Screening for Hepatitis B Virus Infection: A Public Health Imperative

Chronic hepatitis B virus (HBV) infection is a major public health problem, affecting an estimated 400 million persons worldwide. The GBD (Global Burden of Disease) study attributed 786,000 deaths to HBV infection in 2010 as a result of cirrhosis, liver failure, and hepatocellular carcinoma (HCC), making HBV the 15th leading cause of death worldwide. In the United States, 1.25 million persons are infected with HBV and those who develop chronic infection die an average of 22 years earlier than those without infection (1). The burden of HBV infection is expected to increase in the face of immigration patterns into the United States from highly endemic countries.

This issue includes the most recent U.S. Preventive Services Task Force (USPSTF) recommendations on screening for HBV infection in nonpregnant adults and adolescents (2). The new recommendations advocate screening for HBV infection in persons at high risk for infection, such as those born in countries with a prevalence of HBV infection of 2% or greater, HIV-positive persons, injection drug users, household contacts of persons with HBV infection, men who have sex with men, and persons who are immunosuppressed or receiving hemodialysis. The recommendations are given a grade of B, which indicates that there is high certainty that the net benefit is moderate or that there is moderate certainty that the net benefit is moderate to substantial. These recommendations are a dramatic and welcome upgrade from the 2004 USPSTF guidelines, which issued a grade D recommendation against screening asymptomatic persons for HBV infection.

These updated recommendations are long overdue. Since 2001, when its first practice guideline on chronic HBV infection was published, the American Association for the Study of Liver Diseases has recommended screening for HBV infection in high-risk groups (3). The Centers for Disease Control and Prevention has recommended hepatitis B surface antigen screening for high-risk groups, such as pregnant women and infants born to HBV-infected mothers, household contacts and sexual partners of infected persons, and other persons with exposures to infectious blood or body fluids, since at least 2005 (4).

Further, there has been continued progress in treatment of HBV infection. The U.S. Food and Drug Administration has approved 7 antiviral drugs for treating chronic HBV infection: interferon-α2b, pegylated interferon-α2a, lamivudine, adefovir, entecavir, telbivudine, and tenofovir. Entecavir, tenofovir, and pegylated interferon-α2a are the current first-line agents.

The case for suppression of HBV replication is compelling. First, in the REVEAL-HBV (Risk Evaluation of Viral Load Elevation and Associated Liver Disease/Cancer-Hepatitis B Virus) study, serum HBV DNA levels, a marker of replication, were shown to be significantly and independently associated with the incidence of HCC, cirrhosis, and liver-related deaths (5). Second, the preponderance of evidence supports the clinical benefits of virologic suppression, including decreased incidence of hepatic decompensation and HCC, the reversal of cirrhosis, and the clinical stabilization of hepatic failure (6–9).

The USPSTF acknowledged these arguments in its 2014 deliberations. However, considering that the U.S. Food and Drug Administration had already approved several of these anti-HBV agents by 2002 and that much of the data showing clinical benefit of HBV suppression were available by 2004, many would argue that the USPSTF should have endorsed screening for HBV infection in high-risk populations a decade ago or at least soon thereafter. We may have thus missed an opportunity to screen many high-risk persons in the United States.

Although we are glad that the USPSTF now recommends screening, we think that the recommendations would be more useful if they provided a clearer definition of the high-risk patient. The recommendations state that “[c]linicians should exercise their judgment in deciding whether . . . persons are at sufficiently high risk to warrant screening.” We worry that busy generalist clinicians do not have the time to estimate their patients’ risks for HBV infection. The USPSTF should have adopted an approach similar to that used by the Centers for Disease Control and Prevention and listed in table form all factors that render a patient high-risk.

The lack of randomized trials on the health benefits of screening for HBV infection in asymptomatic adolescents and adults contributed to the USPSTF’s previous hesitancy to recommend screening (1). However, given the natural history of HBV infection, during which such clinical outcomes as cirrhosis and HCC develop 20 to 30 years after infection, a randomized, controlled trial of screening for HBV infection in asymptomatic adolescents and adults is unlikely ever to be done. In the absence of such trials, many modeling studies suggest that screening would have a large benefit and be cost-effective. For example, Veldhuijzen and colleagues (10) estimated that 1-time screening for HBV infection in the Netherlands would reduce liver disease–related mortality by 10% and be cost-effective.

Testing asymptomatic persons for chronic HBV infection meets established criteria for screening. It identifies an unrecognized health condition so that treatment can be offered before symptoms of chronic HBV infection, cirrhosis, or HCC develop. Testing for HBV infection also allows interventions to be implemented that reduce the likelihood of continued transmission of the infection to others. In addition, tests for HBV infection are widely available, cheap, and accurate.

We laud the USPSTF for its 2014 recommendations that will enable widespread adoption of screening for HBV
infection in high-risk populations. Under the Patient Protection and Affordable Care Act, most private insurers and all Medicaid programs must cover any preventive service given a grade A or B recommendation by the USPSTF. In light of this powerful mandate, we believe that the USPSTF should make every effort to ensure that its recommendations do not lag behind the evidence, because the administration of potentially high-impact antiviral therapy hinges on timely identification of infected persons.

Ruma Rajbhandari, MD, MPH
Raymond T. Chung, MD
Massachusetts General Hospital
Boston, Massachusetts

Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M14-1153.

Requests for Single Reprints: Raymond T. Chung, MD, Liver Center and Gastrointestinal Division, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114.

This article was published online first at www.annals.org on 27 May 2014.


References

Current Author Addresses: Drs. Rajbhandari and Chung: Liver Center and Gastrointestinal Division, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114.