Chapter 4: Hepatitis B

Lyn Finelli, DrPH; Beth P. Bell, MD, MPH

In infants, young children, and immunosuppressed persons, most newly acquired HBV infections result in chronic infection.[2]

I. Disease Description

Hepatitis B is caused by infection with the hepatitis B virus (HBV), a double-stranded DNA virus of the family hepadnaviridae. HBV replicates in the liver and causes both acute and chronic hepatitis. Although the highest concentrations of virus are found in blood, other serum-derived body fluids, such as semen and saliva, also have been demonstrated to be infectious. Thus, HBV is a bloodborne and sexually transmitted infection and is transmitted by percutaneous and mucosal exposure to infectious body fluids.

The incubation period for acute hepatitis B ranges from 45 to 160 days (average 120 days). The clinical manifestations of acute HBV infection are age dependent. Infants, young children (younger than 10 years of age), and immunosuppressed adults with newly acquired HBV infection are usually asymptomatic.[1] Older children and adults are symptomatic in 30%–50% of infections. When present, clinical symptoms and signs might include anorexia, malaise, nausea, vomiting, abdominal pain, jaundice, dark urine, and clay-colored or light stools. Occasionally, extrahepatic manifestations occur and include skin rashes, arthralgias, and arthritis. Fulminant hepatitis occurs with a case-fatality rate of 0.5%–1%.

During the past 10 years, an estimated 60,000–110,000 persons were infected with HBV annually, and 5,000 died from HBV-related disease in the United States.

Among adults with normal immune status, most (94%–98%) recover completely from newly acquired HBV infections, eliminating virus from the blood and producing neutralizing antibody that creates immunity from future infection. In infants, young children, and immunosuppressed persons, most newly acquired HBV infections result in chronic infection.[2] Infants are at greatest risk, with a 90% chance of developing chronic infection if infected at birth. Although the consequences of acute hepatitis B can be severe, most of the serious sequelae associated with the disease occur in persons in whom chronic infection develops. Persons who acquire chronic HBV infection as infants or young children are often asymptomatic; however, chronic liver disease develops in two-thirds of these persons, and approximately 15%–25% die prematurely from cirrhosis or liver cancer. Persons with chronic HBV infection are often detected in screening programs, such as those for blood donors, pregnant women and refugees. Persons with chronic HBV infection are a major reservoir for transmission of HBV infections. Any person testing positive for hepatitis B surface antigen (HBsAg) is potentially infectious to both household and sexual contacts.

II. Background

Each year during the 1970s and 1980s, an estimated 200,000–300,000 persons were newly infected with HBV. Until recently, hepatitis B was one of the most frequently reported vaccine-preventable diseases in the United States, with 15,000–20,000 cases reported annually to the National Notifiable Diseases Surveillance System (NNDSS). Since 1985, a steady decline has occurred in the number of cases of acute hepatitis B reported to the NNDSS. In 2004, approximately 6,200 cases of acute hepatitis B were reported,[3] which after correcting for underreporting and asymptomatic infections, represented an estimated 60,000 infections. Based on testing from the Third National Health and Nutrition Examination Survey (NHANES III) conducted during 1988–1994, 4.9% of the general U.S. population has serologic evidence of prior HBV infection. An estimated 1.25 million persons have chronic HBV infection.[4]

The extent to which children acquire HBV infection in the United States has not been appreciated, primarily because most infections in this age group are asymptomatic. In the United States, approximately 24,000 HBsAg-positive women give birth in 2005. Without postexposure prophylaxis to prevent perinatal HBV infection, it is estimated that 12,000 infants and children would be infected with HBV annually. Furthermore, before the implementation of universal infant hepatitis B immunization, an additional 16,000 children younger than 10 years

old were infected annually in the United States through exposure to HBsAg-positive household members or community contacts. Populations with the highest rates of these early childhood infections included Alaska Natives, children of Pacific Islander parents, and children of first-generation immigrants from countries where HBV is of high or intermediate endemicity.[5–8]

Screening of all pregnant women for HBsAg to identify infants requiring postexposure prophylaxis has been recommended since 1988, universal childhood hepatitis B immunization since 1991, universal adolescent hepatitis B immunization since 1995,[9, 10] and universal hepatitis B birth dose administration since 2005. In the United States, without postexposure prophylaxis, HBV would annually infect 12,000 infants; without routine childhood immunization, 16,000 children would be infected.

Among older adolescents and adults, the most frequently reported risk factor for acute hepatitis B is heterosexual contact with an infected partner or with multiple partners (40%), followed by injection-drug use (16%), male homosexual activity (15%), household contact with a person with hepatitis B (3%), and healthcare employment with frequent blood contact (1%).[3] Although up to 25% of persons with newly acquired hepatitis B do not report a source for their infection, many of these persons have had a past history of high-risk sex or drug behaviors. Furthermore, more than half of persons with newly acquired hepatitis B were previously seen in medical settings where hepatitis B vaccine is routinely recommended, such as sexually transmitted disease (STD) treatment clinics. Thus, programs to vaccinate older adolescents and adults at increased risk for HBV infection need to be strengthened nationwide in order to have a significant impact on reducing HBV transmission in the next 2 decades.

In 2003, chronic HBV infection became nationally notifiable and is reportable by state health departments to the NNDSS.

III. Importance of Rapid Identification

Rapid identification and prompt reporting of cases of acute hepatitis B is important because measures such as postexposure prophylaxis can be taken to prevent transmission to other persons. Although outbreaks of hepatitis B are unusual, rapid recognition allows for identification of the source and prevention of further transmission. In addition, identification of risk factors for infection provides a means to assess the effectiveness of hepatitis B immunization activities in the community and identify missed opportunities for immunization.

In most states, HBsAg positivity is a laboratory reportable condition. Reporting of HBsAg-positive persons facilitates timely immunization of contacts. For HBsAg-positive pregnant women, reporting allows for initiation of case management to ensure prevention of perinatal HBV transmission (see "Postexposure prophylaxis" below). In 2003, chronic HBV infection became nationally notifiable and is reportable by state health departments to the NNDSS. All states are encouraged to report chronic hepatitis B infection. States should develop registries of persons with HBsAg-positive laboratory results to facilitate postexposure prophylaxis of contacts and reporting to NNDSS (see "Registries/databases for HBsAg-positive persons" below).

Postexposure prophylaxis

Hepatitis B immune globulin (HBIG) is prepared from human plasma known to contain a high titer of antibody to HBsAg (anti-HBs). The plasma from which HBIG is prepared is screened for HBsAg, hepatitis C virus (HCV), and human immunodeficiency virus, and since 1999, all products available in the United States have been manufactured by methods that inactivate HCV and other viruses. A regimen combining HBIG and hepatitis B vaccine is 85%–95% effective in preventing HBV infection when administered at birth to infants born to HBsAg-positive mothers. Regimens involving either multiple doses of HBIG alone or the hepatitis B vaccine series alone are 70%–75% effective in preventing HBV infection. HBIG also has been shown to provide an estimated 75% protection from HBV infection when initiated within 1 week of percutaneous exposure to HBsAg-positive blood, or when initiated within 14 days of sexual exposure to an HBsAg-positive partner. Although the postexposure efficacy of the combination of HBIG and the hepatitis B vaccine series has not been evaluated for occupational or sexual exposures, it can be presumed that the increased efficacy of this regimen observed in the perinatal setting compared with HBIG alone would apply to these exposures.

Postexposure prophylaxis with HBIG and hepatitis B vaccine should be given to infants born to HBsAg-positive mothers, unvaccinated infants whose mothers or primary caregivers have acute hepatitis B, sexual contacts of persons with acute hepatitis B, and healthcare workers after occupational exposure to HBsAg-positive blood depending on their vaccination and vaccine response status. Household and sexual contacts of persons with chronic HBV infection do not need prophylaxis with HBIG but should be vaccinated.

IV. Importance of Surveillance

Disease surveillance is used to 1) identify contacts of case-patients who require postexposure prophylaxis; 2) detect outbreaks; 3) identify infected persons who need counseling and referral for medical management; 4) monitor disease incidence and prevalence; and 5) determine the epidemiologic characteristics of infected persons, including the source of their infection, to assess and reduce missed opportunities for vaccination.

V. Disease Reduction Goals

The primary goal of hepatitis B vaccination is to prevent chronic HBV infection. However, because such a high proportion of persons with chronic HBV infection are asymptomatic and the consequences are not seen for many years, monitoring the direct impact of prevention programs on the prevalence of chronic infection is difficult. Consequently, the disease reduction goals that have been established for hepatitis B are a combination of process and disease outcome measures. Because most HBV infections among children younger than 10 years of age are asymptomatic, programs targeting infants and children are best evaluated by measuring vaccination coverage and not by measuring reduction in acute infection. In older age groups, monitoring the incidence of acute disease as well as measuring vaccine coverage levels provides data useful for measuring the effectiveness of prevention programs.

Healthy People 2010 disease reduction goals have been established for achieving the prevention of HBV transmission in the United States. Disease reduction goals for infants and children include reducing by 90% the estimated number of chronic HBV infections in infants and young children and the number of cases of acute hepatitis B reported among persons 2–18 years of age. *Healthy People 2010* objectives have been developed to increase hepatitis B vaccination coverage levels to at least 90% among children 19–35 months of age and adolescents 13–15 years of age.

Disease reduction goals for adults include reducing the rate of acute hepatitis B to 2.4/100,000 in persons aged 19–24 years, 5.1/100,000 in persons aged 25–39 years, and 3.8/100,000 in persons aged 40 years and older. Among adults in high-risk groups, disease reduction goals include reducing the number of cases of acute hepatitis B by 75% in injection-drug users and men who have sex with men, and by 90% in sexually active heterosexuals. Furthermore, efforts should be made to increase vaccination coverage among men who have sex with men to at least 60%.

VI. Case Definition

The following case definitions for acute hepatitis B, chronic hepatitis B virus infection and perinatal HBV infection have been adopted by the Council of State and Territorial Epidemiologists.[11]

Acute hepatitis B

Clinical case definition

An acute illness with

- A discrete onset of symptoms, and
- Jaundice or elevated serum aminotransferase levels

Laboratory criteria for diagnosis

1. IgM antibody to hepatitis B core antigen (anti-HBc) positive (if done) or hepatitis B surface antigen (HBsAg) positive.
2. IgM anti-HAV negative (if done).

Case classification

Confirmed: *A case that meets the clinical case definition and is laboratory confirmed.*

Chronic hepatitis B virus infection

Clinical description

Persons with chronic HBV infection may have no evidence of liver disease or may have a spectrum of disease ranging from chronic hepatitis to cirrhosis or liver cancer. Persons with chronic infection may be asymptomatic.

Laboratory criteria for diagnosis

IgM anti-HBc negative AND a positive result on one of the following tests: HBsAg, HBeAg, or HBV DNA

OR

HBsAg positive or HBV DNA positive or HBeAg positive two times at least 6 months apart (Any combination of these tests performed 6 months apart is acceptable.)

Case classification

***Confirmed*:** a case that meets either laboratory criterion for diagnosis

Probable: a case with a single HBsAg-positive or HBV DNA-positive or HBeAg-positive laboratory result when no IgM anti-HBc results are available

Comment: Multiple laboratory tests indicative of chronic HBV infection may be performed simultaneously on the same patient specimen as part of a "hepatitis panel." Testing performed in this manner may lead to seemingly discordant results, e.g., HBsAg negative AND HBV DNA positive. For purposes of this case definition, any positive result among the three laboratory tests mentioned above is acceptable, regardless of other testing results. Negative HBeAg results and HBV DNA levels below positive cutoff level do not confirm the absence of HBV infection.

Perinatal HBV infection

Clinical description

Perinatal hepatitis B in the newborn may range from asymptomatic to fulminant hepatitis.

Laboratory criteria for diagnosis

Hepatitis B surface antigen (HBsAg) positive

Case classification

HBsAg positivity in any infant aged >1–24 months who was born in the United States or in U.S. territories to a HBsAg-positive mother.

Comment: Infants born to HBsAg-positive mothers should receive HBIG and the first dose of hepatitis B vaccine within 12 hours of birth, followed by the second and third doses of vaccine at 1 and 6 months of age, respectively. Postvaccination testing for HBsAg and anti-HBs (antibody to HBsAg) is recommended from 3 to 6 months following completion of the vaccine series. If HBIG and the initial dose of vaccine are delayed for more than 1 month after birth, testing for HBsAg may determine if the infant is already infected.

VII. Laboratory Testing

Several well-defined antigen–antibody systems are associated with HBV infection, including HBsAg and anti-HBs; hepatitis B core antigen (HBcAg) and antibody to HBcAg (anti-HBc); and hepatitis B e antigen (HBeAg) and antibody to HBeAg (anti-HBe). Serologic assays are commercially available for all of these except HBcAg because no free HBcAg circulates in blood. One or more of these serologic markers are present during different phases of HBV infection (Table 1). Subtyping of HBsAg has occasionally been used to investigate outbreaks of hepatitis B, but this procedure is not routinely available in commercial laboratories.

The presence of HBsAg is indicative of ongoing HBV infection and potential infectiousness. In newly infected persons, HBsAg is present in serum 30–60 days after exposure to HBV and persists for variable periods. Anti-HBc develops in all HBV infections, appearing at onset of symptoms or in liver test abnormalities in acute HBV infection, rising rapidly to high levels, and persisting for life. Acute or recently acquired infection can be distinguished by presence of the immunoglobulin M (IgM) class of anti-HBc, which persists for approximately 6 months. However, among infected infants, passively transferred maternal anti-HBc may persist beyond the age of 12 months, and IgM anti-HBc may not be present in newly infected children younger than 2 years of age, especially if they acquired their infection through perinatal transmission.

Table 1. Interpretation of serologic test results for hepatitis B virus infection

Serologic Markers				Interpretation
HBsAg*	Total Anti-HBc †	IgM Anti-HBc §	Anti-HBs ¶	
-	-	-	-	Susceptible, never infected
+	-	-	-	Acute infection, early incubation**
+	+	+	-	Acute infection
-	+	+	-	Acute resolving infection
-	+	-	+	Past infection, recovered and immune
+	+	-	-	Chronic infection
-	+	-	-	False positive (i.e., susceptible), past infection, or "low level" chronic infection
-	-	-	+	Immune if titer is >10 mIU/ml

** Hepatitis B surface antigen*
† Antibody to hepatitis B core antigen
§ Immunoglobulin M
¶ Antibody to hepatitis B surface antigen
*** Transient HBsAg positivity (lasting <18 days) might be detected in some patients during vaccination.*

In persons who recover from HBV infection, HBsAg is eliminated from the blood, usually in 2–3 months, and anti-HBs develops during convalescence. The presence of anti-HBs indicates immunity from HBV infection. After recovery from natural infection, most persons will be positive for both anti-HBs and anti-HBc, whereas only anti-HBs develops in persons who are successfully vaccinated against hepatitis B. Anti-HBs can also be present in persons who have received HBIG. Persons who do not recover from HBV infection and become chronically infected remain positive for HBsAg (and anti-HBc), although a small proportion (0.3% per year) eventually clear HBsAg and might develop anti-HBs.

For additional information on laboratory support for surveillance of vaccine-preventable diseases, see Chapter 22.

Special laboratory studies

Occasionally, molecular virologic methods such as polymerase chain reaction (PCR)-based assays are used to amplify and sequence viral genomes. In conjunction with epidemiologic studies, these assays may be helpful for investigating common-source outbreaks of hepatitis B. In addition, these assays are essential for detecting the emergence of potential vaccine-resistant strains. Healthcare professionals with questions about molecular virologic methods or those who identify HBsAg-positive events among vaccinated persons should consult with their state health department or the Epidemiology Branch, Division of Viral Hepatitis, CDC, 404-718-8500.

VIII. Reporting

In the United States, case reports of acute viral hepatitis are classified as hepatitis A, acute hepatitis B, or acute hepatitis C, perinatal HBV infection, chronic HBV infection and hepatitis C, past or present. Serologic testing is necessary to determine the etiology of viral hepatitis, and case reports should be based on laboratory confirmation (see above). Each state and territory has regulations or laws governing the reporting of diseases and conditions of public health importance.[12] These regulations/laws list the diseases and conditions that are to be reported and describe those persons or groups who are responsible for reporting, such as healthcare providers, hospitals, laboratories, schools, day care facilities, and other institutions. Persons reporting these conditions should contact their state health department for state-specific reporting requirements.

Reporting to CDC

Case reports of acute hepatitis B, chronic HBV infection, perinatal hepatitis B virus infection, and other reportable diseases are transmitted by the state health department weekly to CDC via the National Electronic Telecommunications System for Surveillance (NETSS). The NETSS core record includes basic demographic information (excluding personal identifiers)—age, race/ethnicity, sex, date of onset, date of report, county of residence. The Division of Viral Hepatitis has developed an extended Data Collection Worksheet to collect information about symptoms, risk factors and serologic data (Appendix 6). This worksheet can be used for case investigation and data can be directly entered into the state's electronic reporting system.

IX. Vaccination Schedules

Hepatitis B immune globulin (HBIG; for hepatitis B postexposure prophylaxis) and the first dose of hepatitis B vaccine should be administered within 12 hours of birth to infants born to HBsAg-positive women. This combination also should be administered as soon as possible to unvaccinated infants whose primary caregivers have acute hepatitis B, to unvaccinated healthcare workers after occupational exposure (preferably within 24 hours but not longer than 1 week), and to sex partners of persons with acute hepatitis B (within 14 days). For infants, the dose of HBIG is 0.5 mL. For children and adults, the dose is 0.06 mL/kg.

Hepatitis B vaccine

Two single-antigen recombinant hepatitis B vaccines are commercially available, Recombivax HB® (Merck & Company, Inc.) and Engerix-B® (GlaxoSmithKline). Recombivax HB contains 5–40 µg of HBsAg protein per milliliter, depending on the formulation, whereas Engerix-B contains 20 µg/mL. Both vaccines are licensed for persons of all ages (Table 2).

Table 2. Recommended doses of currently licensed single-antigen hepatitis B vaccines

	Recombivax HB*		Engerix-B*	
Group	Dose (µg)	Volume (mL)	Dose (µg)	Volume (mL)
Infants, children and adolescents <20 years of age	5	(0.5)	10	(0.5)
Adolescents 11–15 years†	10	(1.0)		
Adults ≥20 years of age	10	(1.0)	20	(1.0)
Dialysis patients and other immunocompromised persons	40	(1.0)§	40	(2.0)¶

* *Both vaccines are routinely administered in three-dose series. Engerix-B also has been licensed for a four-dose series administered at 0, 1, 2, and 12 months.*

† *Two-dose schedule for adolescents using adult dose of Recombivax HB has been approved by ACIP, administered at 0, 4–6 months.*

§ *Special formulation.*

¶ *Two 1.0-mL doses administered at one site in a four-dose schedule at 0, 1, 2, and 6 months.*

A combined hepatitis A and B vaccine, Twinrix® (GlaxoSmithKline), is also available for use in persons aged 18 years and older. Twinrix is made of the antigenic components used in HAVRIX® (hepatitis A vaccine) and Engerix-B. In addition, there are two combination vaccines (Comvax® [Merck] and Pediarix® [GlaxoSmithKline]) that are used for vaccination of infants and young children. Comvax contains recombinant HBsAg and *Haemophilus influenzae* type b (Hib) polyribosylribitol phosphate conjugated to *Neisseria meningitidis* outer membrane protein complex. Pediarix contains recombinant HBsAg, diphtheria and tetanus toxoids and acellular pertussis adsorbed (DTaP), and inactivated poliovirus (IPV). However, these vaccines may not be administered to infants younger than 6 weeks of age; only single-antigen hepatitis B vaccine may be used for the birth dose. Administration of four-dose hepatitis B vaccine schedules, including schedules with a birth dose followed by a combination vaccine series, is permissible (Table 3).

Table 3. Recommended doses of currently licensed combination hepatitis B vaccines*

	Combination vaccine					
Group	COMVAX		PEDIARIX		TWINRIX†	
	Dose (µg)§, ¶	Volume (mL)	Dose (µg)§, **	Volume (mL)	Dose (µg)§, ††	Volume (mL)
Infants						
Mother HBsAg negative	5	0.5	10	0.5	NA	NA
Mother HBsAg positive	5	0.5	10	0.5	NA	NA
Children (1–10 years)	5§§	0.5	10	0.5	NA	NA
Adolescents						
11–17 years	NA	NA	NA	NA	NA	NA
Adults						
≥18 years	NA	NA	NA	NA	20	1.0

* *Hepatitis B vaccines are administered by intramuscular injection and may be given at the same time as other vaccines. Single-antigen vaccines may be administered with HBIG, but in a separate injection site.*

† *For persons ≥18 years of age at increased risk of both hepatitis B virus and hepatitis A virus infection*

§ *Recombinant HBsAg protein concentration*

¶ *Comvax also contains 7.5 µg Haemophilus influenzae type B polyribosylribitol phosphate (PRP) and 125 µg Neisseria meningitidis outer membrane protein complex (OMPC).*

** *Pediarix also contains 25 Lf diphtheria toxoid, 10 Lf tetanus toxoid, 25 µg inactivated pertussis toxin, 25 µg filamentous hemagglutinin, 8 µg pertactin, 40 D-Wantigen Units (DU) Type 1 poliovirus, 8 DU Type 2 poliovirus, and 32 DU Type 3 poliovirus.*

†† *Twinrix also contains 720 ELISA Units (EL.U) inactivated hepatitis A virus.*

§§ *Maximum age at administration is 71 months.*

Any infant of a HBsAg-positive woman who has not received HBIG and the first dose of hepatitis B vaccine by 12 hours of age or who has not received the third dose of hepatitis B vaccine by the age of 6 months is not adequately vaccinated.[10] Infants born to HBsAg-positive mothers should be tested for HBsAg and antibody to HBsAg after completion of three or more doses in a licensed HepB series, at age 9–18 months (generally at the next well-child visit). The testing should be done 1–2 months after the most recent hepatitis B vaccine dose to avoid a positive HBsAg result due to vaccine. Serologic testing can determine whether these infants are infected or have developed a protective antibody response after vaccination. Infants who do not respond to the primary vaccination series should be given three additional doses of hepatitis B vaccine on a 0, 1–2, 4–6–month schedule.

The vaccination schedule for infants born to HBsAg-negative women includes three doses of vaccine in the first 18 months of life. The first dose should be given at birth, and the minimum interval between doses 1 and 2 is 1 month, and between doses 2 and 3 is 2 months.[10] Dose 3 of hepatitis B vaccine should not be given before 24 weeks of age. Any infant of an HBsAg-negative woman who has not received the third dose of hepatitis B vaccine by the age of 19 months is not up-to-date (Table 4).

Table 4. Hepatitis B vaccine schedules for newborn infants, by maternal hepatitis B surface antigen (HBsAg) status*

Maternal HBsAg Status	Single-Antigen Vaccine		Single Antigen + Combination Vaccine	
	Dose	Age	Dose	Age
Positive	1†	Birth (≤12 hours)	1†	Birth (≤12 hours)
	HBIG§	Birth (≤12 hours)	HBIG§	Birth (≤12 hours)
	2	1-2 mos	2	2 mos
	3¶	6 mos	3	4 mos
			4¶	6 mos (Pediarix) or 12-15 mos (Comvax)
Unknown**	1†	Birth (<12 hours)	1†	Birth (<12 hours)
	2	1-2 mos	2	2 mos
	3¶	6 mos	3	4 mos
			4¶	6 mos (Pediarix) or 12-15 mos (Comvax)
Negative	1†, ††	Birth (before discharge)	1†, ††	Birth (<12 hours)
	2	1-2 mos	2	2 mos
	3¶	6 mos	3	4 mos
			4¶	6 mos (Pediarix) or 12-15 mos (Comvax)

* *Centers for Disease Control and Prevention. A comprehensive 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 2005;54(No. RR-16) p.9.*

† *Recombivax HB or Engerix-B should be used for the birth dose. Comvax and Pediarix cannot be administered at birth or before age 6 weeks.*

§ *Hepatitis B immune globulin (0.5 mL) administered intramuscularly in a separate site from vaccine.*

¶ *The final dose in the vaccine series should not be administered before age 24 weeks (164 days).*

** *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 7 days of age.*

†† *On a case-by-case basis and only in rare circumstances, the first dose may be delayed until after hospital discharge for an infant who weighs ≥2,000 g and whose mother is HBsAg negative. When such a decision is made, a physician's order to withhold the birth dose and a copy of the original laboratory report indicating that the mother was HBsAg negative during this pregnancy should be placed in the infant's medical record.*

Vaccination of preterm infants should be delayed until they weigh 2 kg or are 2 months old, except for infants born to HBsAg-positive women and infants born to women with unknown HBsAg status. Infants born to HBsAg-positive women or women with unknown HBsAg status should be immunized within 12 hours of birth regardless of birthweight.

Children and adolescents

Vaccination is routinely given as three-dose series at 0, 1, and 6 months. Acceptable alternative schedules include 0, 1, 4 months and 0, 2, 4 months.

Adolescents 11–15 years of age

An alternative two-dose vaccination schedule has been developed for use in adolescents. The adult dose of Recombivax HB is administered to the adolescent, with the second dose given 4–6 months after the first dose.

Adults (20 years of age or older)

Routinely given as three-dose series at 0, 1, and 6 months. Acceptable alternative schedules are 0, 1, 4 months and 0, 2, 4 months.

Dialysis patients and other immunocompromised persons

Either given as a three-dose series (0, 1, 6 months) or four-dose series (0, 1, 2, and 6 months), depending on formulation. Larger vaccine doses (Table 2) may be required to induce protective antibody levels in other immunocompromised persons (e.g., those taking immunosuppressive drugs, HIV infected), although few data are available concerning response to higher doses of vaccine in these patients and no data exist for children.

Combined hepatitis A and B vaccine

Primary vaccination of persons aged 18 years and older consists of three doses, administered on a 0, 1, and 6-month schedule.

Providers should be educated about the importance of performing appropriate serologic tests to determine the etiology of viral hepatitis and reporting all cases of acute hepatitis B, chronic hepatitis B, and perinatal HBV.

X. Enhancing Surveillance

Establishing surveillance for acute hepatitis is difficult for several reasons. Five different viruses (A–E) cause viral hepatitis, and the clinical manifestations of the different types of acute hepatitis are similar. Infection with HBV, HCV and HDV can result in both acute and chronic infection. Therefore, serologic testing is necessary to establish an etiologic diagnosis for persons with symptoms of acute hepatitis and to evaluate case reports of persons who are reported with viral hepatitis. However, a lack of understanding about the epidemiology of these diseases and underutilization of serologic testing could result in significant misclassification in reporting of acute viral hepatitis.

Provider education

Providers should be educated about the importance of performing appropriate serologic tests to determine the etiology of viral hepatitis and reporting all cases of acute hepatitis B, chronic hepatitis B, and perinatal HBV. Case investigations of infected persons provide the best opportunity for postexposure prophylaxis of contacts and for reducing transmission.

Case investigation

Case investigation is essential for determining contacts who are eligible for prophylaxis and for collection of risk factor data. Analysis of risk factor data can identify populations where targeted interventions may be needed.

Laboratory reporting

Laboratories should be encouraged to report all persons with serologic markers of acute or chronic hepatitis to the state or local health department. All IgM anti-HBc, and HBsAg positive results should be reported. To facilitate reporting, these laboratory results could be included in the state's list of laboratory-reportable conditions.

Monitoring surveillance indicators

Regular monitoring of surveillance indicators, including date of report, timeliness, and completeness of reporting, may identify specific areas of the surveillance and reporting system that need improvement. Important program indicators that can be monitored through the surveillance, reporting and case investigation system include the following:

- Characteristics of cases of acute hepatitis B that occur in children and adolescents younger than 18 years of age and missed opportunities for vaccination.
- Characteristics of cases of acute hepatitis in which death has occurred.
- Characteristics of cases of acute hepatitis B in persons reporting a history of vaccination.
- Characteristics of cases of acute hepatitis B in persons over 70 years of age.

Registries/databases for HBsAg-positive persons

Reporting of HBsAg-positive test results and establishment of databases/registries for HBsAg-positive persons is encouraged. When any type of database is established, the confidentiality of individual identifying information needs to be ensured according to applicable laws and regulations.

Computerized databases of persons with HBsAg-positive results can be used to

- Distinguish newly reported cases of infection from previously identified cases and facilitate reporting of chronic hepatitis B;
- Facilitate case investigation and follow-up of persons with chronic HBV infection;
- Provide local, state, and national estimates of the proportion of persons with chronic HBV infection who have been identified.

Hospital-based reporting

Hospitals and infection control practitioners should be encouraged to report all persons with acute viral hepatitis (ICD-10 code B16), and all births to HBsAg-positive women.

XI. Case Investigation

Guidelines for investigating a suspected case of acute viral hepatitis include 1) determining a discrete onset of illness, 2) confirming evidence of acute liver disease (jaundice or elevated aminotransferase levels), and 3) obtaining serologic laboratory results. The minimum recommended elements for investigating cases of chronic HBV infection and perinatal HBV infection include obtaining the serologic laboratory results needed to establish the case. Further investigation to determine the clinical characteristics of these cases may also be considered although it is not required to confirm the case.

Information to collect for acute hepatitis B

The following information is epidemiologically important to collect in a case investigation for acute hepatitis B.[13] Additional information may also be collected at the direction of the state health department.

- Demographic information
  - Clinical details
  - Date of illness onset
- Symptoms including pain, jaundice
- Laboratory results
- Vaccination status
- Risk factors
- Contact investigation and prophylaxis

Information to collect for chronic HBV infection

The following information is epidemiologically important to collect in a case investigation for chronic hepatitis B virus infection. Additional information may also be collected at the direction of the state health department.

- Demographic information
- Laboratory results
- Risk factors
- Pregnancy status. All HBsAg-positive pregnant women should be reported to the perinatal hepatitis B program manager so that the women can be tracked and their infants can receive appropriate case management

The recommended elements of case investigation and follow-up of persons with chronic hepatitis B virus infection are detailed elsewhere.[14] They should include the following:

- Contact investigation and prophylaxis: Provision of hepatitis B vaccination for sexual, household, and other (needle-sharing) contacts of persons with hepatitis B, and counseling to prevent transmission to others
- Counseling and referral for medical management, including
  - Assessing for biochemical evidence of chronic liver disease, and
  - Evaluating eligibility for antiviral treatment.

Information to collect for perinatal HBV infection

The following information is epidemiologically important to collect in a case investigation for perinatal HBV infection:

- Demographic information about the child and mother
- Laboratory results
- Immunization history of the child, including date and doses of HBIG and hepatitis B vaccine

Case investigation and follow-up of infants with hepatitis B virus infection should include the following:

- Referral for medical management, including
  - Assessing for biochemical evidence of chronic liver disease, and
  - Evaluating eligibility for antiviral treatment
- Identification of other susceptible infants and children in the household who require vaccination

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