

# Chapter 2

## Hepatitis B Overview



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# HEPATITIS B OVERVIEW

## Hepatitis B Virus

The hepatitis B virus (HBV) belongs to the Hepadnaviridae family and is known to cause both acute and chronic infections in humans. The virus is found in the blood and certain body fluids (serum, semen, saliva, and vaginal secretions) of people infected. It is relatively stable and has been shown to remain infectious on environmental surfaces for more than seven days at room temperature. It is a small, round, enveloped virus with partially double-stranded circular Deoxyribonucleic Acid (DNA) and is highly infectious; the CDC has stated that it is 50 to 100 times more infectious than the Human Immunodeficiency Virus (HIV). There are nine serotypes and eight genotypes of HBV recognized worldwide.

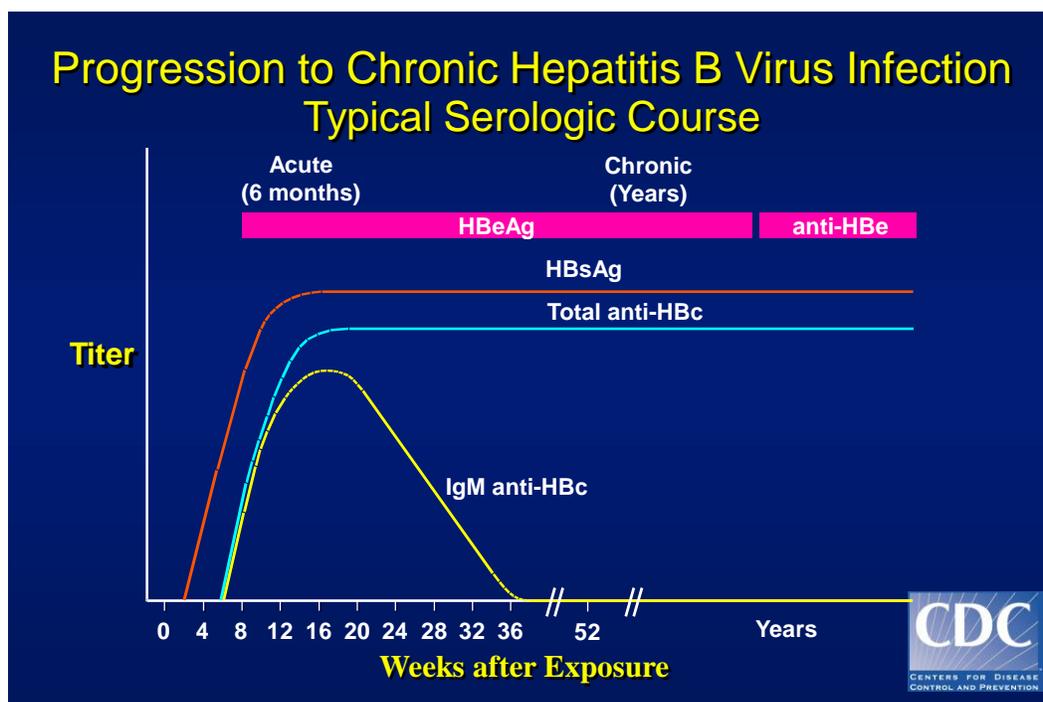
## HBV Infection

HBV infection is a major cause of acute and chronic hepatitis, cirrhosis of the liver, and liver cancer. It is the most prevalent chronic infectious disease in the world, a common cause of morbidity and mortality worldwide, and a major health problem in the US. The World Health Organization (WHO) estimates that two billion people have been infected worldwide with the hepatitis B virus. Two hundred and forty million of those remain chronically infected while more than 780,000 people die every year due to the consequences of the virus.

The highest hepatitis B infection rates are found in sub-Saharan Africa and East Asia; most of whom become infected during childhood. Five to ten percent of the adult population in these areas are chronically infected. Liver cancer caused by hepatitis B is among the top three causes of cancer related death in men and a major cause of cancer in women in these regions. In the US, an estimated 700,000 – 1.4 million people are living with chronic hepatitis B infection.

After exposure, HBV is transported by the bloodstream to the liver, which is the primary site of viral replication. Infection in adults is generally self-limited, meaning the immune system is able to eliminate the virus from the blood and provide lasting immunity against reinfection in about 95 percent of cases. The remainder of adults whose immune system does not eliminate the virus, develops a chronic, lifelong infection. A person with chronic hepatitis B is defined by the CDC as someone with HBsAg present in their bloodstream for greater than six months with continuing viral replication and persistent viremia (Figure 1). These “chronic carriers” are capable of transmitting the virus to other individuals who are unprotected.

Figure 1. Progression to Chronic Hepatitis B Virus Infection Typical Serologic Course



## HBV Lab Tests

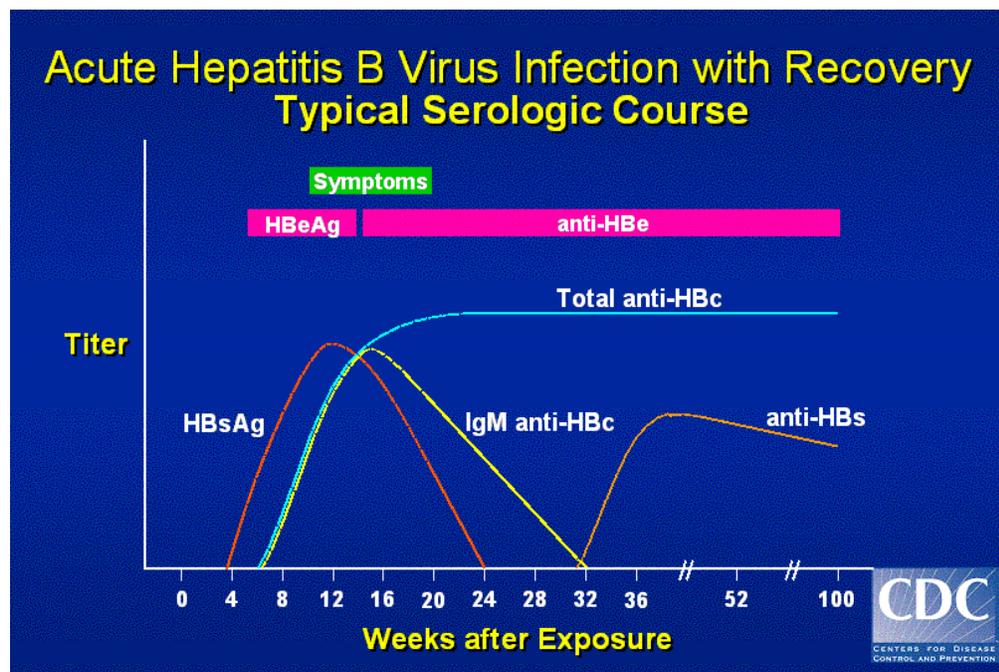
There are several approved laboratory tests available for hepatitis B. The main uses for these tests would be to determine whether a patient's signs and symptoms are due to HBV infection, to diagnose and monitor chronic infection, and to detect previous exposure to the virus. Testing can also be done to:

- screen for infection in at-risk populations or blood donors;
- to determine carrier status; and
- screen for immunity due to vaccination or prior infection.

There are several antigenic components of the virus that can result in a variety of positive laboratory tests (Figure 2).

The HBsAg is found on the surface of the virus and can be identified in serum samples 30 to 60 days after exposure to the virus. This component of the virus is not infectious; however, when present in the blood, it does indicate that the complete virus is present, and the person infected may transmit the virus to others. Once the immune system detects the HBsAg component of the virus due to natural infection or vaccination, it begins to develop antibodies (anti-HBs). The presence of anti-HBs in the serum indicates immunity to the virus. Anti-HBs is also referred to as hepatitis B surface antibody (HBsAb) which can easily be confused with the HBsAg.

**Figure 2. Acute Hepatitis B Virus Infection with Recovery Typical Serologic Course**



### Communicability

Persons with either acute or chronic HBV infection should be considered potentially infectious. When symptoms are present in persons with acute HBV infection, HBsAg can be found in blood and body fluids for one to two months before and after onset of symptoms.

### Clinical Manifestations

The clinical manifestations of acute HBV infection are age dependent. Infants, children younger than ten years of age, and immunosuppressed adults with newly acquired HBV infection are usually asymptomatic (no symptoms); about 30 - 50 percent of adults show symptoms of infection. Because infected persons are often asymptomatic, they are generally unaware that they are infected, resulting in inadvertent transmission to others. When symptoms occur, they are not specific to hepatitis B; therefore, laboratory testing is required to distinguish HBV from other diseases.

### Signs and Symptoms

The incubation period for HBV infection ranges from 60 to 150 days (average of 90 days). The preicteric (before jaundice), or prodromal phase, usually lasts from three to ten days from initial onset of symptoms to jaundice. Symptoms of this phase may include, but are not limited to:

- malaise
- anorexia
- nausea
- vomiting
- fever
- headache
- myalgia
- skin rashes
- arthralgia
- arthritis
- dark urine starting one to two days before the onset of jaundice
- right upper quadrant abdominal pain

The icteric (jaundice) phase is variable but usually lasts one to three weeks. It is characterized by yellowing of the skin, mucous membranes and conjunctiva; light or gray stools; hepatic tenderness, and hepatomegaly (liver enlargement). During convalescence, malaise and fatigue may persist for weeks or months as the other signs and symptoms disappear.

## **Treatment**

No specific treatment exists for acute hepatitis B; supportive care is the mainstay of therapy.

Persons who have chronic HBV infection require medical evaluation and regular monitoring. Therapeutic agents approved by the Food and Drug Administration (FDA) for treatment of chronic hepatitis B can achieve sustained suppression of HBV replication and remission of liver disease in some persons. Patients interested in treatment should seek a referral from their physician to a gastroenterologist, hepatologist, or an infectious disease specialist.

For more information on acute and chronic HBV infections, please consult The Red Book: Report of the Committee on Infectious Diseases (30th Edition) or visit <http://www.cdc.gov/hepatitis/HBV/>.

## **Complications**

The complications of chronic infection include chronic hepatitis, cirrhosis, liver failure, and hepatocellular carcinoma. Persons with chronic HBV infection are at a much higher risk of hepatocellular carcinoma than non-carriers. Approximately 25 percent of persons who become chronically infected die prematurely from cirrhosis or hepatocellular carcinoma. This means that approximately, 3,000 to 4,000 people die each year of HBV-related cirrhosis and approximately 1,000 to 1,500 people die each year from HBV-related liver cancer in the US. HBV infection is estimated to be the cause of 80 percent of hepatocellular carcinoma worldwide.

Generally speaking, the complications that arise are typically associated with chronic HBV infections. However, in a small number of cases, acute infections can result in fulminate hepatic failure and death. Fulminant hepatitis, occurs in about one to two percent of acutely infected persons with mortality rates of 0.5 – 1 percent; although it is suspected to be higher in acutely infected infants. About 200 to 300 Americans die each year of fulminant disease.

## **Epidemiology**

### **Reservoir**

The natural host for the hepatitis B virus is humans. The virus is not known to naturally infect animals, although some non-human primates have been infected under laboratory conditions.

### **Transmission**

The hepatitis B virus is transmitted by parenteral or mucosal exposure to HBsAg-positive body fluids or tissues from persons who have acute or chronic HBV infection.

Parenteral exposure routes include, but are not limited to:

- intravenous (IV) drug use;
- shared razor;
- accidental needle sticks or sharps injuries;
- contaminated multi-dose vials or medical equipment; or
- other breaches of blood-borne pathogen infection control practices.

Mucosal exposure can occur:

- during birth;
- sexual contact;
- accidental blood splash to the eyes or mouth;
- shared household products (i.e., toothbrush); and
- other routes when appropriate barrier precautions are not taken.

The highest concentrations of virus are in blood, serous fluids, and wound exudates; lower titers are found in other fluids, such as saliva and semen. Saliva can be a vehicle of transmission through bites; however, other types of exposure to saliva, including kissing, are unlikely modes of transmission. There appears to be no transmission of HBV via tears, sweat, urine, stool, or droplet nuclei. (Table 1)

**Table 1. Concentration of Hepatitis B Virus in Various Body Fluids**

High	Moderate	Low / Non-detectable
<p><b>Blood</b> <b>Serum</b> <b>Wound exudates</b></p>	<p><b>Semen</b> <b>Vaginal fluid</b> <b>Saliva</b></p>	<p><b>Urine</b> <b>Feces</b> <b>Sweat</b> <b>Tears</b> <b>Breast milk</b></p>

As previously mentioned, HBV infection can also be transmitted through sexual contact, either heterosexual or homosexual, with an infected person. It is thought that transmission occurs among men who have sex with men (MSM), possibly via contamination from asymptomatic rectal mucosal lesions. Fecal-oral transmission does not appear to occur. Transmission in the healthcare setting, long term care facilities, and in the home health setting due to breaches in infection control practices are well described.

Because HBV can survive for more than seven days on environmental surfaces at room temperature, indirect inoculation of HBV can occur via inanimate objects. A ten percent bleach and water solution is recommended to decontaminate a surface after a blood spill.

### **Perinatal Transmission**

Transmission of HBV from mother to infant during the perinatal period represents one of the most efficient modes of HBV infection. The risk of perinatal transmission is directly related to the viral load of the mother. The hepatitis B 'little e' antigen (HBeAg) marker is a commonly

used indicator of active viral replication and thus high viral load. The absence of HBeAg is generally associated with a low viral load, and thus a lower likelihood of transmission to the infant. However, approximately 20 - 30 percent of the chronic infections in the US are due to a variant of HBV call a “pre-core mutant.” This variant of the virus does not produce e-antigen while replicating yet may have a viral load somewhere in between the e-antigen positive and e-antigen negative cases. Using molecular technology, the HBV viral load can be directly measured and quantified.

For a newborn infant whose mother is positive for both HBsAg and HBeAg, the risk for chronic HBV infection is 70 - 90 percent by age six months in the absence of PEP (HBIG and hepatitis B vaccine). On the contrary, if the mother is HBsAg-positive but HBeAg-negative, the risk for chronic infection is less than 10 percent in the absence of PEP.

The exact mechanism of transmission remains unclear, although the mode of delivery (vaginal versus C-section) does not appear to have an impact on the risk of perinatal HBV infection. Infection during pregnancy can occur during the intrauterine, or intrapartum (delivery) periods; however, HBV transmission mainly occurs during delivery. Intrauterine (in utero) transmission is relatively rare, accounting for fewer than two percent of perinatal infections in most studies. Hepatitis B viral DNA and HBsAg have been detected in amniotic fluid, placental cells, and vaginal secretions of HBsAg-positive women during pregnancy and in cord blood of their neonates. Postpartum transmission through exposure to infectious maternal saliva, stool, or urine is quite rare.

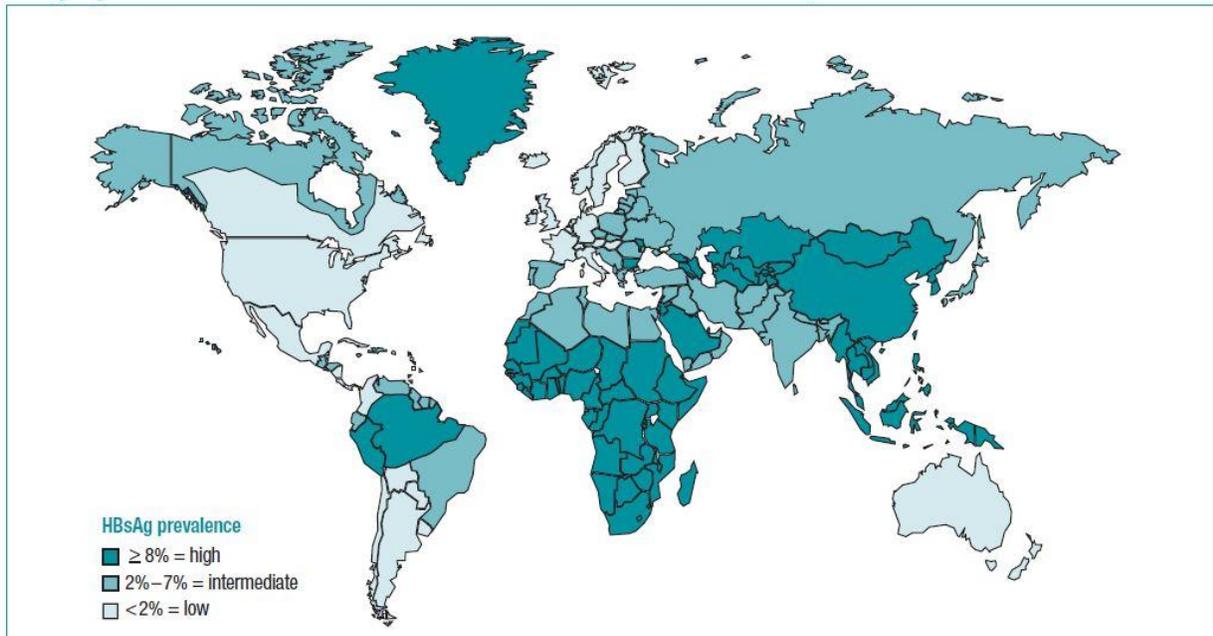
It has been thought that breastfeeding serves as an additional mechanism by which infants may acquire HBV infection. Although trace amounts of HBsAg have been found in breast milk, research strongly suggests that any risk of transmission associated with breast milk is negligible compared to the high risk of exposure to maternal blood and fluids at birth. Because there is no evidence that breastfeeding from an HBV infected mother poses an additional risk to the infant, even without immunization, both the CDC and WHO state that it is safe for an infected woman to breastfeed her child because the benefits outweigh the risks. All mothers who breastfeed should take good care of their nipples to avoid cracking and bleeding.

### **Other Risk Factors Associated with Hepatitis B**

- People born in Asia, Africa, and other regions with moderate or high rates of hepatitis B (Figure 3)
- Unvaccinated people whose parents are from regions with high rates of hepatitis B
- Anyone having sex with a person infected with hepatitis B
- People who live with someone with hepatitis B
- Men who have sexual encounters with other men (MSM)
- People who inject drugs
- People with HIV infection
- People on hemodialysis
- Healthcare workers

**Figure 3. Geographic Distribution of Chronic HBV Infection**

**Geographic Distribution of Chronic HBV Infection — Worldwide, 2006\***



\* For multiple countries, estimates of prevalence of hepatitis B surface antigen (HBsAg), a marker of chronic HBV infection, are based on limited data and might not reflect current prevalence in countries that have implemented childhood hepatitis B vaccination. In addition, HBsAg prevalence might vary within countries by subpopulation and locality.

Source: CDC. Travellers' Health; Yellow Book. <http://www.cdc.gov/travel/yellowbookch4-HepB.aspx>.

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