JOHNS HOPKINS MEDICINE
eLITERATURE REVIEW™
eViralHepatitis Review
Presented by the Johns Hopkins University School of Medicine
Supported by an Educational Grant from Gilead Sciences, Inc.

eViralHepatitis Review
March 2011: VOLUME 1, ISSUE 2

HBV Counseling and How to Treat, Monitor and Refer

In this Issue...

Hepatitis B virus (HBV) infection is a major global health problem, with about one-third of the world's population having been exposed to the virus. Treatment of HBV is aimed at improving survival via remission of liver disease, and preventing cirrhosis, liver failure, and hepatic cancer. Reduction in HBV DNA levels is the primary parameter used to assess therapeutic response.

In this issue, we review the recent literature on: (1) disease prevalence and screening targets; (2) therapeutic options for patients with chronic HBV, including injectable interferons and nucleoside/nucleotide analogues; and (3) the risk for hepatocellular carcinoma and liver-related death among carriers of inactive HBV.

LEARNING OBJECTIVES

After completing this activity, participants will demonstrate the ability to:

- Describe the results of recent research in hepatitis B treatment agents
- Discuss the risk of progression in inactive hepatitis B carriers
- Explain new epidemiological data regarding the geographic prevalence of hepatitis B

IMPORTANT CME/CE INFORMATION

Program Begins Below

ACCREDITATION STATEMENTS
The Johns Hopkins University School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION
The Johns Hopkins University School of Medicine designates this enduring material for a maximum of *1.0 AMA PRA Category1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

SUCCESSFUL COMPLETION
To successfully complete this activity, participants must read the content, then link to the Johns Hopkins University School of Medicine's website to complete the post-test and evaluation. Once you receive a passing grade of 70% or higher, you can access and print your certificate of credit.

NOTE: If you already have registered for other Hopkins CME programs at the CME website simply enter the requested information when prompted.

Provided to registered subscribers without charge or prerequisite

This activity is supported by an educational grant from Gilead Sciences, Inc.

INTERNET CME POLICY
The Office of Continuing Medical Education (CME) at the Johns Hopkins University School of Medicine is committed to protecting the privacy of its members and customers. The Johns Hopkins University SOM CME maintains its Internet site as an information resource and service for physicians, other health professionals, and the public.

The Office of Continuing Medical Education at the Johns Hopkins University School of Medicine will keep your personal and credit information confidential when you participate in an Internet-based CME program. Your information will never be given to anyone outside of The Johns Hopkins University School of Medicine's CME program. CME collects only the information necessary to provide you with the services that you request.

STATEMENT OF RESPONSIBILITY
The Johns Hopkins University School of Medicine takes responsibility for the content, quality, and scientific integrity of this CME activity.

INTENDED AUDIENCE
This activity has been developed for primary care physicians, hepatologists, oncologists, infectious disease specialists, and others involved in the care of patients with viral hepatitis.

Program Information
CME/CE Info
Accreditation
Credit Designations
Intended Audience
Learning Objectives
Internet CME Policy
Faculty Disclosures
Disclaimer Statement

Length of Activity
1.0 hour Physicians

Release Date
March 29, 2011

Expiration Date
March 28, 2013

Next Issue
April 21, 2011

TO ACCESS THE POST-TEST

Step 1.
Review the CE Information and study the educational content.

Step 2.
Click the post-test link at the end of the newsletter.

Step 3.
Follow the instructions to access a post-test.

LAUNCH DATE
February 1, 2011; activities expire 2 years from the date of publication.

DISCLAIMER STATEMENT
The opinions and recommendations expressed by faculty and other experts whose input is included in this program are their own. This enduring material is produced for educational purposes only. Use of the Johns Hopkins University School of Medicine name implies review of educational format design and approach. Please review the complete prescribing information of specific drugs or combination of drugs, including indications, contraindications, warnings, and adverse effects before administering pharmacologic therapy to patients.

FULL DISCLOSURE POLICY AFFECTING CME ACTIVITIES:
As a provider approved by the Accreditation Council for Continuing Medical Education (ACCME), it is the policy of the Johns Hopkins University School of Medicine Office of Continuing Medical Education (OCME) to require signed disclosure of the existence of financial relationships with industry from any individual in a position to control the content of a CME activity sponsored by OCME. Members of the Planning Committee are required to disclose all relationships regardless of their relevance to the content of the activity. Faculty are required to disclose only those relationships that are relevant to their specific presentation. The following relationships have been reported for this activity:

- **Mark S. Sulkowski, MD** has disclosed he has received grants/research support from Merck, Roche, Vertex, Gilead, GlaxoSmithKline, Abbott, Tibotec, and BIPI.
- **David L. Thomas, MD** discloses that he has served as an advisor for Merck and received medications given for clinical trials from Gilead.

Guest Authors Disclosures

HARDWARE & SOFTWARE REQUIREMENTS
Pentium processor or greater, Windows 98/NT/2000/XP or Mac OS 9/X, Microsoft Internet Explorer 5.5 or later, 56K Modem or better, Windows Media Player 9.0 or later, 128 MB of RAM Monitor settings: High color at 800 x 600 pixels, Sound card and speakers, Adobe Acrobat Reader, storage, internet connectivity, and minimum connection speed.

THIS ISSUE

Program Directors

Mark S. Sulkowski, MD
Associate Professor of Medicine
Medical Director
Viral Hepatitis Center
The Johns Hopkins University
School of Medicine
Baltimore, Maryland

David L. Thomas, MD
Professor of Medicine
Director
Division of Infectious Disease
The Johns Hopkins University
School of Medicine
Baltimore, Maryland

GUESTS AUTHOR OF THE MONTH

Commentary & Reviews:

Zhiping Li, MD
Assistant Professor of Medicine
Director, Transplant Hepatology Fellowship Program
Division of Gastroenterology and Hepatology
Johns Hopkins University School of Medicine
Baltimore, Maryland

Guest Faculty Disclosures

Zhiping Li, MD has disclosed that he received financial support as an advisor for Gilead.

Unlabeled/Unapproved Uses

The author has indicated that there will be references to unlabeled/unapproved uses of Truvada.

Program Directors' Disclosures

RECOMMEND TO A COLLEAGUE

NEWSLETTER ARCHIVE

COMMENTARY

It is estimated that approximately 350 million persons worldwide are chronically infected with hepatitis B virus (HBV), with one-third of the world's population exhibiting evidence of exposure to the virus.[1] In the United States, there are an estimated 1.25 million HBV carriers.[2] Current guidelines recommend screening persons who are born in areas with high or intermediate prevalence rates for HBV, including immigrants and adopted children, as well as those with specific risk factors for the virus.[2]

In a recent study (reviewed herein), Rein and colleagues examined the prevalence of hepatitis B surface antigen (HBsAg) among refugees recently entering the United States.[3] The authors reported not only a wide variation in the prevalence of HBsAg among immigrants, but also a changing prevalence over the years among countries that have initiated vaccination or other public health care measures against chronic hepatitis B (CHB) infection.

The overall goal of HBV treatment is to improve survival through remission of liver disease, and to prevent cirrhosis, liver failure, and hepatic cancer. This is accomplished by maintaining sustained suppression of HBV replication. Therefore, reduction in HBV DNA levels is the primary parameter used to evaluate treatment response. Loss of hepatitis B "e" antigen (HBeAg), development of anti-HBe, loss of HBsAg, development of anti-HBs, normalization of serum alanine aminotransferase (ALT) levels, and improvement in liver histology are all additional goals of therapy.

Currently, 7 medications have been approved for treating adults with CHB infection in the United States and Europe. According to current guidelines, treatment is indicated in patients with active HBV disease and elevated ALT and HBV DNA levels, cirrhosis, or evidence of HBV who plan to initiate immunosuppressive therapy.[4] Patients with CHB infection should be evaluated for treatment, but selecting whom to treat remains a challenge, and guidelines and expert opinions are controversial. Because higher HBV DNA levels are significantly correlated with both liver disease progression and hepatocellular carcinoma (HCC) risk, this is another important factor to consider when deciding whom to treat. The association of initial HBV DNA levels with cirrhosis and HCC has been demonstrated repeatedly in a series of studies.[5-7] The recent study by Chen and coworkers, reviewed in this issue, showed that carriers of inactive HBV still have an increased risk for HCC.[8]

The 7 agents currently approved in the United States and Europe for treating CHB can be grouped into 2 classes: (1) the injectable interferons (IFNs), which include standard IFN-alfa and pegIFN-alfa; and (2) the oral nucleoside/nucleotide analogues, which comprise lamivudine, adefovir, entecavir, telbivudine, and tenofovir. In addition, the nucleoside analogue emtricitabine, which is structurally similar to lamivudine, is approved as part of combination therapy for the treatment of HIV infection and is being tested in combination with tenofovir for the treatment of CHB. Standard IFN for the management of CHB has been replaced largely by pegIFN-alfa because of its more favorable dosing schedule and

improved efficacy.[9] In this issue, we review one of the recent studies (by Wong and associates) that demonstrated the durability of pegIFN-alfa-2b treatment at 5 years for patients with CHB.[10]

Lamivudine was the first available nucleoside analogue oral therapy for HBV. The agent has been shown to be safe and effective for treating CHB, even during pregnancy.[11] However, after 5 years, the proportion of persons who develop resistance to the drug is as high as 60% to 70%.[12] In addition, patients with lamivudine-resistant HBV have a higher incidence of resistance to other nucleoside analogues, such as entecavir.13 Because of these high rates of antiviral resistance, lamivudine is no longer considered first-line therapy for the treatment of CHB.

The use of adefovir, a nucleotide analogue, has been replaced largely by tenofovir, which is structurally similar to adefovir but has higher potency, lower resistance, and lower cost.[14] Another nucleoside analogue, telbivudine, has demonstrated superior efficacy to lamivudine for treating CHB. Telbivudine is associated with the same resistance profile as lamivudine, with resistance to the agent reported as 3% to 4% after 1 year of therapy and 9% to 22% after 2 years of therapy.[15]

Entecavir is a nucleoside analogue that exhibits potent antiviral activity. After 1 year of treatment, there is about a 67% and 90% HBV DNA loss in HBeAg-positive and HBeAg-negative patients, respectively.[16,17] Unlike lamivudine and telbivudine, however, the use of entecavir is associated with low antiviral resistance in persons with wild-type HBV infection. In this issue, we review a recent study by Chang and associates, which showed the efficacy and resistance profile of entecavir treatment after 5 years.[18] Given its antiviral efficacy and low resistance profile among nucleoside-naïve patients, entecavir remains a preferred first-line treatment for CHB. However, in persons with resistance to lamivudine (and telbivudine), the development of resistance to entecavir is more rapid. Monotherapy with entecavir is thus not recommended.

Tenofovir is the most recently approved oral antiviral medication for treating CHB. Use of the agent is associated with rates of HBV DNA loss of 76% and 93% in HBeAg-positive and HBeAg-negative patients, respectively, after 1 year treatment.[14] Given its antiviral potency, the rarity of resistance, and its lack of significant side effects, tenofovir is replacing adefovir for the treatment of CHB. Tenofovir is an appropriate first-line treatment that is effective in patients with resistance to lamivudine, telbivudine, or entecavir. In addition, a recent study by Berg and colleagues (reviewed herein) has shown that when substituted for adefovir in treated patients who do not achieve complete viral suppression, tenofovir has been successful in achieving HBV DNA loss.[19]

Commentary References

1. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: management of chronic hepatitis B. *J Hepatology*. 2009;50(2):227-242.
2. Lok AS, McMahon BJ. Chronic hepatitis B: update 2009. *Hepatology*. 2009;50(3):661-662.
3. Rein DB, Lesesne SB, O'Fallon A, Weinbaum CM. Prevalence of hepatitis B surface antigen among refugees entering the United States between 2006 and 2008. *Hepatology*. 2010;51(2):431-434.
4. Sorrell MF, Belongia EA, Costa J, et al. National Institutes of Health consensus development conference statement: management of hepatitis B. *Hepatology*. 2009;49(5 suppl):S4-S12.
5. Chen C-J, Yang H-I, Iloeje UH; REVEAL HBV Study Group. Hepatitis B virus DNA levels and outcomes in chronic hepatitis B. *Hepatology*. 2009;49 (5 suppl):S72-S84.
6. Chen C-J, Yang H-I, Su J, et al; REVEAL HBV Study Group. Risk of hepatocellular carcinoma across a biological gradient of serum hepatitis B virus DNA level. *JAMA*. 2006;295(1):65-73.
7. Iloeje UH, Yang H-I, Su J, Jen CL, You SL, Chen CJ; Predicting cirrhosis risk based on the level of circulating hepatitis B viral load. *Gastroenterology*. 2006;130(3):678-686.
8. Chen J-D, Yang H-I, Iloeje UH, et al; Carriers of inactive hepatitis B virus are still at risk for hepatocellular carcinoma and liver-related death. *Gastroenterology*. 2010;138(5):1747-1754.
9. Cooksley WGE, Piratvisuth T, Lee S-D, et al. Peginterferon a-2a (40 kDa): an advance in the treatment of hepatitis B e antigen-positive chronic hepatitis B. *J Viral Hepat*. 2003;10(4):298-305.
10. Wong VW-S, Wong GL-H, Yan KK-L, et al. Durability of peginterferon alfa-2b treatment at 5 years in patients with hepatitis B e antigen–positive chronic hepatitis B. *Hepatology*. 2010;51(6):1945-1953.

11. Fontana RJ. Side effects of long-term oral antiviral therapy for hepatitis B. *Hepatology*. 2009;49(5 suppl):S185-S195.
12. Lok AS, McMahon BJ. Chronic hepatitis B. *Hepatology*. 2007;45(2):507-39.
13. Tenney DJ, Rose RE, Baldick CJ, et al. Long-term monitoring shows hepatitis B virus resistance to entecavir in nucleoside-naïve patients is rare through 5 years of therapy. *Hepatology*. 2009;49(5):1503-1514.
14. Marcellin P, Heathcote EJ, Buti M, et al. Tenofovir disoproxil fumarate versus adefovir dipivoxil for chronic hepatitis B. *N Engl J Med*. 2008;359(23):2442-2455.
15. Ayoub WS, Keeffe EB. Review article: current antiviral therapy of chronic hepatitis B. *Aliment Pharmacol Ther*. 2008;28(2):167-177.
16. Chang T-T, Gish RG, de Man R, et al; BEHoLD AI463022 Study Group. A comparison of entecavir and lamivudine for HBeAg-positive chronic hepatitis B. *N Engl J Med*. 2006;354(10):1001-1010.
17. Lai C-L, Shouval D, Lok AS, et al; BEHoLD AI463027 Study Group. Entecavir versus lamivudine for patients with HBeAg-negative chronic hepatitis B. *N Engl J Med*. 2006;354:1011-1020.
18. Chang T-T, Lai C-L, Kew Yoon S, et al. Entecavir treatment for up to 5 years in patients with hepatitis B e antigen–positive chronic hepatitis B. *Hepatology*. 2010;51(2):422-430.
19. Berg T, Marcellin P, Zoulim F, et al. Tenofovir is effective alone or with emtricitabine in adefovir-treated patients with chronic-hepatitis B virus infection. *Gastroenterology*. 2010;139(4):1207-1217.

back to top

TENOFOVIR MONOTHERAPY VS TENOFOVIR PLUS EMTRICITABINE IN ADEFOVIR-TREATED PATIENTS WITH CHRONIC HEPATITIS B

Berg T, Marcellin P, Zoulim F, et al. **Tenofovir is effective alone or with emtricitabine in adefovir-treated patients with chronic-hepatitis B virus infection**. *Gastroenterology*. 2010;139(4):1207-1217.

(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)

View journal abstract View full article

Adefovir dipivoxil (ADV) is an oral nucleotide analogue approved in 2002 for treating patients with CHB. It is effective in the setting of lamivudine resistance, but at the approved dose of 10 mg/day, ADV is a relatively weak antiviral agent, compared with other antivirals. Patients who have not responded to ADV or who have viral breakthrough/rebound are usually treated with an added second agent, such as lamivudine, or switched to a more potent drug. Tenofovir disoproxil fumarate (TDF) has been approved for treating CHB and has exhibited greater efficacy than ADV in randomized, controlled trials. Limited clinical data are available, however, on the effectiveness of TDF in the setting of ADV resistance or primary nonresponse/ breakthrough during ADV therapy. Recently, Berg and colleagues conducted a randomized, double-blind, double-dummy study to compare the efficacy of TDF monotherapy or TDF plus emtricitabine in patients who experienced a suboptimal response to ADV.

A total of 105 patients with HBeAg-positive or HBeAg-negative CHB who had persistent HBV replication after ≥24 weeks of ADV treatment were randomly assigned to 1 of 2 treatment groups: (1) TDF monotherapy (n=53) or (2) emtricitabine (FTC)/TDF combination therapy (n=52). The study protocol permitted crossover to open-label TDF/FTC therapy in subjects with HBV DNA ≥400 IU/mL at treatment week 24. At baseline, patients' mean HBV DNA level was 5.97 $\log_{10}$ copies/mL, and 58% of the study participants had received lamivudine. Of the 105 patients randomized and treated, 80 (37 in the TDF group and 43 in the FTC/TDF group) completed 48 weeks of double-blind treatment without switching to open-label FTC/TDF; 23 subjects switched to open-label FTC/TDF therapy. Importantly, no difference was observed in viral decay curves between the treatment groups. At week 48, HBV DNA levels <400 copies/mL were achieved in 81% of patients who initially received TDF or TDF/FTC. Further, the presence of baseline lamivudine-associated or ADV-associated mutations did not affect response, and viral breakthrough caused by resistance was not observed in either group. There were no additional adverse events observed.

This study demonstrates that treatment with TDF alone or in combination with FTC is equally effective in persons with CHB who have exhibited preexisting drug resistance and a prior incomplete response to ADV. A longer follow-up (168 weeks) study is planned.

back to top

ENTECAVIR THERAPY IN PATIENTS WITH HEPATITIS B e ANTIGEN–POSITIVE CHRONIC HEPATITIS B

Chang T-T, Lai C-L, Kew Yoon S, et al. **Entecavir treatment for up to 5 years in patients with hepatitis B e antigen-positive chronic hepatitis B**. *Hepatology*. 2010;51(2):422-430.

(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)

View journal abstract View full article

Along with TDF, entecavir (ETV) is a first-line oral antiviral agent for treating CHB in patients who had not received prior therapy. In one of its registration trials, ETV demonstrated histologic, virologic, and biochemical benefits superior to lamivudine after 48 weeks of treatment in nucleoside-naïve HBeAg-positive patients. Since long-term, sustained virologic suppression is one of the primary goals of HBV therapy, this recently published study by Chang and associates examined the efficacy and the resistance profile of ETV monotherapy for a cumulative duration of up to 5 years.

This is an ongoing, multinational, rollover study designed to provide open-label ETV to patients from previous phase 2 or phase 3 trials. The current study enrolled a total of 183 patients. Of those, 146 patients met the criteria for inclusion in the ETV long-term cohort. The proportion of patients in the cohort who achieved HBV DNA <300 copies/mL increased from 55% in year 1, to 83% in year 2, to 94% in year 5. At year 5, normal ALT levels were exhibited in 80% of patients, with 23% achieving HBeAg seroconversion and 1.4% demonstrating a loss of HBsAg. One patient who received 16 weeks of lamivudine plus ETV combination therapy before being switched to ETV monotherapy developed viral resistance during year 3. The long-term safety profile of ETV treatment was relatively mild and was similar to that observed during the initial 48-week study. No subject discontinued ETV therapy because of an adverse event. Overall, 5 deaths occurred; 1 patient developed HCC. No difference was observed between the cumulative safety profile of ETV in the long-term cohort and that of ETV in the larger patient population treated in the initial study.

The authors concluded that long-term therapy with ETV through 5 years maintained high rates of HBV DNA suppression (<300 IU/mL) and ALT normalization, with minimal viral resistance. In addition, patients continued to achieve HBeAg loss and seroconversion while undergoing long-term ETV therapy.

back to top

PEGINTERFERON ALFA-2B DURABILITY IN PATIENTS WITH HEPATITIS B e ANTIGEN–POSITIVE CHRONIC HEPATITIS B

Wong VW-S, Wong GL-H, Yan KK-L, et al. **Durability of peginterferon alfa-2b treatment at 5 years in patients with hepatitis B e antigen-positive chronic hepatitis B**. *Hepatology*. 2010;51(6):1945-1953.

View journal abstract View full article

In addition to TDF and ETV, peginterferon alfa is recommended by American and European professional societies as a first-line treatment option for patients with CHB. Despite its association with more side effects than oral therapy and the need for weekly subcutaneous administration, peginterferon carries the advantage of a fixed duration of

treatment (48 weeks) with no risk for drug resistance. In some studies, relatively high rates of HBeAg seroconversion at 48 weeks have been observed with peginterferon. In the current study, Wong and coworkers evaluated the long-term durability of seroconversion in HBeAg-positive patients with CHB treated with peginterferon alfa-2b plus lamivudine.

The authors prospectively followed 85 patients with HBV genotype B or C who received peginterferon alfa-2b at a 1.5-?g/kg/week dosage (up to a maximum of 100 ?g/week) subcutaneously for 32 weeks and lamivudine 100 mg/day for 52 or 104 weeks; the mean follow-up was 6.1 ± 1.7 years posttreatment. The rate of HBeAg seroconversion rose progressively, from 37% at the end of the initial treatment period to ~60% at the 5-year follow-up, with no additional therapy. The cumulative incidence of spontaneous posttreatment HBeAg seroconversion at 6 months, 1 year, 2 years, 3 years, 4 years, and 5 years posttreatment was 25%, 33%, 49%, 65%, 67%, and 71%, respectively. At the end of peginterferon treatment and at 5 years, 32% and 13% of the patients had HBV DNA levels <100 copies/mL, respectively. Interestingly, the duration of concomitant lamivudine therapy had no impact on long-term viral suppression. Only 2 patients (2.4%) achieved HBsAg seroclearance. Of note, week 16 HBV DNA levels, end-of-treatment HBeAg seroconversion, and undetectable HBV DNA levels were all independent factors associated with virologic response at 5 years. In other studies, low HBV DNA levels and HBV genotype A were associated with a better response to peginterferon.

Thus, peginterferon may represent an appropriate first-line option for treating patients with HBeAg-positive CHB and compensated liver disease, especially if a fixed course without the risk for antiviral resistance is particularly attractive.

back to top

RISK FOR HEPATOCELLULAR CARCINOMA AND LIVER-RELATED DEATH AMONG CARRIERS OF INACTIVE HEPATITIS B VIRUS

Chen J-D, Yang H-I, Iloeje UH, et al; **Carriers of inactive hepatitis B virus are still at risk for hepatocellular carcinoma and liver-related death**. *Gastroenterology*. 2010;138(5):1747-1754.

(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)

View journal abstract View full article

In the Risk Evaluation of Viral Load Elevation and Associated Liver Disease/Cancer in HBV (REVEAL-HBV) study, the magnitude of the HBV DNA level is significantly correlated with the long-term risk for development of cirrhosis and HCC. However, the risk for disease among carriers of inactive HBV was not well described. In this follow-up study, Chen and coauthors prospectively evaluated 1932 carriers of inactive HBV (defined as being HBsAg seropositive with a normal serum ALT level and an HBV DNA level <10,000 copies/mL or 1900 IU/mL at entry) and 18,137 healthy control subjects (defined as being seronegative for HBsAg and antibodies against hepatitis C virus, yet exhibiting similar clinical liver features). All participants in this analysis contributed 262,122 person-years of follow-up, with a mean follow-up of 13.1 years (standard deviation, 1.8 years).

Compared with the control subjects, carriers of inactive HBV had a significantly higher risk for liver disease. The incidence rate of HCC per 100,000 person-years was 64 in the inactive HBV carriers and 15 in the controls, yielding an incidence rate ratio of 4.4 (95% confidence interval [CI], 3.2 to 5.9). The other significant risk predictors included older age, a high normal baseline serum ALT level, and an alcohol drinking habit. Interestingly, compared with controls, the risk for HCC was greater among inactive HBV carriers with detectable HBV DNA (300 to 10,000 copies/mL). In addition, the liver-related mortality rate per 100,000 person-years was 44 in the inactive HBV carrier subcohort vs. 21 in the control subcohort (crude rate ratio=2.1; 95% CI, 1.5 to 2.9). Risk predictors for liver-related death were similar to those for HCC.

In conclusion, carriers of inactive HBV have a substantially higher risk for HCC and liver-related death compared with persons who are not infected with HBV. This study raises the question of appropriate HBV DNA and ALT levels to be used to determine who is a candidate for HBV treatment. Currently, the American guidelines recommend that both the serum ALT and HBV DNA level be elevated above recommended thresholds before treatment: ALT levels >2 times the upper limit of normal (ULN), and HBV DNA levels >20,000 IU/mL for HBeAg-positive persons and >2000 IU/mL for HBeAg-negative persons. However, although the investigators suggest that even those who do not meet current criteria for treatment are at risk for liver-related death and HCC, the study is observational and cannot evaluate the effect of HBV treatment on the actual risk for these outcomes.

back to top

PREVALENCE OF HEPATITIS B SURFACE ANTIGEN AMONG IMMIGRANTS ENTERING THE UNITED STATES: 2006 TO 2008

Rein DB, Lesesne SB, O'Fallon A, Weinbaum CM. **Prevalence of hepatitis B surface antigen among refugees entering the United States between 2006 and 2008.** *Hepatology*. 2010;51(2):431-434.

(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)

View journal abstract View full article

The Centers for Disease Control and Prevention has recommended testing for HBsAg in all persons born in regions of the world with an HBV prevalence of ≥2.0%. However, few estimates are available of the prevalence of CHB infection in the United States based on country of origin. Currently, the source of such data that is relied on most often is a compilation of screening results from refugees who entered the United States between 1979 and 1991. In the current study, the authors replicated and expanded upon these earlier results using data collected between 2006 and 2008.

A total of 31,980 refugees (approximately 42% of the refugees entering the United States during the observation period) from 9 jurisdictions were screened for HBsAg according to the country of origin. Overall, the estimated HBsAg prevalence was 2.8% (95% CI, 2.6% to 3.0%) for refugees. The prevalence was highest among refugees from Africa (8.1%) and Southeast Asia (10.5%), and lowest among refugees from Europe (2.6%) and South/Central America (1%). The prevalence ranged from 0.6% (Iraq) and 0.7% (Venezuela) to 12.4% (Myanmar) and 15.5% (Eritrea). In 8 countries for which data could be compared with data from 1991, the prevalence of HBV was lower, including Iraq (from 13.0% to 0.6%), Laos (from 15.5% to 2.3%), Thailand (from 14.2% to 6.1%), and Vietnam (from 13.8% to 3.2%). In contrast, the prevalence increased slightly in Afghanistan (from 4.1% to 5.0%).

Taken together, these data indicate that HBV screening should be continued in immigrants from many regions of the world in which the prevalence remains >2.0%. However, the decreased prevalence of HBV infection among refugees from some countries is encouraging.

back to top