Chapter 4: Hepatitis B

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I. Disease description

The clinical manifestations of acute HBV infection are age-dependent. Generally, newborns do not develop any clinical signs or symptoms. Older children and adults are symptomatic in 30%–50% of infections.

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, sexually transmitted infection that is transmitted by percutaneous and mucosal exposure to infectious body fluids.

The incubation period for acute hepatitis B ranges from 45–160 days (average 120 days). Infants, young children (aged < 10 years), 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, it is estimated that annually approximately 150,000–200,000 persons were infected with HBV, and 5,000 died from HBV-related disease in the United States.

In 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. 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 with chronic HBV infection 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, 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, there has been a steady decline in the number of cases of acute hepatitis B reported to the NNDSS. In 2000, there were approximately 8,000 reported cases of acute hepatitis B which, after correcting for underreporting and asymptomatic infections, represented an estimated 20,000 cases and 73,000 infections, respectively. 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 have chronic HBV infection.

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, 16,000–20,000 HBsAg positive women give birth each year. Without post-exposure prophylaxis to prevent perinatal HBV infection, it is estimated that 12,000 infants and children would be infected with HBV annually. Furthermore, prior to implementation of universal infant hepatitis B immunization, an additional 16,000 children < 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 Alaskan Natives, children of Pacific Islander parents, and children of first-generation immigrants from countries where HBV is of high or intermediate endemicity.[2-5]

Screening of all pregnant women for HBsAg to identify infants requiring post-exposure prophylaxis has been recommended since 1988, universal childhood hepatitis B immunization since 1991, and universal adolescent hepatitis B immunization since 1995. In the U.S., without post-exposure prophylaxis, HBV would annually infect 12,000 infants; without routine childhood immunization, HBV would infect 16,000 children.

Most HBV transmission and the morbidity associated with acute hepatitis B occur among older adolescents and young adults, and their most frequently reported risk factor is heterosexual contact with an infected partner or with multiple partners (40%), followed by injecting drug use (17%), male homosexual activity (15%), household contact with a person with hepatitis B (3%), and health-care employment with frequent blood contact (1%). Although up to 25% of persons with newly acquired hepatitis B do not report a known source for their infection, most of these have 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 settings where hepatitis B vaccine is routinely recommended, such as STD treatment clinics. Thus, programs to vaccinate older adolescents and adults at increased risk for HBV infection must be strengthened nationwide to significantly reduce HBV transmission in the next 2 decades.

III. Importance of rapid identification

Rapid identification and prompt reporting of cases of acute hepatitis B is important because measures such as post-exposure prophylaxis can be taken to prevent transmission to other persons. Although outbreaks of hepatitis B are rare, rapid identification 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.

Cases of chronic HBV infection have not been reportable to the National Notifiable Diseases Surveillance System (NNDSS) in the past, but plans are underway to make chronic HBV infection a nationally notifiable condition. All states are encouraged to make an HBsAg-positive test result a reportable condition to facilitate effective immunization of contacts of persons with chronic HBV infection (see "Registries and databases for HBsAg-positive persons"). For HBsAg-positive pregnant women, reporting allows for the initiation of case management to ensure prevention of perinatal HBV transmission (see "Post-exposure prophylaxis").

Post-exposure 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. Multiple doses of HBIG also have been shown to provide an estimated 75% protection from HBV infection following percutaneous exposure to HBsAg-positive blood when initiated within 1 week of exposure and following sexual exposure to an HBsAg-positive partner when initiated within 14 days of exposure. Although the post-exposure 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 compared with HBIG alone observed in the perinatal setting would apply to these exposures.

Post-exposure prophylaxis with HBIG and hepatitis B vaccine should be given to infants born to HBsAg-positive mothers, unvaccinated infants whose mothers or primary care givers have acute hepatitis B, sexual contacts of persons with acute hepatitis B, and health-care 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 cases who require post-exposure prophylaxis; 2) detect outbreaks; 3) identify infected persons who need counseling and referral for medical management; 4) monitor disease incidence in all age groups; 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, established disease reduction goals for hepatitis B combine process outcome and disease outcome measures. Because most HBV infections among children < 10 years of age are asymptomatic, assessment of 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 and measuring vaccine coverage levels provide data to measure the effectiveness of prevention programs.

Healthy People 2010 (HP 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. HP 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 definitions

The following case definitions for acute hepatitis B and for perinatal HBV infection have been approved by the Council of State and Territorial Epidemiologists (CSTE) and were published in 1997.[6]

Acute hepatitis B

Clinical case definition

An acute illness with

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

Laboratory criteria for diagnosis

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

Case classification

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

Comment: The best serologic test to diagnose acute hepatitis B is IgM anti-HBc. For HBsAg-positive persons without an IgM anti-HBc test result, it may be difficult to distinguish between acute and chronic infection. In such situations, a negative IgM anti-HAV test result is helpful to rule out acute hepatitis A.

Clinical description—Perinatal HBV infection acquired in the U.S. or U.S. territories

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 U.S. or in U.S. territories to an HBsAg-positive mother.

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 < 2 years of age, especially if they acquired their infection through perinatal transmission.

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. 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 19, “Laboratory Support for Surveillance of Vaccine-preventable Diseases.”

CDC laboratory special 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 vaccine-resistant strains. For example, the detection of HBV variants or “escape mutants” among vaccinated infants of HBsAg-positive women is important to determine their potential role in vaccine failures.[7] Health-care professionals with questions about molecular virologic methods or those who identify HBsAg-positive events among vaccinated persons should consult their state health department or the Epidemiology Branch, Division of Viral Hepatitis, CDC, 404-371-5910.

VIII. Reporting

In the United States, case reports of acute viral hepatitis are classified as hepatitis A, hepatitis B, or hepatitis C/non-A, non-B hepatitis. Serologic testing is necessary to determine the etiology of viral hepatitis, and case reports should be based on laboratory confirmation (see "Case definitions"). Each state and territory has regulations or laws governing the reporting of diseases and conditions of public health importance.[8]

Reporting to CDC

Case reports of acute hepatitis B and other reportable diseases are transmitted by the state health department weekly to CDC via the National Electronic Telecommunications Surveillance System (NETSS) or National Electronic Disease Surveillance System (NEDSS). The NETSS core record includes basic demographic information (excluding personal identifiers)—age, race or ethnicity, sex, date of onset, date of report, county of residence. The Division of Viral Hepatitis has developed a hepatitis program area module for use in NEDSS where symptoms, risk factors, and serologic data can be entered. The hepatitis module form can be found in **Appendix 5** and can also be found at the following web address:
http://www.cdc.gov/ncidod/diseases/hepatitis/resource/PDFs/vhsp02.pdf
This form can be used for data collection and case investigation, and data collected on the form can be directly entered into NEDSS.

IX. Vaccination schedules

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

Hepatitis B vaccine

Two monovalent recombinant hepatitis B vaccines are commercially available, Recombivax HB™ (Merck & Company, Inc., West Point, Pennsylvania) and Engerix-B® (GlaxoSmithKline, Philadelphia, Pennsylvania). Recombivax HB™ contains 10–40µg of HBsAg protein per mL, whereas Engerix-B® contains 20 µg/mL. Both vaccines are licensed for persons of all ages (Table 2). A combined hepatitis A and B vaccine, Twinrix® (GlaxoSmithKline), is also available for use in persons aged > 18 years. Twinrix® is made of the antigenic components used in HAVRIX® (hepatitis A vaccine) and Engerix-B®. Any person aged > 18 years having an indication for both hepatitis A and B vaccination can be administered Twinrix.

Infants born to HBsAg-positive women

Dose*	Age
1	Birth (within 12 hours)
HBIG†	Birth (within 12 hours)
2	1-2 months
3	6 months

*See **Table 2** for appropriate vaccine dose
†HBIG – 0.5 mL given intramuscularly at separate site from vaccine

Any infant of an 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 3rd dose of hepatitis B vaccine by the age of 6 months is not adequately vaccinated. Infants born to HBsAg-positive women should have serologic testing at 9 to 15 months of age to determine the outcome of immunoprophylaxis and to provide information about the effectiveness of perinatal HBV transmission prevention programs. Serologic testing can also determine whether these infants develop 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 in a 0, 1–2, 4–6 month schedule.

Infants born to HBsAg-negative women*

Dose†	Age
1	Birth–2 months
2	1–4 months
3	6–18 months

* Vaccination of preterm infants should be delayed until they weigh 2 kg or are 2 months old, except for infants born to HBsAg-positive mothers. Infants in populations at high risk of early childhood infections should complete vaccinations by 12 months of age.
†See **Table 2** for appropriate vaccine dose.

The vaccination schedule for infants born to HBsAg-negative women is flexible and includes 3 doses of vaccine in the first 18 months of life. The minimum interval between doses 1 and 2 is one month and between doses 2 and 3 is two months. Dose 3 of hepatitis B vaccine should not be given before 6 months of age. Any infant of a 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.

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

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.

Dialysis patients and other immunocompromised persons

Either given as three-dose series (0, 1, 6) or four-dose series (0, 1, 2, and 6), 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 consists of three doses, given on a 0-, 1-, and 6-month schedule.

X. Enhancing surveillance

Establishing surveillance for acute hepatitis is difficult for several reasons. There are five different viruses (A–E) that 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 in 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 the 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 serology to determine the etiology of viral hepatitis and reporting all cases of acute hepatitis. A common risk factor for persons with acute infection is contact with a previously identified case. Aggressive case-investigations of persons with acute disease provide the best opportunity for post-exposure prophylaxis of contacts and for reducing transmission.

Case investigation. Case investigation is essential to identify contacts eligible for prophylaxis and to collect 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 hepatitis to the state or local health department. All IgM anti-HBc positive results should be reported. To facilitate reporting, these results could be included in the state's list of 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:

- Characteristics of cases of acute hepatitis B that occur in children and adolescents less than 16 years of age and associated missed opportunities for vaccination
- Characteristics of cases of acute hepatitis where death has occurred
- Characteristics of cases of acute hepatitis B in persons reporting a history of vaccination

Registries and databases for HBsAg-positive persons. The reporting of HBsAg-positive test results and the establishment of databases and 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
- 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 codes 070.*), and all births to HBsAg-positive women.

XI. Case investigation

Guidelines for investigating a suspected case of viral hepatitis include:

- Determining a discrete onset of illness
- Confirming evidence of acute liver disease (jaundice or elevated aminotransferase levels)
- Obtaining serologic laboratory results

Information to collect
The following information is epidemiologically important to collect in a case investigation. Additional information may also be collected at the direction of the state health department.

- Demographic information
  - Name
  - Address
  - Date of birth
  - Age

continued on the next page

Information to collect (con't.)

  - Sex
  - Ethnicity
  - Race

- Reporting Source
  - County
  - Earliest date reported

- Clinical details including
  - Date onset of illness
  - Symptoms including pain, jaundice

- Laboratory results

- Vaccine information
  - Dates of vaccination
  - Number of doses received
  - Manufacturer name
  - Vaccine lot number
  - If not vaccinated, reason

- Epidemiological
  - Risk factors
  - Contact investigation and prophylaxis

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

- Assessing pregnancy status for women of childbearing age. All HBsAg-positive pregnant women should be reported to the perinatal hepatitis B program manager, so that the women can be tracked and to ensure their infants receive appropriate case management.

- 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
  - evaluating eligibility for antiviral treatment

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

Serologic Markers				Interpretation
HBs Ag[a]	Total Anti-HBc[b]	IgM Anti-HBc[c]	Anti-HBs[d]	
-	-	-	-	Susceptible, never infected
+	-	-	-	Acute infection, early incubation[e]
+	+	+	-	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

[a] Hepatitis B surface antigen
[b] Antibody to hepatitis B core antigen
[c] Immunoglobulin M
[d] Antibody to hepatitis B surface antigen
[e] Transient HBsAg positivity (lasting < 18 days) might be detected in some patients during vaccination.

Table 2. Recommended doses of currently licensed hepatitis B vaccines

	Recombivax HB[a]	Engerix-B[a]
Group	**Dose µg (mL)**	**Dose µg (mL)**
Infants, children and adolescents < 20 years of age	5 (0.5)	10 (0.5)
Adolescents 11–15 years[b]	10 (1.0)	
Adults > 20 years of age	10 (1.0)	20 (1.0)
Dialysis patients and other immunocompromised persons	40 (1.0)[c]	40 (2.0)[d]

[a] Both vaccines are routinely administered in 3-dose series. Engerix-B also has been licensed for a four-dose series administered at 0, 1, 2, and 12 months.
[b] Two-dose schedule for adolescents using adult dose of Recombivax HB has been approved by ACIP administered at 0, 4-6 months
[c] Special formulation
[d] Two 1.0 mL doses administered at one site in a four-dose schedule at 0, 1, 2, and 6 months

Table 3. Recommended doses of TWINRIX® (combined hepatitis A and B vaccine)

Group	Age	Dose (EL.U.)[a]/mcg	Volume	No. doses	Schedule[b]
Adults	> 18 years	720 A virus/20 mcg HBsAg protein	1.0 mL	3	0, 1, 6

® GlaxoSmithKline
[a] Enzyme-linked immunosorbent assay units
[b] Months; 0 months represents timing of the initial dose and subsequent numbers represent months after the initial dose.

References

1. McMahon BJ, Alward WL, Hall DB, et al. Acute hepatitis B virus infection: relation of age to the clinical expression of disease and subsequent development of the carrier state. *J Infect Dis*. 1985;151:599-603.

2. Franks AL, Berg CJ, Kane MA, et al. Hepatitis B virus infection among children born in the United States to Southeast Asian refugees. *N Engl J Med*. 1989;321:1301-1305.

3. Hurie MB, Mast EE, Davis JP. Horizontal transmission of hepatitis B virus infection to United States-born children of Hmong refugees. *Pediatrics*. 1992;89:269-273.

4. Mahoney FJ, Lawrence M, Scott C, et al. Continuing risk for hepatitis B virus transmission among Southeast Asian infants in Louisiana. *Pediatrics*. 1995;96:1113-1116.

5. Pon EW, Ren H, Margolis H, et al. Hepatitis B virus infection in Honolulu students. *Pediatrics*. 1993;92:574-578.

6. CDC. Case definitions for infectious conditions under public health surveillance. *MMWR Recomm Rep*. 1997;46:1-55.

7. Thomas HC, Carman WF. Envelope and precore/core variants of hepatitis B virus. *Gastroenterol Clin North Am*. 1994;23:499-514.

8. Roush S, Birkhead G, Koo D, et al. Mandatory reporting of diseases and conditions by health care professionals and laboratories. *JAMA*. 1999;282:164-170.