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Silent Epidemic of Viral Hepatitis May Lead to Boom in Serious Liver Disease

Bridget M. Kuehn

WASHINGTON, DC—More than 500 million persons worldwide are infected with hepatitis B or C virus, estimates the World Health Organization, and more than 5 million US residents have such infections, according to the US Centers for Disease Control and Prevention (CDC). Yet these infections often go undetected and untreated because patients and physicians may be unaware of who is at risk or may fail to pursue testing.

Although prevention efforts have helped dramatically reduce the incidence of hepatitis B and C viral infections in the general US population, demographic shifts are leading to growing numbers of chronically infected patients who may develop severe complications such as cirrhosis and hepatic cell carcinoma. A large cohort of individuals infected with hepatitis C virus (HCV) is reaching an age at which liver complications may manifest, and growing numbers of individuals from regions where hepatitis B virus (HBV) infection is endemic are migrating to the United States.

Screening, prevention, and treatment may reduce some of this burden, according to experts who gathered in September in Washington, DC, for a meeting that was cosponsored by the American Gastrointestinal Association Institute, the CDC, the Department of Veterans Affairs, and the National Institute of Allergy and Infectious Diseases. (Gilead, Bristol-Myers Squibb, and Vertex provided funding for the meeting in the form of independent educational grants.)

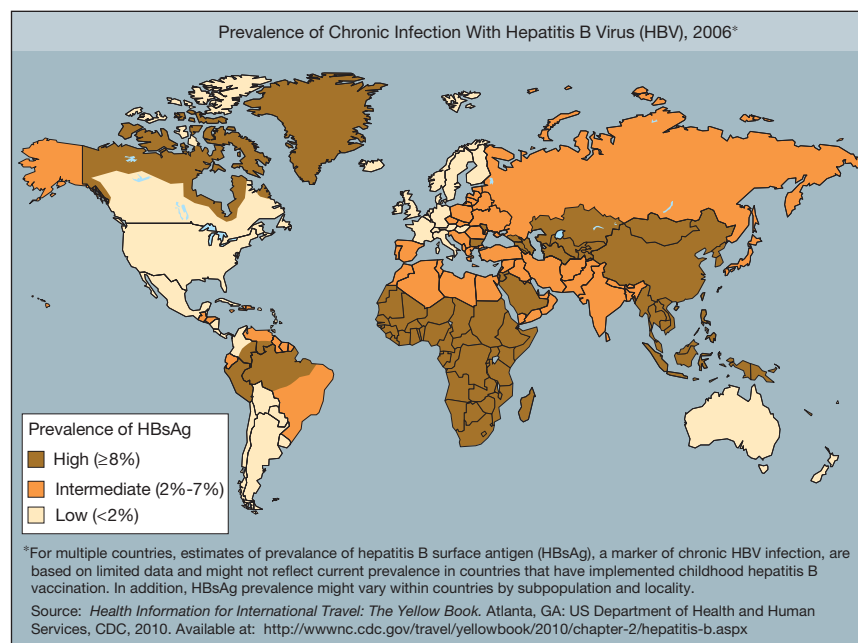
The incidence of viral hepatitis in the United States has declined steadily in

recent decades. The CDC estimates that between 1980 and 2004, the number of new HBV infections dropped from about 200 000 per year to about 60 000, while the estimated number of HCV infections decreased from 180 000 in 1982 to 19 000 in 2006 (<http://www.cdc.gov/hepatitis/Statistics.htm>).

Decreases in the incidence of hepatitis B can be attributed to the introduction of universal HBV vaccination for infants, catch-up vaccinations for children and adults, screening of pregnant women, and educational campaigns on the prevention of sexual, perinatal, and percutaneous transmission of the virus, said Dale J. Hu, MD, MPH, of the CDC's Division of Viral Hepatitis. He added that identification and treatment of chronic HBV infections,

which can keep viral titers low and help prevent the spread of infection among contacts, has also helped.

However, chronic HBV infection remains prevalent worldwide, affecting 400 million people and causing about half a million deaths annually, Hu said. Shifting immigration patterns are bringing more chronically infected individuals to the United States from regions such as Africa, Central America, and Asia, where perinatal transmission of HBV is common. Hu noted, for example, that 50% to 70% of US residents with chronic HBV infections were born in another country, and more than half of new cases identified are in Asians or Pacific Islanders. The vast majority of such individuals are asymptomatic and unaware of their infection status, Hu said.



As more individuals immigrate to the United States from regions where hepatitis B virus infection is prevalent, US physicians may see higher rates of complications from such infection.



“The global burden of hepatitis B infection has important implications for the epidemic in the United States,” he said.

Screening of blood products and other efforts to prevent transmission of HCV via blood transfusion or organ transplantation have helped to reduce the incidence of this infection, said Miriam J. Alter, PhD, of the University of Texas Medical Branch in Galveston. Safer injection practices also have contributed to the overall decline in incidence, noted W. Ray Kim, MD, of the Mayo Clinic College of Medicine in Rochester, Minn.

Even so, incidence remains high among injection drug users, Alter said. And prevalence continues to be disproportionately high among certain subgroups, particularly baby boomers born between the late 1940s and early 1960s, who have a comparatively higher risk of having ever used injection drugs (Armstrong GL. *Arch Intern Med.* 2007; 167[2]:166-173). According to an analysis of data from the National Health and Nutrition Examination Survey (NHANES), the prevalence of HCV infection between 1999 and 2002 was highest in people aged 40 to 49 years (Armstrong GL et al. *Ann Intern Med.* 2006;144[10]:705-714).

Kim cited other subgroups with a disproportionate burden of infection. For example, he noted that HCV infection affects about 1.6% of the general population, but it affects 13% of black males between the ages of 40 and 49 years, 13.8% of HIV-infected individuals, 11% of Vietnam veterans, and about 15% of those who are incarcerated.

Kim cautioned that existing estimates of HBV and HCV prevalence are likely “just the tip of the iceberg” because many infected individuals are disenfranchised and may not be accounted for in surveys. For example, the NHANES excludes persons who are homeless or incarcerated.

COMPLICATIONS

Although many individuals with viral hepatitis infections remain asymptomatic for decades, some develop severe liver disease. About 15% to 40% of in-

dividuals with chronic HBV infection develop serious complications such as cirrhosis or hepatic cell carcinoma, and the risk of hepatic cell carcinoma increases with higher virus loads (Chen CJ et al. *JAMA.* 2006;295[1]:65-73).

Progression in HCV infection also varies, noted Harvey J. Alter, MD, chief of the Infectious Diseases Clinical Studies Section at the National Institutes of Health in Bethesda, Md. “Progression is not linear or inevitable,” he said. Only about 20% to 30% of HCV infections will progress to cirrhosis, he said, and even when an individual develops cirrhosis, it may progress very slowly, with 80% of such patients still alive 10 years later without needing a transplant. About 10% of those with cirrhosis will go on to develop hepatic cell carcinoma in 10 years, he said.

The incidence of hepatic cell carcinoma, to which hepatitis is a major contributing factor, doubled between 1979 and 2004 (Everhart J and Ruhl C. *Gastroenterology.* 2009;136[4]:1134-1144), and many speakers at the meeting expressed concern about snowballing rates of this and other types of serious liver disease as the HCV-infected baby boom cohort ages. “We are finding more and more patients with cirrhosis as a result of the aging of this cohort,” said Hashem B. El-Serag, MD, MPH, of Baylor College of Medicine, in Houston, Tex.

Norah A. Terrault, MD, MPH, of the University of California, San Francisco, explained that 40% to 45% of chronic liver disease in the United States can be attributed to viral hepatitis, with HCV leading to as many as 12 000 deaths each year and HBV contributing to more than 3000 deaths each year. Chronic HCV infection also can substantially reduce patients’ quality of life, she said, but few data are available on the effect of chronic HBV infection on quality of life.

Individuals with comorbidities such as alcohol or substance abuse disorders, mental illness, or HIV infection are at substantially greater risk of poor outcomes. Terrault noted that suicide-related deaths contribute to mortality

in patients with chronic viral hepatitis who also have substance abuse disorders or mental illnesses, particularly among younger patients.

MOVING FORWARD

Shifts in clinical practice and public policy could help prevent viral hepatitis infections and improve outcomes for patients with chronic infection.

Several speakers emphasized the need for comprehensive care of patients with chronic viral hepatitis, particularly when comorbidities such as substance abuse or mental health issues are present. But few good treatment guidelines are available. Litjen Tan, MS, PhD, director of medicine and public health at the American Medical Association, surveyed medical associations and found that few had guidelines for hepatitis care, and those guidelines are often out of date. The best available association guidelines, said Cindy Weinbaum, MD, MPH, of the CDC’s Division of Viral Hepatitis, are those from the American Association for the Study of Liver Diseases (http://www.aasld.org/practiceguidelines/Documents/Bookmarked%20Practice%20Guidelines/Chronic_Hep_B_Update_2009%208_24_2009.pdf and <http://www.aasld.org/practiceguidelines/Documents/Hepatitis%20C%20UPDATE.pdf>).

Speakers also urged physicians to screen more aggressively for viral hepatitis, particularly among high-risk groups. But screening recommendations have not been consistent.

The US Preventive Services Task Force (USPSTF) in 2004 recommended against routine screening for HCV infection in asymptomatic adults who do not have risk factors (<http://www.ahrq.gov/CLINIC/USPSTF/uspshepc.htm>) and found insufficient evidence to recommend for or against routine screening in those at risk. The task force also recommended against routine screening of asymptomatic individuals for HBV (<http://www.ahrq.gov/clinic/3rduspstf/hepbscr/hepbsr.htm>). The USPSTF does, however, recommend routine



screening of pregnant women for HBV (<http://www.ahrq.gov/clinic/uspstf/uspshpbpg.htm>).

The USPSTF stance against routine screening for HBV in asymptomatic individuals conflicts with CDC's recommendations for more comprehensive screening for HBV, updated in 2008 (<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm>). Previously, the agency had recommended routine testing for pregnant women, infants of infected mothers, household contacts and sex partners of infected individuals, persons born in countries where 8% or more of the population is infected, persons who may expose

health workers to HBV, and those with HIV infection. The agency has expanded this list to include persons born in countries where 2% or more of the population is infected, men who have sex with men, and injection drug users.

The USPSTF recommendations for HCV have also been debated. Dr Miriam Alter addressed this issue and the need for greater testing in a 2005 editorial (<http://www.aafp.org/afp/20050815/editorials.html>). Weinbaum said the CDC is currently revamping its HCV recommendations.

Once patients with viral hepatitis infection are identified, the next challenge is ensuring access to care because

many people in high-risk groups are likely to be uninsured. Attendees at the meeting debated whether the Ryan White Comprehensive AIDS Resources Emergency (CARE) Act, which provides funding for community-based HIV treatment programs, should be expanded to include viral hepatitis. Others argued for greater coverage through comprehensive health care reform.

The CDC has commissioned the Institute of Medicine to recommend ways to further reduce the incidence of viral hepatitis infection and to mitigate complications in those with chronic infection. The report is due out in 2010 (<http://www.iom.edu/?ID=59310>). □

New Clinical Guideline for Hoarseness Offers Assessment and Treatment Advice

Mike Mitka

A NEW CLINICAL PRACTICE GUIDELINE offers advice to physicians assessing and treating dysphonia, or hoarseness, a condition that affects a substantial number of individuals at some point in life.

The guideline, created by an expert panel assembled by the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) Foundation, seeks to offer evidence-based recommendations for managing dysphonia and to raise public awareness of the condition's prevalence and its treatment options (Schwartz SR et al. *Otolaryngol Head Neck Surg.* 2009;141[3]:S1-S31). According to the guideline, only about 6% of individuals seek treatment for dysphonia, which is more common in women, children, and older adults. Certain occupations have high prevalence rates, including telemarketers (31%), aerobics instructors (44%), and teachers (58%).

For many individuals, an encounter with dysphonia may be little more than a brief nuisance, or a time-limited adverse effect of an upper res-

piratory tract infection. But it can also be a warning signal of something more serious.

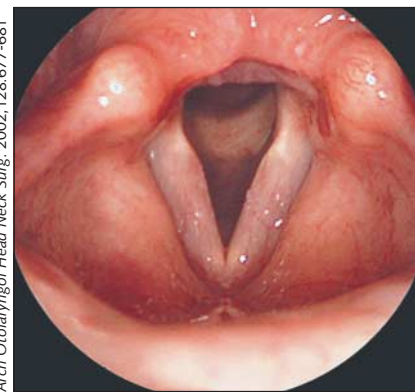
“For the general public, an important message in the guideline is a lot of

experts representing neurology, family medicine, pulmonology, geriatric medicine, internal medicine, otolaryngology–head and neck surgery, pediatrics, nursing, speech-language pathology, professional voice teaching, and consumers.

The document is the sixth published by the AAO-HNS and joins guidelines for benign paroxysmal positional vertigo, cerumen impaction, adult sinusitis, acute otitis externa, and otitis media with effusion. “Guidelines have evolved based on big-ticket inpatient conditions such as cardiac disease and stroke, but some of the outpatient conditions that may be ubiquitous may fall under the radar,” Rosenfeld said. He added that the Centers for Medicare & Medicaid Services (CMS) care about such conditions “because they represent big bucks.”

DON'TS AND DO'S

The dysphonia guideline should please the CMS because it downplays use of several high-cost assessments and treatments. The guideline authors said that based on observational studies, physicians should not obtain computed



A new guideline helps physicians determine when to view vocal cords through laryngoscopy to diagnose dysphonia.

hoarseness can be benign, and a little hoarseness can be a sign of a bigger problem, like cancer,” said Richard M. Rosenfeld, MD, MPH, a coauthor of the document and chair of otolaryngology at the Long Island College Hospital in Brooklyn, NY. In putting together the guideline, Rosenfeld joined