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Hepatitis B: Virology, Epidemiology, Disease, and Prevention, and an Overview of Viral Hepatitis

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Viral hepatitis is a term commonly used for several clinically similar, yet etiologically and epidemiologically distinct, diseases. Hepatitis A (formerly called infectious hepatitis) and hepatitis B (formerly called serum hepatitis) have been recognized as separate entities since the early 1940s and can be diagnosed with specific serologic tests. A third category, known as non-A, non-B hepatitis, includes two epidemiologically distinct types of hepatitis: bloodborne and enterically transmitted non-A, non-B hepatitis. Bloodborne non-A, non-B hepatitis is associated with both community-acquired and posttransfusion cases of acute hepatitis. Hepatitis C virus (HCV) is thought to account for most of the bloodborne non-A, non-B hepatitis occurring in the United States. However, a small percentage of cases of bloodborne non-A, non-B hepatitis are probably due to at least one other, as yet unidentified agent. HCV has been cloned, and assays to detect antibody to this virus have been developed. Hepatitis E (enterically transmitted non-A, non-B hepatitis) is spread by the fecal-oral route. Hepatitis E has not been reported in the United States, but outbreaks have been reported in parts of Asia, Africa, and Mexico. Another distinct type of hepatitis, delta hepatitis, is an infection dependent on the hepatitis B virus (HBV). It may occur as a coinfection with HBV or as superinfection of an HBV carrier.

Hepatitis A

Hepatitis A is caused by the hepatitis A virus (HAV), a 27-nm ribonucleic acid (RNA) agent classified as a picornavirus. Per-

sons who are clinically ill exhibit symptoms similar to those reported by patients with other types of viral hepatitis and may include fever, malaise, anorexia, nausea, abdominal discomfort, dark urine, and jaundice. Symptoms characteristically have an abrupt onset. Most adults are symptomatic; most children younger than six years of age are asymptomatic. Mortality rate is less than 1%. In 1991, 50% of reported cases of viral hepatitis in the United States were due to HAV. In a national seroprevalence survey in 1980, 38% of adults and children surveyed had evidence of past HAV infection.

HAV is transmitted primarily person-to-person through fecal contamination and oral ingestion, and transmission is facilitated by poor personal hygiene, poor sanitation, and intimate contact. In the United States, most cases of hepatitis A occur in community-wide outbreaks, and a high percentage of cases have no identifiable risk factors for infection. In these outbreaks, susceptible children play an important role in transmission of HAV. Young children are often asymptomatic, and HAV infection is usually not recognized until transmission occurs to older household contacts. Persons at risk for HAV infection include (1) household or sexual contacts of a person infected with HAV, (2) employees and children in daycare centers, particularly in centers with diapered children, (3) travelers to areas with high endemicity of HAV infection, (4) residents and staff of prisons and institutions for the disabled when outbreaks of hepatitis A occur, (5) coworkers of a food handler infected with HAV, (6) injection drug users, and (7) persons who ingest food or water contaminated with HAV.

The incubation period for hepatitis A is 15 to 50 days (average, 30 days). Greatest infectivity is during the two-week period immediately before the onset of symptoms, when high concentrations of HAV are present in stool. Virus concentrations excreted in feces diminish rapidly once jaundice appears, and fecal HAV excretion generally persists for less than one week after onset of jaundice. Longer periods of viral excretion have been reported in neonates and in immunocompromised persons. Viremia probably occurs during the period when the virus is shed in feces; however, HAV transmission by blood transfusion is uncommon.

Commercial tests are available to diagnose hepatitis A. Acute

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U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
PUBLIC HEALTH SERVICE



serum hepatitis was repeatedly observed following the use of contaminated needles and syringes in diabetic and venereal disease clinics, following plasma administration for immunoprophylaxis of measles and mumps, and following the administration of vaccines, such as yellow fever vaccines, containing human serum. The role of blood as a vehicle for virus transmission was further documented in 1943 when Beeson and coworkers described jaundice that occurred in seven recipients of blood transfusions. Although some of these cases may have been caused by agents now referred to as non-A, non-B hepatitis viruses, many were undoubtedly caused by HBV.

Hepatitis B was not clearly distinguished from hepatitis A until the 1940s and 1950s, when distinctive incubation periods and modes of transmission were demonstrated in experimental transmission studies in human volunteers. These epidemiologic findings were confirmed in the 1960s with the discovery of Australia antigen (now termed HBsAg) by Blumberg et al. and its association with hepatitis B by Prince. Subsequent development of serologic tests for HBV infection and epidemiologic studies helped clarify the natural history of the disease. Ultimately, HBsAg was prepared in quantity and now constitutes the immunogen in highly effective vaccines used for the prevention of HBV infection.

HBV structure. HBV is a 42-nm double-shelled deoxyribonucleic acid (DNA) virus of the class hepadnaviridae. The outer surface membrane contains HBsAg, which also circulates in blood as 22-nm spherical and tubular particles. The inner core of the virus contains hepatitis B core antigen (HBcAg), hepatitis B e antigen (HBeAg), a single molecule of partially double-stranded DNA, and DNA-dependent DNA polymerase (Figure 1).

HBV infection nomenclature. HBsAg, formerly called Australia antigen or hepatitis-associated antigen, is present on the surface of the virus and is a serologic marker of HBV infection. HBcAg and HBeAg are translated from a common gene but display different antigenic properties in spite of their similar amino acid composition. HBcAg is the nucleocapsid protein and is not detectable in serum by conventional techniques. HBcAg can be detected in liver tissue in patients who have acute or chronic HBV infection. HBeAg is a soluble protein that can be detected in the serum of persons with high virus titers. DNA polymerase repairs the single-stranded region in

the viral DNA to make fully double-stranded molecules of approximately 3,200 base pairs.

Antibody to HBsAg (anti-HBs) develops during convalescence after acute HBV infection or following hepatitis B vaccination. **Antibody to HBeAg (anti-HBe)** indicates infection with HBV at an undefined time in the past. **IgM class antibody to HBcAg (IgM anti-HBc)** indicates recent infection with HBV. **Antibody to HBeAg (anti-HBe)** becomes detectable when HBeAg is lost and is associated with low infectivity of serum.

Chronic HBV infection is determined when (1) HBsAg is detected on two tests at least six months apart or (2) the results of a single serum specimen are HBsAg-positive and IgM anti-HBc-negative. Persons with chronic infection (HBsAg carrier) may be asymptomatic and unaware that they have HBV infection, yet are capable of infecting others.

IG (previously ISG, immune serum globulin, or gamma globulin) contains antibodies to HAV and a low titer of antibodies to HBV. IG is used for passive immunization against HAV and measles virus, but not against HBV. **Hepatitis B immune globulin (HBIG)** is a preparation obtained from the plasma of donors with a high titer of anti-HBs. HBIG is administered with hepatitis B vaccine in some situations to provide postexposure prophylaxis. And, finally, **Hepatitis B vaccine** is used for active immunization against HBV infection.

Epidemiology.

Disease burden in the United States. The acute and chronic consequences of HBV infection are major health problems in the United States. During the 1980s, approximately 300,000 acute HBV infections occurred annually in all age groups in the United States. Of these, 30% to 40% were symptomatic, and 60% to 70% were asymptomatic. Most acute infections occurred in young adults, and more infections occurred in men than in women. Of persons with symptomatic HBV infections, 11,000 to 17,000 were hospitalized and 350 to 450 died of fulminant hepatitis. Overall, in children and adults, 9% to 14% of acute HBV infections progress to chronic infection. Of those with chronic infection, an estimated 4,000 to 5,500 will die prematurely from cirrhosis or liver cancer (Figure 2).

Global distribution. Approximately 45% of the global population live in areas where prevalence of chronic HBV infection is

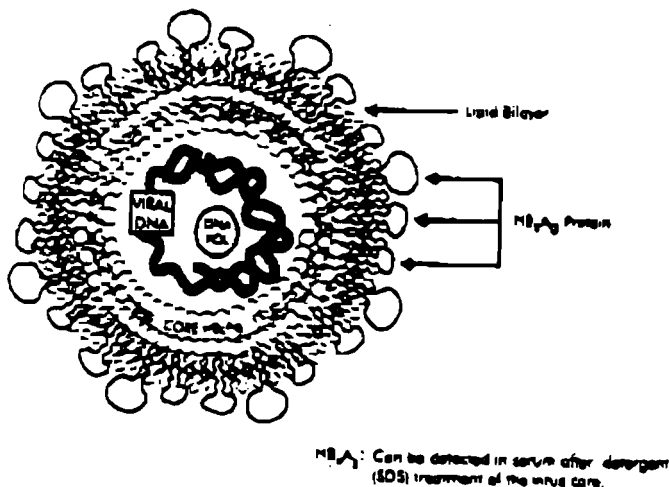


Figure 1. Schematic of Hepatitis B virus.

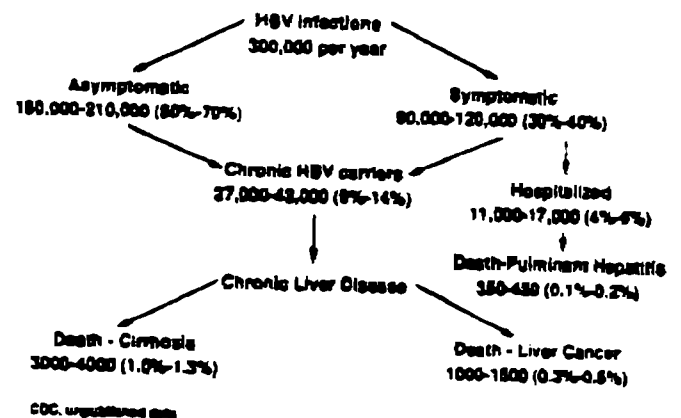


Figure 2. Disease burden of acute and chronic HBV infections. Average annual incidence in all age groups. United States. 1980-1989 estimates.

convalescence, malaise and fatigue may persist for weeks or months, and jaundice, anorexia, and other symptoms disappear.

Outcome of HBV infection. Most acute HBV infections in adults result in complete recovery, with elimination of HBsAg from the blood and the production of anti-HBs creating immunity from future infection. Fulminant hepatitis occurs in about 1% to 2% of patients with acute disease, with mortality rates of 63% to 93%. While the consequences of acute HBV infection can be severe, most of the serious sequelae associated with HBV infection occur in persons in whom chronic infection develops. Persons with chronic infection are often asymptomatic; however, these persons are at high risk for chronic hepatitis, and approximately 15% to 25% may die prematurely from either cirrhosis or liver cancer.

The outcome of acute HBV infection varies substantially depending on the age at which infection occurs (see Figure 5). In children under five years of age, <5% of acute HBV infections are symptomatic; however, chronic infection occurs in about 80% to 90% of infants infected during the first year of life and in about 30% to 50% of children infected between one and four years of age. By comparison, 30% to 50% of adults with acute HBV infection are symptomatic; chronic infection develops in only 5% to 10%.

Diagnosis of HBV infection. Because the clinical course of illness is similar for all types of viral hepatitis, serologic testing is needed to distinguish the etiologic agent in individual patients. Serologic markers of HBV infection vary depending on whether the infection is acute or chronic (Table 1).

HBsAg is detectable in persons with both acute and chronic HBV infection. The presence of HBsAg indicates that a person is infectious, regardless of whether the infection is acute or chronic.

Anti-HBs is a protective, neutralizing antibody. The presence of anti-HBs following acute HBV infection generally indicates recovery and immunity from reinfection. Anti-HBs can also be acquired as an immune response to hepatitis B vaccine or passively transferred by administration of HBIG.

Total anti-HBc includes both IgM and IgG, appears shortly after HBsAg in acute disease, and indicates HBV infection at some undefined time in the past. Anti-HBc generally persists for life and therefore is not a serologic marker for acute infection.

IgM anti-HBc appears in patients with acute disease about the time of illness onset and indicates recent infection with HBV. IgM anti-HBc is generally detectable four to six months

after onset of illness and is the best serologic marker of acute HBV infection. HBeAg present in serum correlates with HBV replication, a high titer of HBV, and increased infectivity. Anti-HBe present in serum correlates with low infectivity of serum.

Acute HBV infection. The first serologic marker to appear in the blood of persons with acute HBV infection is HBsAg (see Figure 6). HBsAg can initially be detected as early as one or two weeks and as late as 11 or 12 weeks (mean 30 to 60 days) after exposure to HBV. In persons who recover following acute HBV infection, HBsAg is detectable for a variable period (mean three months) and disappears with recovery. HBeAg is invariably present in patients with acute infection and indicates that the person is highly infectious. Anti-HBc is the first antibody to become detectable following acute infection, most of which initially is IgM anti-HBc. After the disappearance of HBsAg and before the appearance of anti-HBs, the "window" period occurs when only IgG and IgM anti-HBc and anti-HBe are detectable. Subsequently, the titer of IgM anti-HBc declines, whereas the titer of IgG anti-HBc increases and persists indefinitely. Anti-HBs becomes detectable during convalescence, after the disappearance of HBsAg, in patients who do not progress to chronic infection. The presence of anti-HBs following acute HBV infection generally indicates recovery and immunity from reinfection.

Chronic infection. In patients with chronic HBV infection, HBsAg remains persistently detectable, generally for life (see Figure 7). The presence of HBsAg for six months or more generally indicates chronic infection. HBeAg is variably present in patients with chronic HBV infection. IgG anti-HBc is invariably present in the serum of these patients; however, IgM anti-HBc generally declines to subdetectable levels. A test result negative for IgM anti-HBc and a test result positive for HBsAg in a single blood sample usually indicates that a patient has a chronic HBV infection.

Management of persons with HBV infection.

Acute HBV infection. No specific drugs are available for treating acute HBV infection. Supportive, symptomatic care is the mainstay of treatment. Liver transplantation has been used for patients with fulminant acute hepatitis B, with survival rates of >50%. Since infants have close contact with primary caregivers and have a higher risk of becoming HBV carriers after acute HBV infection, prophylaxis for an infant younger than 12 months of age with HBIG and hepatitis B vaccine is indicated if the mother or primary caregiver has acute HBV infection. Sexual contacts of patients with acute HBV infection should be screened for evidence of HBV infection and, if susceptible, should receive hepatitis B vaccine.

Chronic HBV infection. Persons with chronic HBV infection should be evaluated for evidence of chronic liver disease and the potential need for treatment with alpha-2b-interferon. Chronic HBV infection has been treated with alpha-2b-interferon with limited success. After treatment with interferon, sustained loss of viral replication has been demonstrated in approximately 40% of patients who have chronic HBV infection, and disappearance of HBsAg in serum has been demonstrated in 10% to 20% of treated patients.

Patients who have chronic HBV infection are also at high risk for hepatocellular carcinoma. Serum alpha-fetoprotein (AFP) levels have been reported to be elevated in 55% to 95% of patients who have hepatocellular carcinoma. Some patients

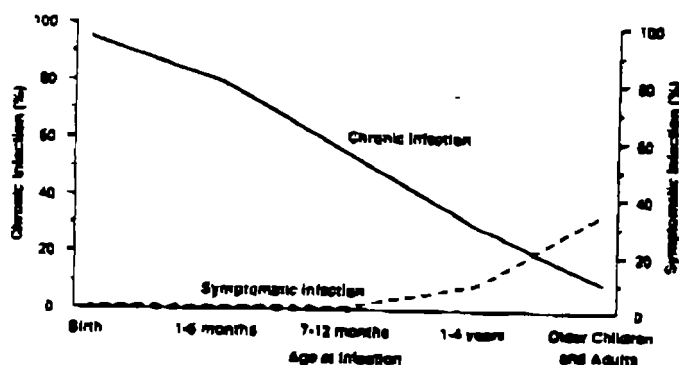


Figure 5. Outcome of hepatitis B virus infection by age at infection.

intact for at least 13 years following hepatitis B vaccination. In persons who initially respond to vaccination, anti-HBs titers may decline over time; however, loss of anti-HBs after vaccination does not imply loss of protection. In vitro studies have demonstrated intact immunologic memory in B cells obtained from vaccine responders who had low or undetectable anti-HBs levels seven to eight years after vaccination. Moreover, natural exposure to HBV long after primary vaccination results in an anamnestic increase in anti-HBs that protects against both clinically significant acute HBV infection and chronic HBV infection. On the basis of these findings, routine booster doses of hepatitis B vaccine are not currently recommended. However, these recommendations should be assessed periodically as more data become available on the duration of protective efficacy.

Vaccine safety. Hepatitis B vaccine has been proven very safe. Soreness at the site of injection is the most common side effect observed, reported in 13% to 29% of adults and 3% to 9% of children. Mild transient systemic symptoms including fatigue, headache, and irritability have been reported in 11% to 17% of adults and 8% to 18% of children, and low-grade fever ($>37.7^{\circ}\text{C}$) has been reported in 1% of adults and 0.4% to 8% of children. Reports of serious or severe adverse events have been minimal. Analysis of reported adverse events indicates no association of Guillain-Barré or other neurologic diseases with the recombinant hepatitis B vaccine.

Only limited data are available on the safety of the hepatitis B vaccine for the developing fetus. However, because the vaccine contains noninfectious HBsAg particles, there should be no risk for the fetus. HBV infection in a pregnant woman may result in severe disease in the mother and chronic infection in the newborn. Therefore, neither pregnancy nor lactation should be considered a contraindication to the vaccination of women.

HBIG. HBIG is prepared by cold ethanol fraction of plasma from donors selected for very high anti-HBs titers. The human plasma from which HBIG is prepared is screened for antibodies to HIV, and the preparation process has been shown to eliminate HIV from the final product. There is no evidence that either HIV or HBV has been transmitted by HBIG commercially available in the United States. IG has no place in the prophylaxis against HBV infection because anti-HBs titers are relatively low. HBIG can be used for postexposure prophylaxis in the following settings: (1) percutaneous and mucous membrane exposures to infectious blood or body fluids; (2) sexual exposure to infected persons, and (3) perinatal exposure of infant born to HBsAg-positive mother. All candidates for HBIG should also be given hepatitis B vaccine.

Evolution of hepatitis B vaccination strategies. When hepatitis B vaccine became available in the United States in 1982, the vaccine was initially recommended for groups at high risk, including health care workers, injection drug users, homosexually active men, and household and sexual contacts of persons with chronic HBV infection (see Appendix 1). When subsequent studies demonstrated the efficacy of HBIG and hepatitis B vaccine in preventing perinatal transmission of HBV, additional recommendations were made to screen all pregnant women for HBsAg to identify infants needing immunoprophylaxis.

Although the strategy of vaccinating persons in high-risk groups was used during most of the decade of the 1980s, it had little impact on the incidence of hepatitis B in the United States (see Figure 8). In fact, the incidence of hepatitis B in the early

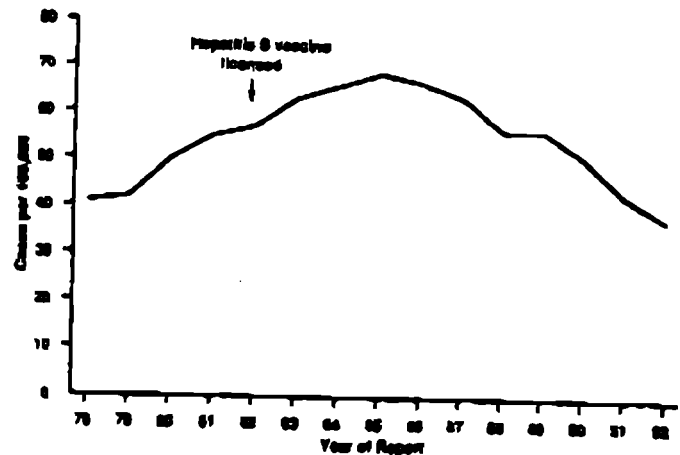


Figure 8. Estimated incidence of acute hepatitis B, United States, 1978-1992.

1990s was similar to that during the late 1970s, before the availability of hepatitis B vaccine.

Several reasons may account for the limited impact of the hepatitis B vaccination strategy targeting high-risk groups: (1) About 25% to 30% of persons with acute hepatitis B do not report a risk factor for infection and would not be identified as candidates for vaccination. (2) Many persons at risk for hepatitis B, including injection drug users and persons with sexual risk factors, are already infected with HBV when they initially present for medical attention. (3) Many persons at risk for hepatitis B are difficult to access for vaccination either because they do not seek health care or because they are not identified as being at risk during routine health care visits. (4) In contrast to vaccination programs for infants, no programs that routinely access adolescents and adults exist.

Current recommendations for hepatitis B vaccination. Based on the knowledge gained from the use of hepatitis B vaccine during the 1980s, a new vaccination strategy was developed with an overall goal of eliminating HBV transmission in the United States (see Figure 9). The major component of this strategy is to provide hepatitis B vaccine for all infants born in the United States as part of their routine childhood vaccination schedule. Other components of the strategy are shown in Figure 9.

Continued screening of pregnant women is needed for several reasons, including the need to administer both HBIG and hepatitis B vaccine to prevent perinatal HBV transmission. It is also necessary for targeted follow-up of infants of HBsAg-positive mothers to ensure the timely administration of three doses of hepatitis B vaccine. "Catch-up" vaccination in populations with high rates of HBV infection among children (Alaskan Natives, Pacific Islanders, and infants of immigrants from countries in which HBV is endemic) is important because HBV transmission continues through early adolescence and the risk of chronic HBV infection in these populations is high. Continued vaccination of adolescents and adults in high-risk groups will prevent HBV infection in those persons who can be reached. Eventually, as successive birth cohorts are vaccinated, vaccination of adolescents and adults in high-risk groups will no longer be necessary.

Additional measures to prevent HBV transmission in the health care setting. Two further measures, infection control

APPENDIX 2

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APPENDIX 3

Hepatitis B Workshop

Answers are in bold.

1. Hepatitis B can be correctly classified as a sexually transmitted disease.
TRUE. Sexual exposure is the primary risk factor for transmission of HBV in the United States.
2. Hepatitis A virus (HAV) and Hepatitis B virus (HBV) are both transmitted by contaminated food or water.
FALSE. HAV is transmitted by the fecal-oral route and has been transmitted by food and water contaminated with HAV. Food and water are not vehicles for the transmission of HBV.
3. A person whose serum contains hepatitis B surface antigen (HBsAg) is infectious.
TRUE. Any person whose serum contains HBsAg, whether from acute or chronic infection, is capable of transmitting the virus and is infectious.
4. Immune globulin (IG; "gamma globulin") and hepatitis B immune globulin (HBIG) are equally effective in preventing hepatitis B when used as postexposure prophylaxis.
FALSE. IG generally contains low titers of hepatitis B surface antibody (anti-HBs) and cannot be relied on to prevent HBV infection when used as postexposure prophylaxis. HBIG is produced from persons prescreened for high titers of anti-HBs and is effective when used promptly after exposure. IG has no place in the prophylaxis of HBV infection.
5. It is not necessary for health care workers to receive hepatitis B vaccine until after they have completed their professional training.
FALSE. Hepatitis B vaccine should be given before or as soon as possible after a person enters a high-risk group. In the health care setting, hepatitis B vaccine should preferably be given before or at the time contact with potentially infectious body fluids begins. This high-risk period usually begins when a student begins clinical rotations.
6. A 45-year-old female nurse is diagnosed as having acute hepatitis B. Her husband, teenage daughter, 6-year-old son, 11-month-old son, and mother-in-law, who lives with them, are all at equal risk of acquiring HBV infection.
FALSE. Only sex contacts, her 11-month-old son, and persons who were exposed to the infected person's blood (e.g., sharing razors or toothbrushes) are at risk.
7. All of the above-named contacts of the nurse should start the three-dose series of hepatitis B vaccine as soon as possible.
FALSE. The sex partner of the nurse and the 11-month-old son would need prophylaxis. HBIG and the first dose of hepatitis B vaccine should be given as soon as possible after the disease is diagnosed. If the nurse becomes a chronic carrier of HBV (defined as HBsAg-positive for more than six months), all members of the household should be given hepatitis B vaccine.
8. A 19-year-old pregnant woman who comes into a maternity clinic for a visit should be screened for HBsAg.
TRUE. All pregnant women should be screened for HBsAg. Infants born to HBsAg-positive mothers should be treated with HBIG and hepatitis B vaccine immediately after birth.
9. A 31-year-old man arriving for treatment of a sexually transmitted disease should be considered for hepatitis B vaccine.
TRUE. Sexually active persons with multiple sex partners are at increased risk of HBV infection; risk increases with increasing numbers of sex partners. Vaccination is recommended for persons who are diagnosed as having recently acquired other sexually transmitted diseases, for prostitutes, and for persons who have a history of sexual activity with multiple partners (>1) in the previous six months.
10. Hepatitis B vaccine is never used for postexposure prophylaxis.
FALSE. In general, hepatitis B vaccine should be used when there will continue to be a risk of HBV infection beyond the immediate exposure situation. Use of hepatitis B vaccine in postexposure prophylaxis is particularly important for health care workers and for infants born to HBsAg-positive mothers.
11. Hepatitis B vaccine may cause mild fever and soreness and swelling of injection site in vaccinees.
TRUE. In clinical trials of hepatitis B vaccine, soreness at the injection site was reported in 13% to 29% of adults and in 3% to 9% of children. Mild transient systemic symptoms including fatigue, headache, and irritability have been reported in 11% to 17% of adults and 8% to 18% of children, and low-grade fever (>37.7° C) has been reported in 1% of adults and 0.4% to 8% of children.
12. Pregnancy should not be considered a contraindication to vaccinating susceptible women at risk for hepatitis B.
TRUE. On the basis of limited experience, there is no apparent risk of adverse effects to developing fetuses when hepatitis B vaccine is administered to pregnant women. The vaccine contains noninfectious HBsAg particles and should cause no risk to the fetus. HBV infection affecting a pregnant woman may result in severe disease for the mother and chronic infection for the newborn. Therefore neither pregnancy nor lactation should be considered a contraindication to vaccination of women.
13. Severe adverse reactions, such as encephalitis, occur more frequently following hepatitis B vaccine than after receipt of most other commonly recommended vaccines.
FALSE. The most common side effect observed following vaccination with each of the available hepatitis B vaccines has been soreness at the injection site. Available data from reporting systems for adverse events do not indicate an association between receipt of recombinant vaccine and Guillain-Barré syndrome.
14. Booster doses of hepatitis B vaccine are routinely recommended.
FALSE. Routine booster doses of hepatitis B vaccine are not recommended even though anti-HBs levels may fall to low or immeasurable levels.

To obtain, for teaching purposes, the hepatitis B slide set or the hepatitis B workshop with separate test questions and answers, contact Rose Marie Matulionis, Program Manager, Association of Teachers of Preventive Medicine, 1015 15th Street, N.W., Suite 405, Washington, D.C. 20005. Telephone (202) 682-1698, Telefax (202) 842-1980.



REPRINTED BY
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FROM THE
MORBIDITY AND MORTALITY WEEKLY REPORT
RECOMMENDATIONS AND REPORTS
November 22, 1991 / Vol. 40 / No. RR-13
Pages 1-25



Hepatitis B Virus: A Comprehensive Strategy for Eliminating Transmission in the United States Through Universal Childhood Vaccination

**Recommendations of the Immunization
Practices Advisory Committee (ACIP)**

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Hepatitis B Virus: A Comprehensive Strategy for Eliminating Transmission in the United States Through Universal Childhood Vaccination

Recommendations of the Immunization Practices Advisory Committee (ACIP)

The following statement updates all previous recommendations on protection against hepatitis B virus infection, including use of hepatitis B vaccine and hepatitis B immune globulin for prophylaxis against hepatitis B virus infection (MMWR 1985;34:313-24,329-35, MMWR 1987;36:353-66, and MMWR 1990;39 [No.RR-2]:8-19) and universal screening of pregnant women to prevent perinatal hepatitis B virus transmission (MMWR 1988;37:341-46,51, and MMWR 1990;39[No.RR-2]:8-19). Recommendations concerning the prevention of other types of viral hepatitis are found in MMWR 1990;39(No.RR-2):1-8, 22-26.

This document provides the rationale for a comprehensive strategy to eliminate transmission of hepatitis B virus in the United States. This prevention strategy includes making hepatitis B vaccine a part of routine vaccination schedules for all infants.

INTRODUCTION

The acute and chronic consequences of hepatitis B virus (HBV) infection are major health problems in the United States. The reported incidence of acute hepatitis B increased by 37% from 1979 to 1989, and an estimated 200,000-300,000 new infections occurred annually during the period 1980-1991. The estimated 1 million-1.25 million persons with chronic HBV infection in the United States are potentially infectious to others. In addition, many chronically infected persons are at risk of long-term sequelae, such as chronic liver disease and primary hepatocellular carcinoma; each year approximately 4,000-5,000 of these persons die from chronic liver disease (1).

Immunization with hepatitis B vaccine is the most effective means of preventing HBV infection and its consequences. In the United States, most infections occur among adults and adolescents (2,3). The recommended strategy for preventing these infections has been the selective vaccination of persons with identified risk factors (1,2). However, this strategy has not lowered the incidence of hepatitis B, primarily because vaccinating persons engaged in high-risk behaviors, life-styles, or occupations before they become infected generally has not been feasible. In addition, many infected persons have no identifiable source for their infections and thus cannot be targeted for vaccination (2).

Preventing HBV transmission during early childhood is important because of the high likelihood of chronic HBV infection and chronic liver disease that occurs when children less than 5 years of age become infected (3). Testing to identify pregnant women who are hepatitis B surface antigen (HBsAg)-positive and providing their infants with immunoprophylaxis effectively prevents HBV transmission during the perinatal period (4,5). Integrating hepatitis B vaccine into childhood vaccination schedules in populations with high rates of childhood infection (e.g., Alaskan Natives and Pacific Islanders) has been shown to interrupt HBV transmission (6).

This document provides the rationale for a comprehensive strategy to eliminate transmission of HBV and ultimately reduce the incidence of hepatitis B and hepatitis B-associated chronic liver disease in the United States. The recommendations for implementing this strategy include making hepatitis B

EPIDEMIOLOGY AND PREVENTION OF HEPATITIS B VIRUS INFECTION

Infections among Infants and Children

In the United States, children become infected with HBV through a variety of means. The risk of perinatal HBV infection among infants born to HBV-infected mothers ranges from 10% to 85%, depending on each mother's hepatitis B e antigen (HBeAg) status (3,7,8). Infants who become infected by perinatal transmission have a 90% risk of chronic infection, and up to 25% will die of chronic liver disease as adults (9). Even when not infected during the perinatal period, children of HBV-infected mothers remain at high risk of acquiring chronic HBV infection by person-to-person (horizontal) transmission during the first 5 years of life (10). More than 90% of these infections can be prevented if HBsAg-positive mothers are identified so that their infants can receive hepatitis B vaccine and hepatitis B immune globulin (HBIG) soon after birth (4,5).

Because screening selected pregnant women for HBsAg has failed to identify a high proportion of HBV-infected mothers (11,12), prenatal HBsAg testing of all pregnant women is now recommended (1,13,14). Universal prenatal testing would identify an estimated 22,000 HBsAg-positive women and could prevent at least 6,000 chronic HBV infections annually (3). Screening and vaccination programs for women and infants receiving care in the public sector have already been initiated through state immunization projects.

Horizontal transmission of HBV during the first 5 years of life occurs frequently in populations in which HBV infection is endemic. The risk of chronic infection is age dependent, ranging from 30% to 60% for children 1-5 years of age (15). Worldwide, it has been recommended that, in populations in which HBV infection is acquired during childhood, hepatitis B vaccine should be integrated into routine vaccination schedules for infants, usually as a part of the World Health Organization's Expanded Programme on Immunization (16). In the United States, racial/ethnic groups shown to have high rates of childhood HBV infection include Alaskan Natives (6,17), Pacific Islanders (18), and infants of first-generation immigrant mothers from parts of the world where HBV infection is endemic, especially Asia (19,20). Vaccination programs to prevent perinatal, childhood, and adult HBV infections among Alaskan Natives were begun in late 1982; as a result, the incidence of acute hepatitis B in this population has declined by over 99% (6). Hepatitis B vaccine was integrated into vaccination schedules for infants in American Samoa beginning in 1986 and by 1990 was incorporated into the schedules of the remaining Pacific Islands under U.S. jurisdiction.

Each year, approximately 150,000 infants are born to women who have immigrated to the United States from areas of the world where HBV infection is highly endemic (3). Children born to HBsAg-positive mothers can be identified through prenatal screening programs. However, children born to HBsAg-negative immigrant mothers are still at high risk of acquiring HBV infection, usually from other HBV carriers in their families or communities (3,19,20). Infections among these children can be prevented by making hepatitis B vaccine part of their routine infant vaccinations (1).

Infections among Adolescents and Adults

In the United States most persons with hepatitis B acquire the infection as adolescents or adults. Several specific modes of transmission have been identified, including sexual contact, especially among homosexual men and persons with multiple heterosexual partners; parenteral drug use; occupational exposures; household contact with a person who has an acute infection or with a chronic carrier; receipt of certain blood products; and hemodialysis. However, over one-third of patients with acute hepatitis B do not have readily identifiable risk factors (1,2).

The rates of HBV infection differ significantly among various racial and ethnic groups (2,21). For example, the prevalence of infection among adolescents and adults has been shown to be threefold to fourfold greater for blacks than for whites and to be associated with serologic evidence of previous infection with syphilis (21,22).

Efforts to vaccinate persons in the major risk groups have had limited success. For example, programs directed at injecting drug users failed to motivate them to receive three doses of vaccine (CDC, unpublished data). Health-care providers are often not aware of groups at high risk of HBV infection and frequently do not identify candidates for vaccination during routine health-care visits (CDC, unpublished data). In addition, there has been limited vaccination of susceptible household and sexual contacts of HBsAg carriers identified in screening programs for blood donors (23). Hepatitis B vaccination of health-care workers appears to have resulted in a substantial decrease in the rate of

widespread vaccination of persons at occupational risk, regulations have had to be developed to ensure implementation of vaccination programs (24).

Educational programs to reduce parenteral drug use and unprotected sexual activity are important components of the strategy to prevent infection with the human immunodeficiency virus (HIV), which causes acquired immunodeficiency syndrome. These programs appear to have reduced the risk of HBV infections among homosexual men but have not had an impact on hepatitis B attributable to parenteral drug use or heterosexual transmission (2). Educational efforts alone are not likely to fully eliminate the high-risk behaviors responsible for HBV transmission.

EPIDEMIOLOGY AND PREVENTION OF HEPATITIS DELTA VIRUS INFECTION

Hepatitis delta virus (HDV) is a defective virus that causes infection only in the presence of active HBV infection (25). HDV infection occurs as either coinfection with HBV or superinfection of an HBV carrier. Coinfection usually resolves; superinfection, however, frequently causes chronic HDV infection and chronic active hepatitis. Both types of infection may cause fulminant hepatitis.

Routes of transmission are similar to those of HBV. In the United States, HDV infection most commonly affects persons at high risk of HBV infection, particularly injecting drug users and persons receiving clotting factor concentrates (26). Preventing acute and chronic HBV infection of susceptible persons will also prevent HDV infection.

STRATEGY TO ELIMINATE HEPATITIS B VIRUS TRANSMISSION

A comprehensive strategy to prevent HBV infection, acute hepatitis B, and the sequelae of HBV infection in the United States must eliminate transmission that occurs during infancy and childhood, as well as during adolescence and adulthood. In the United States it has become evident that HBV transmission cannot be prevented through vaccinating only the groups at high risk of infection. No current medical treatment will reliably eliminate chronic HBV infection and thus eliminate the source of new infections in susceptible persons (27). Therefore, new infections can be prevented only by immunizing susceptible persons with hepatitis B vaccine. Routine visits for prenatal and well-child care can be used to target hepatitis B prevention. A comprehensive prevention strategy includes a) prenatal testing of pregnant women for HBsAg to identify newborns who require immunoprophylaxis for the prevention of perinatal infection and to identify household contacts who should be vaccinated, b) routine vaccination of children born to HBsAg-negative mothers, c) vaccination of certain adolescents, and d) vaccination of adults at high risk of infection.

Infants and children can receive hepatitis B vaccine during routine health-care visits; no additional visits would be required. Costs include that of the vaccine and the incremental expense associated with delivering an additional vaccine during a scheduled health-care visit. Implementation of this immunization strategy would be greatly facilitated by the development and use of multiple-antigen vaccines (e.g., diphtheria-tetanus-pertussis[DTP]/hepatitis B, *Haemophilus influenzae* type b conjugate/hepatitis B). These vaccines would reduce the number of injections received by the infant, reduce the cost of administration, and greatly facilitate widespread vaccine delivery.

Since most HBV infections occur among adults, disease control could be accelerated by vaccinating emerging at-risk populations, such as adolescents and susceptible contacts of chronic HBV carriers. The recommendation for universal infant vaccination neither precludes vaccinating adults identified to be at high risk of infection nor alters previous recommendations for postexposure prophylaxis for hepatitis B (1).

The reduction in acute hepatitis B and hepatitis B-associated chronic liver disease resulting from universal infant vaccination may not become apparent for a number of years. However, universal HBsAg screening of pregnant women to prevent perinatal HBV infection has been shown to be cost saving (28, CDC, unpublished data), and the estimated cost of universal hepatitis B vaccination for infants is less than the direct medical and work-loss costs associated with the estimated 5% lifetime risk of infection (CDC, unpublished data). Currently, the cost of an infant's dose of hepatitis B vaccine delivered in the public sector is about the same as each of the other childhood vaccinations. Vaccinating adolescents and adults is substantially more expensive because of the higher vaccine cost and the higher implementation costs of delivering vaccine to target populations. In the long term,

PROPHYLAXIS AGAINST HEPATITIS B VIRUS INFECTION

Two types of products are available for prophylaxis against HBV infection. Hepatitis B vaccine, which provides long-term protection against HBV infection, is recommended for both preexposure and postexposure prophylaxis. HBIG provides temporary protection (i.e., 3-6 months) and is indicated only in certain postexposure settings.

Hepatitis B Immune Globulin

HBIG is prepared from plasma known to contain a high titer of antibody against HBsAg (anti-HBs). In the United States, HBIG has an anti-HBs titer of $>100,000$ by radioimmunoassay. The human plasma from which HBIG is prepared is screened for antibodies to HIV; in addition, the process used to prepare HBIG inactivates and eliminates HIV from the final product. There is no evidence that HIV can be transmitted by HBIG (29,30).

Hepatitis B Vaccine

Two types of hepatitis B vaccine have been licensed in the United States. One, which was manufactured from the plasma of chronically infected persons, is no longer produced in the United States. The currently available vaccines are produced by recombinant DNA technology.

The recombinant vaccines are produced by using HBsAg synthesized by *Saccharomyces cerevisiae* (common bakers' yeast), into which a plasmid containing the gene for HBsAg has been inserted. Purified HBsAg is obtained by lysing the yeast cells and separating HBsAg from the yeast components by biochemical and biophysical techniques. Hepatitis B vaccines are packaged to contain 10-40 μg of HBsAg protein/mL after adsorption to aluminum hydroxide (0.5 mg/mL); thimerosal (1:20,000 concentration) is added as a preservative.

Routes and sites of administration.

The recommended series of three intramuscular doses of hepatitis B vaccine induces a protective antibody response (anti-HBs ≥ 10 milli-international units [mIU]/mL) in $>90\%$ of healthy adults and in $>95\%$ of infants, children, and adolescents (31-33). Hepatitis B vaccine should be administered only in the deltoid muscle of adults and children or in the anterolateral thigh muscle of neonates and infants; the immunogenicity of the vaccine for adults is substantially lower when injections are administered in the buttock (34). When hepatitis B vaccine is administered to infants at the same time as other vaccines, separate sites in the anterolateral thigh may be used for the multiple injections. This method is preferable to administering vaccine at sites such as the buttock or deltoid.

Compared with three standard doses administered intramuscularly, three low doses of plasma-derived or recombinant vaccine administered intradermally to adults result in lower seroconversion rates (55%-81%) and lower final titers of anti-HBs (35-38), although four doses of plasma-derived vaccine administered intradermally have produced responses comparable with vaccine administered intramuscularly (39). Plasma-derived vaccine administered intradermally to infants and children does not induce an adequate antibody response (40). At this time, low-dose intradermal vaccination of adults should be performed only under research protocol with written informed consent. Persons who have been vaccinated intradermally should be tested for anti-HBs. Those with an inadequate response (anti-HBs <10 mIU/mL) should be revaccinated with three full doses of vaccine administered intramuscularly. Intradermal vaccination should not be used for infants or children.

Vaccination during pregnancy.

On the basis of limited experience, there is no apparent risk of adverse effects to developing fetuses when hepatitis B vaccine is administered to pregnant women (CDC, unpublished data). The vaccine contains noninfectious HBsAg particles and should cause no risk to the fetus. HBV infection affecting a pregnant woman may result in severe disease for the mother and chronic infection for the newborn. Therefore, neither pregnancy nor lactation should be considered a contraindication to vaccination of women.

Vaccine Usage

Preexposure prophylaxis

Vaccination schedule and dose. The vaccination schedule most often used for adults and children has been three intramuscular injections, the second and third administered 1 and 6 months, respectively, after the first. An alternate schedule of four doses has been approved for one vaccine that

would allow more rapid induction of immunity. However, for preexposure prophylaxis, there is no clear evidence that this regimen provides greater protection than that obtained with the standard three-dose schedule.

Each vaccine has been evaluated to determine the age-specific dose at which an optimum antibody response is achieved. The recommended dose varies by product and the recipient's age and, for infants, by the mother's HBsAg serologic status (Table 1). In general, the vaccine dose for children and adolescents is 50%-75% lower than that required for adults (Table 1).

Incorporating hepatitis B vaccine into childhood vaccination schedules may require modifications of previously recommended schedules. However, a protective level of anti-HBs (≥ 10 mIU/mL) was achieved when hepatitis B vaccine was administered in a variety of schedules, including those in which vaccination was begun soon after birth (5,8,41).

→ In a three-dose schedule, increasing the interval between the first and second doses of hepatitis B vaccine has little effect on immunogenicity or final antibody titer. The third dose confers optimal protection, acting as a booster dose. Longer intervals between the last two doses (4-12 months) result in higher final titers of anti-HBs (42,43). Several studies have shown that the currently licensed vaccines produce high rates of seroconversion ($>95\%$) and induce adequate levels of anti-HBs when administered to infants at birth, 2 months, and 6 months of age or at 2 months, 4 months, and 6 months of age (CDC, Merck Sharpe & Dohme, SmithKline Beecham, unpublished data). When the vaccine is administered in four doses at 0, 1, 2, and 12 months, the last dose is necessary to ensure the highest final antibody titer.

→ When hepatitis B vaccine has been administered at the same time as other vaccines, no interference with the antibody response of the other vaccines has been demonstrated (44).

→ ✗ If the vaccination series is interrupted after the first dose, the second dose should be administered as soon as possible. The second and third doses should be separated by an interval of at least 2 months. If only the third dose is delayed, it should be administered when convenient.

The immune response when one or two doses of a vaccine produced by one manufacturer are followed by subsequent doses from a different manufacturer has been shown to be comparable with that resulting from a full course of vaccination with a single vaccine.

Larger vaccine doses or an increased number of doses are required to induce protective antibody in a high proportion of hemodialysis patients (45,46) and may also be necessary for other immunocompromised persons (e.g., those who take immunosuppressive drugs or who are HIV positive), although few data are available concerning response to higher doses of vaccine by these patients (47).

Prevaccination testing for susceptibility. Susceptibility testing is not indicated for immunization programs for children or for most adolescents because of the low rate of HBV infection and the relatively low cost of vaccine. For adults, the decision to do prevaccination testing should include an analysis of cost effectiveness because of the higher cost of the vaccine. Testing for prior infection

TABLE 1. Recommended doses of currently licensed hepatitis B vaccines

Group	Recombvax HB*		Engerix-B*	
	Dose (μ g)	(mL)	Dose (μ g)	(mL)
Infants of HBsAg ⁻ -negative mothers and children <11 years	2.5	(0.25)	10	(0.5)
Infants of HBsAg-positive mothers; prevention of perinatal infection	5	(0.5)	10	(0.5)
Children and adolescents 11-19 years	5	(0.5)	20	(1.0)
Adults ≥ 20 years	10	(1.0)	20	(1.0)
Dialysis patients and other immunocompromised persons	40	(1.0) [†]	40	(2.0) [†]

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

[†]HBsAg = Hepatitis B surface antigen.

[‡]Special formulation.

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

should be considered for adults in risk groups with high rates of HBV infection (e.g., injecting drug users, homosexual men, and household contacts of HBV carriers). The decision for testing should be based on whether the costs of testing balance the costs of vaccine saved by not vaccinating already-infected persons. Estimates of the cost effectiveness of testing depend on three variables: the cost of vaccination, the cost of testing for susceptibility, and the expected prevalence of immune persons. If susceptibility testing is being considered, careful attention should also be given to the likelihood of patient follow-up and vaccine delivery.

For routine testing, only one antibody test is necessary (antibody either to the core antigen [anti-HBc] or anti-HBs). Anti-HBc testing identifies all previously infected persons, including HBV carriers, but does not differentiate carriers and non-carriers. The presence of anti-HBs identifies previously infected persons, except for HBV carriers. Neither test has a particular advantage for groups expected to have HBV carrier rates <2%, such as health-care workers. Anti-HBc may be preferable so that unnecessary vaccination of HBV carriers can be avoided in groups with high carrier rates.

Postvaccination testing for serologic response. Such testing is not necessary after routine vaccination of infants, children, or adolescents. Testing for immunity is advised only for persons whose subsequent clinical management depends on knowledge of their immune status (e.g., infants born to HBsAg-positive mothers, dialysis patients and staff, and persons with HIV infection). Postvaccination testing should also be considered for persons at occupational risk who may have exposures from injuries with sharp instruments, because knowledge of their antibody response will aid in determining appropriate postexposure prophylaxis. When necessary, postvaccination testing should be performed from 1 to 6 months after completion of the vaccine series. Testing after immunoprophylaxis of infants born to HBsAg-positive mothers should be performed from 3 to 9 months after the completion of the vaccination series (see section on Postexposure prophylaxis).

* **Revaccination of nonresponders.** When persons who do not respond to the primary vaccine series are revaccinated, 15%-25% produce an adequate antibody response after one additional dose and 30%-50% after three additional doses (48). Therefore, revaccination with one or more additional doses should be considered for persons who do not respond to vaccination initially.

Postexposure prophylaxis

After a person has been exposed to HBV, appropriate immunoprophylactic treatment can effectively prevent infection. The mainstay of postexposure immunoprophylaxis is hepatitis B vaccine, but in some settings the addition of HBIG will provide some increase in protection. Table 2 provides a guide to recommended treatment for various HBV exposures.

Transmission of perinatal HBV infection can be effectively prevented if the HBsAg-positive mother is identified and if her infant receives appropriate immunoprophylaxis. Hepatitis B vaccination and one dose of HBIG, administered within 24 hours after birth, are 85%-95% effective in preventing both HBV infection and the chronic carrier state (4,5,8). Hepatitis B vaccine administered alone in either a

TABLE 2. Guide to postexposure immunoprophylaxis for exposure to hepatitis B virus

Type of exposure	Immunoprophylaxis	Reference
Perinatal	Vaccination + HBIG*	p. 11-12
Sexual-acute infection	HBIG ± Vaccination	Appendix
Sexual-chronic carrier	Vaccination	p. 12, 15
Household contact-chronic carrier	Vaccination	p. 12, 15
Household contact-acute case	None unless known exposure	Appendix
Household contact-acute case, known exposure	HBIG ± vaccination	Appendix
Infant (<12 months)-acute case in primary care-giver	HBIG + vaccination	Appendix
Inadvertent-percutaneous/per mucosal	Vaccination ± HBIG	Appendix

*HBIG = Hepatitis B immune globulin.

three-dose or four-dose schedule (Table 1), beginning within 24 hours after birth, is 70%-95% effective in preventing perinatal HBV infections (8,41). The infants of women admitted for delivery who have not had prenatal HBsAg testing pose problems in clinical management. Initiating hepatitis B vaccination at birth for infants born to these women will provide adequate postexposure prophylaxis if the mothers are indeed HBsAg positive. The few infections not prevented by either of these treatment regimens were most likely acquired *in utero* or may be due to very high levels of maternal HBV-DNA (49).

Serologic testing of infants who receive immunoprophylaxis to prevent perinatal infection should be considered as an aid in the long-term medical management of the few infants who become HBV carriers. Testing for anti-HBs and HBsAg at 9-15 months of age will determine the success of the therapy and, in the case of failure, will identify HBV carriers or infants who may require revaccination.

Recommendations for postexposure prophylaxis in circumstances other than the perinatal period (Table 2) have been addressed in a previous statement and are reprinted as Appendix A to this document.

Vaccine Efficacy and Booster Doses

Clinical trials of the hepatitis B vaccines licensed in the United States have shown that they are 80%-95% effective in preventing HBV infection and clinical hepatitis among susceptible children and adults (5,33,41,50). If a protective antibody response develops after vaccination, vaccine recipients are virtually 100% protected against clinical illness.

The duration of vaccine-induced immunity has been evaluated in long-term follow-up studies of both adults and children (48,51). Only the plasma-derived hepatitis B vaccine has been evaluated because it has had the longest clinical use; however, on the basis of comparable immunogenicity and short-term efficacy, similar results would be expected with recombinant vaccines. The magnitude of the antibody response induced by the primary vaccination series is predictive of antibody persistence, and a logarithmic decline of antibody levels occurs over time. Among young adults (homosexual men and Alaskan Eskimos) who initially responded to a three-dose vaccine series, loss of detectable antibody has ranged from 13% to 60% after 9 years of follow-up. For children vaccinated after the first year of life, the rate of antibody decline has been lower than for adults (51). The peak antibody titers for infants are lower than those for children immunized after 12 months of age, but the rate of antibody decline is comparable with that observed for adults in the same population.

Long-term studies of healthy adults and children indicate that immunologic memory remains intact for at least 9 years and confers protection against chronic HBV infection, even though anti-HBs levels may become low or decline below detectable levels (48,51,52). In these studies, the HBV infections were detected by the presence of anti-HBc. No episodes of clinical hepatitis were reported and HBsAg was not detected, although brief episodes of viremia may not have been detected because of infrequent testing. The mild, inapparent infections among persons who have been previously vaccinated should not produce the sequelae associated with chronic HBV infection and should provide lasting immunity. In general, follow-up studies of children vaccinated at birth to prevent perinatal HBV infection have shown that a continued high level of protection from chronic HBV infections persists at least 5 years (52,53).

For children and adults whose immune status is normal, booster doses of vaccine are not recommended, nor is serologic testing to assess antibody levels necessary. The possible need for booster doses will be assessed as additional information becomes available. For hemodialysis patients, vaccine-induced protection may be less complete and may persist only as long as antibody levels are ≥ 10 mIU/mL. For these patients, the need for booster doses should be assessed by annual antibody testing, and a booster dose should be administered when antibody levels decline to < 10 mIU/mL.

Vaccine Side Effects and Adverse Reactions

Hepatitis B vaccines have been shown to be safe when administered to both adults and children. Over 4 million adults have been vaccinated in the United States, and at least that many children have received hepatitis B vaccine worldwide.

Vaccine-associated side effects

Pain at the injection site (3%-29%) and a temperature greater than 37.7 C (1%-6%) have been among the most frequently reported side effects among adults and children receiving vaccine (5,31-33,50). In placebo-controlled studies, these side effects were reported no more frequently among vaccinees than

among persons receiving a placebo (33,50). Among children receiving both hepatitis B vaccine and DTP vaccine, these mild side effects have been observed no more frequently than among children receiving DTP vaccine alone.

Serious adverse events

In the United States, surveillance of adverse reactions has shown a possible association between Guillain-Barré syndrome (GBS) and receipt of the first dose of plasma-derived hepatitis B vaccine (54, CDC unpublished data). GBS was reported at a very low rate (0.5/100,000 vaccinees), no deaths were reported, and all reported cases were among adults. An estimated 2.5 million adults received one or more doses of recombinant hepatitis B vaccine during the period 1986-1990. Available data from reporting systems for adverse events do not indicate an association between receipt of recombinant vaccine and GBS (CDC, unpublished data).

Until recently, large-scale hepatitis B vaccination programs for infants (e.g., Taiwan, Alaska, and New Zealand) have primarily used plasma-derived hepatitis B vaccine. No association has been found between vaccination and the occurrence of severe adverse events, including seizures and GBS (55, B. McMahon and A. Milne, unpublished data). However, systematic surveillance for adverse reactions has been limited in these populations, and only a small number of children have received recombinant vaccine. Any presumed risk of adverse events possibly associated with hepatitis B vaccination must be balanced against the expected risk of acute and chronic liver disease associated with the current 5% lifetime risk of HBV infection in the United States. It is estimated that, for each U.S. birth cohort, 2,000-5,000 persons will die from HBV-related liver disease.

As hepatitis B vaccine is introduced for routine vaccination of infants, surveillance for vaccine-associated adverse events will continue to be an important part of the program in spite of the current record of safety. Any adverse event suspected to be associated with hepatitis B vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS). VAERS forms can be obtained by calling 1-800-822-7967.

RECOMMENDATIONS

Prevention of Perinatal Hepatitis B Virus Infection

1. All pregnant women should be routinely tested for HBsAg during an early prenatal visit in each pregnancy, preferably at the same time other routine prenatal laboratory testing is done. HBsAg testing should be repeated late in the pregnancy for women who are HBsAg negative but who are at high risk of HBV infection (e.g., injecting drug users, those with intercurrent sexually transmitted diseases) or who have had clinically apparent hepatitis. Tests for other HBV markers are not necessary for the purpose of maternal screening. However, HBsAg-positive women identified during screening may have HBV-related liver disease and should be evaluated (56).
2. Infants born to mothers who are HBsAg positive should receive the appropriate doses of hepatitis B vaccine (Table 1) and HBIG (0.5 mL) within 12 hours of birth. Both should be administered by intramuscular injection. Hepatitis B vaccine should be administered concurrently with HBIG but at a different site. Subsequent doses of vaccine should be administered according to the recommended schedule (Table 3).
3. Women admitted for delivery who have not had prenatal HBsAg testing should have blood drawn for testing. While test results are pending, the infant should receive hepatitis B vaccine within 12 hours of birth, in a dose appropriate for infants born to HBsAg-positive mothers (Table 1).
 - a. If the mother is later found to be HBsAg positive, her infant should receive the additional protection of HBIG as soon as possible and within 7 days of birth, although the efficacy of HBIG administered after 48 hours of age is not known (57). If HBIG has not been administered, it is important that the infant receive the second dose of hepatitis B vaccine at 1 month and not later than 2 months of age because of the high risk of infection. The last dose should be administered at age 6 months (Table 3).*

*If a four-dose schedule is used (Tables 1 and 3), the second and third doses should be administered at 1 and 2 months of age, respectively, and the fourth dose at 12-18 months of age.

- b. If the mother is found to be HBsAg negative, her infant should continue to receive hepatitis B vaccine as part of his or her routine vaccinations (Tables 3 and 4), in the dose appropriate for infants born to HBsAg-negative mothers (Table 1).
4. In populations in which screening pregnant women for HBsAg is not feasible, *all* infants should receive their first dose of hepatitis B vaccine within 12 hours of birth, their second dose at 1-2 months of age, and their third dose at 6 months of age as a part of their childhood vaccinations and well-child care (Table 3).
5. Household contacts and sex partners of HBsAg-positive women identified through prenatal screening should be vaccinated. The decision to do prevaccination testing of these contacts to determine susceptibility to HBV infection should be made according to the guidelines in the section "Prevaccination testing for susceptibility." Hepatitis B vaccine should be administered at the age-appropriate dose (Table 1) to those determined to be susceptible or judged likely to be susceptible to infection.

Universal Vaccination of Infants Born to HBsAg-Negative Mothers

1. Hepatitis B vaccination is recommended for all infants, regardless of the HBsAg status of the mother. Hepatitis B vaccine should be incorporated into vaccination schedules for children. The first dose can be administered during the newborn period, preferably before the infant is discharged

TABLE 3. Recommended schedule of hepatitis B immunoprophylaxis to prevent perinatal transmission of hepatitis B virus infection

Infant born to mother known to be HBsAg* positive	
Vaccine dose [†]	Age of infant
First	Birth (within 12 hours)
HBIG [‡]	Birth (within 12 hours)
Second	1 month
Third	6 months [§]
Infant born to mother not screened for HBsAg	
Vaccine dose**	Age of infant
First	Birth (within 12 hours)
HBIG [‡]	If mother is found to be HBsAg positive, administer dose to infant as soon as possible, not later than 1 week after birth
Second	1-2 months [¶]
Third	6 months [§]

*HBsAg = Hepatitis B surface antigen.

[†]See Table 1 for appropriate vaccine dose.

[‡]Hepatitis B immune globulin (HBIG)—0.5 mL administered intramuscularly at a site different from that used for vaccine.

[§]If four-dose schedule (Engerix-B) is used, the third dose is administered at 2 months of age and the fourth dose at 12-18 months.

**First dose = dose for infant of HBsAg-positive mother (see Table 1). If mother is found to be HBsAg positive, continue that dose; if mother is found to be HBsAg negative, use appropriate dose from Table 1.

[¶]Infants of women who are HBsAg negative can be vaccinated at 2 months of age.

TABLE 4. Recommended schedules of hepatitis B vaccination for infants born to HBsAg*-negative mothers

Hepatitis B vaccine	Age of infant
Option 1	
Dose 1	Birth—before hospital discharge
Dose 2	1-2 months [†]
Dose 3	6-18 months [‡]
Option 2	
Dose 1	1-2 months [†]
Dose 2	4 months [†]
Dose 3	6-18 months [‡]

*HBsAg = Hepatitis B surface antigen.

[†]Hepatitis B vaccine can be administered simultaneously with diphtheria-tetanus-pertussis, *Haemophilus influenzae* type b conjugate, measles-mumps-rubella, and oral polio vaccines at the same visit.

from the hospital, but no later than when the infant is 2 months of age (Table 4). Because the highest titers of anti-HBs are achieved when the last two doses of vaccine are spaced at least 4 months apart, schedules that achieve this spacing may be preferable (Table 4). However, schedules with 2-month intervals between doses, which conform to schedules for other childhood vaccines, have been shown to produce a good antibody response (Table 4) and may be appropriate in populations in which it is difficult to ensure that infants will be brought back for all their vaccinations. The development of combination vaccines containing HBsAg may lead to other schedules that will allow optimal use of combined antigens.

2. Special efforts should be made to ensure that high levels of hepatitis B vaccination are achieved in populations in which HBV infection occurs at high rates among children (Alaskan Natives, Pacific Islanders, and infants of immigrants from countries in which HBV is endemic).

Vaccination of Adolescents

All adolescents at high risk of infection because they are injecting drug users or have multiple sex partners (more than one partner/6 months) should receive hepatitis B vaccine. Widespread use of hepatitis B vaccine is encouraged. Because risk factors are often not identified directly among adolescents, universal hepatitis B vaccination of teenagers should be implemented in communities where injecting drug use, pregnancy among teenagers, and/or sexually transmitted diseases are common. Adolescents can be vaccinated in school-based clinics, community health centers, family planning clinics, clinics for the treatment of sexually transmitted diseases, and special adolescent clinics.

The 0-, 1-, and 6-month schedule is preferred for vaccinating adolescents with the age-appropriate dose of vaccine (Table 1). However, the choice of vaccination schedule should take into account the feasibility of delivering three doses of vaccine over a given period of time. The use of alternate schedules (e.g., 0, 2, and 4 months) may be advisable to achieve complete vaccination.

Vaccination of Selected High-Risk Groups

Efforts to vaccinate persons at high risk of HBV infection should follow the vaccine doses shown in Table 1. High-risk groups for whom vaccination is recommended include:

1. **Persons with occupational risk.** HBV infection is an occupational hazard for health-care workers and for public-safety workers who have exposure to blood in the workplace (24,58). The risk of acquiring HBV infections from occupational exposures depends on the frequency of percutaneous and permucosal exposure to blood or blood-contaminated body fluids. Any health-care or public-safety worker may be at risk for HBV exposure, depending on the tasks he or she performs. Workers who perform tasks involving contact with blood or blood-contaminated body fluid should be vaccinated (24,58,59). For public-safety workers whose exposure to blood is infrequent, timely postexposure prophylaxis should be considered rather than routine preexposure vaccination.

For persons in health-care fields, vaccination should be completed during training in schools of medicine, dentistry, nursing, laboratory technology, and other allied health professions, before trainees have their first contact with blood.

2. **Clients and staff of institutions for the developmentally disabled.** Susceptible clients in institutions for the developmentally disabled, as well as staff who work closely with clients, should be vaccinated. Susceptible clients and staff who live or work in smaller residential settings with known HBV carriers should also receive hepatitis B vaccine. Clients discharged from residential institutions into community programs should be screened for HBsAg so that appropriate measures can be taken to prevent HBV transmission. These measures should include both environmental controls and appropriate use of vaccine.

Staff of nonresidential day-care programs for the developmentally disabled (e.g., schools, sheltered workshops) attended by known HBV carriers have a risk of infection comparable with that of health-care workers and therefore should be vaccinated (60). The risk of infection for other clients appears to be lower than the risk for staff. Vaccination of clients in day care programs may be considered. Vaccination of classroom contacts is strongly encouraged if a classmate who is an HBV carrier behaves aggressively or has special medical problems (e.g., exudative dermatitis, open skin lesions) that increase the risk of exposure to his or her blood or serous secretions.

3. **Hemodialysis patients.** Hepatitis B vaccination is recommended for susceptible hemodialysis patients. Vaccinating patients early in the course of their renal disease is encouraged because patients with uremia who are vaccinated before they require dialysis are more likely to respond to the vaccine (61). Although their seroconversion rates and anti-HBs titers are lower than those of healthy persons, patients who respond to vaccination will be protected from infection, and the need for frequent serologic testing will be reduced (62).
4. **Recipients of certain blood products.** Patients who receive clotting-factor concentrates have an increased risk of HBV infection and should be vaccinated as soon as their specific clotting disorder is identified. Prevacination testing is recommended for patients who have already received multiple infusions of these products.
5. **Household contacts and sex partners of HBV carriers.** All household and sexual contacts of persons identified as HBsAg positive should be vaccinated. The decision to do prevaccination testing to determine susceptibility to HBV infection should be made according to the guidelines described earlier in the section "Prevaccination testing for susceptibility." Hepatitis B vaccine should be administered at the age-appropriate dose (Table 1) to those determined to be susceptible or judged likely to be susceptible to infection.
6. **Adoptees from countries where HBV infection is endemic.** Adopted or fostered orphans or unaccompanied minors from countries where HBV infection is endemic should be screened for HBsAg (3). If the children are HBsAg positive, other family members should be vaccinated (63).
7. **International travelers.** Vaccination should be considered for persons who plan to spend more than 6 months in areas with high rates of HBV infection and who will have close contact with the local population. Short-term travelers who are likely to have contact with blood (e.g., in a medical setting) or sexual contact with residents of areas with high or intermediate levels of endemic disease should be vaccinated. Vaccination should begin at least 6 months before travel to allow for completion of the full vaccine series, although a partial series will offer some protection. The alternate four-dose schedule (see Table 1) should provide protection if the first three doses can be delivered before departure.
8. **Injecting drug users.** All injecting drug users who are susceptible to HBV should be vaccinated as soon as their drug use begins. Because of the high rate of HBV infection in this population, prevaccination screening should be considered as outlined in the section "Prevaccination testing for susceptibility." Injecting drug users known to have HIV infection should be tested for anti-HBs response after completion of the vaccine series. Those who do not respond to vaccination should be counseled accordingly.
9. **Sexually active homosexual and bisexual men.** Susceptible sexually active homosexual and bisexual men should be vaccinated. Because of the high rate of HBV infection in this population, prevaccination screening should be considered as described in the section "Prevaccination testing for susceptibility." Men known to have HIV infection should be tested for anti-HBs response after completion of the vaccine series. Those who do not respond to vaccination should be counseled accordingly.
10. **Sexually active heterosexual men and women.** Vaccination is recommended for men and women who are diagnosed as having recently acquired other sexually transmitted diseases, for prostitutes, and for persons who have a history of sexual activity with more than one partner in the previous 6 months (2). Most patients seen in clinics for sexually transmitted diseases should be considered candidates for vaccination.
11. **Inmates of long-term correctional facilities.** Prison officials should consider undertaking screening and vaccination programs directed at inmates with histories of high-risk behaviors.

EVOLVING ISSUES IN HEPATITIS B IMMUNIZATION PROGRAMS

Hepatitis B vaccine has now been used extensively throughout the world and is currently being incorporated into the Expanded Programme on Immunization of the World Health Organization (16). New information, vaccines, and technology will have implications for this effort, and adjustments and changes are expected to occur over the years. Some of the issues that can be expected to be addressed in clinical and operational studies include the following:

1. In most developing countries with hepatitis B immunization programs, the first dose of vaccine is administered to all infants soon after birth to prevent perinatal infections; pregnant women are

not screened for HBsAg; and HBIG is not used (8,16,45). The feasibility and effectiveness of incorporating this approach into the hepatitis B prevention strategy for the United States must be evaluated.

2. Booster doses of hepatitis B vaccine have not been recommended because of the persistence of protective efficacy 9 years after vaccination (48,51). The duration of protective efficacy for adolescents who were vaccinated during infancy or childhood must be evaluated; the results will determine future recommendations concerning booster doses.
3. Flexible dosage schedules are required to effectively integrate hepatitis B vaccine into current and future immunization programs for infants. Schedules may change as optimum dosage and timing are studied and new information becomes available.
4. Multiple-antigen vaccines that incorporate HBsAg as one component are currently being evaluated. The routine use of these vaccines may alter childhood vaccination schedules or may result in the administration of additional doses of certain antigens. However, these vaccines should greatly facilitate vaccine delivery and minimize the number of injections.

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APPENDIX A

Postexposure Prophylaxis for Hepatitis B

Adapted from: CDC. Protection against viral hepatitis: recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR* 1990;39(No.RR-2):17-22.

INTRODUCTION

Prophylactic treatment to prevent infection after exposure to HBV should be considered in the following situations: perinatal exposure of an infant born to an HBsAg-positive mother, inadvertent percutaneous or permucosal exposure to HBsAg-positive blood, sexual exposure to an HBsAg-positive person, and household exposure of an infant <12 months of age to a primary care-giver who has acute hepatitis B.

Various studies have established the relative efficacies of HBIG and/or hepatitis B vaccine in different exposure situations. For an infant with perinatal exposure to an HBsAg-positive and HBeAg-positive mother, a regimen combining one dose of HBIG at birth with the hepatitis B vaccine series started soon after birth is 85%-95% effective in preventing development of the HBV carrier state (A1-A3). Regimens involving either multiple doses of HBIG alone or the vaccine series alone have 70%-90% efficacy (A4,A5).

For inadvertent percutaneous exposure, only regimens including HBIG and/or immune globulin (IG) have been studied. A regimen of two doses of HBIG, one given after exposure and one a month later, is about 75% effective in preventing hepatitis B in this setting (A6,A7). For sexual exposure to a person with acute hepatitis B, a single dose of HBIG is 75% effective if administered within 2 weeks of last sexual exposure (A8). The efficacy of IG for postexposure prophylaxis is uncertain; IG no longer has a role in postexposure prophylaxis of hepatitis B because of the availability of HBIG and the wider use of hepatitis B vaccine.

Recommendations on postexposure prophylaxis are based on available efficacy data and on the likelihood of future HBV exposure for the person requiring treatment. In all exposures, a regimen combining HBIG with hepatitis B vaccine will provide both short- and long-term protection, will be less costly than the two-dose HBIG treatment alone, and is the treatment of choice.

Acute Exposure to Blood that Contains (or Might Contain) HBsAg

For inadvertent percutaneous (needlestick, laceration, or bite) or permucosal (ocular or mucous-membrane) exposure to blood, the decision to provide prophylaxis must include consideration of several factors: a) whether the source of the blood is available; b) the HBsAg status of the source; and c) the hepatitis B vaccination and vaccine-response status of the exposed person. Such exposures usually affect persons for whom hepatitis B vaccine is recommended. For any exposure of a person not previously vaccinated, hepatitis B vaccination is recommended.

After any such exposure, a blood sample should be obtained from the person who was the source of the exposure and should be tested for HBsAg. The hepatitis B vaccination status and anti-HBs response status (if known) of the exposed person should be reviewed. The outline below and Table A1 summarize prophylaxis for percutaneous or permucosal exposure to blood according to the HBsAg status of the source of exposure and the vaccination status and vaccine response of the exposed person. For greatest effectiveness, passive prophylaxis with HBIG, when indicated, should be administered as soon as possible after exposure since its value beyond 7 days after exposure is unclear.

1. Source of exposure known and HBsAg positive

- a. Exposed person has not been vaccinated or has not completed vaccination. Hepatitis B vaccination should be initiated. A single dose of HBIG (0.06 mL/kg) should be administered as soon as possible after exposure and within 24 hours, if possible. The first dose of hepatitis B vaccine should be administered intramuscularly at a separate site (deltoid for adults) and can be administered simultaneously with HBIG or within 7 days of exposure; subsequent doses should be administered as recommended for the specific vaccine. If the exposed person has begun but has not completed vaccination, one dose of HBIG should be administered immediately and vaccination should be completed as scheduled.

- b. Exposed person has already been vaccinated against hepatitis B, and anti-HBs response status is known.
- (1) If the exposed person is known to have had adequate response in the past, the anti-HBs level should be tested unless an adequate level has been demonstrated within the last 24 months. Although current data show that vaccine-induced protection does not decrease as antibody level wanes, most experts consider the following approach to be prudent:
 - (a) If the anti-HBs level is adequate, no treatment is necessary.
 - (b) If the anti-HBs level is inadequate,* a booster dose of hepatitis B vaccine should be administered.
 - (2) If the exposed person is known not to have responded to the primary vaccine series, he or she should receive either a single dose of HBIG and a dose of hepatitis B vaccine as soon as possible after exposure, or two doses of HBIG (0.06 mL/kg), one as soon as possible after exposure and the second 1 month later. The latter treatment is preferred for those who have not responded to at least four doses of vaccine.
- c. Exposed person has already been vaccinated against hepatitis B, and the anti-HBs response is unknown. The exposed person should be tested for anti-HBs.
- (1) If the exposed person has adequate antibody, no additional treatment is necessary.
 - (2) If the exposed person has inadequate antibody on testing, one dose of HBIG (0.06 mL/kg) should be administered immediately and a standard booster dose of vaccine administered at a different site.
2. Source of exposure known and HBsAg-negative
- a. Exposed person has not been vaccinated or has not completed vaccination. If unvaccinated, the exposed person should be administered the first dose of hepatitis B vaccine within 7 days of exposure, and vaccination should be completed as recommended. If the exposed person has not completed vaccination, vaccination series should be completed as scheduled.
 - b. Exposed person has already been vaccinated against hepatitis B. No treatment is necessary.
3. Source of exposure unknown or not available for testing.
- a. Exposed person has not been vaccinated or has not completed vaccination. If unvaccinated, the exposed person should be administered the first dose of hepatitis B vaccine within 7 days of

*An adequate antibody level is ≥ 10 mIU/mL.

TABLE A1. Recommendations for hepatitis B prophylaxis following percutaneous exposure

Exposed person	Treatment when source is found to be		Unknown or not tested
	HBsAg positive	HBsAg negative	
Unvaccinated	Administer HBIG x 1* and initiate hepatitis B vaccine†	Initiate hepatitis B vaccine†	Initiate hepatitis B vaccine†
Previously vaccinated			
Known responder	Test exposed person for anti-HBs 1. If adequate, no treatment 2. If inadequate, hepatitis B vaccine booster dose	No treatment	No treatment
Known non-responder	HBIG x 2 or HBIG x 1, plus 1 dose of hepatitis B vaccine	No treatment	If known high-risk source, may treat as if source were HBsAg positive
Response unknown	Test exposed person for anti-HBs† 1. If inadequate, HBIG x 1, plus hepatitis B vaccine booster dose 2. If adequate, no treatment	No treatment	Test exposed person for anti-HBs† 1. If inadequate, hepatitis B vaccine booster dose 2. If adequate, no treatment

*Hepatitis B immune globulin (HBIG) dose 0.06 mL/kg intramuscularly.

†Hepatitis B vaccine dose—see Table 1.

exposure and vaccination should be completed as recommended. If the exposed person has not completed vaccination, vaccination should be completed as scheduled.

- b. Exposed person has already been vaccinated against hepatitis B, and anti-HBs response status is known.
 - (1) If the exposed person is known to have had adequate response in the past, no treatment is necessary.
 - (2) If the exposed person is known not to have responded to the vaccine, prophylaxis as described earlier in section 1.b.(2) under "Source of exposure known and HBsAg-positive" may be considered if the source of the exposure is known to be at high risk of HBV infection.
- c. Exposed person has already been vaccinated against hepatitis B, and the anti-HBs response is unknown. The exposed person should be tested for anti-HBs.
 - (1) If the exposed person has adequate anti-HBs, no treatment is necessary.
 - (2) If the exposed person has inadequate anti-HBs, a standard booster dose of vaccine should be administered.

Sex Partners of Persons with Acute Hepatitis B Virus Infection

Sex partners of HBsAg-positive persons are at increased risk of acquiring HBV infection, and HBIG has been shown to be 75% effective in preventing such infections (A8). Because data are limited, the period after sexual exposure during which HBIG is effective is unknown, but extrapolation from other settings makes it unlikely that this period would exceed 14 days. Before treatment, testing sex partners for susceptibility is recommended if it does not delay treatment beyond 14 days after last exposure. Testing for anti-HBc is the most efficient prescreening procedure to use in this population.

All susceptible persons whose sex partners have acute hepatitis B infection should receive a single dose of HBIG (0.06 mL/kg) and should begin the hepatitis B vaccine series if prophylaxis can be started within 14 days of the last sexual contact or if sexual contact with the infected person will continue. Administering the vaccine with HBIG may improve the efficacy of postexposure treatment. The vaccine has the added advantage of conferring long-lasting protection.

An alternate treatment for persons who are not from a high-risk group for whom vaccine is routinely recommended and whose regular sex partners have acute HBV infection is to administer one dose of HBIG (without vaccine) and retest the sex partner for HBsAg 3 months later. No further treatment is necessary if the sex partner becomes HBsAg negative. If the sex partner remains HBsAg positive, a second dose of HBIG should be given and the hepatitis B vaccine series started.

Household Contacts of Persons with Acute Hepatitis B Virus Infection

Since infants have close contact with primary care-givers and they have a higher risk of becoming HBV carriers after acute HBV infection, prophylaxis of an infant less than 12 months of age with HBIG (0.5 mL) and hepatitis B vaccine is indicated if the mother or primary care-giver has acute HBV infection. Prophylaxis for other household contacts of persons with acute HBV infection is not indicated unless they have had identifiable blood exposure to the index patient, such as by sharing toothbrushes or razors. Such exposures should be treated like sexual exposures. If the index patient becomes an HBV carrier, all household contacts should receive hepatitis B vaccine.

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Hepa s



Hepatitis B is a serious disease caused by a virus that attacks the liver. The virus, which is called hepatitis B virus (HBV), can cause lifelong infection, cirrhosis (scarring) of the liver, liver cancer, liver failure, and death.

Who is at risk?

Hepatitis B can affect anyone. Each year in the United States, more than 200,000 people of all ages get hepatitis B and close to 5,000 die of sickness caused by HBV. If you have had other forms of hepatitis, you can still get hepatitis B.

Get vaccinated!
Hepatitis B
is preventable.

How great is your risk for hepatitis B?

One out of 20 people in the United States will get hepatitis B some time during their lives. Your risk is higher if you

- have sex with someone infected with HBV
- have sex with more than one partner
- are a man and have sex with a man
- live in the same house with someone who has lifelong HBV infection
- have a job that involves contact with human blood
- shoot drugs
- are a patient or work in a home for the developmentally disabled
- have hemophilia
- travel to areas where hepatitis B is common

Your risk is also higher if your parents were born in Southeast Asia, Africa, the Amazon Basin in South America, the Pacific Islands, and the Middle East.

If you are at risk for HBV infection, ask your health care provider about hepatitis B vaccine.



All babies, beginning at birth, should get hepatitis B vaccine.

How do you get hepatitis B?

You get hepatitis B by direct contact with the blood or body fluids of an infected person; for example, you can become infected by having sex or sharing needles with an infected person. A baby can get hepatitis B from an infected mother during childbirth.

Hepatitis B is not spread through food or water or by casual contact.

Who is a carrier of hepatitis B virus?

Sometimes, people who are infected with HBV never recover fully from the infection; they carry the virus and can infect others for the rest of their lives. In the United States, about one million people carry HBV.

How do you know if you have hepatitis B?

You may have hepatitis B (and be spreading the disease) and not know it; sometimes a person with HBV infection has no symptoms at all.

If you have symptoms

- your eyes or skin may turn yellow
- you may lose your appetite
- you may have nausea, vomiting, fever, stomach or joint pain
- you may feel extremely tired and not be able to work for weeks or months

Is there a cure for hepatitis B?

There is no cure for hepatitis B; this is why prevention is so important. Hepatitis B vaccine is the best protection against HBV. Three doses are needed for complete protection.



If vaccine was never given, children 11-12 years of age should get hepatitis B vaccine.

If you are pregnant, should you worry about hepatitis B?

If you have HBV in your blood, you can give hepatitis B to your baby. Babies who get HBV at birth may have the virus for the rest of their lives, can spread the disease, and can get cirrhosis of the liver or liver cancer.



All pregnant women should be tested for HBV early in their pregnancy. If the blood test is positive, the baby should receive vaccine along with another shot, hepatitis B immune globulin (called H-BIG), at birth. The vaccine series should be completed during the first 6 months of life.

Who should get vaccinated?

- » All babies, at birth
- » All children 11-12 years of age who have not been vaccinated
- » Persons of any age whose behavior puts them at high risk for HBV Infection
- » Persons whose jobs expose them to human blood

For information on viral hepatitis call:

Hepatitis Hotline at 1-888-4HEPCDC (1-888-443-7232)

or write:

Hepatitis Branch
Division of Viral and Rickettsial Diseases
National Center for Infectious Diseases
Centers for Disease Control and Prevention
Atlanta, GA 30333

or access:

<http://www.cdc.gov/ncidod/diseases/hepatitis/hepatitis.htm>

Internet Address

Revised - August 1997



**NATIONAL
LESBIAN
GAY HEALTH
CONFERENCE**

and
**16th NATIONAL
AIDS/HIV FORUM
JULY 25-29, 1998**

MEMORANDUM

CONF- 6/98-NLGA
- San Fran

TO: TODD A SUMMERS
FROM: Beverly Saunders Biddle, Executive Director
DATE: June 30, 1998

We have received your registration for the 20th National Lesbian and Gay Health Conference, and 16th National AIDS/HIV Forum. You are now registered to attend the Conference which will be held July 25-29, 1998 at the Hyatt Regency Embarcadero Center, in San Francisco.

Please retain this letter as proof of your registration.

Confirmation Number: 359
Registration: \$0.00
Membership: \$0.00
Scholarship Contribution: \$0.00
Total Amount Paid: \$0.00

Payment: Credit Card*: 0 Check: 0
(*If payment was by credit card, your receipt will be attached below.)

Thank you for your registration and we look forward to seeing you in San Francisco.



The National Lesbian &
Gay Health Association

Legacy of Leadership

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