A CME/CE-certified monograph providing information and expert commentaries on screening and prevention for hepatitis B virus (HBV) infection, and the diagnosis and management of patients with chronic hepatitis B (CHB)

Strategies & Solutions for Hepatitis B Screening, Testing, Linkage to Care, & Treatment

This activity has been endorsed by the Asian Health Foundation (AHF), the Chinese American Medical Society (CAMS), the Korean-American Medical Association (KAMA), and the Vietnamese American Medical Association (VAMA).

This activity is supported by an independent educational grant from Bristol-Myers Squibb.
Dear Health Care Professional:

Chronic hepatitis B (CHB) is a significant cause of liver-related morbidity and mortality. In the absence of early screening, diagnosis, and medical intervention, about 25% of patients with CHB will eventually die of cirrhosis, hepatocellular carcinoma (HCC), or both. In the United States, an estimated 1.4 million to 2.2 million residents have CHB, and the disease causes an estimated 4000 deaths each year. Among the different ethnicities affected by CHB, Asian Americans bear the greatest burden, accounting for more than half of all CHB cases. Furthermore, Asian Americans have the highest rate of HCC among all ethnic groups and a prevalence rate that is 10 times that of the general population.

However, two-thirds of Asian Americans with CHB remain untested, unaware of their infection, and therefore are untreated. To bring all persons with CHB into care and retain them in care, health care providers (HCPs) practicing in communities with at-risk populations need accurate and clinically relevant information and expert guidance on screening, diagnosis, antiviral treatment, and monitoring.

This program provides guidance for HCPs on the management of CHB in Asian Americans based on recommendations from experts and key organizations. Although this program focuses on Asian Americans, much of the information presented is applicable to persons from other immigrant communities as well. Issues addressed include screening, vaccination, treatment criteria, selection of first-line antiviral agents, treatment duration and monitoring, and strategies to improve identification and linkage to care in infected persons. This program also reviews the most recent information and recommendations on the treatment of special populations with CHB, such as pregnant women, patients who are coinfected with hepatitis C virus, and patients undergoing immunosuppressive therapy or chemotherapy.

This continuing medical education (CME) activity will benefit HCPs by providing current information on screening, diagnosis, and management of care for Asian Americans with CHB. In turn, this CME activity will benefit patients with CHB by expanding the knowledge about this disease among HCPs, thereby promoting screening and earlier diagnosis, as well as contributing to the optimal care of patients in populations most at risk.

It is my sincere hope that you will find this program to be a useful part of your continuing education about this challenging disease.

Sincerely,

Myron J. Tong, MD, PhD
Chairperson

Myron J. Tong, MD, PhD
Chairperson
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>CME/CE Information</td>
<td>2</td>
</tr>
<tr>
<td>Overview of the Chronic Hepatitis B Epidemic</td>
<td>4</td>
</tr>
<tr>
<td>Screening and Diagnosis</td>
<td>8</td>
</tr>
<tr>
<td>Considering Treatment</td>
<td>13</td>
</tr>
<tr>
<td>Treatment Options</td>
<td>16</td>
</tr>
<tr>
<td>Patient Counseling</td>
<td>21</td>
</tr>
<tr>
<td>Screening, Diagnosis, and Linkage to Care: Strategies and Solutions</td>
<td>23</td>
</tr>
<tr>
<td>Future Directions</td>
<td>25</td>
</tr>
<tr>
<td>References</td>
<td>27</td>
</tr>
<tr>
<td>CME/CE Posttest</td>
<td>30</td>
</tr>
</tbody>
</table>
PROgRaM OvErVIew

B Aware 4 Care: Strategies & Solutions for Hepatitis B Screening, Testing, Linkage to Care, & Treatment is a CME/CE-certified monograph designed to provide health care providers who care for patients at risk with a thorough review of the epidemiology and natural history of hepatitis B virus (HBV) infection and a discussion of best practices in screening, testing, counseling, linkage to care, and treatment. This CME/CE-certified activity also includes profiles of several existing clinics and programs that have demonstrated success in screening, testing, and treating chronic hepatitis B (CHB) in communities throughout the United States. These models of care will demonstrate strategic insights and examples of successful approaches to prevention, testing, linkage to care, and management of patients with CHB.

EDUCATIONAL OBJECTIVES

• Describe the disproportionate impact that CHB has had among immigrant populations from areas with high or intermediate HBV prevalence rates
• Discuss barriers to care that exist among patients from immigrant populations at risk for CHB
• Explain how to counsel patients on screening for CHB
• Explain follow-up care, treatment, and monitoring for patients diagnosed with CHB
• Identify programs with successful approaches in prevention, testing, screening, linkage to care, and management in high-risk immigrant populations

ACCREDITATION

Physician Continuing Medical Education

Accreditation Statement
This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Global Education Group (Global) and HealthmattersCME. Global is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation
Global Education Group designates this live activity for a maximum of 1.75 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

NURSING CONTINUING MEDICAL EDUCATION

Credit Designation CNA/ANCC
This educational activity for 1.75 contact hours is provided by Global Education Group.
Accreditation Statement
Global Education Group is an approved provider of continuing nursing education by the Colorado Nurses Association, an accredited approver by the American Nurses Credentialing Center’s Commission on Accreditation.

Nurses should claim only the credit commensurate with the extent of their participation in the activity.

GLOBAL CONTACT INFORMATION
For information about the accreditation of this program, please contact Global at 303-395-1782 or inquire@globaleducation-group.com

INSTRUCTIONS TO RECEIVE CREDIT
In order to receive credit for this activity, the participant must fax the completed evaluation form to HealthmattersCME at 646-674-4888.

FEE INFORMATION
There is no fee for this educational activity.

DISCLOSURE OF CONFLICTS OF INTEREST
Global Education Group (Global) requires instructors, planners, managers, and other individuals and their spouse/life partner who are in a position to control the content of this activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified conflicts of interest are thoroughly vetted by Global for fair balance, scientific objectivity of studies mentioned in the materials or used as the basis for content, and appropriateness of patient-care recommendations. The faculty reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

Son T. Do, MD
Consulting Fees: Gilead Sciences, Inc; Vertex
Contracted Research: Centocor
Speaker's Bureau: Bristol-Myers Squibb, Gilead Sciences, Inc.

W. Ray Kim, MD
Consulting Fees: Bristol-Myers Squibb, Gilead Sciences, Inc.

Myron J. Tong, MD, PhD, has no real or apparent conflicts of interest to report, nor any financial relationships to disclose.

Su Wang, MD, MPH
Honoraria: Gilead Sciences, Inc

DISCLOSURE OF UNLABELED USE
This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. Global Education Group (Global) and HealthmattersCME do not recommend the use of any agent outside of the labeled indications. The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of any organization associated with this activity. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

DISCLAIMER
Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed in this activity should not be used by clinicians without evaluation of patient conditions and possible contraindications on dangers in use, review of any applicable manufacturer’s product information, and comparison with recommendations of other authorities.

ACTIVITY AGENDA
Introduction and CME Information: 5 minutes
Monograph: 90 minutes
Posttest and Evaluation: 10 minutes
Overview of the Chronic Hepatitis B Epidemic

An estimated 1.4 million to 2.2 million persons are living with chronic hepatitis B (CHB) in the United States, and the disease causes about 4000 deaths each year.\textsuperscript{1,2} About two-thirds of all persons with CHB in the United States are unaware of their infection and are, therefore, undiagnosed and untreated.\textsuperscript{1,3}
Even among persons who receive a diagnosis of CHB, treatment rates remain unacceptably low. Recent analyses suggest that fewer than half of all patients are referred for appropriate care, and less than 10% of those eligible for treatment ever receive an antiviral prescription. The lack of diagnosis and treatment has serious consequences: according to the Centers for Disease Control and Prevention (CDC), an estimated 15% to 25% of all persons with untreated CHB will eventually die of cirrhosis and/or hepatocellular carcinoma (HCC). The rising rate of HCC in the United States, particularly among populations with high rates of CHB, underscores the pressing need for health care providers to actively engage in expanding the testing, diagnosis, treatment, and prevention of CHB in communities at risk.

Rationale for Screening, Diagnosis, and Treatment

Active replication of hepatitis B virus (HBV) and the inflammation associated with the immune response cause the progression of CHB. Antiviral agents effectively suppress viral replication and provide a rationale for antiviral treatment of CHB to delay or prevent complications. While antiviral treatment does not cure HBV infection, accumulated evidence demonstrates that durable and effective suppression of viral replication with antiviral agents leads to significant improvements in liver inflammation and liver histology, including among Asian patients and patients with advanced fibrosis and cirrhosis. Histologic improvements in CHB with antiviral treatment have been correlated with a decreased risk of liver-related complications. The objectives of antiviral treatment for CHB are the sustained suppression of viral replication and the decrease in liver inflammation to prevent cirrhosis, hepatic failure, and HCC. These goals can be met only when persons with CHB are identified through screening, accurately diagnosed, and linked to medical care.

Populations at High Risk for CHB

CHB disproportionately affects Asian and other immigrant populations. Most persons (47% to 70%) with CHB in the United States were born in geographic regions that are endemic for HBV. (See Sidebar: HBV Transmission Routes.)

CHB in Asian American Communities

The Asian American immigrant community is a very diverse and growing population. Between 1990 and 2000, this segment of the population increased 72% compared with 13% for the general population, and the proportion of the general population...
The prevalence rate for CHB is high in the Asian American community as a whole; however, rates vary according to the country of origin, as shown in Figure 2. Implementation of vaccination programs in Taiwan, Korea, and China has lowered the HBV carrier rates from previously higher levels. Despite the overall high prevalence rate of CHB in Asian Americans, about two-thirds of all persons with CHB in Asian communities are unaware of their infection, and they remain untreated and at risk for cirrhosis, end-stage liver disease, and HCC.

Figure 1. World map of HBsAg prevalence rates, 2006.\(^a\)

\(^a\)Note: For multiple countries, estimates of HBsAg prevalence are based on limited data and might not reflect current prevalence in countries that have implemented childhood hepatitis B vaccination. HBsAg prevalence may vary within countries by subpopulation and locality.


HBsAg, hepatitis B surface antigen.
Evidence suggests that less than one-quarter of Asian Americans with CHB have been diagnosed and up to two-thirds have never been screened. A number of factors related to patients, providers, and the health care system create barriers to timely screening and diagnosis of CHB in this community.

- Patient-related factors include lack of knowledge about HBV, language difficulties, social stigma, denial, cost, and the belief that nothing can be done to control CHB. Evidence suggests that these barriers can be overcome by educating the patient about treatment for CHB and by provider recommendations for screening.

- Provider-related factors that create barriers to HBV screening among Asian Americans include lack of awareness of the higher risk for CHB among Asian Americans, as well as lack of knowledge about testing for HBV infection and CHB treatment options. Knowledge that screening is cost-effective and that insurance coverage is available for HBV vaccination can be important to overcome these barriers.

- The health care system itself also presents barriers to HBV screening through the referral system and language barriers.
Screening and Diagnosis

In 2008, the CDC released revised screening recommendations for CHB. The low prevalence rate of CHB (0.3%) in the US general population makes risk-based screening a more practical strategy than universal screening. All patients identified with HBV infection through screening should receive appropriate care or referral to care.
Current CHB screening recommendations are summarized in Table 1 and specify screening of all immigrants from regions of intermediate to high HBV endemicity, which includes all Asian countries. Screening is also recommended for members of other groups at high risk of HBV infection, including IDUs, men who have sex with men, all pregnant women, patients undergoing hemodialysis, persons infected with human immunodeficiency virus (HIV), and any patients scheduled for immunosuppressive therapy or chemotherapy. (See Select Populations on page 18 for more information on management of pregnant women and patients undergoing immunosuppressive therapy.)

Health care workers should also be screened. Those who are found to have CHB must take precautions to prevent transmission to patients. Recently revised guidelines on the management of health care workers infected with HBV are available from the Society for Healthcare Epidemiology of America and can be found at: www.shea-online.org/Assets/files/guidelines/BBPathogen_GL.pdf. Revised guidelines from the CDC on preventing HBV transmission from health care workers to patients are expected in the near future.

**VACCINATION**

All persons who are susceptible to HBV infection should be vaccinated, including health care workers. The HBV vaccine is highly effective and safe; more than 1 billion doses of vaccine have been administered throughout more than 150 countries.3

The 3-dose vaccine series (given over 6 months) provides more than 90% protection against HBV infection. Implementation of universal HBV vaccination recommendations in newborns has contributed significantly to a decreased incidence of acute HBV in the United States. Between 1990 and 2007, the rate of new acute HBV cases decreased by more than 80% and among infants and children, vaccination contributed to a 98% decline in HBV incidence.

Information on adult vaccine schedules, including HBV, and a downloadable tool to help determine which vaccines are recommended for adults patients, can be found at: http://www.cdc.gov/vaccines/recs/schedules/adult-schedule.htm#hcp. Information on vaccine schedules for neonates, children, and adolescents, including HBV, and downloadable wall charts and publications can be found at: http://www.cdc.gov/vaccines/recs/schedules/child-schedule.htm#hcp

**INTERPRETATION OF HEPATITIS B SEROLOGIC TEST RESULTS**

A number of serologic markers can be tested to assess for HBV (Table 2 on page 10). Some of these markers of HBV infection change as HBV infection progresses from acute to chronic infection.

The American Association for the Study of Liver Diseases (AASLD) recommends testing for hepatitis B surface antigen (HBsAg) and hepatitis B surface antibody (anti-HBs) as a primary screening tool for CHB. Other expert guidelines recommend using HBsAg alone. Tests for total hepatitis B core antibody (anti-HBc), hepatitis B e antigen (HBeAg), hepatitis B e antibody (anti-HBe), and serum HBV DNA levels should not be used for screening. The CDC interpretation of serologic tests for HBV infection is shown in Table 3 on page 10.
Table 2. Serologic markers of HBV infection.

<table>
<thead>
<tr>
<th>Serologic marker</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>• Protein on the surface of HBV</td>
</tr>
<tr>
<td></td>
<td>• Can be detected at high levels in serum during acute HBV infection or in CHB</td>
</tr>
<tr>
<td></td>
<td>• Presence indicates the patient is infected</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>• Antibody to HBsAg</td>
</tr>
<tr>
<td></td>
<td>• Presence may indicate recovery and immunity from HBV infection</td>
</tr>
<tr>
<td></td>
<td>• Also develops in patients successfully vaccinated against HBV</td>
</tr>
<tr>
<td>Total anti-HBc</td>
<td>• Antibody to core antigen of HBV (core antigen is not detectable in blood)</td>
</tr>
<tr>
<td></td>
<td>• Appears at the onset of symptoms in acute HBV infection and remains throughout life</td>
</tr>
<tr>
<td></td>
<td>• Presence indicates previous or ongoing HBV</td>
</tr>
<tr>
<td>IgM anti-HBc</td>
<td>• Immunoglobulin M class antibody to the core antigen of HBV</td>
</tr>
<tr>
<td></td>
<td>• Presence indicates recent acute infection with HBV (≤6 months)</td>
</tr>
<tr>
<td>HBeAg</td>
<td>• Protein produced by the virus when it is actively replicating</td>
</tr>
<tr>
<td></td>
<td>• Can be detected in serum during acute HBV infection and CHB</td>
</tr>
<tr>
<td></td>
<td>• Some strains of HBV do not make e antigen</td>
</tr>
<tr>
<td></td>
<td>• Presence indicates active replication</td>
</tr>
<tr>
<td>Anti-HBe</td>
<td>• Antibody to HBeAg</td>
</tr>
<tr>
<td></td>
<td>• Presence indicates inactive infection except strains of HBV that do not make e antigen</td>
</tr>
<tr>
<td>HBV DNA</td>
<td>• Genetic material of HBV</td>
</tr>
<tr>
<td></td>
<td>• Number of HBV DNA copies in the blood is used to detect active HBV infection and to monitor response to antiviral therapy (10,000 copies/mL = 2000 IU/mL)</td>
</tr>
</tbody>
</table>

Anti-HBc, hepatitis B core antibody; anti-HBe, hepatitis B e antibody; anti-HBs, hepatitis B surface antibody; CHB, chronic hepatitis B; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IgM, immunoglobulin M.


Table 3. Interpretation of common tests for HBV infection.

<table>
<thead>
<tr>
<th>Interpretation of HBV serologic test results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient status</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Susceptible</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Immune due to natural infection</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Immune due to HBV vaccination</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Acutely infected</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Chronically infected</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Anti-HBc, antibody to hepatitis B core antigen; anti-HBs, antibody to hepatitis B surface antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IgM, immunoglobulin M.


CLINICAL STAGES OF CHB IN ASIAN AMERICAN PATIENTS

Asian American patients may be classified into one of several clinical stages of CHB using HBeAg status and alanine aminotransferase (ALT) and HBV DNA levels, as shown in Figure 3 on page 11.35,36 (For a discussion of new values for the upper limit of normal [ULN] for ALT levels, see Sidebar: Interpreting ALT Levels opposite.) These stages can be useful for diagnosis and for making decisions about whether to initiate antiviral treatment.

Immune tolerant. Asian American patients initially presenting for medical care in the first or second decade of life are typically in the immune-tolerant stage.35 Patients in the immune-tolerant stage are clinically asymptomatic, HBeAg-positive, with normal ALT and undetectable-to-low HBV DNA levels (≥10⁴ copies/mL [≥2 million IU/mL]).35 The immune-tolerant phase can last for several decades. This stage typically only occurs in persons with perinatally acquired HBV infection and is rare in Western countries, where CHB usually evolves from acute infection acquired in adulthood.37

Inactive carrier. HBsAg-positive patients may sometimes present for care in the inactive-carrier stage.35 Inactive carriers are HBeAg-negative, with normal ALT and undetectable-to-low HBV DNA levels (≤10⁴ copies/mL [≤2000 IU/mL]). The prognosis for patients in the inactive-carrier stage is typically
Interpreting ALT Levels

The ULN for ALT values currently used by laboratories is typically set at 40 U/L for men and 30 U/L for women. However, a study conducted in Italy found that values for ALT levels that are now considered healthy are lower (<30 U/L for men and <19 U/L for women) than the values currently used as upper reference limits by laboratories. A study among healthy potential liver donors with normal liver histology in Korea reported similar findings. Among the Korean subjects, serum ALT upper limits were found to be lower than previously accepted (45 U/L for men and 34 U/L for women). These lower values (33 IU/L for men and 25 IU/L for women) should be taken into consideration when interpreting test results for patients with HBV infection. When evaluating ALT levels, health care providers (HCPs) must also consider a number of other factors, including the patient’s age, medical history, body mass index (BMI), and cholesterol levels.

Figure 3. Clinical stages of CHB in Asian American patients.

Cirrhosis. Patients may present with established cirrhosis and are often unaware of their advanced liver disease. These patients may be either HBeAg-positive or HBeAg-negative, with or without elevated ALT values, and HBV DNA levels of 10^5 to 10^7 copies/mL (20,000 to 2 million IU/mL). Laboratory test results may show decreased albumin levels and low platelet counts, which suggest cirrhosis. HCC risk is the highest among patients with cirrhosis. HCC can develop at any stage of CHB. As discussed below, surveillance for HCC, therefore, is an essential component of care.

SURVEILLANCE FOR HCC

Patients with CHB are at more than 100 times the risk for HCC compared to those not infected with HBV. Estimates suggest that the annual incidence of HCC in inactive carriers is 0.5% and rises to 3% to 10% in patients with CHB and cirrhosis. Mortality rates for HCC are high, with 5-year survival rates ranging from 0% to 10% for patients who are diagnosed after symptoms emerge. Even with diagnosis and treatment at earlier stages, 5-year survival rates are about 50%. HCC surveillance may facilitate initiation of treatment at a stage when therapy may be most effective. When HCC is detected at early stages, patients may have the option of surgical resection or liver transplantation.

The benefits of HCC surveillance in Asians were shown in a large-scale (N = 18,816) randomized, controlled trial in China that reported a 37% reduction in the 5-year mortality rate among patients with biomarkers for past or current infection with HBV who were monitored for HCC every 6 months with alpha fetoprotein (AFP) and ultrasound. The reduction in mortality was evident despite an adherence rate to the surveillance program of less than 60%.
Table 4. Surveillance for HCC in Asian Americans with CHB.

<table>
<thead>
<tr>
<th>Surveillance candidates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High-risk patients</strong></td>
</tr>
<tr>
<td>• Cirrhosis</td>
</tr>
<tr>
<td>• HCC in blood relatives</td>
</tr>
<tr>
<td>• HBsAg-positive men 40 years and older</td>
</tr>
<tr>
<td>• HBsAg-positive women 50 years and older</td>
</tr>
<tr>
<td><strong>Low-to-moderate-risk patients</strong></td>
</tr>
<tr>
<td>• Inactive carriers</td>
</tr>
<tr>
<td>• Immune-tolerant patients</td>
</tr>
<tr>
<td>• HBsAg-positive men younger than 40 years</td>
</tr>
<tr>
<td>• HBsAg-positive women younger than 50 years</td>
</tr>
<tr>
<td>• Patients with HBsAg loss (especially cirrhosis patients)</td>
</tr>
</tbody>
</table>

**Surveillance tests**

- AFP
- Abdominal ultrasound

**Surveillance interval**

Every 6 months

**Table 5. AASLD recommendations for HCC surveillance in HBV carriers and persons with CHB.**

<table>
<thead>
<tr>
<th>Surveillance candidates</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Asian male HBV carriers older than 40 years&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>• Asian female HBV carriers older than 50 years&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>• HBV carrier with family history of HCC</td>
</tr>
<tr>
<td>• African/North American Blacks with HBV</td>
</tr>
<tr>
<td>• Cirrhotic HBV carriers</td>
</tr>
<tr>
<td>• Caucasian adults with active HBV infection</td>
</tr>
</tbody>
</table>

**Surveillance tests**

- Abdominal ultrasound

**Surveillance interval**

Every 6 months<sup>b</sup>

<sup>a</sup> Surveillance is recommended regardless of replication status or loss of HBsAg.

<sup>b</sup> Surveillance should be continued regardless of spontaneous clearance of virus, antiviral treatment–induced seroconversion, or remission of inflammatory activity.

AFP, alpha fetoprotein; HBsAg, hepatitis B surface antigen; HCC, hepatocellular carcinoma.


Table 4 shows recommendations for HCC surveillance according to the guidelines for the management of CHB among Asian Americans. Both AFP testing and ultrasonography are recommended for Asian Americans. Patients in the high-risk category have established independent risk factors for HCC, such as family history of HCC and cirrhosis. The low-to-moderate-risk category includes patients with risk factors that are probable but less well established as risk factors for HCC. These recommendations include HBsAg-positive men younger than 40 years and women younger than 50 years because some evidence suggests that these persons are at increased risk for HCC; however, the benefit of surveillance in these groups has not been demonstrated.

The AASLD guidelines for management of HCC recommend HCC surveillance tests every 6 months for all persons of Asian descent who are infected with HBV, regardless of replication status or loss of HBsAg. In addition, HCC screening is recommended for Caucasian adults with active HBV infection, regardless of the presence of cirrhosis. Surveillance should be continued in all patients with CHB who receive treatment, regardless of seroconversion or remission of inflammatory activity associated with therapy. The complete AASLD guidelines for management of HCC, including surveillance in persons who do not have HBV infection, can be found at: http://www.aasld.org/practiceguidelines/Documents/Bookmarked%20practice%20Guidelines/Hccupdate2010.pdf

The AASLD recommendations for HCC surveillance in persons who are HBV carriers or who have CHB, shown in Table 5, differ somewhat from those specifically targeted to Asian Americans. The AASLD recommends surveillance of persons at risk for HCC every 6 months with ultrasonography. The AASLD does not currently recommend the routine use of the AFP test for surveillance. The current AASLD guidelines for management of CHB recommend HCC surveillance every 6 to 12 months. The AASLD guidelines for management of HCC recommend HCC surveillance tests every 6 months for all persons of Asian descent who are infected with HBV.

Although supporting data are currently lacking, debate continues about the potential benefits of screening at earlier ages in Asian Americans. Some evidence suggests that HCC among Asians may occur among men and women who fall below the current age thresholds for HCC surveillance; however, the benefit of surveillance in these groups has not been demonstrated. Current recommendations for Asian Americans call for HCC surveillance among younger persons with cirrhosis or other HCC risk factors. Current recommendations for Asian Americans call for HCC surveillance among younger persons with cirrhosis or other HCC risk factors. In addition, studies show that persistently elevated levels of HBV DNA are an independent risk factor for development of HCC. Other factors may also need to be taken into consideration for younger persons when determining whether to initiate HCC surveillance, including male sex, surrogate laboratory test abnormalities for cirrhosis (eg, platelets, total bilirubin, and albumin), smoking, and a family history of HCC. In addition, smoking and alcohol use may exert a synergistic effect.
Considering Treatment

Sustained suppression of HBV DNA replication with antiviral treatment is fundamental to preventing progression of CHB.9,35
Viral replication significantly increases the risk of CHB complications, as demonstrated by findings from the large-scale prospective Risk Evaluation Viral Load Elevation and Associated Liver Disease (REVEAL) study, shown in Figure 4.46,48,49 At the time of study entry, participants were HBsAg-positive, mostly HBeAg-negative, seronegative for antibodies against hepatitis C virus (HCV), and free of HCC.50 Participants were followed for more than 11 years. After adjustment for other HCC risk factors, researchers found that increasing or unchanged levels of HBV DNA over time were the strongest independent predictor of progression to HCC.46

A number of treatment guidelines are available that describe selection of patients for antiviral treatment based on varying levels of ALT and HBV DNA in the setting of CHB or cirrhosis.

These include the AASLD guidelines,9 an Expert Consensus algorithm,7 the European Association for the Study of the Liver (EASL) Clinical Practice Guidelines for Management of Chronic hepatitis B,50 and the Asian-Pacific consensus statement on the management of chronic hepatitis B.51 However, treatment criteria outlined by these guidelines sometimes exclude patients who go on to develop HCC or who die of other liver-related deaths.52,53 For a full discussion of the comparison of the guidelines as they pertain to antiviral treatment criteria and HCC, consult the full publication: Tong MJ, Hsu L, Chang PW, et al. Evaluation of current treatment recommendations for chronic hepatitis B: a 2011 update. J Gastroenterol Hepatol. 2011;26:829-835. This publication is available at: http://onlinelibrary.wiley.com/doi/10.1111/j.1440-1746.2011.06623.x/full

### REVEAL study participants were followed for more than 11 years.

After adjustment for other HCC risk factors, researchers found that increasing or unchanged levels of HBV DNA over time were the strongest independent predictor of progression to HCC.

The guidelines do not recommend antiviral treatment for patients who are in the immune-tolerant stage or who are inactive carriers.35 Antiviral treatment is recommended for patients who have either HBeAg-positive or HBeAg-negative CHB with HBV DNA >10^4 copies/mL (>2000 IU/mL) and ALT levels >ULN. Patients with normal ALT values who have histologic evidence of necroinflammation (ie, histology activity index [HAI] 2–4, Metavir ≥ grade 2) and fibrosis (stage 2 portal fibrosis, Metavir ≥ stage 2) may also be considered for antiviral treatment.35 Antiviral therapy is recommended for patients with cirrhosis who have any detectable level of HBV DNA regardless of HBeAg status or ALT level.35 Patients with compensated cirrhosis and undetectable HBV DNA should be tested every 3 months for any changes in ALT and HBV DNA levels. Antiviral therapy should be initiated in all patients with decompensated cirrhosis, and they should be immediately referred to a liver-transplant center.

Some patients will not meet criteria for treatment or monitoring as outlined in Table 6.35 This group includes patients with CHB who are HBeAg-negative with HBV DNA levels >10^4 copies/
Treatment Considerations

A group of patients has been developed and was presented in the guidelines for management of CHB in Asian Americans. (See Sidebar: Gray Zone: Risk-Impact Score and Treatment Decisions for a review of this approach.)

Table 6. Selection of Asian American candidates for antiviral treatment by clinical stage, HBeAg.

<table>
<thead>
<tr>
<th>Clinical stage</th>
<th>HBeAg</th>
<th>HBV DNA</th>
<th>ALT*</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune tolerant</td>
<td>+</td>
<td>&gt;10⁴ copies/mL (&gt;2000 IU/mL)</td>
<td>≤ULN</td>
<td>Monitor</td>
</tr>
<tr>
<td>Chronic hepatitis(\ast)(\ast)</td>
<td>±</td>
<td>&gt;10⁴ copies/mL (&gt;2000 IU/mL)</td>
<td>&gt;ULN</td>
<td>Treat</td>
</tr>
<tr>
<td>Gray zone</td>
<td>-</td>
<td>&gt;10⁴ copies/mL (&gt;2000 IU/mL)</td>
<td>≤ULN</td>
<td>Further evaluation needed(\ast)</td>
</tr>
<tr>
<td>Gray zone</td>
<td>±</td>
<td>≤10⁴ copies/mL (≤2000 IU/mL)</td>
<td>&gt;ULN</td>
<td>Further evaluation needed(\ast)</td>
</tr>
<tr>
<td>Cirrhosis(\ast)</td>
<td>±</td>
<td>Detectable</td>
<td>NA</td>
<td>Treat</td>
</tr>
<tr>
<td>Cirrhosis(\ast)</td>
<td>±</td>
<td>Undetectable</td>
<td>NA</td>
<td>Monitor</td>
</tr>
<tr>
<td>Inactive carrier</td>
<td>-</td>
<td>≤10⁴ copies/mL (≤2000 IU/mL)</td>
<td>≤ULN</td>
<td>Monitor</td>
</tr>
</tbody>
</table>

ALT, alanine aminotransferase; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; NA, not applicable; ULN, upper limit of normal.

\(\ast\) ALT normal range is based on local laboratory reference range.

\(\ast\) HBV DNA usually 10⁷ copies/mL to 10¹² copies/mL (2 million IU/mL to 200 million IU/mL).

\(\ast\) Liver biopsy grade 1-3 and/or stage 1-3.

\(\ast\) Patients in this category require further evaluation to determine their need for treatment.

\(\ast\) Treatment is recommended for all patients with CHB and decompensated cirrhosis.


mL (>2000 IU/ml) but who have normal ALT values, as well as patients who are HBeAg-positive or HBeAg-negative with HBV DNA ≤ 10⁴ copies/mL (≤2000 IU/mL) but with elevated ALT values. One approach to making treatment decisions for these 2 groups of patients has been developed and was presented in the guidelines for management of CHB in Asian Americans. (See Sidebar: Gray Zone: Risk-Impact Score and Treatment Decisions for a review of this approach.)

Gray Zone: Risk-Impact Score and Treatment Decisions

As presented in the guidelines for management of Asian Americans with HBV infection, the “gray zone” for treatment refers to patients who do not meet the criteria outlined in Table 6 but who are unwilling to undergo liver biopsy.\(\ast\) The gray zone includes 2 groups of patients: those who are HBeAg-negative with HBV DNA levels >10⁴ copies/mL (>2000 IU/mL) but who have normal ALT levels, and those who are HBeAg-positive or HBeAg-negative with HBV DNA ≤ 10⁴ copies/mL (≤2000 IU/mL) but who have elevated ALT levels. The guidelines for Asian Americans with HBV infection present a risk-impact score as an alternative to liver biopsy for these patients (Figure 5).\(\ast\)

The risk-impact score assigns a numerical value to factors that have been identified as independent risk factors for liver-disease progression,\(\ast\) which include sex, age, basal core promoter (BCP) mutations, HCC history in first-degree relatives, and albumin and platelet values.\(\ast\) In addition, if the patient’s ALT levels are within the clinical laboratory’s ULN, but ≥30 U/L in males and ≥19 U/L in females, an additional point is added. The score total can aid in decisions concerning antiviral treatment. For example, antiviral treatment would be considered for a patient with a risk-impact score ≥3 and an HBV DNA level >10⁴ copies/mL (>2000 IU/mL). A patient with a risk-impact score ≥3 but with an HBV DNA level ≤10⁴ copies/mL (≤2000 IU/mL) would be monitored but not started on antiviral treatment. A patient with a risk-impact score <3 would also be monitored but not treated. The risk-impact score is created based on expert consensus and opinion and warrants further clinical experience and validation.\(\ast\)


Figure 5. Evaluation of hepatitis B patients in the gray zone for antiviral treatment using a risk-impact score.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Impact score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥40 years</td>
<td>1</td>
</tr>
<tr>
<td>Male gender</td>
<td>1</td>
</tr>
<tr>
<td>Male ALT &gt;30 U/L, Female ALT &gt;19 U/L</td>
<td>1</td>
</tr>
<tr>
<td>BCP mutation</td>
<td>2</td>
</tr>
<tr>
<td>HCC in first-degree relative</td>
<td>3</td>
</tr>
<tr>
<td>Albumin ≤3.5 g/dL or platelet count ≤130,000 mm³</td>
<td>3</td>
</tr>
</tbody>
</table>

ALT, alanine aminotransferase; BCP, basal core promoter; HBV, hepatitis B virus; HCC, hepatocellular carcinoma.

Currently, 7 antiviral agents are approved for treatment of CHB in the United States.
The 7 antiviral agents currently approved for treatment of CHB in the United States include 5 oral nucleoside or nucleoside analogue (adefovir [ADV], entecavir [ETV], lamivudine [LAM], telbivudine [TVD], and tenofovir [TDF]) and 2 parenteral agents (standard interferon [IFN] and pegylated interferon alfa-2a [pegIFN α2a]). However, standard interferon has largely been replaced by pegIFN.35 Treatment recommendations for Asians are summarized in Table 7.

TDF and ETV are first-line options for Asian patients.35 PegIFN may be considered a first-line choice for Asian patients who may need a finite treatment period.35 Examples of patients for whom pegIFN may be an initial option include female patients who are planning a pregnancy in the near future, patients who are HBeAg-positive and have elevated ALT levels, and patients who cannot commit to long-term antiviral therapy. ADV, LAM, and TVD are associated with a high risk of resistance and are considered second-line agents.35

Tenovir and entecavir are first-line options for Asian patients. Pegylated interferon may be considered a first-line choice for Asian patients who may need a finite treatment period.

IFN is contraindicated in patients with decompensated cirrhosis because hepatic failure is possible.35 ETV and TDF are preferred in these patients because of their low rates of resistance and high potency.35 An indefinite duration of treatment is recommended for patients with CHB and decompensated cirrhosis.

TREATMENT MONITORING

Careful monitoring during treatment for response and adverse events is required for all patients and therapies.35 Recommendations for HBV serologic and other laboratory tests and the timing of these tests are summarized in Table 8 on page 18.

**Treatment Duration**

Duration of oral antiviral treatment depends on HBeAg status, presence of cirrhosis, and response to therapy. IFN is administered for a finite period.

**HBeAg-positive CHB.** Patients who are HBeAg-positive should remain on antiviral therapy until they seroconvert to anti-HBe-positive status, and thereafter consolidation therapy should be continued for at least an additional 1 to 2 years before stopping therapy can be considered.35 Some HBeAg-positive patients may require prolonged consolidation treatment.35 When treatment is stopped, those patients must be closely monitored for relapse, which may be indicated by seroreversion to HBeAg-positive status, reemergence of HBV DNA, and ALT elevation.35 Risk factors associated with HBeAg seroreversion are unclear.35

**HBeAg-negative CHB.** Because the risk of relapse is high in patients with HBeAg-negative CHB, indefinite antiviral treatment is recommended.35 However, if HBsAg becomes undetectable in HBeAg-negative patients, then antiviral therapy may be stopped, but close monitoring of these patients is mandatory. Prompt retreatment is required if elevations in HBV DNA and ALT levels occur. Further research is needed to determine the optimal duration of antiviral treatment in patients with HBeAg-negative CHB.

**Cirrhosis.** In all patients with cirrhosis, antiviral treatment should be continued for the long term.35 In some patients, antiviral treatment may reverse cirrhosis; however, data are lacking to guide how to discontinue treatment in this setting.

**Resistance management**

Recent clinical trial data show that minimal to no resistance has been detected to TDF or ETV through 5 years of treatment in patients with CHB.55,66 Patients with CHB who require long-term antiviral therapy and maintain suppression of HBV DNA to undetectable levels with monotherapy may remain on the initial antiviral agent unless a virologic breakthrough occurs.35 If patients develop a breakthrough infection during antiviral treatment, adherence to therapy should first be confirmed before any additional measures are taken.9,35 Treatment may be resumed for patients who have had a long lapse in adherence. In cases where adherence is not an issue, particularly if secondary agents have been used, drug resistance testing should be
### Table 8. Recommended monitoring tests and timing during and after CHB antiviral therapy for Asian American patients.

<table>
<thead>
<tr>
<th>Antiviral therapy</th>
<th>HBeAg status</th>
<th>Test</th>
<th>Treatment period</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IFN</strong></td>
<td>HBeAg+ and HBeAg-</td>
<td>HBV DNA</td>
<td>Every 3 months until undetectable; then every 3-6 months</td>
</tr>
<tr>
<td></td>
<td>CBC with absolute neutrophil and platelet count</td>
<td>TSH</td>
<td>Every 12 weeks</td>
</tr>
</tbody>
</table>
|                   | HBeAg+                | HBeAg                                     | • Every 6 months until seronegative for HBeAg; then initiate testing for anti-HBe  
|                   |                       |                                           | • Following seroconversion to anti-HBe-positive, test for HBsAg every 12 months |
|                   | HBeAg-                | HBsAg                                     | Every 12 months after sustained suppression of HBV DNA |
| **Oral nucleos(t)ides** | HBeAg+ and HBeAg-     | HBV DNA                                  | Every 3 months until undetectable; then every 3-6 months |
|                   |                       | ALT                                       | Every 3 months until normalized; then every 3-6 months |
|                   | HBeAg+                | HBeAg                                     | • Every 6 months until HBeAg-seronegative; then initiate anti-HBe testing  
|                   |                       |                                           | • Following seroconversion to anti-HBe-positive, test for HBsAg every 12 months |
|                   | HBeAg-                | HBsAg                                     | Every 12 months after sustained suppression of HBV DNA |

ALT, aminotransferase; anti-HBe, antibody to hepatitis B e antigen; CBC, complete blood count; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IFN, interferon; TSH, thyroid stimulating hormone.


All pregnant women need to be tested for HBV infection. The immediate administration of hepatitis B immune globulin and HBV vaccination following delivery (<12 hours) is recommended for all infants born to HBsAg-positive women. Infants should be closely followed after delivery to ensure completion of the 3-dose vaccine series and to verify appropriate antibody response. Antiviral treatment of newborns is not recommended; however, treatment may be warranted for pregnant women who meet certain criteria.

**SELECT POPULATIONS**

Management of CHB in certain patient groups, including pregnant women, patients who are coinfected with HCV or HIV, and patients who are undergoing immunosuppressive therapy or chemotherapy, presents additional challenges for clinicians.
Treatment Options

Figure 6. Risk assessment and prevention of MTCT of HBV.

CHB, chronic hepatitis B; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; LAM, lamivudine; MTCT, mother-to-child transmission; TDF, tenofovir; TVD, telbivudine.

a Signs of preterm labor: woman shows signs of entering into preterm labor that may lead to premature delivery. This is associated with a greater risk of HBV perinatal transmission.

ment screening for CHB when certain immunomodulatory drugs are to be used, but the American Society of Clinical Oncologists (ASCO) does not currently recommend routine HBV screening of patients scheduled for chemotherapy. ASCO, however, does recommend that clinicians consider screening patients belonging to groups at high risk for CHB. Studies suggest that most (about 70%) rheumatologists follow the ACR guidelines on pretreatment screening, but less than 20% of oncologists test their patients for HBV prior to initiating chemotherapy.

Given the high risk of hepatitis flares and associated mortality, the guidelines for CHB management in Asian Americans recommend that all Asian patients should be screened for HBsAg before initiation of chemotherapy or immunosuppressive therapy, and patients who are HBsAg-negative but anti-HBc-positive should be tested for HBV DNA. Antiviral prophylaxis is recommended for all HBsAg-positive patients scheduled to begin chemotherapy, undergo bone-marrow transplant, or initiate immunomodulatory treatment with such agents as corticosteroids or rituximab. In addition, prophylactic therapy should be considered for anti-HBc-positive patients with detectable HBV DNA levels.

HIV and HBV coinfection
HIV and HBV share routes of transmission, and about 15% of all HIV-positive patients also have CHB. Coinfected patients are at greater risk of liver-related mortality and cirrhosis associated with CHB. Selection of antiviral therapy must take into account both viruses. In patients who do not require highly active antiretroviral therapy (HAART), drugs with dual activity against HBV and HIV (eg, LAM, ETV, emtricitabine [FTC], or TDF) should not be given to them as monotherapy for CHB; these drugs may lead to development of antiretroviral resistance. Monotherapy with pegIFN or combination treatment with ADV and TVD may be useful in these patients. However, in coinfected patients with low CD4 cell counts who require HAART, HBV treatment should include a regimen of TDF combined with either FTC or LAM.

Coinfection with HCV
Data suggest that about 7% to 22% of CHB patients are coinfected with HCV. Patients coinfected with HBV and HCV have more severe liver disease, a higher probability of liver cirrhosis and hepatic decompensation, and a greater incidence of HCC than patients with a single infection.

Given the high risk of hepatitis flares and associated mortality, the guidelines for CHB management in Asian Americans recommend that all Asian patients should be screened for HBsAg before initiation of chemotherapy or immunosuppressive therapy, and patients who are HBsAg-negative but anti-HBc-positive should be tested for HBV DNA.

replication can be suppressed in HCV-coinfected patients. Treatment should be directed at the predominant virus. Some evidence suggests that treatment of HCV infection with standard IFN or pegIFN and ribavirin (RBV) for up to 48 weeks is as effective in treating HBV/HCV-coinfected patients as in patients with HCV monoinfection. However, rebounds in HBV DNA levels and reactivation of HBV have been reported in coinfected patients treated with IFN and RBV. HBV reactivation should be treated with antiviral agents active against this virus.
Many Asian Americans and others from immigrant populations will need counseling and education about CHB screening and vaccination. In addition, patients diagnosed with CHB should receive education on treatment, monitoring, and preventing transmission.⁹
Initiating the conversation. Patients should be asked about their understanding of HBV infection and CHB. Patients may have incorrect information or beliefs about CHB and HBV infection that need to be addressed. For example, patients may believe that HBV can be transmitted by eating with infected people or they may have concerns about the safety of the vaccine. Once the patient’s knowledge about CHB and HBV infection is ascertained, education should be provided as needed to dispel any misconceptions or false beliefs that may interfere with screening, vaccination, or treatment.

For patients who are not infected:

Discussing vaccination. Susceptible patients should be informed about the need for vaccination.

- All patients should be assured that the HBV vaccine is both safe and effective. Patients may benefit from learning that the vaccine contains no live virus and that vaccination does not lead to HBV infection.

Discussing treatment and monitoring. Patients who receive a diagnosis of HBV infection should receive education about the appropriateness of treatment for their specific disease parameters and the need for periodic monitoring.

- Patients should be told that many persons who receive a diagnosis of HBV infection do not need treatment immediately, but they do need to be monitored for any changes in their disease status.

Once the patient’s knowledge about CHB and HBV infection is ascertained, education should be provided as needed to dispel any misconceptions or false beliefs that may interfere with screening, vaccination, or treatment.

For patients who are infected:

Discussing treatment and monitoring. Patients who receive a diagnosis of HBV infection should receive education about the measures that they need to take to prevent transmission.

- Notifying all sexual partners or needle-sharing partners and household contacts that they need to be tested for HBV infection and be vaccinated as needed.
- Using barrier protection during sexual contact with susceptible persons.
- Covering all open sores.
- Cleaning all blood spills with bleach or detergent.
- Avoiding donating blood, plasma, semen, or tissue.

These measures include:

- Patients who require treatment should be informed about the need for long-term treatment and provided with support to maintain adherence. Patients may benefit from a discussion about methods to help with adherence, such as alarms, pillboxes, or coordinating medication doses with routine daily tasks.

Discussing prevention of transmission. Patients who receive a diagnosis of HBV infection should be educated about the measures that they need to take to prevent transmission.

- All HBsAg-positive patients should be reminded that they can participate in all types of social activities involving casual contact, including contact sports, and that they can share food and utensils.

Patients should be reassured that treatment is effective and safe, and the objective is to help prevent progression to advanced liver disease, such as cirrhosis or liver cancer. Visual aids, such as photographs of patients or appropriate graphs to explain data (eg, from the REVEAL study), may help patients understand the connection between viral replication and the risk of liver cancer and cirrhosis.
Timely screening for HBV infection among groups most at risk and linking the newly diagnosed patients to appropriate care are essential to reducing the significant burden of viral hepatitis borne by Asian Americans and other immigrant populations. In response to the 2010 report from the Institute of Medicine (IOM), *Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C*, the Department of Health and Human Services (DHHS) released an action plan for the prevention, care, and treatment of viral hepatitis. The action plan describes strategies for improving identification and linkage to care for patients with viral hepatitis, as well as expanding preventive strategies and public education about the disease.

The recommended steps and strategies correspond to 6 specific areas defined by the 2010 IOM report:

- Educating providers and communities to reduce health disparities
- Improving testing, care, and treatment to prevent liver disease and cancer
- Strengthening surveillance to detect viral hepatitis transmission and disease
- Eliminating transmission of vaccine-preventable viral hepatitis
- Reducing viral hepatitis caused by drug-use behaviors
- Protecting patients and workers from health-care-associated viral hepatitis

Several programs in Asian American communities across the United States most affected by CHB have ongoing or completed programs that focus on these recommended strategies: in particular, on screening, testing, and linkage to care. These models of care can provide examples of workable approaches to prevention, control, and treatment of CHB that may be applicable to other clinical settings. Many of these programs rely on public funding, and their level of operation is often variable. However, lessons can still be learned from their results. The Sidebar: Models of Care for CHB in Asian American Communities on page 24 summarizes several key programs and their results.

Other programs or centers that focus on CHB in Asian American communities include:

- **Viral Hepatitis Program at Harborview Medical Center, Seattle, Washington**
- **Vietnamese Community Health Promotion Project at University of California, San Francisco (www.suckhoelavang.org/viethepb/)**
- **Tufts University School of Medicine, Asian-Pacific Liver Wellness Program, Boston, Massachusetts**
- **Asian Pacific Liver Center (APLC), St. Vincent Medical Center, Los Angeles, California (www.asianpacificlivercenter.org)**
- **Hepatitis B Foundation (www.hepb.org)**

*PLEASE NOTE: This information was compiled from various sources, may not be all inclusive, and does not imply endorsement of any kind. It is provided for general informational purposes only.*
<table>
<thead>
<tr>
<th>Program description</th>
<th>Services</th>
<th>Results</th>
</tr>
</thead>
</table>
| **Jade Ribbon Campaign** | • Public-awareness campaigns  
• Local community screenings and education  
• Health care provider education | **Screening**  
• Over the course of 12 months, 1206 participants were tested  
**Vaccination**  
• 85% of those susceptible were vaccinated  
**Awareness**  
• At one year, 67% of those with CHB consulted a physician for liver-cancer screening, and 78% of all participants encouraged family members to be tested for HBV |
| **San Francisco Hep B Free** | • Public and health care provider education  
• Testing  
• Vaccination  
• Linkage to care | **Screening**  
• Between 2007 and 2009, 4427 clients were tested  
**Serologic results**  
• 238 infected (HBsAg-positive); 2227 immune (anti-HBs-positive); 1962 susceptible  
• 7.9% (208) of Asian and Pacific Islander clients born in Asia were chronically infected  
**Screening follow-up**  
• 69% of chronically infected clients were enrolled in follow-up clinical care  
• 52% of susceptible clients received the first vaccine dose; 49% completed the 3-dose series  
**System-wide laboratory results**  
At all hospital and independent diagnostic laboratories serving San Francisco, 2 years into the program:  
• HBsAg test orders increased by 8%  
• Anti-HBs test orders increased by 17% |
| **B Free NYC also known as the Asian American Hepatitis B Program (AAHBP)** (March 2004 to June 2008) | • Free screening  
• Free vaccination  
• Free or low-cost treatment  
• Alternative to treatment: linkage to care | **Screening**  
• 8888 participants were screened; 84% were foreign-born Asian Americans  
**Serological results**  
• 18% infected (HBsAg-positive); 46% protected (anti-HBs-positive); 36% susceptible  
**Screening follow-up**  
• 83% of those screened returned for care  
**Vaccination**  
• 2253/3156 received the first dose  
• 1652/3156 completed the 3-dose series  
**Referral to care**  
• 1533/1632 infected clients returned for test results, and 100% were referred to their providers or program sites for care  
**Care and treatment**  
• 1162 clients were seen at program clinics  
• >90% completed a full clinical evaluation; 15% began antiviral treatment  
**Long-term results**  
• Program screened 3% of the 51,465 CHB cases reported in 2005-2008 in New York City  
• During the program, the annual number of new CHB cases reported from predominantly Asian neighborhoods increased by 34%  
• One year after the program, new case reports declined by 10% |


*PLEASE NOTE: This information was compiled from various sources, may not be all inclusive, and does not imply endorsement of any kind. It is provided for general informational purposes only.*
Improvement is needed in screening, diagnosis, and linkage to care of Asian Americans with CHB. Although a number of programs are making advances, nationwide and publicly funded efforts are essential to increase opportunities for CHB diagnosis and treatment among populations most at risk.
Providers may also find advances in health technology that could have a role in their own practices. Computer applications are available that provide algorithms that can facilitate and streamline testing, treatment, and monitoring. In addition, health technology can be used to improve surveillance and provide public health data to ensure that all at-risk persons receive the appropriate preventive and clinical care services. In particular, electronic medical records (EMRs) may be an important tool for clinicians. The Centers for Medicare and Medicaid Services (CMS) requirements for meaningful use of EMRs mandate the collection of racial and ethnic data for patients, and many clinical practices or health care centers already have or are currently in the process of collecting this data. Although all EMRs are different, programmers may be able to build in pop-up screens or other alerts that are triggered by a patient’s race or ethnicity and that alert the physician to the need for an HBV test for that particular patient. EMRs can be designed that include all essential information about CHB, including ALT, viral load, and ultrasound results, thereby facilitating tracking of patients and helping ensure that they are retained in care. More information on meaningful-use data and EMRs is available at the CMS Website: http://www.cms.gov/EHRIncentivePrograms/

An example of an EMR programmed to track HBV in a patient is shown in Figure 7 opposite. This example, from the Charles B. Wang Community Health Center in New York City, includes elements that clinicians or health care centers may consider when designing their own EMRs to help identify and follow patients with CHB, such as testing for HBV serologic markers, vaccination history, and liver-enzyme levels.
Future Directions

Figure 7. EMR tracking of HBV testing.

<table>
<thead>
<tr>
<th>HBV Registry</th>
<th>Added 06/09/2009</th>
<th>Remove</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>Positive (06/23/2009 9:53:20 am)</td>
<td>Record</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Negative (06/23/2009 9:59:30 am)</td>
<td>Record</td>
</tr>
<tr>
<td>HBeAg</td>
<td>Reactive (01/08/2009 12:55:00 pm)</td>
<td>Record</td>
</tr>
<tr>
<td>HBeAg</td>
<td>Nonreactive (08/10/2009 12:55:00 pm)</td>
<td>Record</td>
</tr>
<tr>
<td>Anti-HBC</td>
<td>Positive (06/23/2009 9:53:20 am)</td>
<td>Record</td>
</tr>
<tr>
<td>Anti-HBC</td>
<td>Negative (06/23/2009 9:59:30 am)</td>
<td>Record</td>
</tr>
</tbody>
</table>

Vaccination History

<table>
<thead>
<tr>
<th>Hepatitis A</th>
<th>Hepatitis B</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFPA VIRAL</td>
<td>495073 e</td>
</tr>
<tr>
<td>AFPTUMORMKRK</td>
<td>6.6</td>
</tr>
<tr>
<td>SGOT (AST)</td>
<td>34.0</td>
</tr>
<tr>
<td>SGPT (ALT)</td>
<td>55.0</td>
</tr>
<tr>
<td>HB IMAGING</td>
<td></td>
</tr>
<tr>
<td>CT OF ABDOME</td>
<td>Reactive</td>
</tr>
<tr>
<td>HEP B E AG S</td>
<td></td>
</tr>
<tr>
<td>HEP B E AB S</td>
<td></td>
</tr>
<tr>
<td>HBVSGAG</td>
<td></td>
</tr>
<tr>
<td>ANTI-HBS</td>
<td></td>
</tr>
<tr>
<td>ANTI-HAV</td>
<td></td>
</tr>
</tbody>
</table>

AFPTUMORMKRK, alpha fetoprotein tumor marker; ALT, alanine aminotransferase; anti-HAV, hepatitis A virus antibody; anti-HBC, hepatitis B core antibody; anti-HBs, hepatitis B surface antibody; AST, aspartate aminotransferase; CHB, chronic hepatitis B; CT OF ABDOME, computed tomography of abdomen; DM, diabetes mellitus; HB, hepatitis B; HBeAb, hepatitis B e antibody; HBeAg, hepatitis B e antigen; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HFPA, hepatic function panel; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase; USG RUQ, ultrasonography right upper quadrant.


REFERENCES

1. What percent of those persons with CHB in the United States were born in regions of intermediate or high HBV endemicity?
   A. <1%  
   B. 25% to 37%  
   C. 47% to 70%  
   D. >80%

2. The estimated prevalence of CHB among foreign-born Asian Americans is about:
   A. <1%  
   B. 4%  
   C. 7%  
   D. 10%

3. The 3-dose HBV vaccine series provides protection against HBV infection in what percent of most responders?
   A. 60%–65%  
   B. 70%–75%  
   C. 80%–85%  
   D. >90%

4. An Asian American patient who is HBeAg-positive with elevated HBV DNA levels and normal ALT levels is in which clinical stage of CHB?
   A. Immune tolerant  
   B. Immune activation  
   C. Low-replicative phase  
   D. Reactivation

5. According to the guidelines for Asian Americans with CHB, surveillance tests for HCC should be performed:
   A. Monthly  
   B. Every 3 months  
   C. Every 6 months  
   D. Every 24 months

6. For patients with CHB who have HBV DNA levels >10^4 copies/mL (>2000 IU/mL) and ALT levels above the upper limit of normal, the guidelines for management of CHB in Asian Americans recommend:
   A. Monitoring  
   B. Antiviral treatment  
   C. Further testing and liver biopsy  
   D. None of the above

7. Which of the following are first-line antiviral treatments for Asian Americans with CHB?
   A. Entecavir  
   B. Lamivudine  
   C. Tenoflovir  
   D. A and C

8. For patients with CHB receiving treatment with oral antiviral agents, HBV DNA levels should be monitored:
   A. Every 3 months until undetectable; then every 3-6 months  
   B. At baseline: then every 6 months until undetectable; then once a year  
   C. Every 12 months until undetectable; then once every 24 months  
   D. Every month for life

9. In patients with HBeAg-negative CHB who respond to antiviral treatment, therapy should be continued for how long?
   A. 24 weeks  
   B. 1 to 2 years after consolidation therapy  
   C. 48 weeks  
   D. Long-term antiviral treatment is recommended

10. For all infants born to HBsAg-positive women, what measures are recommended?
    A. Immediate administration of hepatitis B immune globulin and HBV vaccination following delivery (<12 hours)  
    B. Administration of first dose of oral antiviral treatment  
    C. Immediate initiation of antiviral treatment to the mother  
    D. Testing for HBsAg status within 12 hours of delivery

OUTCOMES QUESTIONS

Question #1:
In the United States, the majority of individuals with CHB are:
   A. Injection drug users  
   B. Immigrants from countries of intermediate to high HBV endemicity  
   C. Organ-transplant recipients  
   D. Patients with HIV

Question #2:
An individual who tests negative for HBsAg, positive for anti-HBc, and positive for anti-HBs is:
   A. Susceptible to HBV infection  
   B. Immune due to natural infection with HBV  
   C. Immune due to HBV vaccination  
   D. Acutely infected with HBV

Question #3
For treatment of Asian Americans with CHB, tenofovir and entecavir are considered:
   A. Alternatives to first-line treatment with pegIFN  
   B. Second-line agents following telbivudine  
   C. First-line agents  
   D. Contraindicated in those with cirrhosis

Case 1:
HM, a male, aged 37 years, born in China but a US resident for 30 years, was screened for CHB by his primary care physician. Test results showed normal ALT and AST levels, he was HBeAg-positive, and had HBV DNA levels >20,000 IU/mL. He had no evidence of HCC on ultrasound. Repeat tests 6 months later showed the same results. What would be your next step for this patient?

Question #4:
   A. Test for alpha-fetoprotein levels  
   B. Refer for a liver biopsy  
   C. Monitor at 3- to 6-month intervals  
   D. Test for HBV genotype

Testing results 24 months from the baseline tests for HM revealed that his HBV DNA remained >20,000 IU/mL and his ALT level was now above the upper limit of normal on repeat testing. He was still HBeAg-positive. What would be your approach to treatment for this patient?

Question #5:
   A. Begin antiviral treatment  
   B. Refer for liver transplantation  
   C. Vaccinate against HBV  
   D. Perform resistance testing

Case 2:
BW, female, aged 25 years, born in Vietnam, in general good health, just tested positive for her first pregnancy. She was 6 weeks pregnant. As part of the initial evaluation, her physician screened BW for HBV infection and liver function. Her results showed that she was HBeAg-positive and anti-HBs negative, with HBV DNA levels <2000 IU/mL and had normal ALT levels. BW had no signs of chronic liver disease or hepato-splenomegaly, and an ultrasound showed no abdominal abnormalities. What would your approach be to treating this patient?
Please write in your answers to the CME/CE POSTTEST and OUTCOMES QUESTIONS in the boxes provided on the application for CME/CE Credit.

If you wish to receive CME credit for completing this activity, please

Provide the information requested below and sign this application

Complete the Activity Evaluation Form on page 32, and

Write in your answers to the CME POSTTEST in the boxes provided

Fax this application to: 646-674-4888

You must complete each of these sections to receive CME credit for completing this activity.

PLEASE PROVIDE THE FOLLOWING INFORMATION

Please print clearly as illegible applications will result in a delay. This application must be submitted by April 18, 2013.

First Name _______________________________  Middle Initial __________  Last Name __________________________________________________

Degree:  □ MD   □ RN   □ NP   □ PA   □ Other _______________________________________________________________________

Mailing Address: ______________________________________________________________________________________________________

City: _____________________________________ State: ______   Zip Code: ________________ Fax: _______________________________________

E-mail Address* (*REQUIRED TO RECEIVE CERTIFICATE):_______________________________________________________________________________

Would you like to receive educational activities on the topic of hepatitis?  □ Yes  □ No

Global Education Group (Global) and HealthmattersCME are interested in adding to our base of faculty and educational development. To help us better plan for education in this area, and to invite you to partake in future educational development, we may contact you for your expertise. If you opt NOT to be contacted in the future, please check the box below:

□ NO, I do NOT want to be contacted in the future.

I certify my actual time spent to complete this educational activity to be (check one):

□ I participated in the entire activity and claim 1.75 credits.

□ I participated in only part of the activity and claim _________ credits.

I certify that I have participated in the continuing education activity entitled, B AWARE 4 CARE: STRATEGIES & SOLUTIONS FOR HEPATITIS B SCREENING, TESTING, LINKAGE TO CARE, & TREATMENT.

Signature: ___________________________________________ Date: ____________________________

Please allow 6-8 weeks to receive your certificate. Thank you for participating in this activity.

For Internal Use Only:  Date Sent: _______________

| CME QUESTION | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | YOUR ANSWER | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |

31
PLEASE COMPLETE THE FOLLOWING ACTIVITY EVALUATION FORM.

I am a(n): □ MD  □ DO  □ PharmD  □ RN  □ NP  □ PA  □ Other ______________________

PLEASE RATE YOUR LEVEL OF AGREEMENT BY CIRCLING THE APPROPRIATE RATING:

<table>
<thead>
<tr>
<th>The learning objectives designed for this activity can help me strive toward:</th>
<th>Significant Improvement</th>
<th>Moderate Improvement</th>
<th>Reinforcement</th>
<th>Not Met</th>
</tr>
</thead>
<tbody>
<tr>
<td>Describe the disproportionate impact that CHB has had among immigrant populations from areas with high or intermediate HBV prevalence rates</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Discuss barriers to care that exist among patients from immigrant populations at risk for CHB</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Explain how to counsel patients on screening for CHB</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Describe immunization strategies against HBV</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Explain follow-up care, treatment, and monitoring for patients diagnosed with CHB</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Identify programs with successful approaches in prevention, testing, screening, linkage to care, and management in high-risk immigrant populations</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

Please indicate the extent of your agreement with the following statements:

<table>
<thead>
<tr>
<th>The information presented in this activity was pertinent to my professional needs.</th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Not Sure</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>The information presented was current.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>The information was presented in a fair and balanced manner and examined the topic with scientific rigor.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>The activity was well organized and well managed.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>The content of this activity contributes valuable information that will assist me in improving patient outcomes.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Based on my experience today, I would recommend future activities for hepatitis similar to this to my colleagues.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

The information presented at this activity was pertinent to my professional needs.  

<table>
<thead>
<tr>
<th>Poor to Fair</th>
<th>Fair to Good</th>
<th>Excellent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Would patient education materials be helpful to your practice?  □ Yes  □ No

Will the information presented cause you to make any changes in your practice?  □ Yes  □ No

Please explain the reason for your answer:

_______________________________________________________________________________________________________________________________________
_______________________________________________________________________________________________________________________________________

Based on your experience, which one of the following is the primary barrier to implementing change in performance? (circle one):

A. Lack of knowledge regarding evidence-based strategies  
B. Misperceptions of or negative attitudes about research and evidence-based care  
C. Demanding patient workloads  
D. Fears about practicing differently than peers

Based on the information presented in this educational activity, which of the following statements best reflects your sentiment toward education for hepatitis? (circle one)

A. I have learned everything I need to learn about hepatitis.  
B. I would like to learn more about hepatitis.

We would be interested in using your topic suggestions as a means to develop future education. What general comments or additional topics would you suggest for future activities?

_______________________________________________________________________________________________________________________________________
_______________________________________________________________________________________________________________________________________

Overall, was this activity satisfactorily free from commercial bias?  □ Yes  □ No

Comments:

_______________________________________________________________________________________________________________________________________
_______________________________________________________________________________________________________________________________________

_______________________________________________________________________________________________________________________________________
This activity has been endorsed by the Asian Health Foundation (AHF), the Chinese American Medical Society (CAMS), the Korean-American Medical Association (KAMA), and the Vietnamese American Medical Association (VAMA).

This activity is supported by an independent educational grant from Bristol-Myers Squibb.

This activity is jointly sponsored by Global Education Group and HealthmattersCME.