

Centers for Disease Control and Prevention  
National Center for Immunization and Respiratory Diseases

**Hepatitis B and Hepatitis B Vaccine**

September 2018  
Chapter 10

Photographs and images included in this presentation are acknowledged to CDC/NCHADS and presenters. No rights are granted outside of the printing of any copies of this CDC slide or printed material.

---

---

---

---

---

---

---

---

**Hepatitis B Virus**

- Hepadnaviridae family (DNA)
- Numerous antigenic components
- Humans are only known host
- May retain infectivity for more than 7 days at room temperature

---

---

---

---

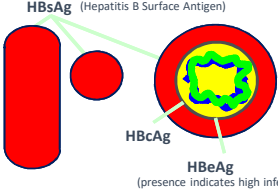
---

---

---

---

**Hepatitis B Virus**



The diagram illustrates the components of the Hepatitis B Virus. On the left, a large red oval represents the HBsAg (Hepatitis B Surface Antigen). To its right is a smaller red circle representing the HBcAg. Further right is a circular structure representing the virus particle, which has a yellow outer shell and a green inner core. A label 'HBeAg' points to the inner core, with a note '(presence indicates high infectivity)' below it.

---

---

---

---

---

---

---

---

### Hepatitis B Virus Infection

- 850,000–2.2 million chronic infections in US
- 257 million chronically infected worldwide
- Established cause of chronic hepatitis and cirrhosis
- Human carcinogen—cause of up to 50% of hepatocellular carcinomas
- Causes about 887,000 deaths worldwide

---

---

---

---

---

---

---

---

### Hepatitis B Infection

- Classified by 2 separate systems: serologic subtype and genotype
  - 9 serologic subtypes
  - 10 genotypes
- Serotypes and genotypes vary geographically
- Infection or immunization with one genotype generally confers immunity to all genotypes

---

---

---

---

---

---

---

---

### Hepatitis B Clinical Features

- Incubation period 60-150 days (average 90 days)
- Illness not specific for hepatitis B
- Nonspecific prodrome of malaise, fever, headache, myalgia
- 30-50% of infections symptomatic

---

---

---

---

---

---

---

---

### Hepatitis B Complications

- Fulminant hepatitis (<1%)
- Hospitalization
- Cirrhosis
- Hepatocellular carcinoma
- Death

---

---

---

---

---

---

---

---

### Chronic Hepatitis B Virus Infection

- 80-90% of persons infected during infancy
- 30% of persons infected before age 6 years
- 1-12% of persons infected as an older child or adult
- Approximately 25% of persons chronically infected during childhood and 15% chronically infected after childhood will die prematurely from cirrhosis or liver cancer

---

---

---

---

---

---

---

---

### Chronic Hepatitis B Virus Infection – 4 Phases

- **Immune tolerant**
  - Minimal or no hepatic inflammation or fibrosis
- **Immune active**
  - Hepatic inflammation with or without fibrosis
- **Immune inactive**
  - Improvement of hepatic inflammation and fibrosis
- **Reactivation**
  - Active hepatic inflammation with or without fibrosis

---

---

---

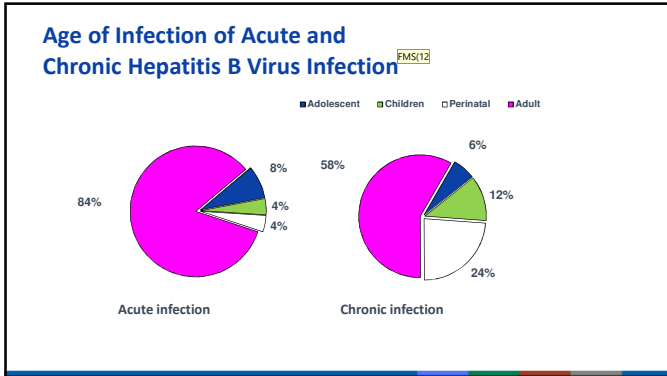
---

---

---

---

---




---

---

---

---

---

---

---

---

### Hepatitis B Epidemiology

|                 |   |
|-----------------|---|
| Reservoir       | Human   |
| Transmission    | Bloodborne<br>Subclinical cases transmit  |
| Communicability | 1-2 months before and after onset of symptoms<br>Persons with either acute or chronic HBV infection with HBsAg present in blood<br>Infectious on environmental surfaces for at least 7 days |

---

---

---

---

---

---

---

---

- ### Risk Factors for Hepatitis B
- Injection drug use
  - 2 or more sexual partners
  - Men who have sex with men
  - Household contacts
  - Developmentally disabled persons in long-term-care facilities
  - Correctional facilities
  - Persons at risk for occupational exposure to HBV
  - Hemodialysis patients
  - Persons with HCV infection
  - Persons with chronic liver disease
  - Travelers to countries where HBV is endemic
  - HIV infection
  - Persons with Diabetes

---

---

---

---

---

---

---

---

## Slide 10

---

**FMS(12** I would delete this slide. The current recs don't discuss prevaccine statistics and these don't match slide 8 which states that 80-90% of persons infected during pregnancy will develop chronic infection.

Freedman, Mark S. (CDC/OPHPR/DEO), 9/7/2018

**Strategy to Eliminate Hepatitis B Virus Transmission—  
United States**

- **Prevent perinatal HBV transmission**
  - Routine testing of all pregnant women for HBsAg
  - Prophylaxis (HepB vaccine and HBIG) for infants born to HepB surface antigen (HBsAg) positive women
  - HBV DNA testing for HBsAg positive women and antiviral therapy if HBV DNA is >200,000 IU/mL
- **Universal vaccination of all infants at birth**
- **Routine vaccination of previously unvaccinated children aged <19 years**
- **Vaccination of adults in high-risk groups**

<https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6404a1.htm>

---

---

---

---

---

---

---

---

---

---

**Hepatitis B-Containing Vaccines**

- **3 single component products**
  - EnderixB
  - Recombivax HB
  - Heplisav-B
- **EnderixB and RecombivaxHB have pediatric and adult formulations**
  - Pediatric formulation
  - Adult formulation
- **2 combination vaccine products**
  - Pediarix–DTaP, IPV and HepB vaccines
  - Twinrix–HepA and HepB vaccines

---

---

---

---

---

---

---

---

---

---

**Heplisav-B**



|                         |  |
|-------------------------|--|
| <b>Storage</b>          | Store in the refrigerator between 2°C and 8°C (36°F and 46°F)  |
| <b>Ages</b>             | 18 years of age and older  |
| <b>Schedule</b>         | Administer 2 doses separated by 4 weeks  |
| <b>Administration</b>   | Intramuscular (IM) injection in the deltoid muscle<br>Can be administered at the same clinical visit as other vaccines. Administer in separate injection sites, 1 inch apart (if possible) |
| <b>Contraindication</b> | History of severe allergic reaction (e.g. anaphylaxis) after a previous dose of <u>any hepatitis B vaccine</u> or to any component of Heplisav-B, including yeast                          |

<https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6404a1.htm>

---

---

---

---

---

---

---

---

---

---

**Engerix and Recombivax HB**

- **Composition**                      Recombinant HBsAg
- **Efficacy**                              95% (Range, 80%-100%)
- **Duration of Immunity**            30 years or more
- **Schedule**                              3 doses
- **Booster doses not routinely recommended**

---

---

---

---

---

---

---

---

**HepB Vaccine Formulations**

- **Recombivax HB (Merck)**
  - 5 mcg/0.5 ml (pediatric)
  - 10 mcg/1 ml (adult)
  - 40 mcg/1 ml (dialysis)
- **Engerix-B (GSK)**
  - 10 mcg/0.5 ml (pediatric)
  - 20 mcg/1 ml (adult)
- **Heplisav-B (Dynavax Technologies)**
  - 20mcg/0.5ml

---

---

---

---

---

---

---

---

**Recommended Dosage of HepB Vaccine**

|  | Recombivax HB<br>Dose (mcg) | Engerix-B<br>Dose (mcg) | Heplisav-B (mcg) |
|--|-----------------------------|-------------------------|------------------|
| Children/Adolescents<br>birth through 17 years | 0.5 mL (5)                  | 0.5 mL (10)             | Not approved     |
| Adolescents 18 years                           | 1.0 mL (10)                 | 1.0 mL (20)             | 0.5 mL (20)      |
| Adults 19 years of age<br>and older            | 1.0 mL (10)                 | 1.0 mL (20)             | 0.5 mL (20)      |

---

---

---

---

---

---

---

---

### Vaccine Supply: Pediatric RecombivaxHB

- Merck is not currently distributing hepatitis B vaccine, pediatric and adult formulations, through 2018
- GSK address the gap for pediatric hepatitis B vaccine using a combination of single-component hepatitis B vaccine and DTaP-HepB-IPV (Pediatrix)
- CDC anticipates there will be approximately 10% less single component pediatric hepatitis B vaccine than normal during the rest of 2018
- GSK has sufficient supplies of adult hepatitis B vaccine to address these anticipated gaps
  - Preferences for a specific presentation (i.e., vial versus syringe) may not be consistently met

CDC Current Vaccine Shortages and Delays <https://www.cdc.gov/nczod/diseases/zoonotic/diseases/vaccine/shortages.html>

---

---

---

---

---

---

---

---

---

---

### Heplisav-B Vaccine ACIP Recommendations



- HEPLISAV-B may be used to vaccinate persons age 18 years and older against infection caused by all known subtypes of HBV
- ACIP does not state a preference for one vaccine product versus another if the patient is eligible for more than 1 product
- The 2-dose HepB vaccine series only applies when both doses in the series consist of Heplisav-B
  - Series consisting of a combination of 1 dose of Heplisav-B and a vaccine from a different manufacturer should consist of 3 total vaccine doses

<https://www.cdc.gov/mmwr/preview/mmwrhtml/aa0001a.htm>

---

---

---

---

---

---

---

---

---

---

### Combination Vaccines

- **Pediatrix DTaP/IPV/HepB**
  - Ages: 6 weeks through 6 years
  - Routine schedule: 2, 4, 6 months of age
  - Approved for dose 1, 2, 3 of Hep B (Do NOT use for the birth dose)
- **Twinrix HepA/HepB**
  - Ages: 18 years of age and older
  - Routine schedule: 3 doses at 0, 1, 6 months, or
  - Alternate schedule: 0, 7, 21- 30 days and a booster dose at 12 months
  - Each dose of Twinrix contains an adult dose of hepatitis B vaccine

---

---

---

---

---

---

---

---

---

---







**Pediarix**

- Can be given at 2, 4, and 6 months in infants who received a dose of HepB vaccine at birth (total of 4 doses)

| Dose1                          | Dose 2     | Dose 3     | Dose 4     |
|--------------------------------|------------|------------|------------|
| Birth                          | 2 mo       | 4 mo       | 6 mo       |
| EngerixB<br>or<br>RecombivaxHB | → Pediarix | → Pediarix | → Pediarix |

Minimum age for dose 3

---

---

---

---

---

---

---

---

**Pediarix**

- Minimum age 6 weeks**
  - Cannot be used for HepB birth dose
- Can be given at 2, 4, and 6 months in infants who received a birth dose of HepB vaccine (total of 4 doses)
- May be used in infants whose mothers are HBsAg positive or status unknown\*

---

---

---

---

---

---

---

---

**HepB Vaccine Adolescent Vaccination**

- Vaccinate previously unvaccinated adolescents and those missing doses
- Routinely recommended through age 18 years
- Integrate assessment and vaccination (if needed) into routine adolescent clinical visits

---

---

---

---

---

---

---

---

**HepB Schedule: Adolescent**

| Dose      | Routine Interval | Minimum Interval                           |
|-----------|------------------|--|
| Primary 1 | ---              | ---  |
| Primary 2 | 1 month          | 4 weeks                                    |
| Primary 3 | 5 months         | 8 weeks and at least 16 weeks from Dose 1* |

\* Third dose must be separated from first dose by at least 12 weeks

---

---

---

---

---

---

---

---

- Alternative Adolescent Vaccination Schedule**
- Two 1.0 mL (10 mcg) doses of Recombivax HB separated by 4 to 6 months only
  - Approved only for adolescents 11–15 years of age
  - Only applies to Merck HepB vaccine

---

---

---

---

---

---

---

---

- Serologic Testing and Children**
- **Prevaccination serologic testing is not indicated before routine vaccination of infants or children**
    - Recommended for all persons born in Africa, Asia, the Pacific Islands, and other regions with HBsAg prevalence of 2% or higher
    - U.S.-born persons not vaccinated as infants whose parents were born in countries with high HBV endemicity
    - Household contacts of HBsAg-positive persons
    - HIV-infected persons
    - Hemodialysis patients
    - Persons needing immunosuppressive therapy

---

---

---

---

---

---

---

---

**Postvaccination Serologic Testing**

▪ Serologic testing is NOT routinely recommended following vaccination of most children and adolescents

▪ Recommended for:

- Infants born to HBsAg-positive women and infants born to women whose HBsAg status remains unknown
- Hemodialysis patients
- HIV-infected persons
- Other immunocompromised persons

---

---

---

---

---

---

---

---

**Management of Nonresponse to HepB Vaccine**

- HBsAg-negative infants with anti-HBs <10 mIU/mL should be revaccinated with a single dose of HepB vaccine and receive postvaccination serologic testing 1–2 months later.
- 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 postvaccination serologic testing 1–2 months after the final dose.

---

---

---

---

---

---

---

---

**Revaccination**

▪ Revaccination is generally not recommended for persons with a normal immune status

▪ Recommended for the following:

- HBsAg-negative infants with anti-HBs <10 mIU/mL
- Hemodialysis patients
- HIV-infected persons
- Other immunocompromised persons

---

---

---

---

---

---

---

---

### Vaccine Administration

▪ **Route: IM Injection**

- Needle gauge: 22–25 gauge
- Needle length\*: 5/8 – 1.5 inch depending on the patient’s age and/or weight

▪ **Site\***:

- Birth–11 months: Vastus lateralis muscle is preferred
- 1–3 years: Vastus lateralis muscle is preferred; deltoid muscle may be used if the muscle mass is adequate
- 4 years and older: Deltoid muscle is preferred; vastus lateralis muscle may be used

\*Professional judgment should be used to determine the proper needle length and site. Factors influencing site including location, number of vaccines to be administered, age and muscle mass.

---

---

---

---

---

---

---

---

---

---

### Vaccine Administration Errors

▪ **Adult formulation administered to a child**

- MORE antigen than the recommended dose was administered
- If the dose meets minimum age and interval, it may be counted

▪ **Pediatric formulation administered to an adult**

- LESS antigen than the recommended dose was administered
- The dose does not count and should be repeated ASAP
  - There is no time/spacing interval that must be met

▪ **HepA instead of HepB vaccine**

---

---

---

---

---

---

---

---

---

---

### Hepatitis B Standing Order Templates Children and Adults

The image shows two side-by-side standing order templates for Hepatitis B vaccination. The left template is titled 'Standing Order for Administering Hepatitis B Vaccine to Children and Teens' and the right is 'Standing Order for Administering Hepatitis B Vaccine to Adults'. Both templates include sections for Purpose, Policy, and Procedure. The Procedure section contains detailed instructions on how to administer the vaccine, including age-specific recommendations and handling instructions. At the bottom of each template is a table with columns for Vaccine Name, Dose, Route, and Frequency. The table for children lists HepB (0, 1, 6 months) and HepB + Hib (12-23 months). The table for adults lists HepB (0, 1, 6 months) and HepB + HepA (0, 1, 6 months).

---

---

---

---

---

---

---

---

---

---

### HepB Vaccine Contraindications and Precautions

- **Contraindication**
  - Severe allergic reaction to a vaccine component or following a prior dose
- **Precaution**
  - Moderate or severe acute illness

---

---

---

---

---

---

---

---

---

---

### HepB Vaccine Adverse Reactions

| Symptom                   | Frequency |
|---------------------------|-----------|
| Pain at injection site    | 3%-29%    |
| Erythema                  | 3%        |
| Swelling                  | 3%        |
| Fever                     | 1%-6%     |
| Headache                  | 3%        |
| Severe systemic reactions | rare      |

---

---

---

---

---

---

---

---

---

---

### Hepatitis B Vaccine Storage and Handling

- Store HepB-containing vaccines in a refrigerator between 2°C - 8°C (36°F - 46°F)
- **DO NOT FREEZE**
- Store in the original packaging with the lids closed in a clearly labeled bin and/or area of the storage unit
- Store pediatric and adult formulations separately, away from each other and other look- or sound-alike vaccines; e.g., HepA, Hib, HPV

**HepB (Envarsis) Pediatric Formulation**

**Age:** Birth through 19 years

**Exc. Mat:** None

**Route:** Intramuscular (IM) injection

Read the package insert that accompanies the product for details for the proper use and handling of this vaccine.

**HepB (Overturnis) IM Pediatric Formulation**

**Age:** Birth through 19 years

**Exc. Mat:** None

**Route:** Intramuscular (IM) injection

Use syringe and vial; always prepare and use aseptically.

**HepB (Envarsis) IM Adult Formulation**

**Age:** 20 years and older

**Exc. Mat:** None

**Route:** Intramuscular (IM) injection

Read the package insert that accompanies the product for details for the proper use and handling of this vaccine.

**HepB (Overturnis) IM Adult Formulation**

**Age:** 20 years and older

**Exc. Mat:** None

**Route:** Intramuscular (IM) injection

Use syringe and vial; always prepare and use aseptically.

Vaccine storage label example  
 #A917818 © 2017 www.cdc.gov/nczod/dpdx/hepbvaccine/immunization.html

---

---

---

---

---

---

---

---

---

---

**What Do You Think?**

▪ Hepatitis B vaccine was inadvertently administered subcutaneously instead of the recommended route, intramuscular injection. Does the dose count?

- Yes
- No

No. For optimal protection, it is crucial that the vaccine be administered IM, not subcutaneously. ACIP recommends repeating the dose.

---

---

---

---

---

---

---

---



PLEASE PLACE QUESTIONS IN THE BASKET

---

---

---

---

---

---

---

---

**Pediarix**

▪ Remember—Minimum age is 6 weeks

- \*Cannot be used for HepB birth dose

▪ Can be given at 2, 4, and 6 months in infants who received a birth dose of HepB vaccine (total of 4 doses)

▪ May be used in infants whose mothers are HBsAg positive or status unknown\*

\*See latest ACIP recommendations

---

---

---

---

---

---

---

---