

# Epidemiology of hepatitis B

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An estimated 200 000 to 300 000 hepatitis B virus infections occur annually in the United States. With acute infection, symptoms develop in fewer than 5% of infants, 5 to 15% of children between the ages of 1 and 5 years and 33 to 50% of older children and adults. However, the risk of chronic infection after acute infection is inversely proportional to age. The risk of chronic infection is highest for infants who acquire infection during the perinatal period (70 to 90%), lower for children younger than 5 years (20 to 50%) and lowest for older children and adults (5 to 10%). Therefore although only approximately 8% of acute infections in the United States occur in children younger than 10 years, these infections account for 20 to 30% of all chronic infections. Children usually acquire infection from infected mothers at the time of birth or from infected household contacts. The risk of hepatitis B virus transmission between children in day-care centers and schools is very low. Among adults and adolescents sexual activity and injecting drug use are the most common risks for acquisition of infection, yet at least 30% of reported hepatitis B among adults cannot be associated with an identifiable risk factor. Because chronic hepatitis B virus infection is associated with long term consequences of cirrhosis and primary hepatocellular carcinoma, prevention of chronic infection is the most important reason for vaccination against hepatitis B. Routine infant immunization is the most feasible, cost-effective means to control hepatitis B virus transmission.

## INTRODUCTION

Infection with the hepatitis B virus (HBV) results in acute illness with symptoms ranging from none or mild to severe hepatitis, liver failure and death. After

acute HBV infection many people clear the virus and develop lifelong immunity; however, chronic infection will develop in some people. Infants and young children who acquire HBV infection are at highest risk of chronic infection and therefore at greatest risk of eventual cirrhosis and primary hepatocellular carcinoma (PHC). Persons with chronic infection are also an important source of infection for others. Therefore although prevention of symptomatic acute HBV infection is important (and prevents deaths that occur occasionally from fulminant hepatitis associated with acute infection), the major reason for vaccination against HBV infection is prevention of chronic infection and its serious consequences.

This paper will review three aspects of the epidemiology of hepatitis B: (1) the incidence of the disease, based upon cases reported to the Centers for Disease Control and Prevention (CDC); (2) the modes of transmission of HBV and the outcomes of infection at different ages; and (3) the experience, both successful and unsuccessful, with various hepatitis B vaccination strategies that has led the CDC and other groups to recommend routine infant immunization, along with universal screening of pregnant women for HBV infection, as the most feasible approach to control HBV transmission in the United States (United States).

## INCIDENCE OF HEPATITIS B

Approximately 300 000 new HBV infections occur each year in the United States, 33 to 50% of which are symptomatic (Fig. 1).<sup>1</sup> An estimated 18 000 to 30 000 new chronic infections result each year from these acute infections. Persons with chronic infection play a crucial role in the epidemiology of HBV infection for two reasons: (1) they are at risk of the chronic complications of HBV infection, including chronic hepatitis, cirrhosis and PHC; and (2) they serve as a source of infection to other individuals. Each year in the United States approximately 6000 people die from the chronic consequences of HBV infection.

In the United States hepatitis B is largely a disease of young adults. The rate of reported cases is highest for persons between the ages of 20 and 39 years (Fig. 2).<sup>2</sup> Rates among children younger than 15 years are relatively low; however, because infection in this age

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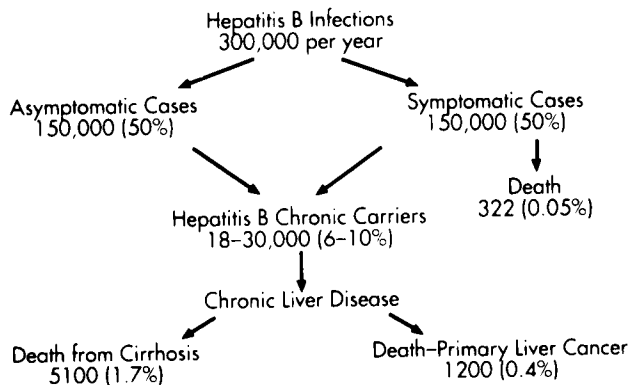


FIG. 1. Outcome of hepatitis B infections in the United States, 1987 estimates. Source: CDC.

group is often asymptomatic and therefore not detected through disease surveillance, the rate of infection is higher than reflected from reported cases.

Sexual transmission accounts for a large proportion of cases reported to the CDC. Based upon data from the Sentinel Counties Studies, in 1991 41% of reported cases were associated with heterosexual activity (including sexual contact with infected persons or with multiple partners); an additional 14% of cases were associated with a history of homosexual behavior. Approximately 12% of persons with hepatitis B had a history of injecting drug use. Hepatitis B cases among household contacts of infected persons and among health care workers account for a relatively small proportion (fewer than 5% each) of reported cases.

Although hepatitis B vaccine has been available since 1982, it has had a limited impact on the incidence of acute hepatitis B.<sup>3</sup> In fact the estimated incidence of the disease in 1990 was greater than in the late 1970s, before vaccine was available (Fig. 3). The decrease in incidence in recent years since the peak of 1986 is thought to be caused predominantly by changes in behavior in response to the acquired immunodeficiency syndrome epidemic, including reductions in high risk sexual behavior and injecting drug use.<sup>3</sup>

#### ACQUISITION OF ACUTE AND CHRONIC HBV INFECTION

The development of symptoms with acute HBV infection is directly related to age. With acute infection, symptoms develop in fewer than 5% of infants, 5 to 15% of children between the ages of 1 and 5 years and 33 to 50% of older children and adults.<sup>4</sup>

The development of chronic infection after acute HBV infection is inversely related to age. The risk of chronic infection is highest (70 to 90%) for infants who acquire infection during the perinatal period, lower (20 to 50%) for children younger than 5 years and lowest (5 to 10%) for older children and adults

<sup>4</sup> CDC, unpublished data.

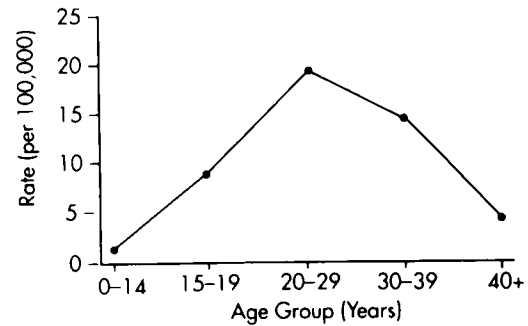


FIG. 2. Rate of reported hepatitis B by age group. United States, 1990. Source: CDC.

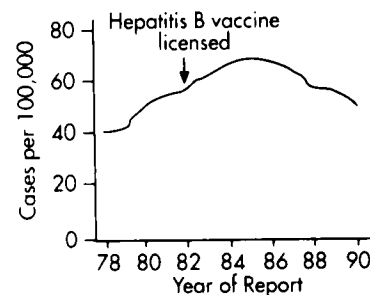


FIG. 3. Estimated incidence of acute hepatitis B. United States, 1978 to 1990. Source: CDC.

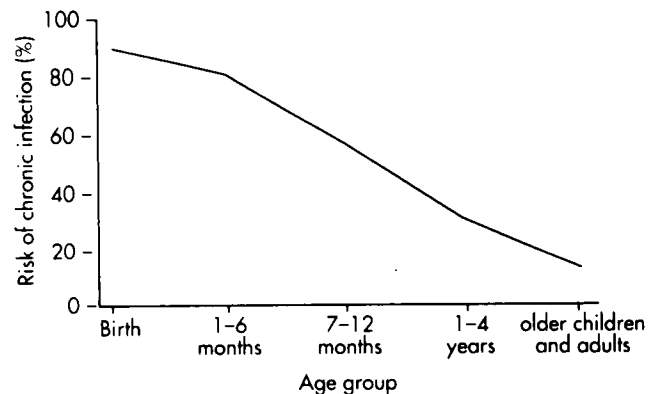


FIG. 4. Risk of chronic hepatitis B virus infection by age group.

(Fig. 4).<sup>4</sup> Therefore although only about 8% of acute infections in the United States occur between birth and 10 years of age, infection during this age period accounts for approximately one-third of all chronic infections.<sup>1</sup> Thus a vaccination strategy targeted at adolescents and adults would fail to prevent many chronic infections.

The risk of PHC or cirrhosis is related to the length of time that a person has chronic infection. Infants who become chronically infected have an estimated 25% lifetime risk of cirrhosis or PHC.<sup>5</sup> In comparison adults who acquire chronic HBV infection have an estimated 15% lifetime risk.

#### HBV TRANSMISSION

**General routes of transmission.** Potential routes of HBV transmission are determined by the body

fluids in which the virus is found in infected individuals. HBV is present in high concentrations in blood, serum and serous exudates and in moderate concentrations in semen, vaginal fluid and saliva.<sup>6, 7</sup> Therefore blood exposure and sexual contact are relatively efficient modes of transmission. HBV has also been detected in low concentrations in feces and breast milk; however, these fluids have not been associated with transmission.<sup>8, 9</sup>

Three types of exposure account for most HBV transmission: (1) exposure to maternal blood during the perinatal period, resulting in mother-to-infant transmission; (2) exposure to blood and blood-derived body fluids through inadvertent needle sticks (health care workers), needles shared among injecting drug users and open wounds (household contacts); and (3) exposure to semen and vaginal secretions via heterosexual or homosexual contact.

**Routes of transmission among infants and children.** Perinatal exposure to maternal blood is the most efficient mode of HBV transmission. During the perinatal period infants are exposed to maternal blood through placental tears, trauma related to birth and contact of conjunctiva and mucous membranes with blood and other fluids during labor and delivery. If mothers are acutely or chronically infected with HBV, their infants are at risk of acquiring HBV infection through these exposures. Infants born to mothers who are positive for hepatitis B e antigen (a marker associated with high circulating titers of virus) have a risk as high as 70 to 90% of acquiring HBV infection during the perinatal period.<sup>10, 11</sup> HBV can also be transmitted to the fetus during the gestational period, but this is not believed to be a major route of transmission.

Among infants who do not acquire infection at birth, almost 40% of infants born to mothers who are hepatitis B e antigen-positive will become infected before the age of 5 years (if they are not vaccinated) because of continued close contact with the mother and other infected persons within the household.<sup>12</sup>

Other settings for HBV transmission among children are listed in Table 1. Person-to-person transmission can occur horizontally from infected household contacts (either adults or other children) through exposure to infected blood or body fluids via bites, scratches or skin lesions. Several studies among southeast Asian immigrant communities in the United States have shown that, even if there is no identified HBV-infected persons in the immediate family,

children are still at risk of infection, perhaps from extended family members who visit only periodically.<sup>13, 14</sup>

Other children at high risk for HBV infection include patients treated in hemodialysis centers, where environmental transmission can occur; hemophiliacs and other children who receive large numbers of blood transfusions; and residents of institutions for the developmentally disabled.

Children adopted from areas where HBV infection is endemic, who may have acquired infection during infancy or early childhood, are a potential source of HBV infection for contacts in their adoptive families.<sup>15</sup> It is therefore recommended that all children adopted from countries where HBV infection is endemic be screened for infection and that family contacts be immunized if the children are found to be infected.<sup>16</sup>

In the United States HBV transmission to other children and staff from HBV carriers in schools and day-care centers has only rarely been observed.<sup>17, 18</sup> Therefore if an HBV-infected child does not have a medical condition that might facilitate transmission, such as exudative dermatitis, or does not exhibit aggressive behavior, such as biting that breaks the skin, then he or she can be admitted to a day-care center or school without restriction.

As children reach adolescence predominant risk factors for acquisition of hepatitis B are similar to those that are observed among adult age groups. Of hepatitis B cases among adolescents with a known source for their infection, 50% can be attributed to sexual contact and 47% to injecting drug use.\*

#### EVOLUTION OF HEPATITIS B VACCINATION STRATEGIES

Knowledge about hepatitis B risk groups formed the basis for recommendations for use of hepatitis B vaccine when it was first introduced in 1982. Initial recommendations called for vaccination of high risk groups, including household and sexual contacts of persons infected with HBV, men with a history of homosexual activity, injecting drug users, hemodialysis patients, hemophiliacs and persons with multiple sexual partners. When studies demonstrated the postexposure efficacy of hepatitis B vaccine and hepatitis B immunoglobulin in preventing infection in infants born to HBV-infected mothers, additional recommendations were introduced for hepatitis B surface antigen (HBsAg) screening of pregnant women to identify infants requiring prophylaxis. Later other studies showed that selective screening of women in high risk groups failed to recognize many infected women; therefore universal screening of all pregnant women was recommended in 1988.<sup>19</sup> This strategy has been shown to be cost-effective compared with other routine perinatal and neonatal screening programs.<sup>20</sup>

**TABLE 1.** Settings of hepatitis B virus transmission among infants and children

Mother-to-infant transmission at birth
Person-to-person contact within the household
Extended family in selected populations
Institutions for the developmentally disabled
High risk groups (e.g. hemodialysis and hemophiliac patients)
Adolescents with high risk behavior

Experience with targeting high risk groups for hepatitis B vaccination has shown that this strategy has not had a major impact on hepatitis B rates.<sup>3</sup> The difficulties in accessing and vaccinating adults in high risk groups are illustrated by results of an intensive vaccination campaign carried out in Worcester, MA, during the mid-1980s. In 1985 an outbreak of hepatitis B associated with delta virus infection occurred in this community, predominantly among injecting drug users and their sexual contacts, resulting in many cases of hepatitis B and several deaths caused by fulminant hepatitis.<sup>21</sup> In response to the outbreak an outreach program to drug treatment programs, jails and other settings was initiated, which offered prevaccination testing and hepatitis B vaccine. Although many injecting drug users and their sexual contacts were identified and screened, a large percentage were already infected with HBV. Moreover although the vaccine was offered free to susceptible persons and intensive follow-up was done, only 15% of the drug users and 22% of their sexual contacts eventually received a full series of three vaccine doses (G. Schatz, personal communication).

This experience illustrates several disadvantages associated with a high risk group hepatitis B vaccination strategy: (1) persons at high risk of HBV infection may already be infected by the age they are reached through vaccination programs; (2) persons at risk for hepatitis B, including drug users and persons with multiple sex partners, are difficult to access since many do not routinely seek health care; (3) in contrast to vaccination programs for infants, programs that routinely access adolescents and adults do not exist.

#### CURRENT RECOMMENDATIONS FOR VACCINATION AGAINST HBV INFECTION

Several important considerations have led to the development of a comprehensive strategy for the elimination of hepatitis B virus transmission which is founded on routine infant immunization with hepatitis B vaccine: (1) appreciation of the difficulty of accessing high risk groups; (2) realization that as many as 30% of persons with hepatitis B do not have identifiable risk factors and therefore would be missed by a high risk group strategy; (3) studies showing the high risk of infection in certain populations, such as southeast Asian immigrant communities; (4) knowledge that infants can be reached through already established vaccination delivery systems before they reach an age of high risk of infection; (5) accumulated data and experience showing that the vaccine confers long term protection against disease,<sup>22, 23</sup> indicating that vaccination during infancy will probably protect through adolescence and beyond; (6) the high cost of the adult dose of vaccine compared with the infant dose; and (7) studies showing that a strategy of routine infant immunization is cost-effective.<sup>24, \*</sup>

The comprehensive strategy for elimination of HBV transmission, as recommended by the CDC, the American Academy of Pediatrics and the Academy of Family Physicians, includes: (1) screening of all pregnant women for HBsAg, immunoprophylaxis of infants born to HBsAg-positive mothers and immunization of susceptible sexual and household contacts of HBsAg-positive women identified through prenatal screening; (2) routine immunization of all infants born to HBsAg-negative mothers, integrated with other childhood immunizations; (3) vaccination of adolescents and adults in high risk groups.<sup>25, 26</sup> Continued screening of pregnant women for HBsAg is necessary because perinatal HBV transmission cannot be eliminated until routine infant immunization is implemented, with all infants being vaccinated starting at birth. HBsAg screening of pregnant women has the additional benefit of providing a method to identify household and sexual contacts of women identified as HBsAg-positive and screening and vaccinating them to prevent HBV infection. Continued vaccination of adolescents and adults in high risk groups will prevent infection in those individuals who can be reached. Eventually as birth cohorts who are vaccinated reach adolescence and older ages, vaccination of household and sexual contacts and vaccination of adolescents and adults in high risk groups will not be necessary.

#### CONCLUSION

Hepatitis B vaccination strategies targeted to high risk groups have had limited impact in reducing the incidence of hepatitis B and in preventing infection during childhood. Because of the difficulties in accessing and vaccinating persons in high risk groups, a comprehensive strategy involving routine infant immunization with hepatitis B vaccine has been recommended by immunization advisory groups. With this strategy eventually all persons will be vaccinated against HBV infection, and transmission of HBV, with its serious consequences, can be eliminated.

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