HEPATITIS B (Perinatal)

REPORTING INFORMATION

- **Class B (perinatal hepatitis B):** Report by the end of the next business day after the case or suspected case and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism: Viral Hepatitis Case Report form, Ohio Confidential Reportable Disease form (HEA 3334), Positive Laboratory Findings for Reportable Disease form (HEA 3333), the local health department via the Ohio Disease Reporting System (ODRS), electronic laboratory reporting (ELR), or telephone.
- Special Notes on Reporting: Local health departments should report all new pregnancies for women identified with acute or chronic hepatitis B infection, even if the case was reported prior to the pregnancy or during a previous pregnancy.

AGENT

Hepatitis B virus (HBV) is classified in the *Hepadnaviridae* family, and is a member of the *Orthohepadnavirus* genus. The hepatitis B virus is a partially double-stranded DNA virus, 40-48 nm in diameter.

TEST NAME ABBREVIATIONS

IgM anti-HAV	Immunoglobulin M antibody to hepatitis A virus
Anti-HBe	Antibody to hepatitis B e antigen
Anti-HBs	Antibody to hepatitis B surface antigen
HBeAg	Hepatitis B e antigen
HBsAg	Hepatitis B surface antigen
HBV DNA	Hepatitis B virus DNA
IgM anti-HBc	Immunoglobulin M antibody to hepatitis B core antigen
Total anti-HBc (IgM/IgG)	Immunoglobulin M and Immunoglobulin G antibodies to hepatitis B core antigen
Anti-HDV	Antibody to hepatitis D virus

CASE DEFINITION

Hepatitis B, Perinatal Virus Infection Acquired in the United States or U.S. Territories

Clinical Criteria

Perinatal HBV infection in a child ≤ 24 months of age may range from asymptomatic to fulminant hepatitis.

Laboratory Criteria for Diagnosis

Laboratory evidence of HBV infection in a child consists of one or more of the following:

- Positive HBsAg test (only if at least 4 weeks after the last dose of hepatitis B vaccine)
- Positive HBeAg test, or
- Detectable HBV DNA

Epidemiologic Linkage

Born to a HBV-infected mother.

Case Classification

Suspected: Child 1-24 months of age born in the US to an HBV-infected mother or mother with unknown HBV infection status.

Probable: Child born in the US and positive for HBsAg at ≥ 1 month of age and ≤ 24 months of age **OR** positive for HBeAg or HBV DNA ≥ 9 months of age and ≤ 24 months of age, but whose mother's hepatitis B status is unknown (i.e. epidemiologic linkage not present).

Confirmed: Child born in the US and positive for HBsAg at ≥ 1 month of age and ≤ 24 months of age **OR** positive for HBeAg or HBV DNA ≥ 9 months of age and ≤ 24 months of age.

Perinatal Hepatitis B Prevention: Public Health Management

I. Background about The Disease

Great progress has been made in identifying hepatitis B surface antigen (HBsAg)-positive pregnant women and immunizing their infants with hepatitis B (Hep B) vaccine and hepatitis B immune globulin (HBIG) to prevent vertical infection, but there are still infants who acquire hepatitis B virus (HBV) infection. This is because either their mothers are not recognized as infected and the infant does not receive HBIG and the full hepatitis B vaccine series or the intervention does not prevent infection. Without post-exposure prophylaxis with HBIG and hep B vaccine, approximately 45% of infants born to HBV-infected mothers will become infected and up to 90% of those infected will develop chronic, life-long infection. Among infants who develop infection, 25% will die prematurely of liver cirrhosis or cancer. It is estimated that 1,000 newborns are infected annually in the US (1); approximately 300 infants are exposed annually in Ohio (2). Although treatment of HBV infection is now possible and can attenuate the impact of infection, hepatitis B cannot yet be cured (3).

It is important to assure adequate immunity in infants of HBV-infected mothers and to determine if infection of the infant occurred with or without post-exposure prophylaxis. The Centers for Disease Control and Prevention (CDC) and the Advisory Committee on Immunization Practices (ACIP) recommend universal testing of pregnant women for HBsAg, post-exposure prophylaxis within 12 hours of birth with HBIG and the first dose of hep B vaccine for infants born to HBV-infected mothers, universal birth dose administration within 24 hours of birth to all infants regardless of the mother's HBsAg status (4), completion of a valid three dose vaccine series in all infants, and post-vaccination serologic testing (PVST) for HBsAg and anti-HBs at 9-12 months for infants born to HBV-infected mothers or infants born in regions of high and intermediate HBV endemicity (3). The CDC Perinatal Hepatitis B Prevention Program helps promote these recommendations and provides case management of HBV-infected mothers and their infants. Evaluation of the program depends on the follow-up of exposed infants.

II. Fundamentals of Perinatal Hepatitis B Prevention

A. Serologic screening of pregnant females

1. All pregnant females should be screened for hepatitis B infection (i.e. HBsAg) during each pregnancy as a part of routine prenatal care. All HBV-infected women must be reported to the local health department according to Ohio Administrative Code.
    a. This screening should be done on all pregnant females during each pregnancy.
    b. Screening should be repeated later in the pregnancy in those females who are at high risk for the acquisition of hepatitis B during pregnancy.
    c. If a pregnant female is found to be HBsAg positive, a nucleic acid test for hepatitis B virus DNA (HBV-DNA), including qualitative, quantitative and

genotype testing, is recommended to guide the use of maternal antiviral therapy during pregnancy for the prevention of perinatal HBV transmission.

2. Report pregnancy status along with test results for women who are positive for any one of the following three laboratory tests:
   a. Hepatitis B surface antigen (HBsAg)
   b. Hepatitis B e antigen (HBeAg)
   c. Nucleic acid test for hepatitis B virus DNA (HBV-DNA) (including qualitative, quantitative and genotype testing)
3. Immediately determine HBsAg status on all pregnant women presenting for labor and delivery without documentation of HBsAg test results for current pregnancy and those with risk factors regardless of previous HBsAg test results.
4. For common hepatitis B serological profiles, see Table 1.

Table 1: Common Hepatitis B Serological Profiles

HBsAg	Anti-HBs	IgM anti-HBc	Total anti-HBc	HBeAg	Interpretation
+	**-**	**+**	**-**	**+**	Acute hepatitis B
-	**-**	**+**	**-**	**+ or -**	Acute hepatitis B
+	**-**	**-**	**+**	**-**	Chronic hepatitis B, low viral replication
+	**--**	**-** (very rarely **+**)	**+**	**+**	Chronic hepatitis B, high viral replication
-	**+**	**-**	**-**	**-**	Vaccination-induced immunity
-	**+**	**-**	**+**	**-**	Natural recovery from hepatitis B infection (now immune)

B. Hepatitis B vaccine and HBIG usage in term infants born to HBsAg-positive mothers

1. At birth (within 12 hours of birth): Give first dose of vaccine plus HBIG.
2. At 1-2 months of age: Give second dose of vaccine (if using single-antigen vaccine).
3. At 6 months of age: Give third dose of vaccine (if using single-antigen vaccine).
4. For doses, see Table 2.
5. For immunoprophylaxis of preterm and low birth weight infants, see Table 3.
6. See Table 4 for schedule by vaccine type, which includes the use of combination vaccines.

Table 2: Recommended Dosages of Hepatitis B Vaccine [Adapted from the *Red Book: 2015 Report of the Committee on Infectious Diseases**]

Patients	Recombivax** Dose: µg (ml)	Engerix-B** Dose: µg (ml)
Infants of HBsAg-positive mothers (HBIG) [0.5 mL] is also recommended	5 (0.5)	10 (0.5)
Infants of HBsAg-negative mothers and children and adolescents younger than 20 years of age	5 (0.5)	10 (0.5)
Adults 20 years of age or older	10 (1.0)	20 (1.0)
Adults undergoing dialysis and other immunosuppressed adults	40 (1.0) special formulation for dialysis patients	40 (2.0) two 1.0 ml doses given in one site in a 4-dose schedule

* American Academy of Pediatrics. Hepatitis B. In: Kimberline DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015: 400-423.
** For other hepatitis B-containing vaccines and multiple antigen vaccines such as Pediarix and Comvax, which cannot be used for the birth dose, see the Red Book, 2015.

Table 3: Hepatitis B Immunoprophylaxis by Birthweight for Infants Born to HBsAg-positive or HBsAg-unknown Mothers (including abandoned and safe haven babies)
[Adapted from the *Red Book: 2015 Report of the Committee on Infectious Diseases**]

Maternal Serostatus	Infant = or >2,000g	Infant <2,000 g
HBsAg-positive	• Hepatitis B vaccine and HBIG within 12 hours of birth • Continue vaccine series beginning at 1-2 months of age according to Table 4	• Hepatitis B vaccine and HBIG within 12 hours of birth • Do not count birth dose as part of 3-dose vaccine series; begin vaccine series at 1 month of age
HBsAg-unknown (including abandoned and safe haven babies)	• Test mother immediately for HBsAg • Hepatitis B vaccine and HBIG within 12 hours of birth (preferred by ODH Perinatal Hepatitis B Prevention Program and ODH Immunization Program)** • Or await HBsAg result and if positive, give HBIG as soon as possible but in less than seven days (*Red Book* recommendation) • Continue vaccine series beginning at 1-2 months of age according to Table 4	• Test mother immediately for HBsAg • Hepatitis B vaccine and HBIG within 12 hours of birth • Do not count birth dose as part of 3-dose vaccine series; begin vaccine series at 1 month of age

* American Academy of Pediatrics. Hepatitis B. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015: 400-423.** The rationale for giving HBIG within 12 hours (unless HBsAg is determined to be negative within 12 hours) is that the ODH Perinatal Hepatitis B Prevention Program has seen cases where HBIG was held pending the HBsAg determination (which proved to be positive); the patient was discharged and lost to follow-up, and, therefore, did not receive HBIG.

Table 4: Hepatitis B Vaccine Schedules for Infants > or = 2000g* by Maternal Hepatitis B Surface Antigen (HBsAg) Status
[Adapted from the *Red Book: 2015 Report of the Committee on Infectious Diseases***]

Maternal HBsAg Status	Single-Antigen Vaccine		Single-Antigen + Combination	
	Dose	Age	Dose	Age
Positive	• 1 • HBIG • 2 • 3	• Birth (12 h or less) • Birth (12 h or less) • 1-2 months • 6 months	• 1 • HBIG • 2 • 3 • 4	• Birth (12 h or less)*** • Birth (12 h or less) • 2 months • 4 months • 6 mo (Pediarix)
Unknown	• 1 • HBIG • 2 • 3	• Birth (12 h or less) • Birth (12 h or less) • 1-2 months • 6 months	• 1 • HBIG • 2 • 3 • 4	• Birth (12 h or less)*** • Birth (12 h or less) • 2 months • 4 months • 6 mo (Pediarix)
Negative	• 1 • 2 • 3	• Birth (24 h or less) • 1-2 months • 6-18 months	• 1 • 2 • 3 • 4	• Birth (24 h or less)*** • 2 months • 4 months • 6 mo (Pediarix)

*For infants weighing <2000g, the birth dose of hepatitis B vaccine should NOT be counted toward completion of the hepatitis B vaccine series. See the Red Book, 2015 for further information.
** American Academy of Pediatrics. Hepatitis B. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015: 400-423.
*** Combination vaccines should not be used for birth dose (or any dose through 6 weeks of age).

C. Hepatitis B vaccine and HBIG usage in term infants born to mothers of unknown HBsAg status (including abandoned and safe haven babies)

1. At birth (within 12 hours): Give first dose of vaccine. Draw maternal blood for HBsAg.
2. Give HBIG within 12 hours of birth (strongly preferred by the ODH Perinatal Hepatitis B Prevention Program [PHBPP] Bureau of Infectious Diseases) or await HBsAg result and, if positive, give HBIG as soon as possible but in less than seven days (American Academy of Pediatrics *Red Book* recommendation).
3. At 1-2 months of age: Give second dose of vaccine (if using single-antigen vaccine).
4. At 6 months of age: Give third dose of vaccine (if mother is found to be positive). If mother is found to be negative, give third dose of vaccine at 6-18 months of age. (If using single-antigen vaccine)
5. For doses, see Table 2.
6. For preterm and low birth weight infants, see Table 3.
7. For vaccination schedule by vaccine type, see Table 4.

D. Post-vaccination serological testing among infants born to HBsAg-positive mothers (and mothers whose serostatus remains unknown)

1. After the completion of the vaccine series, these infants should be tested for HBsAg (to determine whether immunoprophylaxis failed) and anti-HBs (to determine whether the immune response was sufficient to ensure continuing protection).
2. This should be done at least 4 weeks after completion of the primary vaccination series, preferably at 9-12 months of age, but at least by 18 months of age (three to nine months after the completion of the series, but never earlier than nine months of age).

E. Additional vaccination

1. Infants who test HBsAg-negative and anti-HBs-negative (anti-HBs <10 mIU/mL) should be revaccinated with a single dose of hepatitis B vaccine and receive post-vaccination serologic testing (PVST) 1–2 months later. Infants whose anti-HBs remains (<10 mIU/mL) following single dose revaccination, should receive two additional doses of Hepatitis B vaccine to complete the second series, followed by PVST 1–2 months after the final dose. Or, based on clinical circumstances or family preference, HBsAg-negative infants with anti-HBs <10 mIU/mL may instead be revaccinated with a second, complete 3-dose series, followed by PVST performed 1–2 months after the final dose of vaccine.
2. If after the sixth dose, the child does not seroconvert, no more doses are indicated, and the child should be considered still susceptible to disease.

F. Screening of household and sexual contacts of pregnant HBsAg-positive females

1. Household and sexual contacts who have a history of three doses of hepatitis B vaccine and are immune to HBV, or who have been found previously to be hepatitis B positive, need not be screened.
2. If the contact has no history of disease or vaccination, they should have serology drawn and vaccine started.

G. Hepatitis B vaccine and HBIG usage among household and sexual contacts of pregnant HBsAg-positive females

1. Household and sexual contacts of pregnant HBsAg-positive females should have screening serology drawn and receive the full series of hepatitis B vaccine.
    a. If a household contact or sexual partner received an exposure (in the past 14 days) to blood from a pregnant HBsAg-positive female regardless of whether the female has acute or chronic hepatitis, HBIG should be given at the same time as the first dose of vaccine (in a different anatomical site).
2. Post vaccine serology testing should be performed on sexual contacts 1-2 months after administration of the last dose of vaccine.
    a. Sexual contacts who do not seroconvert, should receive a second 3-dose series of vaccine, followed by repeat serology 1-2 months after the last dose.
    b. If, after the sixth dose, the contact has not seroconverted, no more doses are indicated.
    c. If it has been greater than 6 months since the last vaccine was administered, give one dose of vaccine and test one month later.

III. Identification and Reporting of HBsAg-positive Pregnant Females: Local Health Department Recommendations

A. All pregnant females should be screened for HBsAg during each pregnancy.

B. All positive laboratory test results

1. All positive laboratory test results of Class B reportable diseases, such as acute, chronic, and perinatal hepatitis B, are required to be reported to the local health department (LHD) within the jurisdiction the individual resides per Ohio Administrative Code 3701-3.
2. This means that any physician, healthcare agency, or laboratory that detects a positive result for one or more hepatitis B serological markers (except anti-HBs) is required to report it to the appropriate LHD. (The presence of anti-HBs indicates

immunity from either previous vaccination or resolved infection.)

C. All females of childbearing age (i.e. 10-50 years of age) and both male and female children (age 15 and below) with one or more positive hepatitis B markers should be entered into the electronic Ohio Disease Reporting System (ODRS) regardless of clinical status as acute or chronic hepatitis B.

1. The pregnancy status of all females of childbearing age should be entered into ODRS.
2. If the pregnancy status is unknown for a female of childbearing age who has one or more positive serological markers for hepatitis B (e.g. HBsAg, HBeAg, HBV-DNA, hepatitis B genotype testing), the female's physician should be contacted to determine the pregnancy status. This should be entered into ODRS.
   a. If the physician does not know the pregnancy status, the female should be contacted directly.
   b. If the female has recently delivered, the LHD should collect clinical, diagnostic, and serological marker data that allows a determination of the status of hepatitis B (e.g. acute, chronic). This should be entered into ODRS.

D. Case information should be entered into ODRS.

IV. Case Management of HBsAg-positive Pregnant Females: Local Health District Recommendations

A. The pregnant female should be interviewed by the LHD within five business days of report to identify all household and current sexual contact(s). If the pregnant female has been followed by the ODH PHBPP during a previous pregnancy, she should be asked if there have been new household and/or sexual contact(s).

1. This information should be entered into ODRS as it is acquired.

V. Management of Infants Born to HBsAg-positive Mothers or Mothers of Unknown Serostatus (including abandoned and safe haven babies)

A. Ensure/facilitate the receipt of the full series of hepatitis B vaccination and HBIG administration as needed.

1. Birth information will be sent to the LHD from the ODH PHBPP, if ODH receives the information from the delivery facility.
2. If notification of delivery is not received within three weeks of estimated date of delivery, the LHD should contact the prenatal care provider or delivery facility to determine pregnancy/delivery status.

B. Ensure/facilitate the determination of post-vaccination serology.

1. Upon completion of the full vaccination series, the LHD should ensure that post-vaccination serology is determined by following up as needed with the infant's medical provider and/or the mother.

C. Determine whether additional vaccination is needed.

1. If post-vaccination serology results are not received from the medical provider, the LHD should contact the infant's medical provider for the results.
2. If post-vaccination serology results indicate hepatitis B infection in the infant, the LHD should:
   a. Contact the ODH PHBPP.
   b. Report the infected infant as a confirmed case in ODRS per ODH guidelines.
   c. Refer the infant for further medical follow-up.
3. If post-vaccination serology indicates that the infant has had an insufficient immune response, the LHD should ensure/facilitate a second three-dose vaccine series, followed one month after the last dose by repeat testing.

D. ODRS should be used to record and track the entire management and follow-up of the infant. All data should be entered into ODRS as it is acquired during management and follow-up.

VI. Management of Household and Sexual Contacts

A. Household and sexual contacts that have a history of three doses of vaccine

and immune to HBV, or who have been found previously to be hepatitis B positive, need not be screened or vaccinated.

B. Serologic testing should be done on all household and sexual contacts that have no history of disease or vaccination.

1. The LHD should provide appropriate educational counseling to each household and sexual contact regarding the importance of screening and vaccination.
2. The serologic testing information should be entered into ODRS for contact investigations.
3. Any new cases of hepatitis B infection (including those in a pregnant female) need to be entered into ODRS.

C. Susceptible household and sexual contacts should be immunized.

1. The first dose of vaccine should be given at the same visit the serology is drawn
2. If a household contact or sexual partner received an exposure (in the past 14 days) to blood from a pregnant HBsAg-positive female regardless of whether the female has acute or chronic hepatitis, HBIG should be given at the same time as the first dose of vaccine (in a different anatomical site).

D. Sexual contacts should have post-vaccination serology (PVS) done 1-2 months after the administration of the last dose of vaccine.

1. Sexual contacts that do not seroconvert should receive a second three-dose series of vaccine, followed by testing for anti-HBs and HBsAg.
2. If, after the sixth dose, the contact has not seroconverted, no more doses are indicated.

VII. Case Closure

A. By the time the infant is 18 months of age, the LHD should make at least three contacts with the infant's parents, guardians or physician; contacts can be via phone, mail and/or in person.

B. Upon both completion of the infant's three-dose series (or six doses if indicated) and documentation of seroconversion with post-vaccination serology (i.e. anti-HBs 10 mU/Ml or more), as well as a negative HBsAg test result, the infant case in ODRS should be closed.

1. As noted above, if seroconversion does not occur after six doses, the infant case in ODRS can still be closed because no further vaccination is recommended.
2. HBsAg should be drawn simultaneously with anti-HBs.

C. The household and sexual contact section can be closed if several reasonable attempts have been made to complete this part of the investigation and case management.

D. In the event that a pregnant HBsAg-positive pregnant female and/or an exposed infant transfers out of the jurisdiction, the LHD will update the ODRS record with the most current address available. To transfer a case, the LHD must provide a street address, city and state. The LHD will transfer the case within Ohio. If the case transfers out-of-state, the ODH PHBPP staff will transfer the case to another state PHBPP coordinator and update the ODRS record.

References

1. A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States. Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part 1: Immunization of Infants, Children, and Adolescents. *MMWR* December 23, 2005; 54 (RR16); 1-23. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5416a1.htm

2. ODH Perinatal Hepatitis B Prevention Program, 2018.

3. American Academy of Pediatrics. Hepatitis B. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015: 400-423.

4. Robinson CL, Romero JR, Kempe A, Pellegrini C. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger — United States, 2017. MMWR Morb Mortal Wkly Rep 2017;66:134–135. DOI: http://dx.doi.org/10.15585/mmwr.mm6605e1

5. Schillie S, Vellozzi C, Reingold A, et al. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2018;67(No. RR-1):1–31.