

# Chapter 4

## Postexposure Prophylaxis (PEP)



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## Prevention

The CDC has released two comprehensive documents pertaining to the elimination of HBV infection in the US. These documents provide recommendations of the Advisory Committee on Immunization Practices (ACIP) and strategies to implement these recommendations in both children and adults. The primary focus of the ACIP childhood recommendations is the universal vaccination of infants as a “safety net” to prevent early childhood HBV infection.

The strategies to prevent hepatitis B infection in children include, but are not limited to:

- Universal vaccination of infants beginning at birth;
- Routine screening of all pregnant women for HBsAg;
- PEP of infants born to HBsAg-positive women or to women with unknown HBsAg status; and
- Routine vaccination of previously unvaccinated children and adolescents.

In these documents, the CDC also provides strategies to enhance implementation of the ACIP recommendations such as:

- Establishing standing orders for administration of hepatitis B vaccination at birth; and
- Implementing policies and procedures to improve identification of and administration of PEP to infants born to:
  - mothers who are HBsAg positive; and
  - mothers with unknown HBsAg status at the time of delivery.

The CDC and ACIP recommend that providers who practice in primary care and at-risk specialty settings should implement standing orders to identify their at-risk patients and subsequently vaccinate them.

Part one of the document (Recommendations for Infants, Children, and Adolescents) can be accessed electronically at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5416a1.htm>. Part two of the document (Immunization of Adults) can be accessed electronically at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5516a1.htm>.

The Institute of Medicine (IOM) also released a report on preventing and controlling viral hepatitis infections in the US. After reviewing evidence on the prevention and control of hepatitis B and hepatitis C, the committee identified the underlying factors that impeded current efforts to prevent and control these diseases. In this report, hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C, the committee offers recommendations in four categories: surveillance, knowledge and awareness, immunization, and services for viral hepatitis. This document, along with recommendations from ACIP can be found at the following web site:

<http://www.cdc.gov/hepatitis/pdfs/iom-hepatitisandlivercancerreport.pdf>.

## Postexposure Prophylaxis (PEP)

### Hepatitis B Immune Globulin (HBIG)

Hepatitis B immune globulin (HBIG) is derived from human plasma. The plasma, which is processed from select human donors with high anti-HBs titers, contains antibodies that are specific to the hepatitis B virus. Although HBIG is derived from humans, it is purified to prevent passing along disease to the person who receives it. In the case of perinatal hepatitis B, HBIG is intended to give the infant short-term protection against the hepatitis B virus which they might have been exposed to during birth. HBIG that is commercially available in the US does not contain thimerosal, a common mercury-containing preservative found in some immunizations.

HBIG is used as passive immunization for individuals who might have been exposed to the virus. It is important to keep in mind that immune globulin does not provide long-term protection in the same way that vaccinations do. The protection is only short term, usually only lasting a few weeks to a few months. For infants exposed during labor and delivery, they should receive HBIG and the birth dose of hepatitis B vaccine within 12 hours of birth. After the immune globulin is no longer effective, the infant's immune system should already be producing its' own antibodies (anti-HBs) to the hepatitis B virus in response to the vaccine. It is important that the infant complete the vaccine series on time, in order to give the infant the best chance of developing immunity against the virus.

<b>HBIG Product Information for Perinatal Exposure</b>			
<b>Product Name</b>	<b>Manufacturer</b>	<b>Perinatal Dosing</b>	<b>Presentation*</b>
HepaGamB®	Cangene Corporation	0.5 mL	1.0 mL single use <i>vial</i>
HyperHEPB®	Grifols	0.5 mL	0.5 mL single dose <i>syringe</i>
Nabi-HB®	Biotest Pharmaceuticals	0.5 mL	1mL single dose <i>vial</i>

\*as relevant only to perinatal administration

### Hepatitis B Vaccine

The hepatitis B vaccine is the best protection against the hepatitis B virus. In 1986, research led to a recombinant hepatitis B vaccine that was synthetically modified and did not contain any blood products. It was later licensed for use in the US in 1989. This was the first vaccine licensed in the US that was produced by recombinant DNA technology. HBV infection cannot result from use of the recombinant vaccine, since no potentially infectious viral DNA or complete viral particles are produced in the recombinant system.

As of March 2000, all hepatitis B vaccines produced for distribution in the US are thimerosal-free.

The hepatitis B vaccine is available as a single-antigen formulation (monovalent vaccine) as well as in fixed combination with other vaccines (combination vaccine).

## Postexposure Prophylaxis (PEP) for Infants at Birth

Born to HBsAg-positive mother	
HBIG	Administer within 12 hours.
Hepatitis B birth dose	Administer within 12 hours.
Born to HBsAg-unknown mother	
HBIG	If positive results are received, administer <b>immediately</b> .
	If discharge is planned before day seven and results are still unknown, HBIG should be administered before the infant is discharged from the delivery facility.
	If negative results are received before discharge, no HBIG needed.
Hepatitis B birth dose	Administer within 12 hours.

### Importance of the Hepatitis B Vaccine Birth Dose

Hepatitis B vaccine was first recommended for administration to all infants in 1991 by the ACIP as the primary focus of a strategy to eliminate HBV transmission in the United States. The recommended timing of administration of the first dose of hepatitis B vaccine to infants has evolved since then to optimize prevention of perinatal and early childhood HBV infections. In 1991, the first dose was recommended to be administered at birth before hospital discharge or at age 1 - 2 months. In 2002, ACIP indicated a preference for the first dose to be administered to newborns before hospital discharge. In December 2005, ACIP issued revised recommendations specifying that all medically stable newborns who weigh > 2,000 g (4.4 lbs.) receive their first dose of hepatitis B vaccine before hospital discharge.

The CDC recommends that *all* infants born to HBsAg-positive mothers, or mothers whose status is unknown, should receive the birth dose of hepatitis B vaccine at birth, *regardless* of birth weight. All infants weighing < 2,000 g (4.4 lbs.) at birth and who received the birth dose of hepatitis B vaccine should have the series reinitiated at ≥ 1 month of age; the birth dose should not be considered a valid dose as part of the series in these infants. These infants will receive between four and five doses of hepatitis B vaccine, depending on the formulation of vaccine used after the birth dose.

Exceptions to the universal birth dose should be rare and considered on a case-by-case basis. Any health care provider who decides to delay the birth dose must document the order to do so, and ensure that a copy of the mother's laboratory report, indicating she was HBsAg-negative during *this* pregnancy and at delivery, is present in the infant's medical record. **The birth dose should not be delayed in infants whose mother tested HBsAg-positive prenatally and / or at delivery.**

The hepatitis B vaccine birth dose serves as a "safety net" in the event that a mother was misdiagnosed as HBsAg-negative prenatally and / or at delivery. Children born to HBsAg-positive mothers who do not become infected during the perinatal period remain at high risk of infection during early childhood. In one study, 40 percent of infants who were not infected perinatally became infected by the age of five years. Guidelines for standing orders in labor and delivery and nursery units to prevent hepatitis B virus transmission to newborns can be found in Appendix D of this manual or on the DSHS Immunization Branch PHBPP website at [www.texasperinatalhepb.org](http://www.texasperinatalhepb.org).

## Vaccination Schedule and Use

### Infants and Children

Hepatitis B vaccination is recommended for all infants soon after birth and before hospital discharge, regardless of birthweight.

- Engerix-B® (GSK)
  - 0.5 mL (10 mcg) / dose
  - Approved: 0 - 19 years of age
  - three doses – administered Intramuscular (IM)
  - Schedule: Birth, 1 - 2 months, 6 months
- Recombivax HB® (Merck)
  - 0.5 mL (5 mcg) / dose
  - Approved: 0 - 19 years of age
  - three doses – administered IM
  - Schedule: Birth, 1 - 2 months, 6 months
- Pediarix® (GSK): DTaP+Hep B+IPV
  - 0.5 mL (10mcg) / dose
  - Approved: 6 weeks – 6 years of age
  - three doses\* – administered IM
  - Schedule: 2 months, 4 months, 6 months

\* It is important to note that although Pediarix® is approved as a three dose series, children who receive Pediarix® on the appropriate schedule, will receive four doses of hepatitis B vaccine, including the birth dose; this is safe and will not harm the child.

It is preferred that the same vaccine / manufacturer be used for completion of a series. The FDA licenses combination vaccines based on their efficacy (and safety) when compared to monovalent vaccines. If the vaccine that the child previously received is not immediately available, or is unknown, vaccination should not be delayed; the child should receive available age appropriate vaccine.

**Infants should not receive the final dose of hepatitis B vaccine prior to six months of age.** If the third dose is inadvertently given before six months (24 weeks) of age, the dose should be repeated and administered once the child is at least 24 weeks of age.

Because the highest anti-HBs are achieved when the last two doses of vaccine are spaced at least four months apart, schedules that achieve this spacing are preferable. However, schedules with two month intervals between doses (i.e., Pediarix®), which conform to schedules for other childhood vaccines, have been shown to produce good antibody responses and may be appropriate in populations in which it is difficult to ensure that infants will be brought back for all of their vaccinations. The minimum intervals for the hepatitis B vaccine schedule to produce a good antibody response in infants are as follows:

- The second dose should be administered at least four weeks after the first dose.
- The third dose should be administered at least eight weeks after the second dose.
- The third dose should be administered at least 16 weeks after the first dose.
- The third dose should not be administered any earlier than 24 weeks of age (six months).

It is not necessary to add doses or restart the series if the interval between doses is longer than recommended. Doses administered too soon (before the minimum intervals noted above), should be re-administered, using the correct interval. The minimum interval that should be used when a dose is administered too soon should be calculated from the incorrectly administered dose. For example, children who incorrectly received their third dose of hepatitis B at age five months, should not receive the correct final dose until eight weeks after the wrong dose was given, meaning the child should not receive the correct / final dose until age seven months.

### **Preterm Infants**

Preterm infants born to HBsAg-positive women and women with unknown HBsAg status must receive PEP with hepatitis B vaccine and HBIG within 12 hours of birth.

Preterm infants with low birth weight < 2,000 g (4.4 lbs.) have a decreased response to hepatitis B vaccine administered before one month of age. However, by one month of age, preterm infants, regardless of initial birth weight or gestational age, are as likely to respond as adequately as full-term infants. Furthermore, preterm infants, or those weighing < 2,000 g (4.4 lbs.), should restart the hepatitis B vaccine series, at one month of age. Although the birth dose is not considered a valid dose in the series for these infants, it is **imperative** that the infants born to HBsAg-positive and unknown status mothers receive the birth dose in addition to HBIG for the best protection.

If ordered by the physician, preterm infants of low birth weight whose mothers are HBsAg-negative, during this pregnancy and at delivery, can receive the first dose of the hepatitis B vaccine series at one month of age, so long as the mother's lab report is documented in the infant's chart by the ordering physician. Preterm infants discharged from the hospital before one month of age can also receive the hepatitis B vaccine at discharge if they are medically stable and have gained weight consistently. The full recommended dose should be used. Divided or reduced doses are not recommended.

### **Vaccine Administration and Contraindications**

Hepatitis B vaccine can be given concurrently with other vaccines. Pregnancy and lactation are not contraindications to receiving hepatitis B vaccine. The vaccine is to be administered intramuscular (IM) in the anterolateral thigh or deltoid area depending on age of the recipient. The choice of site is based on the volume of the injected material and the size of the muscle. In children younger than three years of age, the anterolateral aspect of the thigh provides the largest muscle and is the preferred site; the deltoid muscle can be used in children older than 12 months of age if the muscle mass is adequate. In children three years and older, the deltoid muscle is usually large enough for IM injection. The upper, outer aspect of the buttocks should never be used for vaccine administration because of diminished immunogenicity and the possibility of damaging the sciatic nerve.

## Adverse Reactions

The most common adverse reaction associated with hepatitis B vaccine administration is pain at the injection site. Less frequent adverse reactions include fatigue, headache, irritability, and a fever greater than 99.9°F. There is no scientific data or evidence to show an association between hepatitis B vaccine and sudden infant death syndrome (SIDS), multiple sclerosis (MS), autoimmune diseases, chronic fatigue syndrome, or autism.

## Postvaccination Serologic Testing (PVST)

Postvaccination seroprotection is achieved in 98 percent of healthy full-term infants who received a three dose or four dose hepatitis B vaccine series; infants of low birthweight < 2,000 g (4.4 lbs.) will generally have a lower seroprotection. Because not all infants will adequately respond to the hepatitis B vaccine series, it is important that all infants born to HBsAg-positive mothers be tested for vaccine response after completion of the series. This will ensure that an adequate immune response is reached.

Testing for immunity following hepatitis B vaccination is routinely recommended by the CDC for at-risk infants who are born to HBsAg-positive women. The CDC recently published an update regarding a shortened interval for PVST in infants born to mothers infected with hepatitis B. This update, titled [\*Update: Shortened Interval for Postvaccination Serologic Testing of Infants Born to Hepatitis B-Infected Mothers\*](#) can be found in MMWR 64(39); 1118 - 20. The guidance on timing of PVST provided by the CDC indicates that the optimal time to collect PVST in infants who completed the vaccine series on time is between nine and 12 months of age. For infants whose series was delayed, the PVST should be collected 1 - 2 months after completion of the series. Please note, testing is not recommended before age nine months of age to avoid possible detection of anti-HBs passively transferred from the mother or from HBIG administered during infancy and to maximize the likelihood of detecting late HBV infection. **It is important to test for HBsAg and anti-HBs to determine the success or failure of vaccination.** It is important to keep in mind that testing delays after series completion can lead to false negative anti-HBs results.

Infants who completed the vaccine series on time at six months of age, should have PVST performed three months after the final dose of the hepatitis B vaccine series has been administered; ideally at the next well-child visit at nine months of age to determine the success of PEP.

Infants who were delayed or delinquent in completing the vaccine series should receive the PVST one to two months after completion, as long as the infant is at least nine months of age. For example, an infant who did not receive their final dose of hepatitis B vaccine until eight months of age, can still complete the PVST on time at nine months of age, so long as one month (28 days or four weeks) has passed. Please note, testing delays after series completion can lead to false negative anti-HBs results.

Providers should not order a hepatitis panel when performing PVST, as it typically does not include testing for immunity, but rather only screens for acute hepatitis infection. Providers should order the individual serology markers, HBsAg and anti-HBs. Refer to Chapter 5 for additional information on specific serology markers and their interpretation.

## Procedures for Ordering HBIG and Hepatitis B Vaccine

The HBIG and hepatitis B vaccine are costly and delicate biological products. Keeping a large inventory increases the risk for expiration. Review the expiration dates on the vaccines received and use the shortest-dated vaccines first.

Hospitals, pediatricians, and other medical providers may order HBIG and the hepatitis B vaccine directly from the manufacturer. Providers should contact the manufacturer for ordering instructions. The DSHS HSRs and LHDs must ensure in advance that the hospital has HBIG on hand when a positive HBsAg woman is planning to deliver at the facility to ensure administration of HBIG and hepatitis B vaccine birth dose to the infant within 12 hours of delivery. HBIG can be ordered from the DSHS Immunization Branch on an emergency basis, see below for Ordering Instructions. The LHDs must order HBIG and hepatitis B vaccine through their DSHS HSR. Both biologics must be shipped to a DSHS HSR or LHD.

### HBIG and Hepatitis B Vaccine Ordering Instructions from DSHS:

To order HBIG and hepatitis B vaccine for newborns, DSHS HSRs and LHDs must email the DSHS Immunization Branch Vaccine Call Center at [vaccallcenter@dshs.state.tx.us](mailto:vaccallcenter@dshs.state.tx.us) with the following information:

- **The Provider Identification Number (PIN)**
- **Clinic Days and Hours:** List the hours the clinic will be open to accept vaccine shipments for each day of the work week and note lunch period when no one is available to receive the vaccine. Be sure to note any holidays or clinic closings.
- **Contact Person:** Name of person that is physically present at the clinic to accept the shipment.
- **Phone:** Phone number of the contact person.
- **Clinic Address:** Provide complete name and address of clinic.
- **Pick from List:** Provide the vaccine needed and the vaccine formulation requested and the request for HBIG.
- **Order Amount:** Indicate number of doses needed.
- **Date of Order:** Date the order was completed.

Upon receiving a vaccine request, the DSHS Immunization Branch Vaccine Call Center will forward the request to the Vaccine Management Group to submit the order in the Inventory Tracking Electronic Assets Management System (ITEAMS).

The order will be shipped via the DSHS Pharmacy Branch. The DSHS Pharmacy Branch ships orders on Monday, Tuesday, and Wednesday of each week. In order to meet shipping deadlines, orders must be received before 2:00 p.m. on these days. In the event of an emergency, please call the DSHS Immunization Branch at (800) 252 – 9152. For after hour emergencies, call the DSHS emergency telephone number (512) 776 – 4911 and ask for the physician on call then give the physician the information concerning your emergency.

## Handling and Storage

Careful handling of hepatitis B vaccine and HBIG is extremely important (see package insert for detailed storage and handling procedures). These procedures should be strictly followed:

- Transport only in insulated boxes with coolant to maintain proper temperature.
- Store biologics at 2 - 8°C (35 - 46°F). **DO NOT FREEZE**. Freezing destroys the potency of these biologics.
- Special care should be taken to avoid waste because of the high cost of the biologics. If biologics on hand are provided to your clinic by the Texas Vaccines for Children (TVFC) Program and are due to expire within 90 days, please contact your DSHS HSR or LHD for assistance in transferring the product.

If your vaccine is provided by the Texas Vaccines for Children (TVFC) Program, be sure to follow all TVFC Program requirements. For more information on TVFC Program Requirements and Vaccine Storage and Handling, please visit [www.dshs.state.tx.us/immunize/tvfc/ProviderResources.shtm](http://www.dshs.state.tx.us/immunize/tvfc/ProviderResources.shtm).