Prevention of Hepatitis B in the Newborn Infant Clinical Pathway

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Rationale
To institute the American Academy of Pediatrics recommendations on Hepatitis B vaccine administration to sick and premature infants in the neonatal intensive care unit

Background / Published Data and Levels of Evidence

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 post exposure immunoprophylaxis with hepatitis B vaccine and immune globulin.

Chronic hepatitis B infection occurs in up to 90% of infants infected with hepatitis B at birth or in the first year of life. 25% ultimately will die of hepatocellular carcinoma or liver cirrhosis if left untreated.

When post exposure prophylaxis at birth is not given to an infant who is born to a mother who is hepatitis B surface antigen (HBsAg) positive, the risk of perinatal transmission is substantial. The risk of acquiring hepatitis B infection 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. The true risk to an individual newborn infant is generally unknown because maternal HBe antigen (HBeAg) is frequently unknown.

Hepatitis B vaccine alone is 75% to 95% effective in preventing perinatal hepatitis B transmission when given within 24 hours of birth. When post exposure prophylaxis with both hepatitis B vaccine and hepatitis B immune globulin (HBIG) is given, is timed appropriately (i.e. within 12 hours of birth) and is followed by completion of the infant hepatitis B immunization series, perinatal infection rates range from 0.7% to 1.1%.
These findings are the basis for the rationale for the current change in the recommendation regarding birth vaccination.

The birth dose also provides protection to infants at risk from household exposure after the perinatal period.

The US Department of Health and Human Services has set a goal of 0 perinatal hepatitis B transmission in the United States by 2020. The overall hepatitis B immunization rate of newborn infants is suboptimal. Only 72% of infants received the birth dose of hepatitis B vaccine, which is less than the Healthy People 2020 target of 85%.

The permissive language allowing practitioners the option to delay the birth dosed of Hepatitis B vaccine was rescinded by the Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practices (ACIP) in October 2016.

The ACIP instead issued a new statement: “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.”

Clinical Management
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.

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.

A. **Administration of the birth dose of hepatitis B vaccine**

*Please refer to Figure 1 under Pathway / Algorithm*

1. **Infants > 2000 grams**
   a. 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.
   b. All infants with birth weight ≥ 2000 g born to HBsAg-negative mothers, administer hepatitis B vaccine as a universal routine prophylaxis within 24 hours
of birth.

c. For all infants born to HBsAg unknown mothers, administer hepatitis B vaccine within 12 hours of birth. Administer HBIG by 7 days of age or by hospital discharge (whichever occurs first) if maternal HBsAg status is confirmed positive or remains unknown.

2. Infants < 2000 grams
   a. 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. The birth dose should not be counted as part of the HBV immunization series.
   b. Infants with birth weight < 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). The birth dose should not be counted as part of the HBV immunization series.
   c. Infants born to HBsAg unknown mothers, administer hepatitis B vaccine within 12 hours of birth. Administer HBIG by 12 hours of birth unless maternal HBsAg status is confirmed negative by that time.

B. Administration of subsequent doses of hepatitis B vaccine

Please refer to Table 1 under Pathway / Algorithm

Infants who remain in the NICU beyond one month of age will need to complete their series of hepatitis B immunization if they remain in the nursery 6 months or longer.

I. Infants > 2000 grams

For all maternal HBsAg status (positive, unknown, negative)

1. Second dose of hepatitis B vaccine given at 1-2 months age.
2. Third dose of hepatitis B vaccine given at 6 months age. -The final dose of should not be administered before age 24 weeks (164 days).
II. Infants < 2000 grams

1. For maternal HBsAG positive and unknown status
   a. Second dose at 1 month age.
   b. Third dose at 2-3 months age.
   c. Fourth dose at 6 months age - The final dose of should not be administered
      before age 24 weeks (164 days).

2. For maternal negative HBsAg
   a. Second dose at 2 months of age
   b. Third dose at 6 months of age - The final dose of should not be administered
      before age 24 weeks (164 days).

C. Hepatitis B Vaccine Dosage

Only single antigen HepB vaccine should be used between birth and 6 weeks.
Pediarix should not be administered before age 6 weeks.
Give at a different extremity from where hepatitis B immune globulin (HBIG) was administered.

A. Birth dose of hepatitis B vaccine (single antigen vaccine only)
   Two vaccines are available for use:
   1. Recombivax HB- 5 micrograms (0.5 ml) given Intramuscular (IM)
   2. Engerix-B- 10 micrograms (0.5 ml) given Intramuscular (IM)

B. Subsequent dosing of hepatitis B vaccine-
   1. RecombivaxHB- 5 micrograms (0.5 ml) given Intramuscular (IM)
   2. Engerix-B- 10 micrograms (0.5 ml) given Intramuscular (IM)
   3. Pediarix (Approved for use only at age 6 weeks through 6 years)- 10 micrograms
      (0.5 ml) given IM.
      - Pediarix may be used to complete subsequent doses of the hepatitis B vaccine.
D. Hepatitis B Immune Globulin (HBIG) Dosage

Dose: 0.5 ml given Intramuscular (IM) given at a different extremity from where hepatitis B Vaccine was administered.

1. Given to all infants whose mothers are hepatitis B antigen positive within 12 hours of Birth.

2. Given to infants whose mother’s hepatitis B antigen status is unknown.
   A. Infant’s >2,000 grams
      - Given within 7 days of birth if maternal status is confirmed positive after maternal admission HBsAG lab is resulted.
      - By 7 days of life or at hospital discharge, whichever comes first if hepatitis B status remains unknown.
   A. Infants <2,000 grams HBIG given within 12 hours of birth unless maternal status is confirmed negative by that time.

E. Postvaccination Serologic Testing

1. Postvaccination serologic testing consists of measuring hepatitis B surface antibody (anti-HBs) to document protection and HBsAg to rule out perinatal infection at 9-12 months of age.

2. Postvaccination serologic testing should be performed on infants born to HBsAg positive mothers and infants whose mother’s HBsAG status remains unknown.

4. Infants born to mothers who are HBsAg negative, post vaccination serologic testing is not needed.

5. HBsAg-negative infants with anti-HBs levels ≥10 mIU/ml are protected and need no further medical management.

F. Revaccination With Hepatitis B Vaccine

1. HBsAg-negative infants with anti-HBs levels <10 mIU/ml should be revaccinated with a single dose of HepB vaccine and receive post vaccination serologic testing 1–2 months later (new recommendation).

2. Infants whose anti-HBs remains <10 mIU/mL following single dose revaccination
should receive two additional doses of HepB vaccine to complete the second series followed by post vaccination serologic testing 1–2 months after the final dose.

3. 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.

G. Hepatitis B Vaccine Consent

1. Federal law requires that you give parents a Hepatitis B Vaccine Information Statement (VIS) before vaccine administration.

2. If the HepB vaccine is given as a treatment due to exposure to hepatitis B, it is considered a treatment and is covered by the general consent for treatment.

3. If hepatitis B vaccine is given as a prophylaxis discussion with the parent must occur prior to giving it. Documentation by the provider should be reflected in the chart of the discussion and agreement of the parents to give their baby the vaccine.

4. The parents of Infants who are delivered at Bayfront Baby Place will be given by the Stork Team a copy of the Vaccine Information Statement (VIS). A provider (neonatologist, neonatal fellow, pediatric resident or NNP) will discuss hepatitis B Immunization within 24 hour of birth with the parents and document in the medical record whether they consent or not for their infant to receive the vaccine. Hepatitis B vaccine immunization can only be given after this process occurs.

5. For infants who are transferred from an outlying hospital, the Transport Team will give the parents a copy of the Vaccine Information Statement (VIS). A provider (neonatologist, neonatal fellow, pediatric resident or NNP) will discuss hepatitis B immunization within 24 hour of birth with the parents and document in the medical record whether they consent or not for their infant to receive the vaccine. Hepatitis B vaccine immunization can only be given after this process occurs.
Pathway / Algorithms:

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

Table 1. Hepatitis B vaccine schedules for infants, by infants birth weight and maternal hepatitis B schedule

<table>
<thead>
<tr>
<th>Birthweight</th>
<th>Maternal HBsAg status</th>
<th>Single-antigen vaccine</th>
<th>Single-antigen + combination vaccine†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Dose</td>
<td>Age</td>
</tr>
<tr>
<td>≥2,000 g</td>
<td>Positive</td>
<td>1</td>
<td>Birth (≤12 hrs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>1–2 mos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>6 mos³</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unknown*</td>
<td>1</td>
<td>Birth (≤12 hrs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>1–2 mos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>6 mos³</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>1</td>
<td>Birth (≤24 hrs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>1–2 mos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>6–18 mos³</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2,000 g</td>
<td>Positive</td>
<td>1</td>
<td>Birth (≤12 hrs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>1 mos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>2–3 mos</td>
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<tr>
<td></td>
<td></td>
<td>4</td>
<td>6 mos³</td>
</tr>
<tr>
<td></td>
<td>Unknown*</td>
<td>1</td>
<td>Birth (≤12 hrs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>1 mos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>2–3 mos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4</td>
<td>6 mos³</td>
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<tr>
<td></td>
<td>Negative</td>
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<td>Hospital discharge or age 1 mo</td>
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<td>3 mos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4</td>
<td>6 mos³</td>
</tr>
</tbody>
</table>

Abbreviations: HBIG = hepatitis B immune globulin; HBsAg = hepatitis B surface antigen.
* Mothers should have blood drawn and tested for HBsAg as soon as possible after admission for delivery; if the mother is found to be HBsAg positive, the infant should receive HBIG as soon as possible but no later than age 7 days.
† Pediarix should not be administered before age 6 weeks.
³ HBIG should be administered at a separate anatomical site from vaccine.
* The final dose in the vaccine series should not be administered before age 24 weeks (164 days).

Glossary

hepatitis B e antigen (HBeAg)
hepatitis B surface antigen (HBsAg)
hepatitis B immune globulin (HBIG)
HBV (hepatitis B vaccination)
hepB (hepatitis B)
Vaccine Information Statement (VIS)

References

1. Elimination of Perinatal Hepatitis B: Providing the First Vaccine Dose Within 24 Hours of Birth: Pediatrics 2017; Vol. 140; number 3: e20171870
3. Hepatitis A, B, and C, Pediatric in Review: October 2016; Vol. 37, No.10; p4264
4. Immunization of Preterm and Low Birth Weight Infants, Pediatrics 2003;112;193
Clinical Pathway Team

Prevention of Hepatitis B in the Newborn Infant

Clinical Pathway

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Clinical Pathways are intended to assist physicians, physician assistants, nurse practitioners and other health care providers in clinical decision-making by describing a range of generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. The ultimate judgment regarding care of a particular patient must be made by the physician in light of the individual circumstances presented by the patient.

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