

# **HBV Screening, Testing, and Diagnosis**

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Module 3: Screening and Diagnosis

Lesson 2: <u>HBV Screening, Testing, and Diagnosis</u>

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# **HBV Screening Recommendations**

# recommendations for Hepatitis B Screening and Testing in the United States

In March 2023, the Centers for Disease Control and Prevention (CDC) updated its hepatitis B screening and testing guidance to recommend universal hepatitis B virus (HBV) screening for all adults, as well as risk-based and repeat testing for selected groups, utilizing a 3-test panel, which includes hepatitis B surface antigen (HBsAg), antibody to hepatitis B surface antigen (anti-HBs), and total antibody to hepatitis B core antigen (anti-HBc).[1] In these recommendations, the term "screening" refers to conducting serologic testing of asymptomatic persons not known to be at increased risk for exposure to HBV; the term "testing" refers to conducting serologic testing of persons with HBV-related symptoms or who have increased risk for HBV.[1] The following list summarizes the CDC recommendations.[1] Note that certain indications for screening depend on country-level HBV prevalence (Table 1).[2]

## **Universal Hepatitis B Screening**

- Universal HBV screening in all adults 18 years of age or older at least once in a lifetime.
- The HBV testing should consist of HBsAg, anti-HBs, and anti-HBc.
- For persons undergoing universal hepatitis B screening, repeat testing does not need to occur if no subsequent risk for HBV acquisition occurs following screening with the 3-test panel.

#### **Screening Pregnant Women**

- HBV screening for all pregnant women during each pregnancy, preferably in the first trimester, regardless of vaccination status or prior screening history.
- The HBV testing should consist of HBsAg, anti-HBs, and anti-HBc.

#### Risk-based Testing

- HBV testing should be performed for all individuals at increased risk for HBV, regardless of age, provided they were susceptible to HBV at the time of increased risk.
- Periodic, repeat testing should be performed for susceptible persons with ongoing risk factors, regardless of age.

#### **Definition for HBV Susceptible**

• The CDC defines susceptible persons to be those who



Have never been infected with HBV (e.g., HBsAg negative and anti-HBc negative),

AND

• Have not received a hepatitis B vaccine that is licensed in the United States or are known to be vaccine nonresponders.

#### **Definition of Increased Risk for HBV Infection**

- The CDC identifies the following groups of people to be at increased risk for HBV:
  - Persons currently or formerly incarcerated in jail, prison, or another detention setting
  - Persons with current or past sexually transmitted infections (STIs) or multiple sex partners
  - Persons with current or past hepatitis C virus (HCV) infection
  - Persons born in regions with an HBV prevalence equal to or greater than 2%
  - United States-born persons who were not vaccinated as infants and whose parents were born in a region of high HBV prevalence (equal to or greater than 8%)
  - · Persons with HIV infection
  - Persons with current or past injection drug use
  - Men who have sex with men
  - Infants born to people who are HBsAg-positive
  - Household contact with a person who has HBV infection
  - Needle-sharing or sexual contacts of persons with known HBV infection
  - Patients receiving predialysis, hemodialysis, peritoneal dialysis, or home dialysis
  - Persons with elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels of unclear etiology
  - Persons who request HBV testing due to the potential reluctance to disclose stigmatizing risk factors

#### **Additional Clinical Considerations for HBV Screening**

The CDC does not provide guidance on the number of sex partners that confer increased risk for HBV acquisition.[1] Medical providers should consider the number of sex partners, type of sexual activity, and timing of prior HBV testing when deciding on repeat testing for people at risk for HBV acquisition.[1] Similarly, there is no clear guidance on the frequency in which HBV testing should be repeated for persons who remain at risk for infection. Decisions regarding the timing and frequency of repeat testing should be individualized based on risk factors, patient age, and immune status.[1]

# **Rationale for Universal HBV Screening in Adults**

Chronic HBV is an indolent and often silent disease that over time can lead to serious health consequences, including cirrhosis, decompensated liver disease, hepatocellular carcinoma (HCC), and death.[] Universal screening for HBV has the advantage of averting substantial morbidity and mortality and it has been shown to be cost-effective.[3] In addition, universal screening has a number of benefits at the individual and population levels, which are outlined below.[1]

- Chronic HBV infection can be easily detected before the onset of significant liver disease using reliable and inexpensive tests.[1]
- Multiple safe and effective antiviral options are available for persons who have an indication for treatment and can reduce the morbidity and mortality associated with chronic HBV.[4,5]
- Persons identified to have chronic HBV can undergo evaluation for cirrhosis, and if diagnosed with cirrhosis,& can receive further evaluation, management, and prevention of cirrhosis-related complications.[4,5,6]
- Persons with chronic HBV can be evaluated to see if they have an indication for hepatocellular carcinoma surveillance; if indicated, regular surveillance for hepatocellular carcinoma can identify early-stage cancer lesions in the liver that have the potential for cure. [7]
- Persons diagnosed with chronic HBV can receive hepatitis A immunization (if nonimmune) and receive counseling on how to minimize additional liver damage, such as avoiding alcohol intake or excessive acetaminophen ingestion.[2]
- Screening can identify persons who would benefit from hepatitis B vaccination or those who are at risk for HBV reactivation.[1]
- Identifying persons with chronic HBV can reduce the population spread of HBV through treatment of HBV and appropriate treatment and prevention measures.[4]
- Screening of pregnant women can facilitate appropriate management to reduce the risk of perinatal infection.[1]



## **HBV Tests**

A range of serologic tests is utilized to diagnose HBV infection and to determine whether a person lacks immunity to HBV. In addition, there are multiple serologic and non-serologic tests used to risk-stratify and monitor patients with chronic HBV. The following discusses the major tests used for hepatitis B diagnosis and monitoring. The interpretation of these tests, as well as the progression of these markers with acute HBV infection, resolved HBV infection, chronic HBV infection, and response to immunization are summarized below in the section on *Interpretation of HBV Serologic Tests*.

- Hepatitis B Surface Antigen (HBsAg)Play animation: Hepatitis B Surface Antigen (HBsAg): Structurally, HBsAg is the main outer surface (envelope) protein of intact HBV. In addition, excess HBsAg proteins that are produced can form free subviral spherical and tubular particles that do not contain other viral elements. These subviral particles outnumber the intact hepatitis B virions by at least 100 to 1. The HBsAg is detected by enzyme immunoassay (EIA). After initial infection, HBsAg becomes detectable in blood on average at about 4 weeks. The presence of HBsAg indicates active infection, except in the situation whereby HBsAg is transiently present after receipt of a dose of hepatitis B vaccine.
- Hepatitis B Surface Antibody (anti-HBs)Play animation: Antibody to Hepatitis B Surface Antigen (Anti-HBs): The appearance of anti-HBs follows declining HBsAg titers and indicates recovery from HBV infection. The anti-HBs binds to the HBsAg that is present on the surface of the intact virions and on the HBsAg subviral lipoprotein particles (spheres and filaments). Early in the course of infection, most of the anti-HBs is bound to HBsAg and thus not detectable in blood. If a vigorous T-cell immune response clears most of the intact virions and subviral particles from the circulation, free (unbound) anti-HBs becomes detectable at high titers. The presence of anti-HBs indicates either recovery from natural infection and immunity to HBV or a response to HBV vaccination with the development of immunity. For those with prior infection or prior vaccination, immunity is defined by anti-HBs levels of 10 mlU/mL or greater or 12 mlU/mL or greater (depending on the assay). In addition, with a treatment-related cure of HBV, which is uncommon, anti-HBs will appear.
- Total Antibody to Hepatitis B Core Antigen (Total anti-HBc)Play animation: Total Antibody to Hepatitis B Core Antigen (Total anti-HBc): The HBV core (or nucleocapsid) is the shell-like inner region of the virus that encloses HBV DNA and the HBV polymerase enzyme. The total anti-HBc includes IgM anti-HBc and IgG anti-HBc. The anti-HBc forms in response to hepatitis B core antigen (HBcAg) peptides, which are small fragments of the HBcAg. The HBcAg peptides are formed when intact virions are degraded inside macrophages (antigen presenting cells) or when HBcAg is newly synthesized and processed within hepatocytes. The HBcAg peptides do not circulate in significant quantity in the blood, and there is no existing assay for HBcAg. The immune system is triggered to form anti-HBc when the HBcAg peptides are shuttled to the surface of cells by major histocompatibility complex (MHC) class 1 or 2 molecules. Anti-HBc does not bind to intact virions since the core is completely surrounded by the viral envelope. The formation of anti-HBc indicates past exposure to the virus, and it is not seen following HBV immunization. The role, if any, of anti-HBc in controlling or preventing HBV infection is not known. Anti-HBc remains persistently detectable in most individuals following HBV infection, with the persistent anti-HBc predominantly consisting of IgG anti-HBc.
- IgM Antibody to Hepatitis B Core Antigen (IgM anti-HBc)Play animation: IgM Antibody to Hepatitis B Core Antigen (IgM Anti-HBc): Anti-HBc is the first antibody to appear following acute HBV infection and it typically becomes detectable within 6 to 8 weeks after infection. Most of the early anti-HBc consists of IgM anti-HBc. The detection of IgM anti-HBc indicates infection within the prior 6 months. The IgM anti-HBc is the most reliable test for distinguishing acute from chronic HBV infection, although rarely, some patients with chronic HBV can demonstrate recurrent anti-HB core IgM during acute flares of their disease. By about 6 months after acute HBV infection, most of the IgM anti-HBc is replaced by IgG anti-HBc and therefore IgM anti-HBc is generally not detectable in persons with chronic HBV infection.
- **Hepatitis B e Antigen (HBeAg)**Play animation: Hepatitis B e Antigen (HBeAg): Within hepatocytes, HBeAg and HBcAg are generated from the same region of the HBV DNA. The newly formed HBeAg is



then secreted from the hepatocyte into the blood circulation. In contrast, the HBcAg is assembled into the HBV core and incorporated into the intact virion. Although abundant HBeAg is produced, it is not a component of the intact hepatitis B virion or subviral particles, and it is not required for viral infection, assembly, or replication. The function of HBeAg is unclear, but it may play an immunomodulatory role in natural infection by suppressing cytotoxic T-lymphocyte responses. The presence of HBeAg is typically associated with elevated HBV DNA levels and high infectivity, but it is variably present in persons with chronic HBV infection. Certain precore and basal core promoter mutations are associated with reduced or abolished HBeAg protein production.

- Antibody to Hepatitis B e Antigen (anti-HBe)Play animation: Antibody to Hepatitis B e Antigen (Anti-HBe): The appearance of anti-HBe generally is associated with declining HBeAg titers and indicates a favorable immune response to HBV infection. In some instances, initial detection of anti-HBe may occur weeks after HBeAg disappears from blood. For reasons that are not clear, anti-HBe usually appears in blood only after the immune system has controlled most of the initial HBV infection and cleared most of the HBeAg from the systemic circulation. The anti-HBeAg that appears following HBeAg clearance will generally persist, but unlike anti-HBs, it does not have a known role in controlling or neutralizing HBV infection, nor does it have any known role in preventing HBV infection.
- **HBV DNA**Play animation: HBV DNA: The HBV DNA is found in the intact virion but not in the spherical or filamentous particles, since these particles contain only HBsAg. The presence of HBV DNA indicates active infection (acute or chronic). Detection of HBV DNA is not usually used for diagnostic purposes, but it does play a major role in risk stratification and monitoring response to antiviral therapy.



# **Recommended Screening Tests**

# **Universal Screening**

The CDC recommends universal HBV screening for all adults (18 years of age and older) using a 3-test panel, which includes:[1]

- 1. Hepatitis B surface antigen (HBsAg)
- 2. Antibody to hepatitis B surface antigen (anti-HBs)
- 3. Total antibody to hepatitis B core antigen (anti-HBc)

The benefits of using a 3-test panel are that it can identify individuals with current HBV infection, those with prior HBV infection, those with immunity due to prior vaccination, and those who are susceptible to HBV and would benefit from vaccination.[1]

# **Screening of Pregnant Women**

Pregnant women should be screened for HBV using the 3-test panel of HBsAg, anti-HBs, and anti-HBc. Pregnant women who have previously undergone HBV screening with a 3-test panel and do not have any subsequent risk for HBV can be screened using HBsAg alone.[1]

# **Risk-Based Testing**

Susceptible persons at increased risk for HBV should be screened using the 3-test panel of HBsAg, anti-HBs, and anti-HBc.[1]



# **Incorporation of HBV Screening into Clinical Workflows**

# **HBV Screening in Clinical Setting**

In the clinic setting, when interacting with non-pregnant adults, the decision to screen for HBV should be based on an individual's prior screening status, vaccination status, and risk factors for HBV (Figure 1) .[1] All individuals who have not been previously screened for HBV should be offered HBV serologic screening, regardless of vaccination status.[1] Similarly, individuals who have previously been screened for HBV but remain susceptible due to lack of vaccination should undergo repeat HBV testing if they have experienced an activity or exposure associated with increased risk for HBV since their last screening. Vaccinated individuals who have previously been screened but experienced increased risk for HBV following their screening (but before vaccination) also warrant repeat testing.[1]

# Initiating HBV Immunization Concurrent with Screening

There is no need to wait for serologic results to return prior to initiating hepatitis B vaccination, and individuals who have not completed the hepatitis B vaccine series should be offered vaccination concurrent with HBV screening. When HBV screening and vaccination are offered on the same day, it is important that vaccination occurs after the collection of blood, as hepatitis B vaccination can result in a transient HBsAg positivity for up to 18 days following vaccination.[1] In settings where persons refuse hepatitis B testing, or when serologic testing is not possible, vaccination should not be delayed, and serologic testing can be offered at a subsequent visit, as long as subsequent serologic screening occurs outside the 18 day window for transient HBsAg positivity.[1] Although results of HBV serologic testing need not delay the initiation of the hepatitis B vaccine series, results should guide the need for additional vaccine doses.[1]



# **Evolution of Serologic Tests after Infection and Vaccination**

To understand and interpret HBV serologic diagnostic tests, it is important to understand how serologic markers evolve over time after initial infection and after receiving hepatitis B vaccine. Following acute HBV infection, the evolution of the pattern of serologic markers depends on the outcome of the host immune response, which typically correlates with the patient's age.[2,8,9] Adults have resolution of HBV infection approximately 90% of the time, whereas 30 to 90% of young children will fail to resolve the infection and thus develop chronic HBV infection.[8,9] The following discussion will summarize the evolution of key serologic markers during acute HBV infection with recovery, chronic HBV, and post-immunization, with each topic accompanied by corresponding animations from the Centers for Disease Control and Prevention Hepatitis B Serology Training as audio-visual guides to aid in understanding.

# **Acute HBV Infection with Recovery**

Following acquisition of HBV, the first detectable serologic marker in blood is HBsAg. Detection of HBsAg typically occurs at 4 weeks following infection, with a range of 1 to 9 weeks following infection. Typically, when HBsAg is detectable during acute infection, HBV DNA can also be detected in blood. During early infection, persons may also test positive for HBeAg, which is a marker of infectivity and higher HBV DNA levels. Nearly all persons who recover from acute HBV infection will test negative for HBsAg and HBV DNA by 15 weeks after the onset of symptoms. With acute HBV infection, IgM anti-HBc is typically detectable at the onset of symptoms and persists for 6 to 9 months following infection. Total anti-HBc, which consists of IgM anti-HBc and IgG anti-HBc, can similarly be detected at the onset of symptoms but persists indefinitely as a marker of prior infection (mostly as IgG). During recovery and after the disappearance of HBsAg, persons who have immunologic control of acute infection will develop antibodies to HBs (anti-HBs), which may persist indefinitely or wane over time. It is important to note that following the disappearance of HBsAg and prior to the appearance of anti-HBs, there is a period of time when IgM anti-HBc and total anti-HBc may be the only detectable serologic markers. This period of time is known as the window period.

## **Chronic HBV Infection**

Persons who do not resolve their acute infection will progress to have chronic hepatitis B. In these cases, HBsAg and total anti-HBc will remain positive for the duration of infection. HBV DNA is also typically detectable in serum. HBeAg, a marker of infectivity and higher viral load, is also generally present in chronic infection. Over time, patients can lose their ability to produce e antigen through the selection of replicating HBV with spontaneous mutations in the precore or basal core promoter region of the HBV genome.[10] In addition to HBeAg loss, they can eventually develop anti-HBe, a change that can be associated with lower HBV DNA levels if they become an inactive carrier. A diagnosis of chronic HBV can be made in the following 2 ways:

- 1. Detection of HBsAq, HBeAq, or HBV DNA on two separate samples 6 months apart, or
- 2. Detection of HBsAg, HBeAg, or HBV DNA on a single sample with a concurrent negative IgM anti-HBc

### **Vaccination**

Vaccination against hepatitis B results in the development of anti-HBs. Following hepatitis B vaccination, seroprotection is defined by anti-HBs levels of at least 10 to 12 mIU/mL (depending on the assay used) 1 to 2 months after completion of the vaccine series. In the absence of repeated exposure, anti-HBs levels may wane over time, although in immunocompetent hosts, immunity is likely maintained, even when anti-HBs levels fall below 10 mIU/mL.[11,12] Because the hepatitis B vaccine contains HBsAg, hepatitis B vaccination may cause a transient false-positive HBsAg for 2 to 3 weeks following vaccination. This result is clinically insignificant and does not represent infection.



# **Interpretation of HBV Serologic Tests**

The three major tests used for hepatitis B screening are HBsAg, anti-HBs, and anti-HBc. The following summarizes the interpretation of test results with these three serologic markers (Table 2).[13,14,15] The anti-HBc test may consist of a total anti-HBc or an IgM anti-HBc. The IgM anti-HBc has value primarily when considering acute hepatitis B infection. For diagnostic purposes, testing for HBeAg and anti-HBe is usually not performed, since they typically do not provide additional diagnostic information. For persons who are diagnosed with HBV infection, evaluation of HBeAg, anti-HBe, and HBV DNA are all usually performed, and monitoring these labs can be important in persons on treatment for chronic HBV.

- **Never Infected and Susceptible**: Persons who have never been infected with HBV or vaccinated with HBV vaccine are susceptible to HBV and will have a negative HBsAg, negative total anti-HBc, negative IgM anti-HBc, and negative anti-HBs. In addition, prior HBV vaccine nonresponders who have never been infected with HBV can also have this same serologic profile.
- Acute HBV Infection: Following exposure to the hepatitis B virus, HBsAg is the first detectable serologic marker in blood. Detection of HBsAg typically occurs approximately 4 weeks following HBV acquisition (range 1 to 9 weeks). In early acute infection, HBsAg may be the only detectable serologic marker, unless HBV DNA is tested, which would also be positive. In addition, most patients with acute HBV also test positive for HBeAg, which is a marker of infectivity and higher HBV DNA levels. During this early period, it can be challenging to make the diagnosis of acute HBV infection, especially in the absence of symptoms and IgM anti-HBc, but typically the serum aminotransferases (ALT or AST) are quite elevated in this setting and additional history of exposure risk can provide additional information.
- Recovered from Past Infection and Immune: Following acute HBV infection most adults will spontaneously clear their infection and subsequently test negative for HBsAg and HBV. In this situation, persons who have cleared the HBV infection have positive tests for anti-HBc and anti-HBs. In contrast, persons who receive HBV immunization, which consists of pure HBsAg, will develop anti-HBs, but not anti-HBc.
- **Chronic HBV Infection**: Persons who do not resolve their acute infection will progress to have chronic hepatitis B. With chronic HBV, HBsAg and total anti-HBc will remain positive for the duration of infection. In addition, most persons with chronic HBV have persistently positive serum HBV DNA levels. Although persons with chronic HBV almost always have a negative anti-HBs test, there are a few reports of the simultaneous presence of HBsAg and anti-HBs in persons with chronic HBV.[16,17] For diagnostic purposes, testing for HBeAg and anti-HBe are not performed, since these tests do not provide any additional diagnostic value over standard recommended tests.
- Immune from Vaccination: All modern HBV vaccines utilize recombinant HBsAg as the primary immunogen. The host serologic response to the vaccine is the development of anti-HBs. The hepatitis B vaccines do not generate an anti-HBc immune response. A positive anti-HBs in conjunction with negative HBsAg and negative anti-HBc indicates immunity as a result of vaccination, whereas a positive titer for both anti-HBs and anti-HBc indicates immunity from past infection with HBV. An anti-HBs titer greater than 10 to 12 mIU/mL correlates with protective immunity.[18,19]

For additional guidance on interpreting HBV serologies, please see the mini-lecture Interpreting <u>Hepatitis B Serologies</u> (included below).



# **Summary Points**

- The CDC recommends universal HBV screening for all adults 18 years of age and older.
- Pregnant women should be screened for HBV during each pregnancy.
- Susceptible persons at increased risk for HBV should undergo periodic testing for HBV, regardless of age, while their risk for exposure persists. These individuals should also be offered vaccination against HBV.
- The CDC recommends using a 3-test panel to screen for HBV, which includes HBsAg, anti-HBs, and anti-HBc.
- The serologic hallmark of acute HBV infection is the detection of IgM anti-HBc, which is typically detectable at the onset of symptoms and persists for 6 to 9 months following infection.
- Because HBsAg is detected first following infection with HBV, in early acute infection, HBsAg may be the only detectable serologic marker. Early after infection, HBV DNA is also detectable.
- Chronic HBV can be diagnosed by detection of HBsAg, HBeAg, or HBV DNA on two separate samples 6
  months apart, or by detection of HBsAg, HBeAg, or HBV DNA on a single sample with a concurrent
  negative IgM anti-HBc.
- Following hepatitis B immunization, seroprotection is defined by anti-HBs level of 10 to 12 mlU/mL or greater (depending on the assay) 1 to 2 months after completion of the vaccine series.
- Following resolution of HBV infection, serologic studies will show a positive anti-HBs anti-HBs, but anti-HBs levels may wane over time.
- Persons who have never been infected with HBV and are susceptible to HBV will have a negative HBsAq, negative total anti-HBc, negative IgM anti-HBc, and negative anti-HBs.



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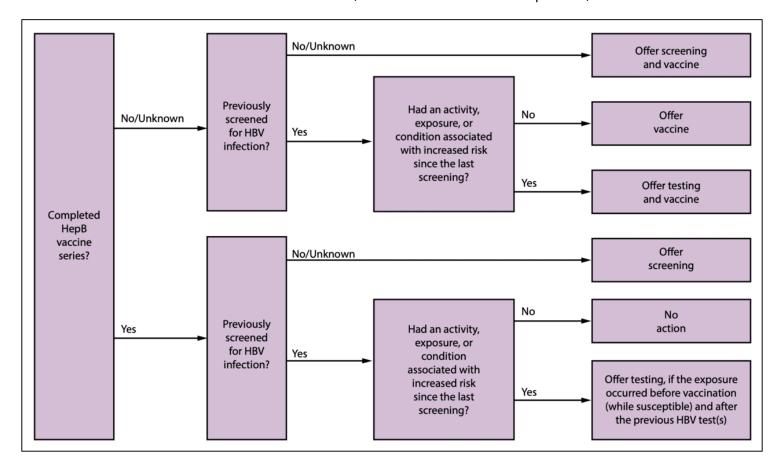
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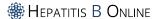


# **Figures**

# Figure 1 Incorporating HBV Screening and Testing into a Clinic Workflow: Nonpregnant Adults Aged ≥18 Years without a Known History of HBV Infection

Source: Conners EE, Panagiotakopoulos L, Hofmeister MG, et al. Screening and Testing for Hepatitis B Virus Infection: CDC Recommendations - United States, 2023. MMWR Recomm Rep. 2023;72:1-25.





#### Table 1.

#### Global Prevalence of Chronic HBV Infection, by Country

### **Prevalence Category** Country

**High** Angola, Cabo Verde, (≥8%) Central African Repu

Central African Republic, Chad, Eswatini, Ghana, Guinea, Guinea-Bissau, Kiribati, Lesotho, Liberia, Mali, Mauritania, Niger, Nigeria, Philippines, Sao Tome and Principe, Sierra Leone, Solomon Islands, Taiwan, Timor-Leste, Togo, Tonga, Turkmenistan, Tuvalu, and Zimbabwe. Albania, Benin, Burkina

Intermediate

(5.0-7.9%)

Albania, Benin, Burkina
Faso, Cameroon, China,
Côte d'Ivoire, Democratic
People's Republic of Korea,
Djibouti, Eritrea, Ethiopia,
Federated States of
Micronesia, Gabon,
Indonesia, Kyrgyzstan,
Moldova, Mongolia,

Mozambique, Myanmar, Papua New Guinea, Senegal, Somalia, South Sudan, Syria, Tajikistan, Uzbekistan, Vanuatu, and

Vietnam.

Low Intermediate

(2.0-4.9%)

Afghanistan, Azerbaijan, Bangladesh, Belarus,

Bosnia and Herzegovina,

Bulgaria, Burundi, Cambodia, Comoros, Congo, Democratic Republic of Congo,

Gambia, Georgia, Guyana, Haiti, Hong Kong, India, Iraq, Jamaica, Jordan, Kazakhstan, South Korea, Laos, Madagascar, Malawi, Malaysia, Marshall Islands, Oman, Pakistan, Romania,

Rwanda, Samoa,

Singapore, South Africa, Sri Lanka, Sudan, Tanzania, Thailand, Trinidad and Tobago, Tunisia, Turkey, Uganda, Yemen, and

Zambia.

**Low** Algeria, Argentina,

### **Prevalence Category** Country

 $(\leq 1.9\%)$ 

Armenia, Australia, Austria, Bahrain, Belgium, Belize, Bhutan, Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Croatia, Cuba, Czechia, Denmark, Dominican Republic, Ecuador, Egypt, El Salvador, Estonia, Fiji, Finland, France, Germany, Greece, Guatemala, Honduras, Hungary, Iran, Ireland, Israel, Italy, Japan, Kenya, Kosovo, Kuwait, Lebanon, Libya, Mexico, Morocco, Nepal, Netherlands, New Zealand, Nicaragua, Norway, Palestine, Panama, Paraguay, Peru, Poland, Portugal, Qatar, Russia, Saudi Arabia, Slovakia, Slovenia, Spain, Suriname, Sweden, Switzerland, Ukraine, United Arab Emirates, United Kingdom, United States, and Venezuela.

# Unknown prevalence (data not available)

American Samoa, Andorra, Anguilla, Antigua and Barbuda, Aruba, Bahamas, Barbados, Bermuda, Bonaire Sint Eustatius and Saba, Botswana, British Virgin Islands, Brunei, Cayman Islands, Cook Islands, Curação, Cyprus, Dominica, Equatorial Guinea, Falkland Islands, Faroe Islands, French Guiana, French Polynesia, Gibraltar, Greenland, Grenada, Guadeloupe, Guam, Holy See, Iceland, Isle of Man, Latvia, Liechtenstein, Lithuania, Luxembourg, Macao, Macedonia, Maldives, Malta, Martinique, Mauritius, Mayotte, Monaco, Montenegro, Montserrat, Namibia,



## **Prevalence Category** Country

Nauru, New Caledonia, Niue, Northern Mariana Islands, Palau, Puerto Rico, Réunion, Saint Barthélemy, Saint Helena, Saint Kitts and Nevis, Saint Lucia, Saint Martin, Saint Pierre and Miquelon, Saint Vincent and the Grenadines, San Marino, Serbia, Seychelles, Sint Maarten, Tokelau, Turks and Caicos Islands, U.S. Virgin Islands, Uruguay, Wallis and Futuna, and Western Sahara.

**NOTE**: This table is based on data from the Centers for Disease Control and Prevention (CDC) Source:

 Conners EE, Panagiotakopoulos L, Hofmeister MG, et al. Screening and Testing for Hepatitis B Virus Infection: CDC Recommendations - United States, 2023. MMWR Recomm Rep. 2023;72:1-25. [PubMed Abstract]



Table 2.			

HbsAg	Total ar	nti-HBc	IgM anti-H	Вс	Anti-HBs	НВ	V DNA	Interpretat	tion	1	
-		101120	-		-	11-	10.0.	-		<u>-</u>	Never infected; susceptible
+	_		-		-			-	4	- or -	Early acute infection (positive or negative HBV DNA), <i>or</i> Transient (up to 18 days) after vaccination with negative HBV DNA
+	-		+		+			-		+	Acute infection
-	•		+		+		-	⊦or-	-	or -	Acute resolving infection
-	-		+		-			+		-	Recovered from past infection and immune
+	-		+		-			-		+	Chronic infection
_			+		-			+		- or -	Isolated core antibody  False-positive (susceptible), or Past infection (resolved), or "low-level" chronic infection (unlikely to be infectious), or Passive transfer of anti-HBc to infant born to HBsAg-positive mother  Immune if anti-
											HBs concentration is ≥10 mIU/mL after completing vaccine series, or Passive transfer after hepatitis B immune globulin administration (for 3-6 months)

**Abbreviations**: anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen; HBsAg = hepatitis B surface antigen; HBV DNA = hepatitis B virus deoxyribonucleic acid; IgM =



HbsAg	Total anti-HBc	IgM anti-HBc	Anti-HBs	HBV DNA	Interpretation
immunog	lobulin class M.				

## Source:

• Schillie S, Vellozzi C, Reingold A, et al. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep. 2018;67:1-31. [PubMed Abstract]