



Hepatitis B: Screening, Awareness, and the Need to Treat

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Despite the availability of an effective hepatitis B vaccine, the global prevalence has not substantially declined, and significant barriers remain to screening and care.

Globally, chronic hepatitis B virus (HBV) infection is the leading cause of liver-related morbidity and mortality. Worldwide, more than 2 billion people have been exposed to HBV, and about 250 million are chronically infected.¹

The prevalence of hepatitis B surface antigen (HBsAg), the serologic marker of chronicity, varies significantly worldwide. The highest rates of HBsAg are reported in Asia, Sub-Saharan Africa, and the Amazon basin. The overall prevalence of chronic HBV infection in the U.S. is low, 800,000 to 1.4 million persons. The disease is predominantly seen in immigrants, with > 90% of cases in persons from countries of intermediate or high HBV prevalence, such as East Asia, Africa, Pacific Islands, parts of Africa, and Eastern Europe.²

The prevalence of chronic HBV infection in the U.S. may be underestimated and closer to 2.2 million persons, because many foreign-born persons are generally excluded from national prevalence surveys.³ More worrisome, studies suggest that a majority of individuals with chronic HBV infection are unaware of their diagnosis, and consequently, many patients who might benefit from therapy do not receive appropriate care or treatment.⁴ This review will discuss screening recommendations for HBV in the U.S., identify knowledge gaps regarding the disease, and present a cogent argument for why treatment-eligible patients should be entered into management programs and evaluated for therapy.

HEPATITIS B SCREENING

Chronic hepatitis B meets the criteria established by the

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World Health Organization as a disease for which screening would be beneficial to public health. Chronic HBV infection is an important health problem that can result in serious sequelae, such as cirrhosis, hepatocellular carcinoma, and liver-related mortality. Moreover, persons unaware of their diagnosis may unwittingly transmit the virus to unprotected individuals.

A simple, relatively inexpensive test is widely available to identify chronic HBV infection. The test allows physicians to confirm a diagnosis before symptoms develop and offer a safe and effective therapy. Modeling studies suggest that screening populations with a prevalence of chronic HBV infection $\geq 2\%$ also would be cost-effective in reducing the burden of HBV-associated liver cancer and chronic liver disease in high-risk populations.^{5,6} However, a number of barriers exist that limit screening (Table 1).

Who to Screen?

All guidelines recommend that persons at high risk for HBV infection should be screened. Broadly, these include persons from geographic areas with a high prevalence of chronic infection, persons at high risk for acquiring HBV infection, persons with increased risk of transmitting HBV, and persons at risk for reactivation of HBV. In addition to previous recommendations, the Centers for Disease Control and Prevention (CDC) updated 2008 guidelines now recommend testing all persons born in geographic areas with a HBsAg prevalence $\geq 2\%$, U.S.-born persons not vaccinated as infants whose parents were born in regions with HBsAg prevalence $\geq 8\%$, persons who inject drugs, men who have sex with men, persons with elevated alanine transaminase and aspartate transaminase of unknown etiology, and persons with selected medical conditions that

Table 1. Barriers to Screening

Patient Barriers	<ul style="list-style-type: none"> • Lack of information and education about disease • Cultural beliefs limiting physician contact • Preference for alternative therapy • Fear of stigmatization • Cost
Provider Barriers	<ul style="list-style-type: none"> • Lack of knowledge of who should be screened • Communication and linguistic difficulties
Environmental Barriers	<ul style="list-style-type: none"> • Lack of access to routine care • Lack of insurance • Difficulty accessing health system • Lack of social support

require immunosuppressive therapy (Table 2).⁷ In 2014, the U.S. Preventive Services Task Force provided updated guidance on screening of nonpregnant adolescents and adults that aligned with the CDC guidelines and also recommended screening individuals at high risk for HBV infection.⁸ The American Association for the Study of Liver Diseases and other professional liver organizations support these recommendations.⁹

Which Test to Use

Serologic testing for HBsAg is the recommended method to identify persons with chronic HBV infection. Testing for HBV infection in high-risk groups should be performed with a FDA-licensed or FDA-approved serologic assay for HBsAg (sensitivity and specificity of > 98%) according to the manufacturer's recommendations. Initially, reactive specimens should be confirmed with a licensed confirmatory test.

A positive HBsAg result indicates active infection, either acute or chronic. Other serological markers of HBV infection, such as presence of hepatitis B core IgM antibody, and the clinical context are used to differentiate between acute, chronic, or resolving infection. For identification of individuals who are at risk for chronic infection, the screening strategy should be with HBsAg only. For identifying susceptible persons who should be offered HBV vaccination, or patients that are at risk of reactivation or transmission of HBV, screening should include testing for HBsAg, hepatitis B core antibody (anti-HBc) and hepatitis B surface antibody (anti-HBs).

The interpretation of HBV screening serology is shown in Table 3. Persons with chronic HBV infection are treated, if needed, per practice guidelines based on the initial test results and interpretation of the stage of the disease and counseled regarding transmission of infection.^{9,10} Vaccination is recommended for uninfected persons.

HEPATITIS B EDUCATION

There is relatively poor awareness of HBV among high-risk individuals and health care professionals (HCPs). A study examining the prevalence of chronic hepatitis B in an Asian and Pacific Islander population reported that about 15% of participants had not been previously tested for hepatitis B.¹¹ Another study that surveyed 3,163 Asian American adults in the San Francisco Bay Area found that of those screened and identified with chronic HBV infection (8.9%), two-thirds were unaware that they were infected.¹²

Primary care providers in San Francisco correctly identified that Chinese immigrants have a higher prevalence of chronic hepatitis B than that of non-Hispanic white or U.S.-born Chinese people, but the providers incorrectly identified persons with HIV infection, men who have sex with men, and persons who inject drugs as having higher prevalence than that of Chinese immigrants in a survey.¹³ Lack of awareness probably contributes to poor outcomes from the infection among at-risk persons as well as continued transmission to susceptible individuals. Furthermore, lack of knowledge is a barrier to testing, prevention, and care. Increased awareness to identify the at-risk population and early treatment is an important step to prevent morbidity and mortality from chronic hepatitis B.

Public Awareness

Many at-risk populations are unaware of HBV, its possible routes of transmission, or that a safe and effective vaccine exists for HBV prevention. Moreover, many foreign-born persons with chronic HBV infection feel stigmatized by others or have cultural barriers against Western medicine and prefer alternative therapies. As a result, the Institute of Medicine (IOM) has suggested that innovative approaches need to be developed to promote a better understanding of transmission, prevent and treat HBV, increase HBV vaccination rates among children and at-risk adults, educate women about vertical transmission risk, reduce stigmatization, and provide culturally sensitive and understandable educational material.¹⁴

Table 2. CDC Recommendations for Screening

At-Risk Population	Initial Screening Tests
Persons born in regions with HBV prevalence \geq 2%	HBsAg
U.S. born persons not vaccinated as infants and whose parents were born in regions with HBV prevalence \geq 8%	HBsAg
Injection drug users	HBsAg, anti-HBc, or anti-HBs
Men who have sex with men	HBsAg, anti-HBc, or anti-HBs
Prior to immunosuppression	HBsAg, anti-HBc, and anti-HBs
Elevated ALT/AST of unknown etiology	HBsAg
Donors of blood, plasma, organs, tissues, or semen	HBsAg, anti-HBc, and HBV DNA
Hemodialysis patients	HBsAg, anti-HBc, and anti-HBs
All pregnant women	HBsAg
Infants born to HBsAg positive mothers	HBsAg and anti-HBs after 1-2 months of completion of vaccination series
Household, needle sharing, or sex contacts with persons who are HBsAg positive	HBsAg, anti-HBc, or anti-HBs
Source person in sexual assault or needlestick injury	HBsAg
Persons who are HIV positive	HBsAg, anti-HBc, and/or anti-HBs

Abbreviations: anti-HBc, hepatitis B core antibody; anti-HBs, hepatitis B surface antibody; HBsAg, hepatitis b surface antigen.

Adapted from: Weinbaum CM, Williams I, Mast EE, et al; Centers for Disease Control and Prevention. Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. *MMWR Recomm Rep*. 2008;57(RR-8):10-11.

Awareness Among Health Care Professionals

Studies have identified knowledge gaps among HCPs regarding the prevalence of HBV in the general U.S. population, outcome of infection, who should be screened and vaccinated against HBV, appropriate methods for screening and interpretation of serologic tests for HBV, and proper treatment of persons with chronic infection. As a consequence, the IOM recommended educational programs for HCPs on the prevalence of HBV infection in the general U.S. population and at-risk populations, particularly foreign-born persons. In addition, these educational programs should target all levels of HCPs, including undergraduates and postgraduates, and include information on screening and prevention, testing, and interpretation of tests.¹⁴

Need to Treat

The global HBV disease burden remains high despite the existence of an effective vaccine. Worldwide, there are an

estimated 4.5 million new infections and 780,000 HBV-related deaths each year.¹⁵ In the U.S., the highest rates of mortality are seen in Asians and Pacific Islanders and among persons aged 55 to 64 years. Asians and Pacific Islanders also have the highest rate of liver cancer deaths.^{16,17}

The natural history of chronic hepatitis B is highly variable and dependent on a complex interplay between the virus and the host immune response. It is estimated that between 25% and 40% of persons with chronic hepatitis B will be at risk for progression to cirrhosis.^{7,18,19} In a study among persons with cirrhosis, the 5-year cumulative risk of developing hepatocellular carcinoma was 17% in Asian patients and 10% in white Americans and Europeans. The 5-year liver-related death rate was 14% among East Asians and 15% among white Europeans.¹⁸

A significant proportion of individuals infected with HBV are unaware of their diagnosis, not enrolled in care, or not receiving therapy.^{7,12,20-24} Data from several prospective and retrospective cohort studies have

Table 3. Screening Results

HBsAg	Total anti-HBc	IgM anti-HBc	Anti-HBs	Interpretation
Negative	Negative	Negative	Negative	Never infected and no evidence of infection
Positive	Positive	Negative	Negative	Chronic infection
Positive	Positive	Positive	Negative	Acute infection
Negative	Positive	Negative	Positive	Recovered from past infection and immune
Negative	Negative	Negative	Positive	Immune (Immunization or natural)

Abbreviations: anti-HBc, hepatitis B core antibody; anti-HBs, hepatitis B surface antibody; IgM anti-HBc, hepatitis B core IgM antibody.

Adapted from: Weinbaum CM, Williams I, Mast EE, et al; Centers for Disease Control and Prevention. Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. *MMWR Recomm Rep*. 2008;57(RR-8):4.

demonstrated that prolonged viral suppression achieved with therapy is associated with regression of fibrosis and reversal of cirrhosis in a substantial proportion of individuals.^{25,26} Treatment has also been associated with a reduction in rates of liver decompensation, HCC, liver-related, and all-cause mortality among patients with liver cirrhosis.²⁷

Given the risk of serious complications and the availability of safe and effective therapy, it is imperative that persons identified as having chronic hepatitis B be referred for evaluation to determine whether therapy is warranted. However, it is also important to recognize that a cure for HBV infection is currently not available, and most patients who initiate therapy will require long-term treatment. In addition, persons who are not currently treatment candidates may become candidates due to changes in disease activity. This underscores the point that patients with chronic hepatitis B require life-long monitoring regardless of whether they are receiving treatment.

CONCLUSIONS

The primary reasons to screen for HBV are to reduce morbidity and mortality related to liver disease and to prevent transmission. Significant barriers remain to screening and referral for care for HBV in the U.S. Educational programs to increase knowledge and awareness among HCPs and the public together with improved access to care are critical to improve disease outcomes and prevent transmission. Despite the availability of an effective vaccine for 3 decades, the global prevalence of HBV has not substantially declined.

Further research is needed to explore strategies to overcome screening barriers, improve vaccination rates, and to develop new models of health care delivery to reduce the burden of disease-related to HBV. ●

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