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Hepatitis B

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HBV Infections in U.S. Under-Reported by 800,000—True Number Is 2 Million

In a letter to the editor of the *Journal of Viral Hepatitis*, researchers from the Hepatitis B Foundation asserted that the true number of people in the United States chronically infected with the hepatitis B virus (HBV) is about 2 million, instead of 1.2 million cited by the U.S. Centers for Disease Control and Prevention (CDC).

The under-reporting of infections results from under-representation of HBV-infected immigrants and members of high-risk groups among those surveyed, they wrote.

HBV infection estimates come from National Health and Nutrition Examination Surveys 1976-1994 (NHANES II, III),

which did not include significant numbers of Asians and Pacific Islanders (API), the ethnic groups most affected by hepatitis B. This makes it difficult to obtain accurate prevalence estimates, researchers wrote. "Also, the large influx of foreign-born individuals from countries with moderate or high incidence of hepatitis B increases the limitation of the NHANES estimate."

Using U.S. Census data (2005) and prevalence estimates, the foundation calculated that among just APIs, there are about 832,433 infected individuals. "This number was reached using hepatitis B prevalence estimates of 8.9% for foreign and 1.4% for U.S.-born APIs, based on HBV survey data of API pregnant women," they wrote. "These estimates are conservative in comparison with recent studies, which have found the prevalence among for-

eign-born APIs to be between 10-15%."

"We calculated a chronic HBV burden of 1,157,137 individuals in the Caucasian, African American, and 'other' ethnicities, with a prevalence estimate of 0.42% in these groups (based on NHANES III data)," they wrote.

"Adding our estimate for the API population (832,433) brings the total burden estimate to 1,989,570. This represents an increase of almost 800,000 individuals from the currently accepted HBV prevalence estimate, and it does not account for undocumented APIs, which could increase the number of chronically-infected by another 100,000."

With the number of new infections remaining steady despite the availability of a vaccine, hepatitis B must be prioritized as an important public health concern, foundation staff

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stressed. “An accurate assessment of the true prevalence of chronic hepatitis B that includes updated estimates from high-risk, undercounted populations, is a crucial first step towards significantly reducing the burden of chronic hepatitis B in this country,” they added.

Screening Asian-Americans Essential to Identify, Treat and Prevent Hepatitis B

Stanford University researchers conducted a prevalence study in the San Francisco Bay area between 2001 and 2006 of 3,163 adult Asian-Americans to gauge the incidence of chronic hepatitis B infections.

They discovered 8.9% were chronically infected with HBV, and of those half to two-thirds (65.4%) were unaware that they were infected. Of those not infected, 44.8% lacked protective antibodies and had not been vaccinated and were susceptible to future infection. Men were twice as likely as women to be chronically infected (12.1% vs. 6.4%).

Asian-Americans born in East Asia, Southeast

Asia or the Pacific Islands were 19.4 times more likely to be infected than those born in the United States.

Among the 12% who reported having been vaccinated, 5.2% were chronically infected, and 20.3% lacked protective antibodies, according to the report published in the July 2007 issue of *Hepatology*.

2% of HIV-Infected Women Have Occult or Undiagnosed HBV Infections

U.S. researchers screened 400 women infected with the human immunodeficiency virus (HIV) to see how many had hidden or occult hepatitis B infections. Occult HBV infections occur when there is no detectable hepatitis B surface antigen (HBsAg) in an individual’s blood, but there is HBV DNA (also called viral load).

U.S. researchers, reporting in the journal of *Clinical Infectious Diseases*, discovered that 2% of the 400 HIV-infected women who had antibodies to hepatitis B core antigen had occult HBV infection. Lower CD4 cell counts (less than 200 cells/mm³)

were more common among these HBV-infected women than those without HBV infection.

Researchers noted that these HBV- and HIV-infected women did not appear to have elevated alanine aminotransferase (ALT) levels, which rise above normal when liver cells are damaged or die.

Researchers Find a 5.8% HBV and HCV Infection Rate in HIV-Infected Children

A group of 228 HIV-infected U.S. children was screened for coinfection with either HBV or the hepatitis C virus (HCV) virus. They had an infection rate of 5.8%, according to a report published in a recent issue of the journal of the *Clinical Infectious Diseases*.

“This analysis suggests that chronic hepatitis is prevalent and should be routinely screened for in the pediatric HIV-infected population,” the researchers concluded.

HBeAg and Detectable HBV DNA Increase Risk of Mother-to-Child HBV Transmission

Researchers studied 144 children, born to HBV-infected mothers, who received both the hepatitis B vaccine and HBIG (hepatitis B immune globulin or antibodies) within 24 hours of birth to determine why some of them became infected.

Seventeen of the children (11.8%) developed chronic hepatitis B. The rate of infection transmission was:

- 12% born to mothers with the hepatitis B surface antigen (HBsAg)
- 0% born to mothers who tested negative for the hepatitis B “e” antigen (HBeAg)
- 21% born to HBeAg-positive mothers
- 0% born to mothers with undetectable HBV DNA
- And, 27% born to mothers with detectable HBV DNA.

Infection was significantly higher in mothers who were positive for HBeAg and HBV DNA. “To identify those children at high risk of HBV (prevention) failure, maternal HBeAg and HBV DNA need to be assessed prior to childbirth,” the researchers recommended in the report published in the August 2007 issue of the *European Journal of Pediatrics*.

Older Children and Adolescents, Vaccinated as Infants, Have Waning HBV Immunity

For how long does the hepatitis B vaccine protect those who were immunized during infancy? And, do some types of vaccines work better than others?

CDC researchers measured how 378 children and teens who had been vaccinated during infancy responded to a vaccine booster shot. If they were still immune from immunization during infancy, they should immediately generate antibodies.

Researchers reported in a recent issue of *Pediatrics* that 99% of children ages 5-7 and 83% of those ages 10-15 who received a recombinant hepatitis B vaccine responded to the booster, indicating they had continued immunity.

Of teens who received a plasma-derived vaccine during infancy, 69% had immunity against hepatitis B. Researchers reported that the older the children were, the weaker their immune protection against hepatitis B. About 60% of 14-year-olds had a protective antibody response, compared to 97 percent of 5-year-olds.

While most responded to the vaccine booster, “the significance of the increased proportion of non-responses among older adolescents might indicate waning immune memory,” researchers wrote.

Today’s hepatitis B vaccines come in higher doses. While there are low rates of HBV transmission today, researchers want to make sure that there is not a resurgence in HBV infection in adults who were vaccinated as young children and may have weakening immunity.

In another vaccine study, published in the August issue of the journal *Vaccine*, Taiwanese researchers studied 395 teenagers (ages 15-18) who had been immunized as infants and had low levels of surface antibodies to see if they retained hepatitis B immunity when they received boosters. They reported that a significant number of teens with low antibody levels before the booster shot quickly lost antibodies after receiving the booster shot.

“Our observations indicate that a booster dose of hepatitis B vaccine maybe unable to induce sufficient immunological response in adolescents who had undetectable residual (surface antibodies),” they noted.

HBeAg and Detectable HBV DNA Lower Survival Rates Over 25 Years in Caucasian Adults

How do HBV-infected Caucasian patients fare over 25 years? Italian researchers followed 70 Caucasian patients, who all originally tested positive for HBeAg, over 25 years.

They reported in the August 2007 issue of *Gut* that 61 (87%) patients spontaneously lost HBeAg and developed “e” antibodies. Over 23 years after HBeAg seroclearance, 40 (66%) of patients became inactive carriers, with no apparent liver damage. However, the remaining 21 (34%) experienced elevated ALT levels. One (1%) reverted and became HBeAg positive again, nine (15%) had detectable HBV DNA but tested negative for HBeAg, and 3 (5%) had non-alcoholic fatty liver disease.

Liver-related death occurred in 11 (15.7%) patients, caused by liver cancer in five and liver failure in six.

The 25-year survival rate was:

- 40% in HBeAg-positive patients
- 50% in HBeAg-negative patients with de-

tectable HBV DNA or HBeAg reversion

- And 95% in inactive carriers.

Older age, male gender, early development of cirrhosis and return of HBeAg lowered survival rates.

“Most patients with HBeAg seroconversion became inactive carriers with very good prognosis,” researchers wrote. “The risk of liver-related mortality in Caucasian adults with chronic hepatitis is strongly related with sustained disease activity and ongoing high level of HBV replication independent of HBeAg status.”

Core Mutation, Linked to Aggressive Liver Disease, Often Found in HIV-HBV Coinfected People

Researchers, reporting in the August 2007 journal *AIDS*, have discovered a mutation in the HBV core antigen region, which is frequently found in people coinfecting with HBV and HIV.

While antiviral treatment has improved survival in many HIV-infected people, a number of HBV-HIV coinfecting people die from liver failure. Researchers determined that a

mutation in the core antigen, which is known to cause more aggressive liver disease in those infected with only HBV, was prevalent in 10 HBV-HIV coinfecting individuals.

“Mutations in the HBV core and precore genes may be contributing to disease pathogenesis in HIV/HBV co-infected individuals,” they concluded.

MRI Most Accurate Tool to Find Liver Cancer, AFP Was a Weak Indicator

To screen people for liver cancer, doctors often test their alpha fetoprotein (AFP) levels annually during routine blood tests. AFP can be elevated when tumors are present, but AFP can be inaccurate. Researchers at Baylor University Medical Center in Texas compared AFP, a CAT scan ultrasound (CT) and magnetic resonance imaging (MRI) to see which diagnostic tool identified cancer most accurately.

Their report, published in the August 2007 issue of the journal of *Alimentary Pharmacology & Therapeutics*, examined which tool most accurately identified tumors in 239 patients with proven liver cancer. The cause of

cirrhosis and liver cancer in these patients was HCV (55%), HBV (17%), alcohol abuse (9%) and unknown causes (19%).

While AFP was elevated in 62% of those with liver cancer, the levels were low and unremarkable. Only 26%, 15% and 13% of patients had AFP levels more than 100, 400 and 1000 ng/mL respectively. AFP levels were elevated in 20% without liver cancer but exceeded 100 ng/mL in only 3% with cancer.

“The overall accuracy of AFP was poor regardless of the cutoff,” researchers wrote. MRIs proved to be more accurate than CT or ultrasound in detecting tumors, they concluded. “AFP is insensitive and adds little to screening strategies, but has prognostic value when extremely elevated.”

CAD Increases Accuracy in Diagnosing Liver Fibrosis

Magnetic resonance CAD is effective in diagnosing fibrosis of the liver, according to a study by Japanese radiologists, published in July issue of the *American Journal of Roentgenology*.

It is important to identify fibrosis, which includes inflammation and

mild scarring of the liver, because it is a precursor to liver cancer. Fifty-two patients’ magnetic resonance images (MRIs) were reviewed by two radiologists, and their diagnosis was then compared to data provided by the CAD computer diagnostic system. CAD, when compared to the review of the images by two radiologists, was more accurate in diagnosing liver fibrosis.

If successful, the CAD system could replace more invasive liver diagnostic tools, such as liver biopsies, to assess liver fibrosis.

HBV DNA Levels Dictate Frequency of Monitoring in HBeAg-Negative Patients

What happens once people seroconvert, become HBeAg-negative and have normal ALT levels? How closely should they be monitored for liver damage? Canadian researchers followed 74 HBeAg-negative individuals every three months for up to five years and compared them with 32 HBeAg-positive patients.

For HBeAg-negative patients, viral load predicted whether liver dam-

age would occur and ALT levels would rise. Only one HBeAg-negative patient in the study, who had normal ALT and low HBV DNA levels, experienced elevated ALT levels. In contrast, 67% of HBeAg-negative patients with HBV DNA levels greater than 100,000 copies/mL experienced a rise in ALT levels within one year.

Researchers, reporting in a recent issue of *Hepatology*, recommended that HBV DNA levels lower than 10,000 copies/mL, “predict persistently normal ALT for at least one year. Patients with HBV DNA values between 10,000 and 100,000 copies/mL can safely be followed at six monthly intervals, whereas HBV DNA values greater than 100,000 copies/mL are highly predictive of future ALT elevation and should prompt regular follow-up.”

Entecavir More Effective in Lowering HBV DNA Than Lamivudine

Chinese researchers treated HBeAg-positive patients, who normally have high viral loads, with two antivirals, either lamivudine (Epivir-HBV) or entecavir (Baraclude), to see which was most effec-

tive in lowering viral load.

They treated 21 people with lamivudine and 21 with 0.5 mg per day of entecavir for 48 weeks. Up to 71.4% of the entecavir group achieved undetectable HBV DNA, compared to 38% of the lamivudine group. The entecavir group also had a higher rate of normal ALT levels (85.7%), compared to 76.2% of the lamivudine-treated group, according to the report published in the August 2007 issue of the *World Journal of Gastroenterology*.

Experimental Antiviral Clevudine Appears Effective in HBeAg-Negative Patients

Clevudine, a new antiviral currently in clinical trials, was administered at 30 mg daily for 24 weeks in 63 HBeAg-negative patients. Researchers continued to follow the patients for an additional 24 weeks to assess the long-term impact of treatment.

After 24 weeks of treatment, viral load declined by about 1,000-fold, and 24 weeks after therapy ended, the patients sustained a HBV DNA decline of about 1,000-fold from their pretreatment levels.

At week 24 and week 48, 92.1% and 16.4% respectively of patients had undetectable HBV DNA levels, and 74.6% achieved normal ALT levels at week 24, which were maintained during the additional 24-week follow-up period.

No resistance to clevudine was detected during treatment. Researchers, reporting in the July 2007 issue of *Hepatology*, suggest that treatment for longer than 24 weeks is needed to achieve sustained response, including undetectable HBV DNA and normal ALT levels.

60 Weeks, Instead of 48 Weeks, of Pegylated Interferon Treatment Better in HBeAg-Negative Patients

While a 48-week regimen of pegylated interferon is currently recommended, researchers at the California Pacific Medical Center treated 13 HBeAg-negative patients with 60 weeks of pegylated interferon alone or with lamivudine to assess its effectiveness and to monitor any changes in the quantity of HBsAg.

Nine of the 13 (69%) achieved a 100-fold decrease in HBV DNA and

nearly undetectable HBV DNA 24 weeks after treatment ended (at week 84).

At week 84, HBV DNA was undetectable in five (38%) of patients, and three additional patients had a sustained 100 to 1,000-fold reduction in HBV DNA. Five patients had a 90% decrease in HBsAg concentration at week 60, including three with undetectable HBV DNA at week 84.

The researchers, reporting in the July 2007 issue of the *American Journal of Gastroenterology*, concluded that 60 weeks of pegylated interferon with or without lamivudine produced a better response than the 48-week regimen in HBeAg-negative individuals.

“Larger studies are necessary to assess if longer duration therapy is more effective than the standard regimen and results in a greater decline in HBsAg concentration,” they wrote.

Among Lamivudine-Resistant, Females and Those with Low HBV DNA Fare Best with Adefovir

A team of Spanish researchers treated 54 pa-

tients, who had developed viral resistance to lamivudine, with adefovir (Hepsera) alone or in combination with lamivudine, and then followed them closely for 30 months to see who responded best to the new antiviral. About half of the patients were HBeAg-positive.

Thirty-eight patients (70.4%) achieved low HBV DNA within the first 12 months of treatment. Six (24%) of 25 HBeAg-positive patients exhibited HBeAg loss and 20% seroconverted to “e” antibodies. Eight patients (14.8%) developed viral resistance to adefovir.

Patients who responded best tended to have low viral load to begin with, were female and were HBeAg-negative. Those who seroconverted and developed “e” antibodies had low viral load and HBV genotype D, researchers reported in the September 2007 issue of the *Journal of Hepatology*.

