

# Appendix C

## Serology Interpretation



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## **Hepatitis B Antigens and Markers**

### **1) Hepatitis B DNA (HBV DNA)**

HBV DNA is one of the first tests that can be detected in the bloodstream after initial infection. It can be detected as early as one week after infection. The amount of HBV DNA in the patient's blood indicates how fast the virus is replicating within the liver. This test measures the patient's viral load. High viral loads indicate rapid viral replication while low or undetectable levels indicate inactive infections. Tests for HBV DNA are not performed as a standard test and are generally only used as indicators of disease progression, suitability for therapy, and research purposes.

### **2) HBV-DNA genotype**

HBV DNA genotype testing identifies which of the genetic strains of hepatitis B virus a patient is infected with. It is most often used to predict or monitor therapy, detect mutations, or in epidemiologic investigations to assess transmission linkages.

### **3) Hepatitis B Surface Antigen (HBsAg)**

HBsAg is found on the surface of the virus and can be identified about 30 - 60 days after exposure to the virus. The surface antigen component of the virus is not infectious, however, it does indicate that the virus is present and can be transmitted to others. HBsAg testing is the current standard to indicate current infection with hepatitis B. If HBsAg is present for more than six months this generally indicates a chronic infection.

### **4) Hepatitis B 'little e' Antigen (HBeAg or 'e' antigen)**

HBeAg is contained within the core of the virus rather than on the surface. When the virus replicates, HBeAg is produced in excess. The 'little e' antigen is only detectable when the hepatitis B virus is actively reproducing. HBeAg indicates high infectivity due to the active replication of the virus and indicates a greater risk of progression to liver disease. HBeAg and HBsAg are generally detectable at the same time; however, HBeAg disappears before HBsAg.

There are mutant strains of HBV exist that replicate without producing HBeAg. In many cases, infection with these mutant strains is more aggressive than HBe producing strains.

### **5) Hepatitis B 'little e' Antibody (anti-HBe)**

Antibodies to HBeAg only become detectable when the HBeAg is no longer presence indicating that there is no active viral replication. Serology that is anti-HBe positive would indicate low infectivity.

### **6) Hepatitis B Core Antigen (HBcAg)**

The core antigen (HBcAg) is a viral protein that is produced and contained within the infected hepatocyte and is the most antigenic component of the virus. It does not freely

circulate in a detectable amount within the blood, therefore, there is no specific lab test to detect the core antigen. However, it can be detected in the sample of liver cells taken after a liver biopsy. Because of the antigenicity of the core antigen, the immune system does produce antibodies to HBcAg (anti-HBc) that are detectable.

### 7) Hepatitis B Core Antibody (anti-HBc)

Anti-HBc positive serum indicates that the individual has been infected with the hepatitis B virus at some point, but it is not possible to determine when that infection occurred. Any individual that has been infected with the virus will test positive for anti-HBc; it will remain positive for life.

### 8) Hepatitis B Immunoglobulin M (IgM anti-HBc)

IgM anti-HBc is detectable around six to eight weeks after infection occurs and indicates acute infection. It is generally not detectable after six months, and therefore generally indicates a recent infection. This is the best serologic marker of acute HBV infection.

### 9) Hepatitis B Surface Antibody (anti-HBs)

This is a protective antibody. The presence of anti-HBs following a known acute infection indicates recovery and immunity against reinfection. Anti-HBs can also be acquired as an immune response to hepatitis B vaccine indicating that the individual adequately responded to the vaccine and is protected from infection.

Figure 1. Acute Hepatitis B Virus Infection with Recovery

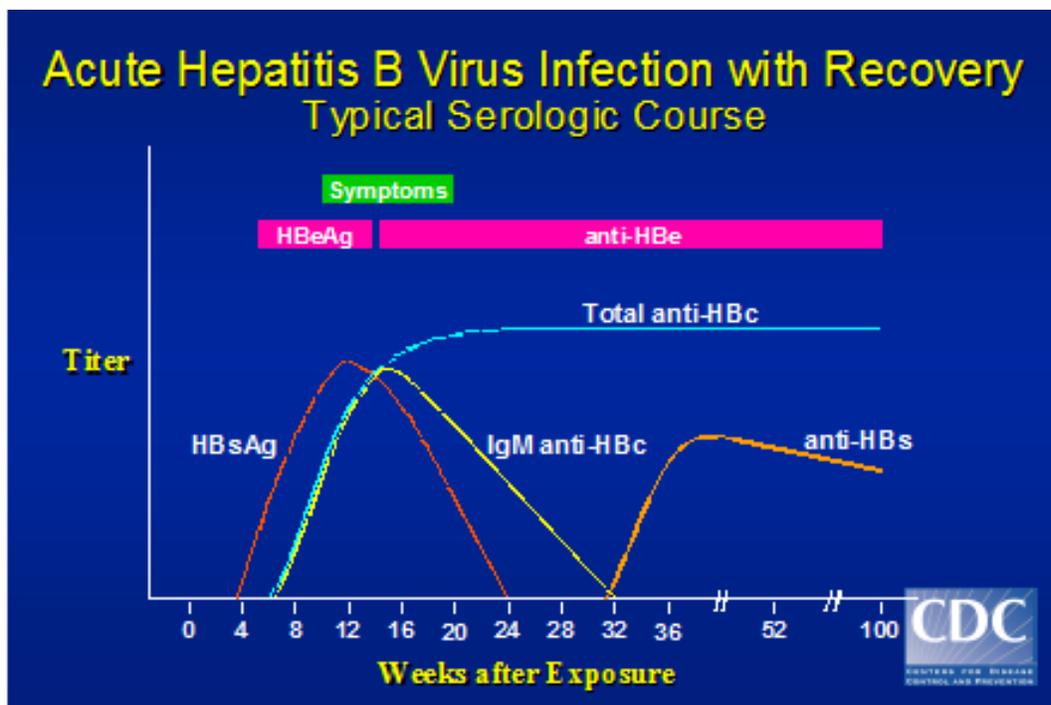
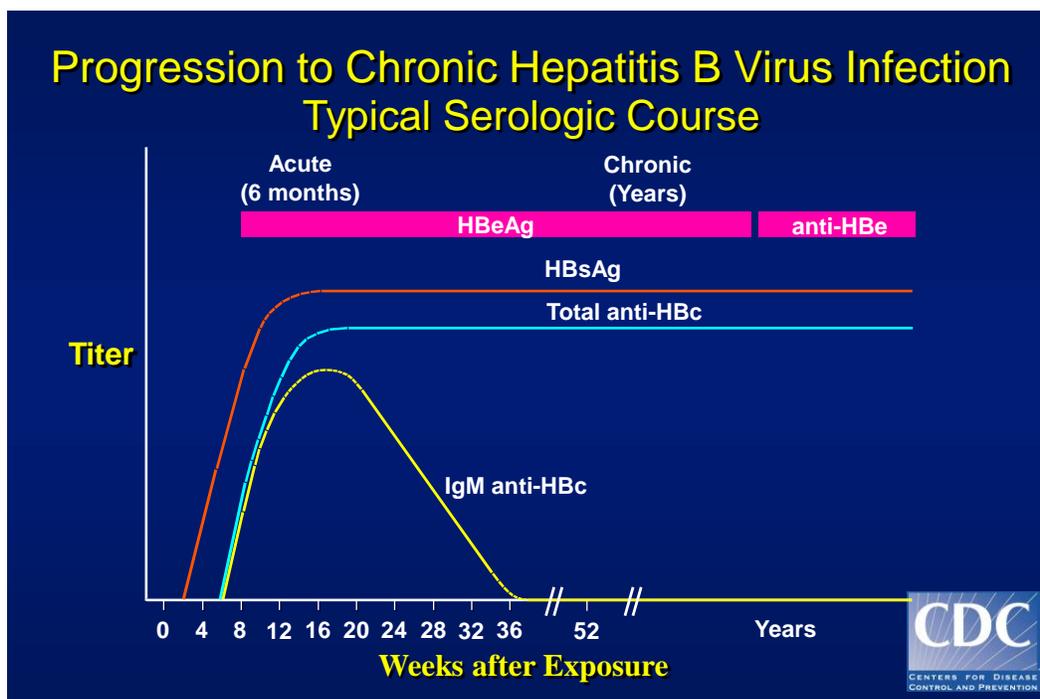


Figure 2. Progression to Chronic Hepatitis B Virus Infection



### Interpretation of Post-Vaccination Serologic Testing and Action for Infants

HBsAg	Anti-HBs	Interpretation and Necessary Action
-	+	The infant is immune to HBV. Case management services are considered complete.
-	-	The infant is NOT immune to hepatitis B. The infant <b>must</b> receive a <b>second</b> series of hepatitis B vaccine. The first dose of the second series should be given as soon as post-vaccination serology results are known and follow the 0, 1, and 6 month schedule. The infant should be tested again for HBsAg and anti-HBs (PVST), 1 - 2 months after completion of the second series. These infants will receive a total of at least six doses of hepatitis B vaccine.
+	-	The vaccination effort failed. The infant is infected with HBV ( <b>perinatal hepatitis B infection</b> ) and is likely to become a chronic carrier. All confirmed cases of perinatal hepatitis B virus infection should be reported to the state through the NEDSS as soon as they are identified and to the perinatal hepatitis B coordinator through the submission of the <i>Infant case Management form</i> along with a copy of the laboratory report. Refer the child for clinical follow-up. Case management services are considered complete.  <b>Note:</b> The surveillance case definition for perinatal hepatitis B virus infection is HBsAg positivity in any infant aged 1 - 24 months who was born in the US or in US territories to an HBsAg-positive mother.

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# Interpretation of Hepatitis B Serologic Test Results

Hepatitis B serologic testing involves measurement of several hepatitis B virus (HBV)-specific antigens and antibodies. Different serologic “markers” or combinations of markers are used to identify different phases of HBV infection and to determine whether a patient has acute or chronic HBV infection, is immune to HBV as a result of prior infection or vaccination, or is susceptible to infection.

Tests	Results	Interpretation
HBsAg anti-HBc anti-HBs	negative negative negative	Susceptible
HBsAg anti-HBc anti-HBs	negative positive positive	Immune due to natural infection
HBsAg anti-HBc anti-HBs	negative negative positive	Immune due to hepatitis B vaccination
HBsAg anti-HBc IgM anti-HBc anti-HBs	positive positive positive negative	Acutely infected
HBsAg anti-HBc IgM anti-HBc anti-HBs	positive positive negative negative	Chronically infected
HBsAg anti-HBc anti-HBs	negative positive negative	Interpretation unclear; four possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. “Low level” chronic infection 4. Resolving acute infection

**Adapted from:** A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. Part I: Immunization of Infants, Children, and Adolescents. MMWR 2005;54(No. RR-16).



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[www.cdc.gov/hepatitis](http://www.cdc.gov/hepatitis)

## ■ Hepatitis B surface antigen (HBsAg):

A protein on the surface of hepatitis B virus; it can be detected in high levels in serum during acute or chronic hepatitis B virus infection. The presence of HBsAg indicates that the person is infectious. The body normally produces antibodies to HBsAg as part of the normal immune response to infection. HBsAg is the antigen used to make hepatitis B vaccine.

## ■ Hepatitis B surface antibody (anti-HBs):

The presence of anti-HBs is generally interpreted as indicating recovery and immunity from hepatitis B virus infection. Anti-HBs also develops in a person who has been successfully vaccinated against hepatitis B.

## ■ Total hepatitis B core antibody (anti-HBc):

Appears at the onset of symptoms in acute hepatitis B and persists for life. The presence of anti-HBc indicates previous or ongoing infection with hepatitis B virus in an undefined time frame.

## ■ IgM antibody to hepatitis B core antigen (IgM anti-HBc):

Positivity indicates recent infection with hepatitis B virus ( $\leq 6$  mos). Its presence indicates acute infection.

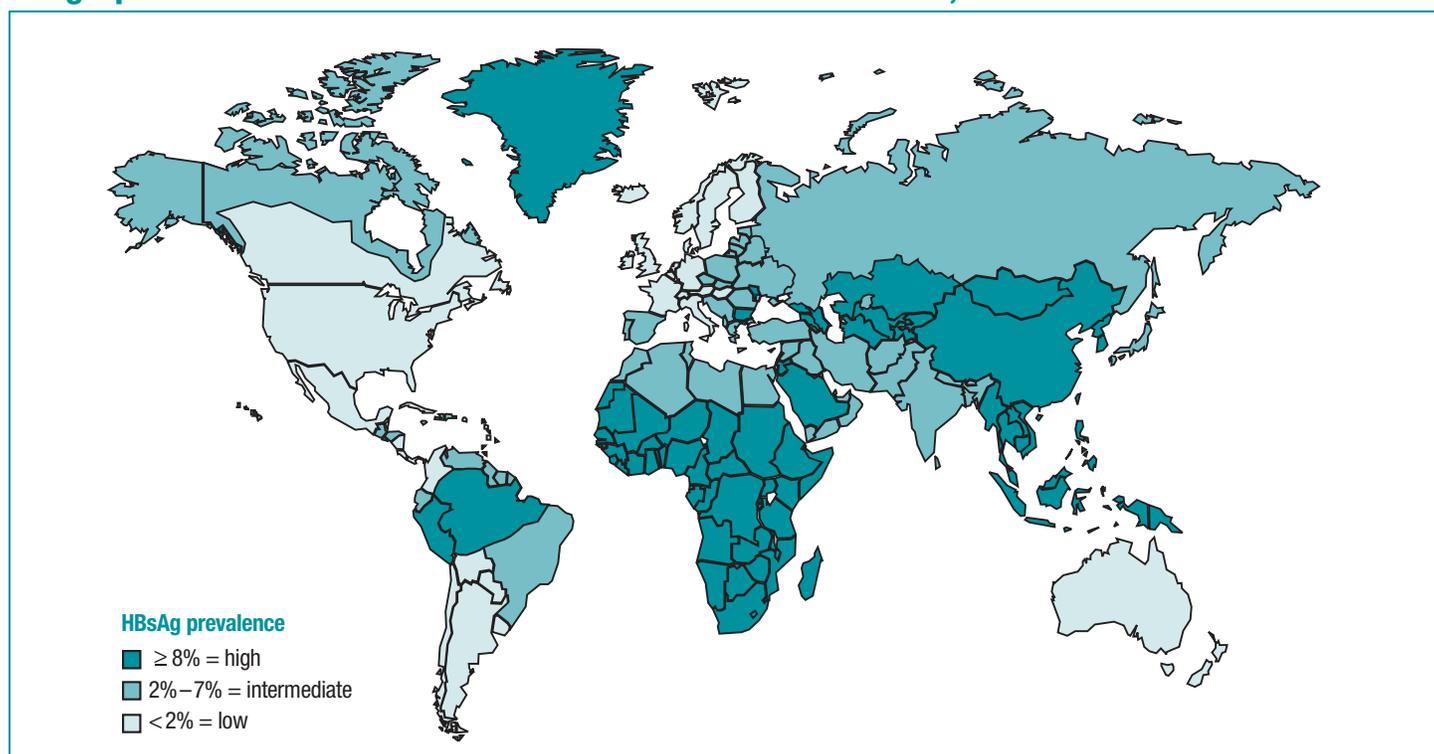
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# Recommendations for Routine Testing and Follow-up for Chronic Hepatitis B Virus (HBV) Infection

Population	Recommendation	
	Testing	Vaccination/Follow-up
Persons born in regions of high and intermediate HBV endemicity (HBsAg prevalence $\geq 2\%$ )	Test for HBsAg, regardless of vaccination status in their country of origin, including <ul style="list-style-type: none"> <li>– immigrants</li> <li>– refugees</li> <li>– asylum seekers</li> <li>– internationally adopted children</li> </ul>	If HBsAg-positive, refer for medical management. If negative, assess for on-going risk for hepatitis B and vaccinate if indicated.
US born persons not vaccinated as infants whose parents were born in regions with high HBV endemicity ( $\geq 8\%$ )	Test for HBsAg regardless of maternal HBsAg status if not vaccinated as infants in the United States.	If HBsAg-positive, refer for medical management. If negative, assess for on-going risk for hepatitis B and vaccinate if indicated.

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## 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>.

## Routine Testing and Follow-up for Chronic HBV Infection (continued)

Population	Recommendation	
	Testing	Vaccination/Follow-up
Injection-drug users	Test for HBsAg, as well as for anti-HBc or anti-HBs to identify susceptible persons.	First vaccine dose should be given at the same visit as testing. Susceptible persons should complete a 3-dose hepatitis B vaccine series to prevent infection from ongoing exposure.
Men who have sex with men	Test for HBsAg, as well as for anti-HBc or anti-HBs to identify susceptible persons.	First vaccine dose should be given at the same visit as testing. Susceptible persons should complete a 3-dose hepatitis B vaccine series to prevent infection from ongoing exposure.
Persons needing immunosuppressive therapy, including chemotherapy, immunosuppression related to organ transplantation, and immunosuppression for rheumatologic or gastroenterologic disorders	Test for all markers of HBV infection (HBsAg, anti-HBc, and anti-HBs).	Treat persons who are HBsAg-positive. Monitor closely persons who are anti-HBc positive for signs of liver disease.
Persons with elevated ALT/AST of unknown etiology	Test for HBsAg along with other appropriate medical evaluation.	Follow-up as indicated.
Donors of blood, plasma, organs, tissues, or semen	Test for HBsAg, anti-HBc, and HBV-DNA as required.	
Hemodialysis patients	Test for all markers of HBV infection (HBsAg, anti-HBc, and anti-HBs). Test vaccine nonresponders monthly for HBsAg. HBsAg-positive hemodialysis patients should be cohorted.	Vaccinate against hepatitis B to prevent transmission and revaccinate when serum anti-HBs titer falls below 10mIU/mL.
All pregnant women	Test for HBsAg during each pregnancy, preferably in the first trimester. Test at the time of admission for delivery if prenatal HBsAg test result is not available or if mother was at risk for infection during pregnancy.	If HBsAg-positive, refer for medical management. To prevent perinatal transmission, infants of HBsAg-positive mothers and unknown HBsAg status mothers should receive vaccination and postexposure immunoprophylaxis in accordance with recommendations and within 12 hours of delivery.
Infants born to HBsAg-positive mothers	Test for HBsAg and anti-HBs 1–2 mos after completion of at least 3 doses of a licensed hepatitis B vaccine series (i.e., at age 9–18 months, generally at the next well-child visit to assess effectiveness of postexposure immunoprophylaxis). Testing should not be performed before age 9 months or within 1 month of the most recent vaccine dose.	Vaccinate in accordance with recommendations.
Household, needle-sharing, or sex contacts of persons known to be HBsAg positive	Test for HBsAg, as well as anti-HBc or anti-HBs to identify susceptible persons.	First vaccine dose should be given at the same visit as testing. Susceptible persons should complete a 3-dose hepatitis B vaccine series to prevent transmission from ongoing exposure.
Persons who are the sources of blood or body fluids resulting in an exposure (e.g., needlestick, sexual assault) that might require postexposure prophylaxis	Test source for HBsAg.	Vaccinate healthcare and public safety workers with reasonably anticipated occupational exposures to blood or infectious body fluids. Provide postexposure prophylaxis to exposed person if needed.
HIV-positive persons	Test for HBsAg, as well as for anti-HBc or anti-HBs to identify susceptible persons.	Vaccinate susceptible persons against hepatitis B to prevent transmission.

Adapted from: Centers for Disease Control and Prevention. Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection. MMWR 2008; 57 (No. RR-8).

