# Screening for Hepatitis B

Dianne Tarrant, FNP-BC, Joan Block, BSN, and Brian McMahon, MD

**ABSTRACT**

Patients with chronic hepatitis B virus (HBV) infection are often asymptomatic, but they are at risk for serious health consequences, including cirrhosis, liver failure, and hepatocellular carcinoma if they have active disease, and may need antiviral therapy. As primary care providers, nurse practitioners (NPs) may be the first and sometimes the only health care provider an HBV-infected individual may encounter. This article describes a new algorithm that can aid NPs in knowing whom to screen for HBV infection and how to follow up based on screening results, including what additional tests to order, necessary monitoring, and when to refer.

**Keywords:** chronic, disease management, hepatitis B, liver, liver cancer, screening



Chronic infection with the hepatitis B virus (HBV) remains a serious public health problem in the United States, despite the availability of an effective vaccine and universal infant vaccination.[1,2] It is estimated that as many as 2 million people (1%-2% of the population) may have chronic HBV infection.[3]

Although the Centers for Disease Control and Prevention (CDC), the American Association for the Study of Liver Diseases (AASLD), and others have issued evidence-based guidelines for HBV screening and management, a recent Institute of Medicine (IOM) study raises concerns about significant gaps in identification and follow-up care of patients chronically infected with HBV.[4-6] The IOM report states that about 65% of HBV-infected persons in the US are unaware that they are infected.[6] In addition, CDC estimates that 40,000-45,000 people enter the US every year from countries where HBV is endemic.[2]

To help address these concerns, the Hepatitis B Foundation convened an expert panel of primary care providers to review existing evidence-based guidelines. Primary care panelists included a nurse practitioner (NP), a physician assistant, and physicians from family medicine, general internal medicine, pediatrics, and obstetrics/gynecology, as well as several experts in HBV disease. The panel recently published a decision flowchart that can help NPs and other primary care providers more effectively implement HBV screening, vaccination, and management guidelines in the primary care setting (Figure 1).[7]

This article highlights how NPs can use this algorithm in everyday practice to help determine which patients should be screened for HBV, what tests to order, and how to interpret the screening results. If a patient is found to be positive for HBV infection, the algorithm will provide guidance on what additional tests to order, how to manage infected persons, and when to consult with a liver specialist.

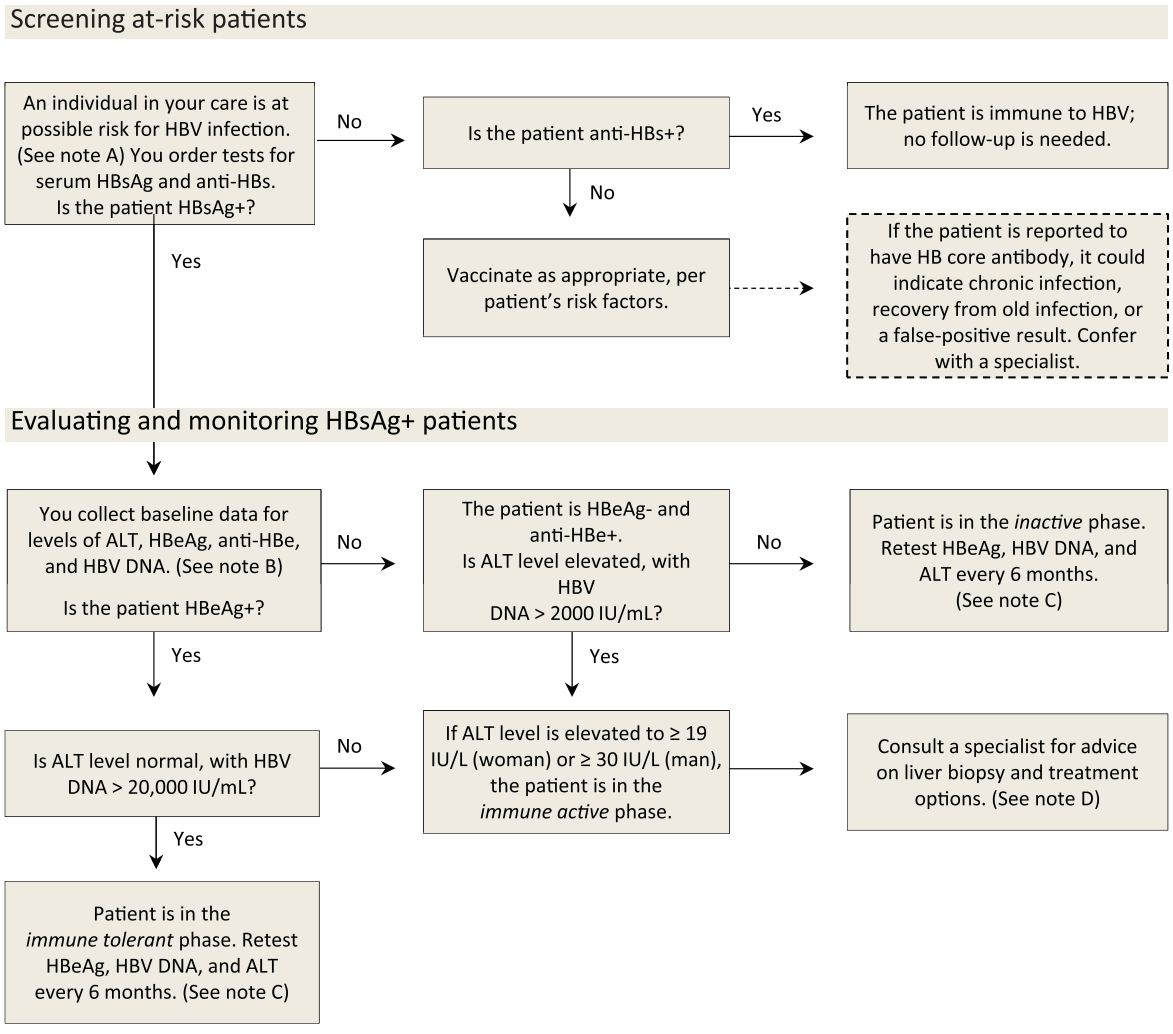
## PRESENTATION

Infection with HBV is often asymptomatic and patients may not even know they have the disease. Most adults infected with HBV develop acute hepatitis and fully recover. After an acute infection, approximately 5% of adults and adolescents, up to 50% of young children, and nearly 90% of infants will go on to develop chronic HBV infection.[5]

In those who develop chronic HBV infection, 3 phases can be indentified: the immune tolerant, immune active, and inactive phases. In the *immune tolerant* phase, there is little or no liver inflammation or fibrosis, and serum levels of the liver enzyme alanine aminotransferase (ALT) are normal, even though levels of circulating virus (measured as HBV DNA levels) are very high.[8,9]

As the immune system begins to mount a response to the virus, patients move into the *immune active* phase,

**Figure 1.** HBV Screening Algorithm for At-Risk Patients

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characterized by elevated serum ALT and the development of liver inflammation and fibrosis. Even in this phase, most individuals do not have overt signs of liver disease. Some patients in the immune active phase with moderate or severe liver inflammation or fibrosis can benefit by antiviral therapy.

Most patients will eventually enter an *inactive carrier* phase (naturally or as a result of antiviral treatment) where circulating virus decreases and may even become undetectable, ALT levels return to normal, and liver inflammation is minimal to none. Not all patients, however, move into the inactive carrier phase, and some that do may face reactivation of HBV disease at any time during their life. These individuals are at risk for serious health consequences, including cirrhosis, liver failure, and hepatocellular carcinoma (HCC). This is why it is so important that persons with chronic HBV infection have lifelong follow-up at regular intervals by an NP or other primary care provider.

## PATIENTS AT RISK

The majority of patients with chronic HBV infection will be asymptomatic. Therefore, it is likely that NPs will encounter patients in their practices who have unrecognized HBV infections. NPs should be alert for elevated ALT levels of unknown cause on routine metabolic panels and screen these patients for HBV.

**Figure 1.** *Continued*

## 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, Columbia, 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/mL (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 or woman ≥ 50
  - > 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)

Nearly 90% of persons in the US with chronic HBV infection are immigrants born in countries where the virus is endemic (Figure 1, Note A lists regions where HBV prevalence is greater than 2%). Others may have acquired HBV through intimate or close contact with an HBV-infected household member or individual in the community. HBV can remain viable on environmental surfaces for at least 1 week, and transmission can occur via open cuts and scratches or sharing of toothbrushes, razors, nail clippers, or other personal items. HBV can also be transmitted through risky behaviors (eg, intravenous drug use or unprotected sexual contact with an infected person).

Infants born to HBV-infected mothers are at the highest risk of contracting HBV as transmission of the virus occurs at birth via exposure to the mother's blood. A newborn's risk of developing chronic HBV

infection is further increased if he or she does not receive hepatitis B immune globulin (HBIG) and hepatitis B vaccine immediately after birth. As such, it is especially important to know the HBV status of pregnant patients for their own health and that of their infant.

Patients on long-term immunosuppressive or immune-modifying therapy who have chronic asymptomatic HBV infection are at risk for hepatitis flares that may lead to elevated liver enzymes, icteric hepatitis, and even death from fulminate liver failure. Thus, all patients undergoing chemotherapy for cancer or immunosuppressive therapy, including persons on potent immune modulating therapy for rheumatoid arthritis, inflammatory bowel disease, psoriatic arthritis, and other immunologic diseases, should be screened for HBV infection before initiation of these types of therapy, as pre-emptive HBV antiviral therapy may prevent or decrease the risk of reactivation (Figure 1, Note A also lists individuals at risk for HBV infection).

## SCREENING AND INTERPRETING RESULTS

Screening for HBV involves a simple and relatively low-cost blood test to detect the presence of hepatitis B surface antigen (HBsAg) and antibody to HBsAg (anti-HBs) in serum. Patients who are HBsAg-negative and do not have antibodies should be given the hepatitis B vaccine. Those who are HBsAg-negative and have detectable anti-HBs are already immune (generally from prior vaccination or recovery from an acute infection) and do not require further intervention or testing.

A patient who tests positive for HBsAg has an active HBV infection, and further testing is needed to determine the phase of disease and course of action (Figure 1). Recommended initial follow-up testing includes serum ALT and HBV DNA levels, as well as serology for hepatitis B e antigen (HBeAg) and antibody to HBeAg (anti-HBe). Individuals with chronic HBV infection have circulating HBsAg persistently present in their serum for more than 6 months (without developing anti-HBs).

## EVALUATION, MONITORING, AND REFERRAL

If a patient's ALT level is elevated on initial follow-up testing or at any point during routine monitoring, and HBV DNA levels are above 2,000 IU/mL, then the patient has entered the immune active phase and consultation with a liver specialist or other provider experienced in HBV disease management is warranted. The specialist can recommend appropriate treatment strategies and discuss whether ultrasound, liver biopsy, or other testing is advisable to monitor for development of cirrhosis.

Patients in the inactive and immune tolerant phases do not require treatment, and testing for serum ALT and HBV DNA levels should be repeated every 6 months to monitor disease progression (Figure 1, Note C lists all recommended tests and frequency). It is important to note that, even if a patient remains in the inactive carrier phase for many years, HBV can reactivate at any time. Patients with chronic HBV infection require lifelong monitoring, initially every 6 months and later; if the patient remains in the inactive carrier phase for several years, then at least every 12 month thereafter.[5]

Additional surveillance is recommended for patients with chronic HBV infection who are at high risk for developing HCC. Men with chronic HBV have a 100 times greater risk of developing HCC than an uninfected person. The risk for women is lower than that for men but is still very high, especially after menopause. As early detection and treatment of liver tumors can improve outcomes, AASLD recommends screening men with chronic HBV infection for HCC starting at age 40 and women at 50, including liver ultrasound every 6 to 12 months[10] (Figure 1, Note C lists groups at high risk for HCC and recommended tests).

Note that high levels of serum HBV DNA may be observed during routine monitoring of patients who are in the immune tolerant phase, but this does not necessarily indicate that active liver inflammation and fibrosis are present. Antiviral treatment based on HBV DNA level alone is not recommended, and inappropriate treatment with antiviral drugs can lead to the development of drug-resistant virus strains, limiting the patient's options later in life if active disease develops. Antiviral treatment is generally reserved for patients in the immune active phase who have high levels of serum ALT or moderate to severe liver inflammation or fibrosis found on liver biopsy or identified via surrogate markers for fibrosis.

Currently, 7 medications are licensed in the US for the treatment of chronic HBV infection, including 5 antiviral nucleos(t)ide analogs that work by suppressing HBV DNA levels. Once initiated, treatment may need to be lifelong, as HBV may reactivate if treatment is stopped.

NPs providing prenatal care should also be aware that HBsAg-positive pregnant women who have normal ALT throughout pregnancy can develop a hepatitis flare postpartum that is often asymptomatic. As such, monitoring ALT level postpartum in HBsAg-positive mothers is important. In addition, any changes during pregnancy (elevated serum ALT, change in serology to HBeAg positive, or increasing HBV DNA levels) warrant immediate referral to a specialist.[11,12]

## CONCLUSION

Even in today's fast-paced clinical environment, it is important not to miss opportunities for detection, intervention, and prevention of chronic hepatitis B infection. As primary care providers, NPs play a key role in ensuring the appropriate screening of at-risk patients, initial clinical and laboratory evaluation, strategic management (including routine periodic monitoring), and referral of those who have chronic HBV infection. This is especially important because an NP may the only health care provider with which a patient may come into contact. The use of this simple and easy algorithm—developed by a panel of representative primary care providers, including the primary author, who is an NP—will aide NPs in the early diagnosis and management of persons with chronic HBV infection. JNP


**References**

1. Mast EE, Margolis HS, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children, and adolescents. *MMWR Recomm Rep.* 2005;54:1-31.
2. Mast EE, Weinbaum CM, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 2: immunization of adults. *MMWR Recomm Rep.* 2006;55:1-25.
3. Cohen C, Evans AA, London WT, Block J, Conti M, Block T. Underestimation of chronic hepatitis B virus infection in the United States of America. *J Viral Hepat.* 2008;15:12-13.
4. Weinbaum CM, Williams I, Mast EE, et al. Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. *MMWR.* 2008;57(RR08):1-20.
5. Lok AS, McMahon BJ. Chronic hepatitis B: update 2009. AASLD Practice Guideline. *Hepatology.* 2009;50:661-662.
6. Institute of Medicine. *Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C.* Washington, DC: The National Academies Press; 2010.
7. 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.
8. Hoofnagle JH, Doo E, Liang TJ, Fleischer R, Lok ASF. Management of hepatitis B: summary of a clinical research workshop. *Hepatology.* 2007;45:1056-1075.
9. McMahon BJ. Natural history of chronic hepatitis B. *Clin Liver Dis.* 2010;14:381-396.
10. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. AASLD Practice Guideline. 2010. http://www.aasld.org/practiceguidelines/Documents/Bookmarked%20Practice%20Guidelines/HCCUpdate2010.pdf. Accessed October 8, 2012.
11. Apuzzio J, Block JM, Cullison S, et al. Chronic hepatitis B in pregnancy: a workshop consensus statement on screening, evaluation, and management, part 1. *Female Patient.* 2012;37(4):22-27.
12. Apuzzio J, Block JM, Cullison S, et al. Chronic hepatitis B in pregnancy: a workshop consensus statement on screening, evaluation, and management, Part 2. *Female Patient.* 2012;37(5):30-34.



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*In compliance with national ethical guidelines, the authors report no relationships with business or industry that would pose a conflict of interest.*

### *Disclosure*

*All authors were members of the Hepatitis B Foundation Panel on the Role of Primary Care Providers in Hepatitis B. Dianne Tarrant was an expert primary care provider, and Joan Block and Brian McMahon were experts on hepatitis B who advised the panel during their deliberations.*


1555-4155/13/$ see front matter



http://dx.doi.org/10.1016/j.nurpra.2013.02.003