

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



### Hepatitis B and Hepatitis B Vaccine

**Adult Track**

Chapter 10

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### 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

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### 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

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### 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

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### Hepatitis B Complications

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

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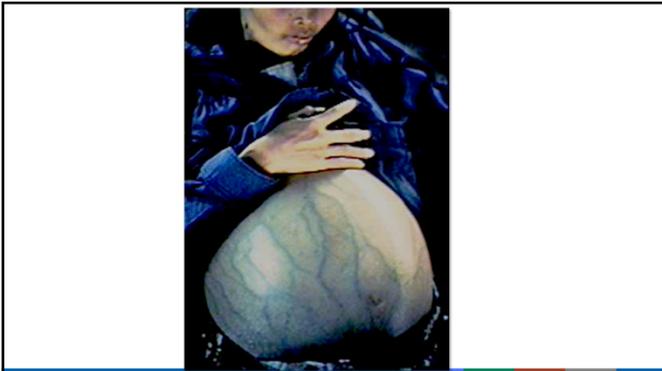
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**Chronic Hepatitis B Virus Infection**

- 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

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**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

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**Hepatitis B Epidemiology**

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

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**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

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**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**

<http://www.cdc.gov/mmwr/preview/mmwrhtml/aa0601a.htm>

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**Hepatitis B-Containing Vaccines**

- **3 single component products**
  - EngerixB
  - Recombivax HB
  - Heplisav-B
- **EngerixB 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

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**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 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

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**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**

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**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

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### Recommended Dosage of HepB Vaccine

	Recombivax HB Dose (mcg)	Engerix-B Dose (mcg)	Heplisav-B (mcg)
Adults 19 years of age	0.5 mL (5)	0.5mL (10)	0.5 mL (20)
Adults 20 years of age and older	1.0 mL (10)	1.0 mL (20)	0.5 ml (20)

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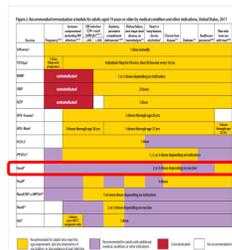
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### ACIP HepB Vaccine Recommendations Adult

- Recommended for previously unvaccinated high-risk adults




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### Vaccine Supply: Adult Recombivax HB

- Merck is not currently distributing its adult hepatitis B vaccine and does not expect to be distributing adult hepatitis B vaccine throughout the remainder of 2018
- GSK has sufficient supplies of adult hepatitis B vaccines to address the anticipated gap in Merck's supply of adult hepatitis B vaccine during this period. In addition, Dynavax makes an adult hepatitis B vaccine that is available for use

CDC Current Vaccine Shortages and Delays: <https://www.cdc.gov/vaccines/imz/downloads/resource/shortages.html>

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**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/000000a0.htm>

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**HepB Schedule: Adult**

Vaccine	Routine Interval	Minimal Interval
2-dose series (Heplisav_B)	4 weeks	4 weeks
3-dose series (Energix B, Recombivax HB)	Dose 1 to dose 2: 1 month Dose 2 to dose 3: 5 months	Dose 1 to dose 2: 4 weeks Dose 2 to dose 3: 8 weeks and at least 16 weeks from dose 1

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**Combination Vaccines**

- **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

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### Hepatitis B and Diabetes Mellitus

- Compared with adults without diabetes, adults with diabetes have a 60% higher prevalence of past or present HBV infection and twice the odds of acquiring acute HBV
- Repeated outbreaks of HBV infection associated with assisted blood glucose monitoring underscore the continued risk for this population
- Data also suggest the possibility of a higher case-fatality proportion among persons with diabetes acutely infected with HBV compared with those without diabetes

CDC webpage: Infection Prevention during Blood Glucose Monitoring and Insulin Administration <https://www.cdc.gov/infectioncontrol/blood-glucose-monitoring.html>

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### ACIP Recommendation for Persons with Diabetes Mellitus

- HepB vaccine (2 or 3-dose series) should be administered to unvaccinated adults (19 through 59 years of age) with diabetes (insulin and non-insulin dependent)
- HepB vaccine (2 or 3-dose series) may be administered to unvaccinated adults (60 years of age and older) with diabetes (insulin and non-insulin dependent)

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### Adults at Risk for HBV Infection

- **Other groups**
  - International travelers to regions with high or intermediate levels (HBsAg prevalence of 2% or higher) of endemic HBV infection
  - Persons with HIV infection



FIGURE 1. Prevalence of Hepatitis B surface antigen (HBsAg) by region, 2004-2005. Data are based on the 2004-2005 World Health Organization (WHO) Global Hepatitis B (HBV) Survey. The prevalence of HBsAg is defined as the percentage of individuals with HBsAg among a representative sample of adults.

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**Prevaccination Serologic Testing**

▪ **Recommended for:**

- Household, sexual, or needle contacts of HBsAg–positive persons
- HIV-positive persons
- Persons with elevated alanine aminotransferase/aspartate aminotransferase of unknown etiology
- Hemodialysis patients
- Men who have sex with men
- Past or current persons who inject drugs
- Persons born in countries of high and intermediate HBV endemicity
- U.S.-born persons not vaccinated as infants whose parents were born in countries with high HBV endemicity
- Persons needing immunosuppressive therapy
- Donors of blood, plasma, organs, tissues, or semen

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**Postvaccination Serologic Testing**

▪ **Serologic testing is NOT routinely recommended following vaccination of most infant, children, or adults**

▪ **Recommended for:**

- Infants born to HBsAg–positive mothers or mothers whose HBsAg status remains unknown
- Health care personnel
- Hemodialysis patients and others who might require outpatient hemodialysis
- HIV-infected persons
- Other immunocompromised persons
- Sex partners of HBsAg-positive persons

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**Postvaccination Serologic Testing**

- Testing should be performed **1 to 2 months** after administration of the final dose of the vaccine series
- Testing HCP with documentation of complete HepB vaccination, followed by one or more additional doses of HepB vaccine for HCP with anti-HBs <10 mIU/mL, helps to ensure that HCP will be protected if they have an exposure to HBV-containing blood or body fluids.

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**Management of Nonresponse to HepB Vaccine**

- Complete a second series of 3 doses
- Follow the routine schedule of 0, 1, and 6 months
  - May be given on a 0, 1, and 4 months
- Retest 1-2 months after completing the second series

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**Persistent Nonresponse to HepB Vaccine**

- Less than 5% of vaccinees do not develop anti-HBs after 6 valid doses
- May be nonresponder or “hypo-responder”
- Check HBsAg status
- If exposed, treat as nonresponder with postexposure prophylaxis

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**Revaccination**

- Revaccination is generally not recommended for persons with a normal immune status
- Recommended for the following:
  - Completely vaccinated HCP with anti-HBs < 10 mIU/mL
  - Hemodialysis patients should be assessed by annual anti-HBs testing and booster dose administered when anti-HBs < 10 mIU/mL
  - Immunocompromised persons should be considered for annual anti-HBs testing if have ongoing risk for exposure

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## Slide 35

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**SRA(10** No; fig 3 in ACIP recs says to do testing first, then if negative, give one dose of vaccine.

Strikas, Raymond A. (Ray) (CDC/OID/NCIRD), 9/7/2018

**FMS(18 Updated**

Freedman, Mark S. (CDC/OPHPR/DEO), 9/10/2018





### 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 (Engerix-B) Pediatric Formulation**

**Age:** Birth through 19 years

**Use:** See above in the notes

**Route:** Intramuscular (IM) injection

Keep the original vial that contains the vaccine in the bin for protection against other vials

**HepB (Recombivax-B) Pediatric Formulation**

**Age:** Birth through 19 years

**Use:** See above in the notes

**Route:** Intramuscular (IM) injection

Use copper and orange plunger cap and 4 mm needle

**HepB (Engerix-B) Adult Formulation**

**Age:** 20 years and older

**Use:** See above in the notes

**Route:** Intramuscular (IM) injection

Keep the original vial that contains the vaccine in the bin for protection against other vials

**HepB (Recombivax-B) Adult Formulation**

**Age:** 20 years and older

**Use:** See above in the notes

**Route:** Intramuscular (IM) injection

Use copper and orange plunger cap and 16 mm needle

Vaccine storage label example  
Available at [www.cdc.gov/vaccines/imz/downloads/pdf/11p/11p0001.pdf](http://www.cdc.gov/vaccines/imz/downloads/pdf/11p/11p0001.pdf)

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### What Do You Think?

- How often should I test HCP after they've received the hepatitis B vaccine series and have documentation of a positive response to make sure they're protected?
- Every year
- Every 5 years
- Periodic testing is not routinely recommended for these HCP

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PLEASE PLACE QUESTIONS IN THE BASKET

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