

Hepatitis B and C



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KEYWORDS

- Hepatitis B • Hepatitis C • Sustained virologic response • Pegylated interferon
- Direct-acting antiviral agents • Spontaneous viral clearance

KEY POINTS

- The disease burden for both hepatitis B virus (HBV) and hepatitis C virus (HCV) infection in the pediatric population is high because most infected children acquire the virus via maternal fetal transmission.
- Without spontaneous viral clearance or indications to treat, most HBV-infected and HCV-infected children will become adults with chronic viral hepatitis and liver disease.
- The treatment goal for HCV infection is to achieve a sustained virologic response (ie, sustained viral clearance). The treatment goal for HBV infection is to achieve a functional cure, meaning that circulating markers of viral infection are negative but there may be residual covalently closed circular (ccc) HBV DNA in the liver.
- Successful antiviral treatment in adults with HBV and HCV infection gives promise to guide therapy in children; however, there are differences between adults and children with these infections, including in natural history, pharmacokinetics, responses to therapy, and short-term and long-term adverse effects of antiviral agents.
- Apart from antiviral therapies, prevention of these diseases is important because transmission largely occurs during the perinatal period.

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Viral hepatitis has been a global health concern and economic burden for the past century. Hepatitis B virus (HBV) and hepatitis C virus (HCV) are the most common causes of chronic viral hepatitis in the United States, as well as worldwide. However, the presentation depends on the type of virus and the age of the patients. Children with HBV rarely have acute severe hepatitis. Most children with HBV and HCV are asymptomatic during childhood but are at risk for developing cirrhosis and hepatocellular carcinoma (HCC) in adulthood. In this article, human immunodeficiency virus (HIV) coinfection is not discussed in depth.

HEPATITIS B VIRUS

Epidemiology and Natural History

The number of cases of chronic HBV (CHB) infection has been estimated at almost 400 million worldwide (~5% of world's population). HBV has 8 genotypes (A–H) which are associated with moderate differences in response to therapy.¹ Children with CHB (genotypes B and C) have a high frequency of hepatitis B envelope antigen (HBeAg) positivity and high HBV DNA levels compared with those with other genotypes. The timing of HBeAg seroconversion in genotype C is more delayed compared with genotype B. Genotype C results in more aggressive hepatitis and is associated with an increased risk of HCC.² However, the development of HCC was associated with genotype B in a Taiwanese pediatric study.² The prevalence of CHB infection in pregnant women in urban areas of the United States varies by race and ethnicity.³ Although the highest rate was observed in Asian women (6%), the rates in black, white, and Hispanic women were 1, 0.6%, and 0.14%, respectively.

Maternal-fetal transmission is currently the most common route of HBV transmission because meticulous screening for HBV has been performed in individuals receiving transfusion of blood products. Perinatal transmission occurs at or close to the time of birth as a result of exposure to maternal blood and cervical secretions. Transplacental transmission is presumably responsible for perinatal infections, depending on risk factors, including maternal HBeAg positivity, hepatitis B surface antigen (HBsAg) titer, and HBV DNA level.⁴ Infants born to mothers positive for HBeAg and mothers with very high serum DNA levels ($\geq 10^9$ copies per mL) are at risk for acquiring HBV despite receiving active and passive immunization within 24 hours postpartum.^{5–7} Transplacental transmission can occur due to leakage, such as during a threatened abortion. Amniocentesis in HBsAg-positive mothers can be another risk of HBV transmission.⁸ Although HBsAg and HBV DNA can be detected in the colostrum and breast milk of HBV-infected mothers, several studies have shown that there is no additional risk of transmission of HBV to breast-fed infants of infected mothers, provided that completed active and passive immunoprophylaxis is received.^{9,10}

Wang and colleagues¹¹ compared outcomes among 3 groups of infants of HBsAg-positive mothers: 144 born by spontaneous vaginal delivery, 40 by forceps or vacuum extraction, and 117 by cesarean section, all of whom received the HBV vaccine and the hepatitis B immunoglobulin (HBIG). Because the response rates to recommended passive and active immunoprophylaxis were similar in all groups, in the 1-year-old infants, hepatitis B surface antibody (anti-HBs) was detected in 78.9% of the infants born by normal vaginal delivery, 84.6% by forceps or vacuum extraction, and 86.4% by cesarean section, with CHB incidence of 7.3%, 7.7%, and 6.8%, respectively. The mode of delivery does not likely influence HBV transmission. A higher incidence of low birth weight and prematurity has been reported in infants born to mothers infected with HBV compared with those born to uninfected mothers.¹²

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