

National Response Needed to Control Hepatitis

BY JEFF EVANS

WASHINGTON — A new, coordinated national response is needed to screen and treat hepatitis B and C viral infections because too many infected patients are unaware of their disease and go untreated, speakers said at a national forum on chronic viral hepatitis.

Acute hepatitis B virus (HBV) infections peaked in 1985 at about 12/100,000 people, whereas acute hepatitis C virus (HCV) infections topped out at about 2.5/100,000 in 1992. The burden of disease now remains primarily in people with chronic infections. Current estimates suggest that 2 million people are infected with HBV and 4 million are infected with HCV, totaling 2% of the U.S. population, according to Dr. W. Ray Kim.

"One can argue that of this 6 million, we know only of the tip of the iceberg that has been diagnosed," said Dr. Kim of the division of gastroenterology and hepatology at the Mayo Clinic, Rochester, Minn.

Despite the effectiveness of vaccines for HBV to lower the incidence of acute hepatitis B, immigrants from endemic countries who are unaware of their chronic infection continue to bring it into the United States.

To illustrate this point, Dr. Kim presented data contrasting the population of patients with chronic HBV infection at the Mayo Clinic with the general population of Olmsted County, where the institution is located. Most of the cases of chronic HBV infection occurred in minorities, many of whom were foreign born. Asian patients composed 53% of the chronic HBV patients and 99% of them were foreign born. Similarly, 29%

of patients with chronic HBV were black and 91% of them were foreign born. In comparison, 13% of Mayo's patients with chronic HBV were white, but only 16% were foreign born. Olmsted County as a whole is 95% white.

Although the prevalence of HCV infection is declining because the incidence of the infection has been decreasing since the 1990s, chronically infected patients are becoming older and are experiencing more long-term complications associated with the virus, such as chronic liver disease and hepatocellular carcinoma, he said.

"All of those consequences of hepatitis B and hepatitis C infection have culminated in an epidemiologic trend" that may be a substantial contributor to the increasing incidence of hepatocellular carcinoma (HCC), in the United States, Dr. Kim said. "This is one of the few cancers whose incidence is increasing."

Most HCC cases still occur in whites, but the rate is highest in foreign-born individuals, especially Asians and Hispanics, he said.

Many variables work together to reduce the clinical effectiveness of therapies for viral hepatitis, compared with the efficacy that they showed in clinical trials, observed Dr. Hashem El-Serag, professor of medicine at Baylor College of Medicine and GI section chief at the Michael E. DeBakey Veterans Affairs Medical Center, both in Houston.

In one survey of 128 VA facilities, an average of about 20% of patients at each center received treatment for hepatitis C. However, treatment rates at individual centers ranged from nearly 0% to 40%.

This variation may be partly the result of legitimate underuse of treatment

when it is not clinically appropriate for some patients or when patients prefer not to undergo treatment. But the rest of the difference between the expected and observed use of treatment may be the result of disparities in access to health care, legal and regulatory issues, and discrimination and bias, he said.

In another study of 4,084 veterans who presented for treatment at 24 VA medical centers, researchers found that only 32% met standard criteria for eligibility for antiviral treatment and 40% were deemed treatment candidates by a clinician (*Am. J. Gastroenterol.* 2005;100:1772-9).

If clinicians are to translate the efficacy seen in clinical trials into real-world effectiveness, they must figure out if the remaining 60% or more of patients have reversible or treatable contraindications, which include ongoing substance use, comorbid medical disease, psychiatric disease, and advanced liver disease, Dr. El-Serag said.

In the VA study, 76% of patients who met standard criteria for treatment agreed to be treated. "The reasons for nonacceptance may also be modifiable," depending on the way treatment options are presented to them. "Some of them want to defer diagnosis until better therapies arrive; others are concerned about side effects," he said.

This VA study is a "very nice example" of how the efficacy of antiviral therapy can drop "tremendously" when put in terms of real-world clinical effectiveness, Dr. El-Serag said.

HBV presents "virtually similar issues [as HCV] but with less data in the United States," he said.

Resources must be allocated to screen more patients with viral hepatitis, par-

ticularly hepatitis C, for HCC, as it becomes "increasingly more of a liver disease, rather than an infectious disease," he said.

Screening patients with cirrhosis for HCC to detect cancer at an earlier stage has been shown to be efficacious in one randomized, controlled trial and in several observational cohort studies. But, even in studies of insured patients with HCC, few patients are appropriately screened.

For example, in a yet-to-be-published study of 3,903 Medicare patients with HCC, 57% had received at least one screening test for the cancer in the 3 years prior to their diagnosis. But only 7% were screened according to standard-of-care guidelines.

In the same study, physicians were nearly three times more likely to screen for HCC if they were affiliated with a medical school than if they had a solo or group practice. Gastroenterologists were three to four times more likely to screen than were primary care physicians alone, which illustrates that viral hepatitis is "becoming more and more not a primary care disease as it progresses," he said.

The conference was endorsed by the American Association for the Study of Liver Diseases and was cosponsored by the American Gastroenterological Association Institute, the Centers for Disease Control and Prevention, the Department of Veterans Affairs, and the National Institute of Allergy and Infectious Diseases.

Dr. Kim reported serving as a consultant to Bristol-Myers Squibb Co., Gilead Sciences Inc., and Roche Pharmaceuticals. He disclosed receiving grant and research support from Romark Laboratories LC. Dr. El-Serag had nothing to disclose. ■

Hepatitis C Will Be 'The Big Virus' Over Next 20 Years

BY BETSY BATES

LAS VEGAS — Amid the alphabet soup of hepatitis virus types, the one that should most concern physicians these days is hepatitis C.

"This is going to be the big virus in the next 20 years in the U.S.," Dr. Marsha H. Kay predicted at a meeting sponsored by the American Academy of Pediatrics.

Hepatitis C virus already infects 1.6% of the general U.S. population—4 million people—but "the vast majority of people who are infected do not know it," said Dr. Kay, a pediatric gastroenterologist and director of pediatric endoscopy at the Cleveland Clinic.



Known to be at risk are infants born to mothers with hepatitis C; young adult survivors of leukemia, childhood malignancies, and childhood cardiac surgery; hemophilia patients; dialysis patients; intravenous drug users; sexual partners of a person with hepatitis C; recipients of blood transfusions prior to 1989; first responders; and health care workers.

Alarming, though, 32% of the current cases involve no known risk factor. "We don't know exactly how this virus is transmitted," Dr. Kay said. There is no way to prevent hepatitis C, and there is no vaccine.

Among those infected, 80%-85% will develop chronic hepatitis, and of those, half will develop cirrhosis, putting them at highly elevated risk for hepatocellular carcinoma. Hepatitis C is already the leading cause of liver transplantation in the nation.

All things considered, the perfect storm of hepatitis C constitutes "a really terrible outcome compared to hepatitis B infection," she said.

Among children, the leading cause of hepatitis C transmission is perinatal exposure, with transmission risk correlated to the mother's viral load at delivery.

Unfortunately, drugs used to treat acute hepatitis C are teratogenic and cannot be used during pregnancy. Hepatitis C acquired via perinatal transmission has an increased likelihood to be chronic. Anti-HCV testing is ideally performed between 15 and 18 months of age. Although HCV RNA testing may be positive at 2 months and 6 months, the results may be a response to the mother's sera at that time.

Other patients who should be considered at risk in a primary care practice include young people who overcame serious illnesses early in life and those who received blood products before 1989.

Individuals who received Gammagard (immune

globulin) during 1993 and 1994 may also be at risk.

Health care providers, especially those who work in emergency departments, surgery, or procedurally related specialties, have an estimated 1% prevalence rate that is rising, she said.

"I have to say, the majority of the kids I see in my practice with hepatitis C are the children, typically, of a nurse—a health care provider who likely got it occupationally," she noted.

New data suggest that prompt treatment with interferon and ribavirin may produce a sustained virologic response in up to 80% of patients with acute hepatitis C. "If you're sure of [acute infection], you want to treat them early," she said.

Antibody testing has been available for nearly 20 years, but the antibody just signals exposure to the virus, not immunity. Current detection modes include PCR (polymerase chain reaction), which can sometimes detect virus within 1-2 weeks of exposure but may be intermittently negative even in positive patients; ELISA (enzyme-linked immunosorbent assay)-IgG, which is highly sensitive and specific late in the course of the disease but may be inaccurate early; and RIBA (recombinant immunoblot assay)-IgG, a confirmatory test.

Clinically, liver function tests may generate variable results throughout the course of the disease.

Dr. Kay disclosed no relevant conflicts of interest regarding her talk. ■

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