The role of primary care physician assistants in managing chronic hepatitis B

Geoff A. Beckett, PA-C, MPH; Joan M. Block, RN, BSN; Chari Cohen, MPH; Brian J. McMahon, MD

ABSTRACT

This article informs physician assistants of an algorithm designed for primary care practice to guide the screening of patients for hepatitis B virus infection. The algorithm also provides guidance on evaluation, follow-up, and referral of patients who screen positive. The algorithm is a synthesis of several published, evidence-based practice guidelines and reports.

Keywords: hepatitis B virus, hepatocellular carcinoma, chronic HBV infection, antiviral, immunization, cirrhosis

Although immunization has dramatically reduced the incidence of hepatitis B virus (HBV) infections in the United States, an estimated 1 to 2 million Americans are chronically infected with HBV, and have a significant lifetime risk of developing cirrhosis, liver failure, and hepatocellular carcinoma.[1-3]

HBV can be transmitted perinatally, through sexual or close household contact, and by direct contact with infected blood, body fluids, tissues, and organs (for example, percutaneous or mucosal exposure, or transplantation). In the United States, most patients with chronic HBV infection are immigrants or refugees born in countries in which HBV is highly endemic, and where most transmission occurs perinatally and during early childhood. A substantial proportion of these countries are in sub-Saharan Africa and Asia (**Figure 1**). Chronic HBV infection can persist without overt symptoms for many years, and more than half of people infected with HBV may be unaware of their status.[4]

Although chronic HBV infection has no cure, active disease can be managed effectively with antiviral treatments.[5] The primary care physician assistant (PA) can play a key role in the early diagnosis of chronic HBV infection and in the lifelong periodic monitoring that is necessary for patients with chronic HBV.

PUTTING THE GUIDELINES INTO PRACTICE

Many primary care providers do not follow the guidelines for routine screening for HBV, and many have only limited knowledge of the follow-up recommended for patients with chronic HBV infection.[4] To aid primary care providers, including PAs, in incorporating guidelines into everyday practice, the Hepatitis B Foundation convened a meeting in 2010 to develop an algorithm for screening, evaluation, and monitoring (**Figure 1**).[6] This practical tool, published by a panel of experts in primary care medicine, maternal and fetal medicine, and hepatitis and liver diseases, is based on current, evidence-based guidelines and reports from the CDC and the American Association for the Study of Liver Diseases.[3,5,6]

IDENTIFYING PATIENTS THROUGH SCREENING

Because HBV infection is often asymptomatic, and because the potential consequences of untreated active disease can be severe or fatal, screening of at-risk patients is essential. Screening should be targeted to persons at risk for chronic HBV infection, including persons born in Asia and Africa, and in other countries where HBV prevalence is greater than 2% (**Figure 1**).

As described in the first section of the algorithm, screening for HBV involves serologic testing for the presence of hepatitis B surface antigen (HBsAg) and antibody to

Geoff A. Beckett is chief of the Prevention Branch, Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, at the Centers for Disease Control and Prevention in Atlanta, Ga. **Joan M. Block** is executive director and co-founder of the Hepatitis B Foundation in Doylestown, Pa. **Chari Cohen** is director of public health at the Hepatitis B Foundation. **Brian J. McMahon** is scientific program and clinical director of the Liver Disease and Hepatitis Program of the Alaska Native Tribal Health Consortium at the Alaska Native Medical Center in Anchorage, Alaska. The authors have disclosed no potential conflicts of interest, financial or otherwise.

Acknowledgment: The authors would like to acknowledge **Theresa Wizemann, PhD,** for help in preparing this manuscript.

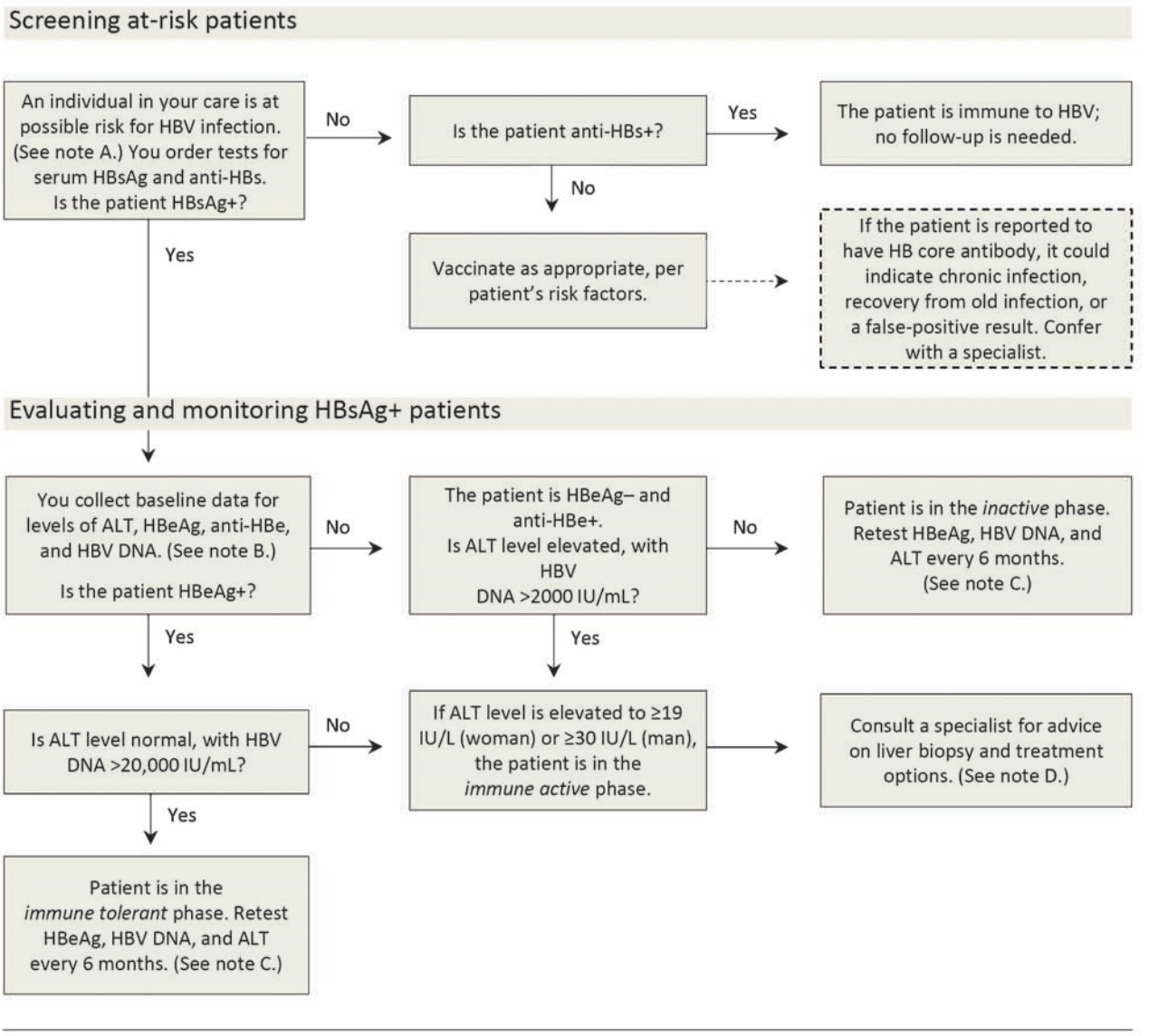
Disclaimer: The material presented in this article expresses the opinions of the authors and does not necessarily express the opinion of the CDC.

Roy A. Borchardt, PA-C, PhD, department editor.

DOI: 10.1097/01.JAA.0000443972.61728.33

FIGURE 1.

Suspect HBV infection? Use this algorithm to screen and intervene



ALT, alanine aminotransferase; anti-HBe, antibody to HBeAg; anti-HBs, antibody to HBsAg; AST, aspartate aminotransferase; DNA, deoxyribose nucleic acid; HBeAg,hepatitis B e-antigen (protein produced by HBV, indicating heightened viral activity); HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HIV, human immunodeficiency virus; HCC, hepatocellular carcinoma.

Source: Primary Care Provider Workshop on Hepatitis B, sponsored by the Hepatitis B Foundation in Doylestown, Pa (March 10-11, 2010).

McHugh JA, Cullison S, Apuzzio J, et al. Chronic hepatitis B infection: a workshop consensus statement and algorithm. J Fam Pract. 2011;60(9):E1-E8. Reprinted with permission of The Journal of Family Practice, © 2011 Quadrant HealthCom Inc.

HBsAg (anti-HBs). Patients who are persistently HBsAg-positive for more than 6 months are chronically infected and require further evaluation. A patient who is HBsAg-negative but anti-HBs positive is already immune due to prior acute infection or vaccination, and no additional follow-up is needed. Importantly, patients who test negative for both HBsAg and anti-HBs have not been exposed to HBV and are unprotected; these patients should receive the HBV vaccine series.

EVALUATION, MANAGEMENT, AND REFERRAL

For evaluating the patient identified as having chronic HBV infection, the second section of the algorithm guides providers through determining which of the three major

Algorithm notes

A Individuals at risk for HBV infection

- Blood or tissue donors
- Hemodialysis patients
- HIV-positive patients
- Household members or sexual contacts of infected individuals
- Individuals with conditions that may require immunosuppressive or immune-modifying therapy (beyond 2 weeks of corticosteroids)
- Individuals with elevated ALT/AST of unknown cause
- Infants born to HBV-infected mothers
- Injection drug users
- Men who have sex with men
- Pregnant women
- Individuals born in regions where HBV prevalence is ≥2%:
  - Africa
  - Asia
  - Caribbean: Antigua-Barbuda, Dominica, Grenada, Haiti, Jamaica, St. Kitts-Nevis, St. Lucia, Turks and Caicos
  - Central America: Guatemala and Honduras
  - Eastern Europe, except Hungary
  - Middle East, except Cyprus and Israel
  - North America: indigenous peoples of Alaska, Northern Canada, and Mexico
  - South America: Amazonian areas of Bolivia; Brazil, Colombia, Ecuador, Guyana, Peru, Suriname, Venezuela
  - South Pacific, except Australia and New Zealand

B Postdiagnosis education and counseling

- Screen close family members, household contacts, and sexual partners
- Vaccinate uninfected close family members, household contacts, and sexual partners
- Provide infected individuals with disease-management information and consult with a specialist

C Recommended management of chronic HBV infection

- Measure ALT every 6 months, HBV DNA at baseline and every 6 months if ALT is elevated ≥19 IU/L (women) or ≥30 IU/L (men)
- Measure HBeAg yearly
- Measure alpha-feto protein and perform liver ultrasound every 6-12 months for those at high risk for HCC:
  - –Family history of HCC
  - –Cirrhosis
  - –Man ≥40 years or woman ≥50 years
  - –>20 years old and born in Africa
  - –Co-infection with HCV or HIV

D Potential candidates for referral

- HBeAg-positive, ALT elevated; with or without advanced fibrosis or cirrhosis
- HBeAg-negative, ALT elevated, HBV DNA >2000 IU/mL; with or without advance fibrosis or cirrhosis
- Patients undergoing immunosuppressive or sustained immune-modifying therapy (eg., >2 weeks of corticosteroids or other modifying agents)

phases of disease the patient is in. This determination is made by obtaining a complete liver panel (including alanine aminotransferase [ALT]), HBV DNA level, and screening tests for the presence in serum of the hepatitis B e-antigen (HBeAg) and antibody to HBe (anti-HBe).

Patients with normal or minimally elevated ALT and high levels of circulating HBV DNA, but no active immune response against the virus, are in the *immune-tolerant phase*. Patients who remain in the immune-tolerant phase for a prolonged period were likely infected at birth. Antiviral therapy is not helpful in this phase.

A patient with both elevated serum ALT and elevated HBV DNA (above 2,000 IU/mL) is considered to be in the *immune active phase* of disease, in which an immune response against the virus is under way, and liver inflammation and fibrosis can develop. Some of these patients with moderate or severe liver inflammation or fibrosis are candidates for antiviral therapy.

Patients who have been infected for a prolonged period will often go into the *inactive carrier phase* characterized by normal or minimally elevated ALT and low levels of HBV DNA (below 2,000 IU/mL or undetectable).

Clinicians must determine the phase of disease in patients with newly identified chronic HBV infection because antiviral treatment is only appropriate during the immune active phase, when ALT levels are elevated and HBV DNA is above 2,000 IU/mL. Treatment has no established benefit in the inactive carrier or immune-tolerant phases, and inappropriate use of antiviral medications can lead to the development of drug-resistant viral strains and incurs high costs, because treatment may be needed indefinitely.

For patients in the immune active phase of chronic HBV infection, prompt consultation with a liver specialist or other experienced provider is advised to determine treatment strategies and assess the need for further workup such as liver biopsy (**Figure 1**).

Clinicians must determine the phase of disease in patients with newly identified chronic HBV infection because antiviral treatment is only appropriate during the immune active phase.

Long-term follow-up is essential for patients in all phases of chronic HBV infection. Active liver disease may develop at any time in persons in the immune-tolerant phase (when the immune system "wakes up" and recognizes the virus as foreign). In addition, up to 20% of patients in the inactive carrier phase can have reactivation of active disease, even after decades of inactivity. Patients in the immune-tolerant and inactive carrier phases should be retested for HBeAg, HBV DNA, and ALT every 6 months for life. PAs should be aware that high levels of circulating HBV DNA may be observed when monitoring patients in the immune-tolerant phase, but this is not necessarily an indicator of active disease as long as ALT levels are normal.

The algorithm also includes information on routine screening for hepatocellular carcinoma, to help facilitate detection while the cancer is small and still in a treatable stage (**Figure 1**).[7] Patients with HBV who are at a particular risk for hepatocellular carcinoma include those with evidence of cirrhosis or a family history of hepatocellular carcinoma, as well as Asian American men and women starting at age 40 years and 50 years, respectively. In these persons, the risk for hepatocellular carcinoma persists even when HBV DNA levels are low and HBeAg is absent. Regular hepatocellular carcinoma screening for patients at risk should continue for life, even among patients who remain in the inactive disease phase.

PAs should ensure that all pregnant women are screened for HBsAg, as recommended by CDC and the American Congress of Obstetricians and Gynecologists.[8,9] Monitor HBsAg-positive patients during pregnancy and postpartum, being especially alert for postpartum hepatitis flares.[8,9] Communicate with colleagues providing care for newborns of HBsAg-positive women so that hepatitis B vaccine and hepatitis B immune globulin are administered to the newborn in the delivery room to prevent perinatal transmission.

CONCLUSION

PAs in primary care have a critical role in reducing HBV-related morbidity and mortality by identifying patients with chronic HBV infection, and ensuring they receive appropriate follow-up, care, and long-term monitoring. Proper prevention and treatment is also essential to reducing horizontal and vertical transmission of HBV. The algorithm described is intended to support PAs in the implementation of national hepatitis B prevention and care guidelines through routine screening and appropriate evaluation, management, and referral.[3,5,6] **JAAPA**

REFERENCES

1. Cohen C, Evans AA, London WT, et al. Underestimation of chronic hepatitis B virus infection in the United States of America. *J Viral Hepat*. 2008;15(1):12-13.
2. Kowdley KV, Wang CC, Welch S, et al. Prevalence of chronic hepatitis B among foreign-born persons living in the United States by country of origin. *Hepatology*. 2012;56(2):422-433.
3. Weinbaum CM, Williams I, Mast EE, et al. Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. *MMWR. Recomm Rep* 2008;57(RR-8):1-20.http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm. Accessed June 6, 2013.
4. Colvin HM, Mitchell AE, eds. *Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C*. Washington, DC: The National Academies Press; 2010. http://books.nap.edu/openbook.php?record_id=12793. Accessed June 6, 2013.
5. Lok AS, McMahon BJ. Chronic hepatitis B: update 2009. *Hepatology*. 2009;50(3):661-662. http://www.aasld.org/practiceguidelines/documents/bookmarked%20practice%20guidelines/chronic_hep_b_update_2009%208_24_2009.pdf. Accessed June 6, 2013.
6. McHugh JA, Cullison S, Apuzzio J, et al. Chronic hepatitis B infection: a workshop consensus statement and algorithm. *J Fam Pract*. 2011;60(9):E1-E8.
7. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. AASLD Practice Guideline. 2010. *Hepatology*. 2011;53(3):1020-1022. http://www.aasld.org/practiceguidelines/Documents/Bookmarked%20Practice%20Guidelines/HCCUpdate2010.pdf. Accessed June 6, 2013.
8. Apuzzio J, Block JM, Cullison S, et al. Chronic hepatitis B in pregnancy: a workshop consensus statement on screening, evaluation, and management, part 1. *The Female Patient*. 2012;37(4):22-27.
9. Apuzzio J, Block JM, Cullison S, et al. Chronic hepatitis B in pregnancy: a workshop consensus statement on screening, evaluation, and management, part 2. *The Female Patient*. 2012;37(5):30-34.