Perinatal transmission risk and consequences of perinatal transmission
- Modes of transmission
- Prevention of HBV transmission to contacts
- Importance of PEP
- Substance abuse treatment, if appropriate

Please refer to the acute and chronic hepatitis B Investigative Guidelines for details on case investigation.

To ensure that proper screening and PEP occurs, hospitals should have policies and procedures in place to identify HBsAg-positive or unknown mothers, test as necessary, administer immunoprophylaxis (HBIG and vaccine birth dose), and report to the LPHA and document the date and time of immunoprophylaxis in the Oregon Vital Events Registration System (OVERS).

Table 1. Hepatitis B vaccines: Recommended dosage and schedules.

Vaccine	Age group	Dose (µg)[1]	Volume (mL)	# Doses	Schedule/Dose interval
Single Antigen Vaccines					
Engerix-B*	0–19 years	10	0.5	3	Age: birth[2], 1–4, 6–18 months[3] Dose intervals (older children): 0, 1–2, 4 months
	≥20 years	20	1.0	3	Dose intervals: 0, 1, 6 months
Recombivax HB*	0–19 years	5	0.5	3	Age: birth[2], 1–4, 6–18 months[3] Dose intervals (older children): 0, 1–2, 4 months
	11–15 years	10	1.0	2	Dose intervals 0, 4–6 months[4]
	≥20 years	10	1.0	3	Dose intervals: 0, 1, 6 months
HEPLISAV-B	≥18 years	20	0.5	2	Dose interval: 0 and 1 month
Combination vaccines					
Pediarix[5] DTaP+HepB+IPV	6 weeks–6 years	10 (Engerix)	0.5	3	Age: 2, 4, 6 months[3,6] A single antigen hepB dose should be given at birth
Twinrix HepA+HepB	≥18 years	20 (Engerix)	1.0	3	Dose intervals: 0, 1, 6 months
		20 (Engerix)	1.0	4	Dose intervals: 0, 7, 21–30 days, 12 months

1. Recombinant hepatitis B surface antigen protein dose.
2. Birth dose should be administered within 24 hours of birth.
3. The final dose (third or fourth) in the hepatitis B vaccine series should be administered no earlier than age 24 weeks.
4. If an adult formulation of Recombivax HB is used, the vaccine is administered in a 2 dose series.
5. Cannot be administered before 6 weeks of age, but can be used to complete the hepatitis B vaccine series for all infants, including those born to HBsAg+ mothers. Use a single antigen vaccine for the hepatitis B birth dose prior to hospital discharge.
6. Administration of a total of 4 doses of hepatitis B vaccine is permitted when a combination vaccine containing hepatitis B is administered after the birth dose.

*** NOTE:** For individuals who are immunocompromised or on dialysis, use single antigen vaccines. Dosage and schedules for children (<20 years) remain the same, however they differ for adults. For adults (≥ 20 years):
Engerix-B: Dose, 40 µg; volume, 2.0mL. Two 1.0 mL doses administered at one site, on a 4 dose schedule at 0, 1, 2, and 6 months
Recombivax HB: Special dialysis formulation available. Dose, 40 µg; volume, 2.0mL. Dialysis formulation administered on a 3-dose schedule at 0, 1, and 6 months.

5.2 Case Management of Infants

Refer to Table 2 for a summary of case management activities.

1. Mother has HBV Infection (HBsAg, HBeAg, or HBV DNA Positive)

All infants born to HBV-infected women should receive single-antigen hepatitis B vaccine and HBIG ***within 12 hours of birth***. The hepatitis B vaccine and HBIG should be administered concurrently, by intramuscular injection, and at different injection sites.

The vaccine series should be completed according to the recommended schedule for infants born to HBV-infected women (Table 2). The final dose in the vaccine series should not be administered before the infant is 24 weeks (164 days) of age. For infants exposed to HBV, the hepatitis B vaccine series is recommended to be completed at 6 months of age.

Post-vaccination serologic testing (PVST) consists of testing for anti-HBs and HBsAg after completion of the vaccine series at age 9–12 months of age (see §5.2.4). HBeAg and HBV DNA testing completed between 9 and 24 months of age are considered acceptable alternatives to HBsAg to ensure perinatal cases are not missed.

Infant is low birth weight [<2,000g]

- The infant should receive single-antigen hepatitis B vaccine and HBIG ***within 12 hours of birth***. The hepatitis B vaccine and HBIG should be administered concurrently, by intramuscular injection, and at different injection sites. However, the birth dose should not be counted as part of the vaccine series because of the potentially reduced immunogenicity of hepatitis B vaccine in these infants.
- The vaccine series (3 additional doses) should begin when the infant reaches 1 month of age in accordance with the recommended schedule for infants born to HBV-infected women (Table 2). The final (4^{th}) dose in the vaccine series should not be administered before the infant is 24 weeks (164 days) of age. For infants exposed to HBV, the hepatitis B vaccine series should be completed at 6 months of age.
- Post-vaccination testing for anti-HBs and HBsAg should be performed after completion of the vaccine series at 9–12 months of age. HBeAg and HBV DNA testing completed between 9 and 24 months of age are considered acceptable alternatives to HBsAg to ensure perinatal cases are not missed (see §5.2.4).

2. Mother's HBV Status is Unknown at Delivery

If a pregnant woman presents for delivery without documented hepatitis B test results, testing should be completed as soon as possible. While test results are pending, all infants born to women without documentation of hepatitis B test results should receive the first dose of single-antigen hepatitis B vaccine ***within 12 hours of birth***. Case management should proceed based on the mother's test results:

- **If the mother is determined to have hepatitis B**, her infant should receive the additional protection of HBIG as soon as possible, but no later than 7 days of age. The efficacy of HBIG administered after 48 hours of age, however, is not known. Case management should continue according to the recommendations for infants born to hepatitis B-infected mothers above.
- **If the mother is not tested to determine her HBsAg status,** the vaccine series should be completed according to the recommended schedule for infants born to hepatitis B status-unknown women (Table 2). Administration of HBIG is not necessary for these infants.
- **If the mother is determined to be HBsAg-negative**, the vaccine series should be completed according to a recommended schedule for infants born to hepatitis B-negative women (Table 2).

Infant is low birth weight [<2,000g]

- The infant should receive single antigen hepatitis B vaccine within 12 hours of birth.
- Due to the potentially decreased immunogenicity of vaccine in preterm infants weighing <2,000g, infants should also **receive HBIG if the mother's hepatitis B status cannot be determined within 12 hours of birth**. The hepatitis B vaccine series should begin when the infant reaches 1 month of age in accordance with the appropriate schedule (Table 2).
- If the mother is found to have hepatitis B, post-vaccination testing should be performed on the infant after completion of the vaccine series. See §5.2.4 for more information.

3. Note on Infants Born to HBV-Negative Mothers

Infants born to HBV-negative women should be immunized against hepatitis B. Medically stable infants weighing ≥2,000g should receive the birth dose of hepatitis B vaccine within 24 hours of birth.[3] Refer to Table 1 and Table 2 for the appropriate vaccination schedule for these infants.

Table 2. Summary of perinatal hepatitis B infant case management activities by maternal hepatitis B status and infant's birth weight.		
Maternal hepatitis B status	**Infant's weight**	**Recommendations**
Positive	≥2,000g	1. HBIG* and hepatitis B vaccine within 12 hours of birth 2. Administer 2–3 additional doses at 1–2 and 6 months (single-antigen) or 2, 4 and 6 months (Pediarix®)‡ 3. Test for HBsAg and anti-HBs† after completion of the vaccine series at 9–12 months of age
	<2,000g	1. HBIG* and hepatitis B vaccine within 12 hours of birth 2. Do not count birth dose as part of the vaccine series 3. Administer 3 additional doses at 1,2–3 and 6 months (single-antigen) or 2, 4 and 6 months (Pediarix®)‡ 4. Test for HBsAg and anti-HBs† after completion of the vaccine series at 9–12 months of age
Unknown	≥2,000g	1. Test mother for HBsAg ASAP 2. Administer hepatitis B vaccine within 12 hours of birth 3. If mother is HBsAg-positive, administer HBIG within 7 days of birth. Follow the recommendations for infants born to HBsAg-positive mothers If mother remains HBsAg-unknown, HBIG administration is not necessary. Follow recommendations for infants born to HBsAg-negative mothers
	<2,000g	1. Test mother for HBsAg ASAP 2. Administer hepatitis B vaccine within 12 hours of birth 3. If no test results within 12 hours of birth, administer HBIG 4. Do not count birth dose as part of the vaccine series 5. Administer 3 additional doses at 1, 2–3 and 6 months (single-antigen) or 2, 4 and 6 months (Pediarix®)‡ 6. If mother is found to be HBsAg-positive, test for HBsAg and anti-HBs† after completion of the vaccine series at 9–12 months of age
Negative	≥2,000g	1. Administer hepatitis B vaccine within 24 hours of birth 2. Complete vaccine series following the recommended schedule
	<2,000g	1. May delay first dose of hepatitis B vaccine to the time of hospital discharge or 1 month of age 2. Complete the vaccine series following the recommended schedule
* Hepatitis B immune globulin. ‡ For infants exposed to HBV, the hepatitis B vaccine series is recommended to be completed at 6 months of age † Antibody to HBsAg.		

4. Post-vaccination Serologic Testing

PVST of children born to HBV-infected mothers should be performed following the completion of the vaccine series at 9–12 months, generally at the next well-child check. If the vaccine series is completed at >6 months of age, PVST

is done 1–2 months after vaccine completion but not before 9 months of age. Test for anti-HBs and HBsAg.

A 2015 study conducted by the CDC found that anti-HBs was less likely to be detected at a protective level (≥10 mIU/mL), the further PVST was done after completion of the vaccine series.[5] Therefore, the recommended testing window provides the opportunity to complete blood draws at the 9- or 12-month well-child checks and reduces the amount of time an unprotected infant is exposed to infected household contacts. In addition, earlier completion of PVST enables prompt revaccination in infants who do not respond to the primary vaccine series.

PVST includes serological screening for two different markers, each for a specific reason:

- HBsAg to determine whether a child has become infected with HBV; AND
- Anti-HBs to determine whether the vaccine was effective in mounting an immune response in the recipient.

If, however, a provider orders HBeAg or HBV DNA tests when the child is 9–24 months of age, the test results can be used in place of HBsAg to determine a child's disease status. This ensures that no perinatal cases are missed due to inappropriate testing. Anti-HBs testing should still be completed for these children.

See Table 3 for hepatitis B markers and interpretation of serologic test results. Below are some notes on serologic testing for infants.

- **Testing should not be performed before age 9 months** to avoid detection of anti-HBs from HBIG administered during infancy and to maximize the likelihood of detecting late HBV infection. A late HBV infection has a delayed incubation period, resulting in disease presentation later than is typical. It can occur after the administration of HBIG.
- **Anti-HBc testing of infants is NOT recommended** because passively acquired maternal anti-HBc might be detected in infants born to HBV-infected mothers to age 24 months.
- **HBsAg-negative infants with anti-HBs levels ≥10 mIU/mL, or greater than or equal to the cut off value for the test method,** are protected and need no further medical management.
- **HBsAg-negative infants with anti-HBs levels <10mIU/mL, or less than the cut off value for the test method,** should be revaccinated with a single dose of hepatitis B vaccine and receive post-vaccination serologic testing 1–2 months later. Infants whose anti-HBs remains <10mIU/mL following a single dose revaccination should receive two additional doses of vaccine, 2 months and 6 months after the first dose of the second vaccine series. Vaccination should be followed by retesting 1–2 months after the last dose. Alternatively, infants may be revaccinated with a second 3-dose series, followed by retesting 1–2 months after the final dose of vaccine.

Note. A study of infants born to HBsAg-positive mothers who did not respond to a primary vaccine series indicated that all those not infected with HBV responded satisfactorily to a repeat 3-dose revaccination series. Data suggest that children who have no detectable antibody after 6 doses of vaccine would NOT benefit from additional hepatitis B vaccine doses.[6]

- **HBsAg, HBeAg, or HBV DNA positive infants** are considered to be infected with hepatitis B, and infectious to others through the usual modes of transmission. The HBV infected child should receive appropriate follow-up. In addition, they must be reported to the LPHA and ACDP as soon as possible, but no later than the end of the calendar week of initial physician/lab report.

Table 3. Typical interpretation of serologic test results for hepatitis B virus infection.[3]

Serologic Marker					
HBsAg	**Total anti-HBc**	**IgM anti-HBc**	**Anti-HBs**	**HBV DNA**	**Interpretation**
negative	negative	negative	negative	negative	Never infected, not immune
positive[a]	negative	negative	negative	**positive** or negative	Early acute infection; transient (up to 18 days) after vaccination
positive	**positive**	**positive**	negative	**positive**	Acute infection
negative	**positive**	**positive**	**positive** or negative	**positive** or negative	Acute resolving infection
negative	**positive**	negative	**positive**	negative	Recovered from past infection and immune
positive	**positive**	negative	negative	**positive**	Chronic infection
negative	**positive**	negative	negative	**positive** or negative	False positive (i.e., susceptible); past infection; "low-level" chronic infection;[b] or passive transfer of anti-HBc to infant born to HBsAg-positive mother
negative	negative	negative	**positive**	negative	Immune if concentration is ≥10mIU/mL, [c d] passive transfer after hepatitis B immune globulin administration

Abbreviations: HBsAg = hepatitis B surface antigen; anti-HBc = antibody to hepatitis B core antigen; IgM = immunoglobulin M; anti-HBs = antibody to hepatitis B surface antigen; HBV DNA = hepatitis B virus deoxyribonucleic acid

[a.] To ensure that an HBsAg-positive test result is not a false positive, samples with repeatedly reactive HBsAg results should be tested with a licensed (and, if appropriate, neutralizing confirmatory) test.

[b.] Persons positive for only anti-HBc are unlikely to be infectious except under circumstances in which they are the source for direct percutaneous exposure of susceptible recipients to large quantities of virus (e.g., blood transfusion or organ transplant).

[c.] Milli-International Units per milliliter.

[d.] Is dependent on the cut off value for the test methodology; may also be ≥11mIU/mL or ≥12mIU/mL.

Note: No-cost testing is available to LPHAs through the Oregon State Public Health Laboratory. This will be maintained as long as funding is available to support this testing. There is a charge for testing ordered by private providers.

5. Documentation

All case management activities (HBIG, vaccine doses, and PVST) should be reported in Orpheus for each infant contact born to a hepatitis B case. Information should be recorded as soon as possible, but no later than the end of the week in which it was reported. Orpheus perinatal hepatitis B data entry instructions are available at www.bit.ly/2J2bKxr.

6. Closing Case Management

If case management for the infant is complete, close the infant contact in Orpheus and include the date and reason for completion.

Lost to Follow-up

A mother-infant pair is considered closed to case management at the county level for the reason lost to follow-up when:

- At least three attempts have been made to contact the family at different days and times (including, when possible, one evening and one weekend attempt), and using different methods (calls, mailing, certified mailings, home visit, etc.), and
- During the same timeframe, the provider is unable to make contact after multiple attempts.

If a mother-infant pair meets these requirements and the child is <24 months of age, they will enter an “inactive” state of case management. To enter a child into "inactive" case management, select the reason of "County - Lost to follow-up/unable to locate" as the reason for closing case management, and enter a date of closure in the electronic communicable disease database. During the "inactive" period, the county is no longer responsible for case management. The state perinatal hepatitis B coordinator will periodically check ALERT Immunization Information System (IIS) until the child is 24 months of age to see whether they have received care elsewhere or a new address becomes available. If no contact information is found, the state perinatal hepatitis B coordinator will fully close the child to case management at 24 months of age with the reason of "State - Lost to follow-up/unable to locate." If contact information is found, case management will again become the LPHA’s responsibility.

8. Reimbursement

The reimbursement for completed case management of mother-infant pairs is paid annually in the fall for the previous fiscal year (July 1–June 30). Partial reimbursement is also given based on how much follow-up is completed when an infant is closed to case management.

5.3 Management of Household and Sexual Contacts of HBV-infected women

Household contacts, sex partners, and needle-sharing contacts of HBV-infected women identified through prenatal screening should be contacted and referred to the LPHA for:

- Testing for HBV infection,
- Administration of the first dose of hepatitis B vaccine immediately after collection of a blood sample for serologic testing, and

- Appropriate counseling on methods to prevent or reduce the risk of HBV transmission.

1. Pre-vaccination Serologic Testing for Susceptibility

Pre-vaccination testing is recommended for *unvaccinated* household, sexual, and needle-sharing contacts of HBV-infected individuals. Anti-HBc is the test of choice for pre-vaccination testing.

- Unvaccinated individuals who are **anti-HBc-negative** are **susceptible** and should complete the vaccine series.
- Unvaccinated individuals who are **anti-HBc-positive** should be tested for HBsAg.
- HBsAg testing may be performed on the same specimen collected for anti-HBc testing. Refer to table 3 for interpreting results.

2. Vaccination and Counseling

- Administer the first hepatitis B vaccine dose at the same time blood is drawn for serologic testing of susceptibility.
- For those found to be free of HBV infection and susceptible to HBV, complete the vaccine series using an age-appropriate vaccine dose and schedule (see Table 1). Incompletely vaccinated persons should complete the vaccine series.
- HBV-infected individuals and sex partners of HBV-infected individuals should be counseled on methods to prevent or reduce the risk of HBV transmission.
- In the event that the case has had sexual contact with a new partner in the past two weeks, HBIG is recommended.

3. Post-vaccination Testing for Serologic Response

Testing after vaccination is recommended only for certain individuals whose subsequent clinical management depends on knowledge of their immune status. This includes the sex partners of HBV-infected individuals in order to determine the need for revaccination and for counseling on methods to prevent or reduce the risk of hepatitis B transmission.

- Testing should be performed 1–2 months after administration of the last dose of the vaccine series, using a method that allows determination of a protective level of anti-HBs (usually ≥10 mIU/mL but dependent on the test methodology).
- Persons found to have anti-HBs levels of <10 mIU/mL, or less than the cutoff value for the test methodology, after the primary vaccine series should be revaccinated.
- Persons who do not respond to revaccination should be tested for HBsAg.
- HBsAg-positive individuals should receive appropriate management, be added as a case in Orpheus, and any household, sexual, or needle-sharing contacts should be identified, tested, and vaccinated.
- Non-responding HBsAg-negative individuals should be considered susceptible and should be counseled on methods to prevent or reduce the

risk of hepatitis B transmission as well as the need to obtain HBIG post-exposure prophylaxis for any known or likely parenteral exposure to HBsAg-positive blood.

4. Documentation, Closing Case Management, and Reimbursement

Pre- and post-vaccination serologic testing and vaccine doses should be reported in Orpheus for household and sexual contacts. Once case management is done, contacts should be closed to case management. LPHAs will be reimbursed for recorded case management of household and sexual contacts identified within one year of an infant's date of birth. Reimbursement is paid annually in the fall for the previous fiscal year (July 1–June 30). Partial reimbursement is also given based on how much follow-up is completed upon closure.

GLOSSARY OF TERMS

anti-HBc (aka total anti-HBc or total core): Antibody to hepatitis B core antigen (anti-HBc) serves as a marker of past infection. Generally, anti-HBc remains elevated for at least two years after transient infection and may remain elevated for life. Vaccination does not produce anti-HBc. Passively transferred maternal anti-HBc is detectable for up to 24 months among infants born to HBV-infected women.

anti-HBs: Antibody to hepatitis B surface antigen (HBsAg) usually indicates the development of immunity, either from past infection or immunization. Most carriers never develop anti-HBs (but if they do, they remain HBsAg positive as well). Anti-HBs levels may decline to undetectable levels over time (years), especially if resulting from immunization and not infection.

HBeAb (aka anti-HBe): Hepatitis B e antibody is produced by the immune system temporarily during acute HBV infection and may persist in chronic infections. Spontaneous conversion from e antigen to e antibody (seroconversion) is a predictor of long-term clearance of HBV in patients undergoing antiviral therapy and indicates lower levels of HBV. Chronic HBsAg carriers can be positive for either HBeAg or anti-HBe, but are less infectious when anti-HBe is present.

HBeAg: Hepatitis B e antigen is a core protein exported from infected liver cells and a marker of high levels of infectivity. Similar to HBsAg, it is seen (albeit transiently) as part of acute infection and may persist in the chronic carrier state. Needlestick exposure data suggest that HBeAg-positive individuals are 3–5x more infectious than HBeAg-negative counterparts.

HBsAg: Hepatitis B surface antigen, a marker of replicating virus. It occurs as part of acute infection and persists in chronic infection. Its presence indicates that the patient is considered infectious.

HBV DNA (aka viral DNA, HBV NAT): Signifies active replication of the virus and indicates that the patient is infectious. It is usually measured to test for chronic infection, and the viral load may be used to decide whether treatment is warranted. HBV DNA rises to high concentrations during incubation and falls with the onset of hepatic disease in transient infection. It is detectable in about 50% of chronic carriers and can be present when HBsAg is undetectable.

IgM anti-HBc: IgM antibody to hepatitis B core antigen, indicative of recent infection with HBV (usually <6 months). Antibody to core antigen is produced only following infection, not immunization. Used in the identification of people with acute or recent HBV infections (including HBsAg-negative people during the "window" phase of infection).

Late HBV infection: A hepatitis B infection with a delayed incubation period, resulting in a later presentation than is typical. This can sometimes occur after the administration of HBIG.

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UPDATE LOG

June 2018: Added new testing recommendations for pregnant women; added information on HEPLISAV-B® vaccine; added HBV DNA column to table 3; ensured consistent language with acute and chronic hepatitis B guidelines; edits for clarity. (Peters)

April 2017: Added probable case definition; updated case definitions to include HBeAg and HBV DNA test results; separated §5.2.5 Documentation, closing case management, and reimbursement into three separate sections; added

§5.2.7 Lost to follow-up, with an updated definition and tracking in the communicable disease database to reflect recommendations from the CDC; updated language around birth dose administration for infants born to women without hepatitis B based on the ACIP vote in October 2016; updated language regarding revaccination for infants who are non-responders to the first vaccine series based on the ACIP vote in February 2017; updates throughout the document to reflect these changes. (Peters)

December 2015: Reorganized case management sections. Reformatted table on vaccine recommendations and combined tables on case management for normal birth weight and low birth weight infants. Removed information related to Comvax. Updated recommended timeframe for completing post vaccination serologic testing. Added HBsAg-negative section. Added an update log. Added glossary of terms. Updated references. Removed contact information section. Reformatted to align with layout of other Investigative Guidelines. (Schrauben)

November 2015: Placed into new template and corrected spelling and link errors. (Byster)