POLICY STATEMENT Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Elimination of Perinatal Hepatitis B: Providing the First Vaccine Dose Within 24 Hours of Birth

COMMITTEE ON INFECTIOUS DISEASES, COMMITTEE ON FETUS AND NEWBORN

abstract

After the introduction of the hepatitis B vaccine in the United States in 1982, a greater than 90% reduction in new infections was achieved. However, approximately 1000 new cases of perinatal hepatitis B infection are still identified annually in the United States. Prevention of perinatal hepatitis B relies on the proper and timely identification of infants born to mothers who are hepatitis B surface antigen positive and to mothers with unknown status to ensure administration of appropriate postexposure immunoprophylaxis with hepatitis B vaccine and immune globulin. To reduce the incidence of perinatal hepatitis B transmission further, the American Academy of Pediatrics endorses the recommendation of the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention that all newborn infants with a birth weight of greater than or equal to 2000 g receive hepatitis B vaccine by 24 hours of age.

FREE

DOI: https://doi.org/10.1542/peds.2017-1870

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: AAP COMMITTEE ON INFECTIOUS DISEASES and AAP COMMITTEE ON FETUS AND NEWBORN. Elimination of Perinatal Hepatitis B: Providing the First Vaccine Dose Within 24 Hours of Birth. *Pediatrics.* 2017;140(3):e20171870

Approximately 1000 new cases of perinatal hepatitis B infection are identified annually in the United States.[1,2] Chronic hepatitis B infection occurs in up to 90% of infants infected with hepatitis B at birth or in the first year of life. When untreated, approximately 25% ultimately will die of hepatocellular carcinoma or liver cirrhosis. In the absence of postexposure prophylaxis at birth, the risk of perinatal transmission is substantial when an infant is born to a mother who is hepatitis B surface antigen (HBsAg) positive. The proportion of infants acquiring infection in this circumstance ranges from approximately 30% when mothers are hepatitis B e antigen (HBeAg) (a marker of infectivity) negative to approximately 85% when mothers are HBeAg positive. Because maternal HBeAg status frequently is unknown, the true risk to an individual newborn infant also generally is unknown. Postexposure prophylaxis is highly effective. Hepatitis B vaccine alone is 75% to 95% effective in preventing perinatal hepatitis B transmission when given within 24 hours of birth.[3,4] When postexposure prophylaxis with both hepatitis B vaccine and hepatitis B immune globulin (HBIG) is given, is timed appropriately,

and is followed by completion of the infant hepatitis B immunization series, perinatal infection rates range from 0.7% to 1.1%.[5,6] These findings are the basis for the rationale for the current change in the recommendation regarding birth vaccination.

Prevention of perinatal transmission of hepatitis B is part of a national strategy for hepatitis B prevention that relies on testing all pregnant women for hepatitis B infection by testing women for HBsAg routinely during pregnancy and providing appropriate and timely prophylaxis to all newborn infants.[6] Appropriate prophylaxis consists of HBIG and/or hepatitis B vaccine, depending on the HBsAg status of the mother and the weight of the infant (Fig 1). The birth dose of hepatitis B vaccine is a critical safety net to protect infants born to hepatitis B–infected mothers not identified at the time of birth. The birth dose can prevent infection of infants born to infected mothers in situations in which the mother's results are never obtained, are misinterpreted, are falsely negative, are transcribed or reported to the infant care team inaccurately, or simply not communicated to the nursery. The Immunization Action Coalition reported greater than 500 such errors in perinatal hepatitis B prevention from 1999 to 2002.[7] The birth dose also provides protection to infants at risk from household exposure after the perinatal period. For infants born to HBsAg-negative mothers, the birth dose is the beginning of appropriate lifelong prophylaxis. Because the consequences of perinatally acquired hepatitis B are enduring and potentially fatal, the safety net of the birth dose is critically important. The incidence of new hepatitis B infections has increased in some states as a result of the opioid epidemic in the United States,[8] underscoring the urgency

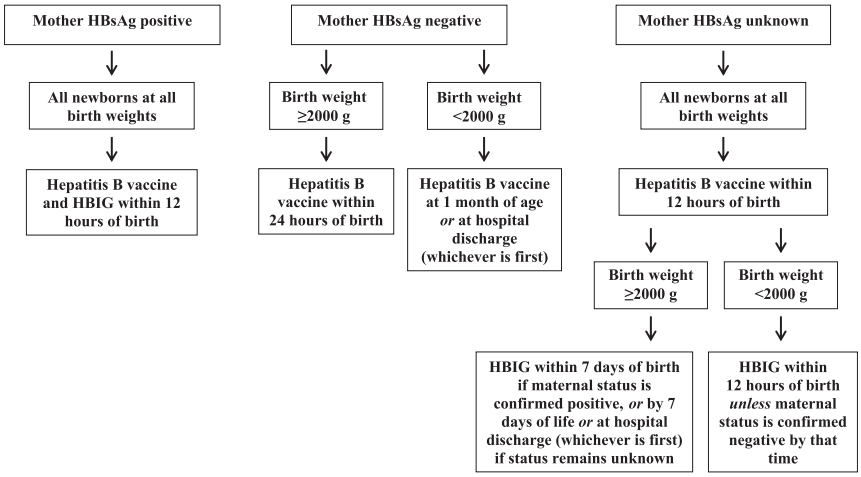

FIGURE 1
Administration of the birth dose of hepatitis B vaccine by maternal HBsAg status.

of improving perinatal prevention strategies.

Hepatitis B antiviral therapy now is offered during pregnancy to hepatitis B–infected women with high hepatitis B viral loads. Antiviral therapy started from 30 to 32 weeks' gestational age and continued until postpartum week 4 in the mother, in addition to newborn prophylaxis with hepatitis B vaccine and HBIG, has been associated with significantly reduced rates of perinatal hepatitis B virus transmission from highly viremic mothers.[9] There is no evidence, however, that maternal antenatal treatment alone without infant prophylaxis is sufficient to reduce the risk for perinatal transmission.[10]

The US Department of Health and Human Services has set a goal of 0 perinatal hepatitis B transmission in the United States by 2020.[6] Although 95% of infants born to infected women who are identified by the Centers for Disease Control and Prevention's Perinatal Hepatitis B Prevention Program do receive prophylaxis with HBIG and hepatitis B vaccine within 12 hours of birth, the overall hepatitis B immunization rate of newborn infants is suboptimal.[11] In 2005, the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) issued hepatitis B vaccine recommendations that contained permissive language around administration of the birth dose of hepatitis B vaccine, allowing practitioners the option to delay this dose.[5] By 2014, a quality improvement study found that only 72% of infants received the birth dose of hepatitis B vaccine, which is less than the Healthy People 2020 target of 85%.[12] In October 2016, the ACIP rescinded the permissive language and instead stated the following: "For all medically stable infants weighing greater than or equal to 2000 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 hepatitis B vaccine should be used for the birth dose."[13,14]

RECOMMENDATIONS

The American Academy of Pediatrics Committee on Infectious Diseases and the Committee on Fetus and Newborn support removal of permissive language for delaying the birth dose of hepatitis B vaccine, endorse the recommendation of the ACIP for giving the birth dose within the first 24 hours of life in all medically stable infants

weighing greater than or equal to 2000 g, and provide guidance for implementation.[15]

Vaccine Issues

After completion of a 3- or 4-dose hepatitis B vaccine series, 98% of healthy term infants achieve protective antibody concentrations. Protection may be lower in infants with birth weights less than 2000 g.[5] The optimal time to perform serologic testing to detect a vaccine response in infants is 1 to 2 months after the final dose of the hepatitis B vaccine series. Recommendations for postvaccination serologic testing of infants born to hepatitis B–infected mothers have been updated recently.[16] For infants born to HBsAg-positive mothers, postvaccination serologic testing by measuring hepatitis B surface antibody (anti-HBs) to document protection and HBsAg to rule out perinatal infection now is recommended at 9 to 12 months of age instead of 9 to 18 months. Infants who are HBsAg negative with anti-HBs levels less than 10 mIU/mL (nonprotective) require additional vaccine doses. The ACIP considered revaccination strategies in February 2017 and recommended that HBsAg-negative infants with anti-HBs levels less than 10 mIU/mL receive a single additional dose of hepatitis B vaccine and be retested for anti-HBs 1 to 2 months after that vaccine dose. If the anti-HBs level is still less than 10 mIU/mL, the infant should receive 2 additional doses of hepatitis B vaccine followed by retesting 1 to 2 months later. Infants with anti-HBs levels less than 10 mIU/mL after 2 3-dose series of hepatitis B vaccine are nonresponders, and available data do not suggest benefit from additional vaccinations. The ACIP noted that, on the basis of clinical circumstance or family preference, HBsAg-negative infants with anti-HBs levels less than 10 mIU/mL may be vaccinated instead with a second complete series followed by postvaccination testing 1 to 2 months after the final dose.

Hepatitis B vaccine is well tolerated in infants.[17,18] Commonly reported mild adverse events after hepatitis B vaccination in people of all ages from postmarketing surveillance data include pain (3%–29%), erythema (3%), swelling (3%), fever (1%–6%), and headache (3%). Safety of hepatitis B vaccines has been examined extensively; no evidence of a causal association between receipt of hepatitis B vaccine and neonatal sepsis or death, rheumatoid arthritis, Bell's palsy, autoimmune thyroid disease, hemolytic anemia in children, anaphylaxis, optic neuritis, Guillain-Barré syndrome, sudden-onset sensorineural hearing loss, or other chronic illnesses has been demonstrated through analysis of data from the Vaccine Safety Datalink.[5] Perinatal hepatitis B–prevention strategies are considered cost-effective, with a cost-effectiveness ratio of $2600 per quality-adjusted life-year.[19]

Implementation

The following are key steps for implementing appropriate administration of the birth dose of hepatitis B vaccine (see also Fig 1):

- Identify HBsAg-positive mothers before delivery and document maternal HBsAg status in infant records;
- Resolve unknown HBsAg status of mothers as soon as possible around delivery, and document maternal status in infant records;
- For all infants born to HBsAg-positive mothers, administer both hepatitis B vaccine and HBIG within 12 hours of birth, regardless of any maternal antenatal treatment with antiviral medications;
- For all infants with birth weight greater than or equal to 2000 g born to HBsAg-negative mothers, administer hepatitis B vaccine as a universal routine prophylaxis within 24 hours of birth;
- For all infants with birth weight less than 2000 g born to HBsAg-negative mothers, administer hepatitis B vaccine as a universal routine prophylaxis at 1 month of age or at hospital discharge (whichever is first);
- For all infants born to HBsAg-unknown mothers, administer hepatitis B vaccine within 12 hours of birth, and:
  - For infants with birth weight greater than or equal to 2000 g, administer HBIG by 7 days of age or by hospital discharge (whichever occurs first) if maternal HBsAg status is confirmed positive or remains unknown;
  - For infants with birth weight less than 2000 g, administer HBIG by 12 hours of birth unless maternal HBsAg status is confirmed negative by that time;
- Document infant vaccination accurately in birth hospital records and in the appropriate CDC Immunization Information Systems and state immunization registry. Review documentation accuracy periodically and address identified errors; and
- Develop procedures to educate all personnel involved in newborn care about recommendations for the birth dose of hepatitis B vaccine, including those personnel who provide care at planned home births.

COMMITTEE ON FETUS AND NEWBORN, 2016–2017

Kristi Watterberg, MD, FAAP, Chairperson
William Benitz, MD, FAAP
Ivan Hand, MD, FAAP
Eric Eichenwald, MD, FAAP
Brenda Poindexter, MD, FAAP
Dan L. Stewart, MD, FAAP
Susan W. Aucott, MD, FAAP
Karen M. Puopolo, MD, PhD, FAAP
Jay P. Goldsmith, MD, FAAP

ABBREVIATIONS

ACIP: Advisory Committee on Immunization Practices
Anti-HBs: hepatitis B surface antibody
HBeAg: hepatitis B e antigen
HBIG: hepatitis B immune globulin
HBsAg: hepatitis B surface antigen

REFERENCES

1. Centers for Disease Control and Prevention, Division of Viral Hepatitis. Surveillance for viral hepatitis—United States 2014. Revised September 26, 2016. Available at: https://www.cdc.gov/hepatitis/statistics/2014surveillance/. Accessed March 23, 2017
2. Ko SC, Fan L, Smith EA, Fenlon N, Koneru AK, Murphy TV. Estimated annual perinatal hepatitis b virus infections in the United States, 2000-2009. *J Pediatric Infect Dis Soc*. 2016;5(2):114–121
3. Beasley RP, Hwang LY, Lee GC, et al. Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine. *Lancet*. 1983;2(8359):1099–1102
4. Lee C, Gong Y, Brok J, Boxall EH, Gluud C. Effect of hepatitis B immunisation in newborn infants of mothers positive for hepatitis B surface antigen: systematic review and meta-analysis. *BMJ*. 2006;332(7537):328–336
5. Mast EE, Margolis HS, Fiore AE, et al; Advisory Committee on Immunization Practices (ACIP). 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 Recomm Rep*. 2005;54(RR-16):1–31
6. US Department of Health and Human Services. Action plan for the prevention, care, & treatment of viral hepatitis. Updated 2014–2016. Available at: https://www.hhs.gov/sites/default/files/viral-hepatitis-action-plan.pdf. Accessed March 23, 2017
7. Immunization Action Coalition. Reducing medical errors: case reports. Available at: www.immunize.org/protect-newborns/guide/chapter2/case-reports.pdf. Accessed March 23, 2017
8. Harris AM, Iqbal K, Schillie S, et al. Increases in acute hepatitis b virus infections — Kentucky, Tennessee, and West Virginia, 2006–2013. *MMWR Morb Mortal Wkly Rep*. 2016;65(3):47–50
9. Pan CQ, Duan Z, Dai E, et al; China Study Group for the Mother-to-Child Transmission of Hepatitis B. Tenofovir to prevent hepatitis B transmission in mothers with high viral load. *N Engl J Med*. 2016;374(24):2324–2334
10. Chen HL, Lee CN, Chang CH, et al; Taiwan Study Group for the Prevention of Mother-to-Infant Transmission of HBV (PreMIT Study); Taiwan Study Group for the Prevention of Mother-to-Infant Transmission of HBV PreMIT Study. Efficacy of maternal tenofovir disoproxil fumarate in interrupting mother-to-infant transmission of hepatitis B virus. *Hepatology*. 2015;62(2):375–386
11. Schillie S, Walker T, Veselsky S, et al. Outcomes of infants born to women infected with hepatitis B. *Pediatrics*. 2015;135(5). Available at: www.pediatrics.org/cgi/content/full/135/5/e1141
12. Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kolasa M. National, state, and selected local area vaccination coverage among children aged 19-35 months - United States, 2014. *MMWR Morb Mortal Wkly Rep*. 2015;64(33):889–896

13. Kim DK, Riley LE, Harriman KH, Hunter P, Bridges CB. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older — United States, 2017. . *MMWR Morb Mortal Wkly Rep*. 2017; 66(5);136–138

14. US Department of Health and Human Services, Centers for Disease Control and Prevention. Advisory committee on immunization practices. summary report. 2016. Available at: https://www.cdc.gov/vaccines/acip/meetings/downloads/min-archive/min-2016-10.pdf. Accessed May 3, 2017

15. Committee on Infectious Diseases. Recommended childhood and adolescent immunization schedule—United States, 2017. *Pediatrics*. 2017;139(3):e20164007

16. Schillie S, Murphy TV, Fenlon N, Ko S, Ward JW. Update: shortened interval for postvaccination serologic testing of infants born to hepatitis B-infected mothers. *MMWR Morb Mortal Wkly Rep*. 2015;64(39):1118–1120

17. Eriksen EM, Perlman JA, Miller A, et al. Lack of association between hepatitis B birth immunization and neonatal death: a population-based study from the vaccine safety datalink project. *Pediatr Infect Dis J*. 2004;23(7):656–662

18. Lewis E, Shinefield HR, Woodruff BA, et al; Vaccine Safety Datalink Workgroup. Safety of neonatal hepatitis B vaccine administration. *Pediatr Infect Dis J*. 2001;20(11):1049–1054

19. Barbosa C, Smith EA, Hoerger TJ, et al. Cost-effectiveness analysis of the national perinatal hepatitis B prevention program. *Pediatrics*. 2014;133(2):243–253

Elimination of Perinatal Hepatitis B: Providing the First Vaccine Dose Within 24 Hours of Birth

COMMITTEE ON INFECTIOUS DISEASES and COMMITTEE ON FETUS AND NEWBORN

Pediatrics 2017;140;; originally published online August 28, 2017;
DOI: 10.1542/peds.2017-1870

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Elimination of Perinatal Hepatitis B: Providing the First Vaccine Dose Within 24 Hours of Birth

COMMITTEE ON INFECTIOUS DISEASES and COMMITTEE ON FETUS AND NEWBORN

Pediatrics 2017;140;; originally published online August 28, 2017;
DOI: 10.1542/peds.2017-1870