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Hepatitis B

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“Occult” Hepatitis B—without the Surface Antigen—Increases Liver Cancer Risk Eight-Fold

Researchers, writing in the November 2009 issue of the *Journal of Viral Hepatitis*, found that Japanese patients who have “occult hepatitis B” infection—which means they test negative for the hepatitis B surface antigen (HBsAg) but have HBV DNA circulating in their bloodstream—face up to an eight-fold higher risk of liver cancer after they develop cirrhosis (severe liver scarring).

The researchers followed 82 cirrhotic patients, all of whom tested negative for either the hepatitis B virus (HBV) or the hepatitis C virus (HCV), for more than five years. Nine of the patients tested positive

for the hepatitis B core antigen (which shows evidence of past infection) and HBx DNA, which is believed to embed itself in liver cells and lead to a higher rate of liver cancer, in addition to HBV DNA (viral load) in their bloodstream. These nine patients tended to be younger and had lower alanine aminotransferase (ALT) levels—characteristics that usually indicate an absence of liver damage. However, liver cancer rates for these patients with HBV DNA were 27% after five years and 100% after 10 years. In contrast, the liver cancer rate for the other cirrhotic patients who did not have occult hepatitis B was 13.5% and 24.6% after five and 10 years respectively. The presence of diabetes also increased the risk of liver cancer.

The researchers encour-

aged additional studies to determine if some other co-existing condition, such as fatty liver disease, autoimmune liver disease, or past alcohol consumption might also contribute to the rise in liver cancer among patients with occult hepatitis B.

Health Officials Call for Better Prevention, Monitoring, and Treatment of Hepatitis B in the U.S.

The U.S. Centers for Disease Control and Prevention estimate that between 1980 and 2004 the number of new HBV infections dropped from about 200,000 per year to about 60,000, and the estimated number of new HCV infections decreased from 180,000 in 1982 to

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19,000 in 2006. But beneath the good news is a lurking, silent epidemic unless adequate prevention efforts are implemented, according to a report published in the Nov. 10, 2009, issue of the *Journal of the American Medical Association*.

The report summarized recommendations from a meeting of viral hepatitis experts held in September sponsored by the American Gastrointestinal Association Institute, the CDC, the Department of Veterans Affairs, and the National Institute of Allergy and Infectious Diseases.

Decreases in hepatitis B have resulted from 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. However, chronic hepatitis B remains prevalent worldwide, affecting 400 million people and causing about 500,000 deaths annually. Shifting immigration patterns are bringing more chronically infected individuals to the U.S. from Africa, Central

America, and Asia.

Currently about 50% to 70% of U.S. residents with chronic hepatitis B were born in another country, and more than half of new cases identified were born in Asia or the Pacific Islands. The vast majority have no symptoms and are unaware of their infections.

“The global burden of hepatitis B infection has important implications for the epidemic in the United States,” wrote Bridget M. Kuehn. Researchers fear the spread of HBV infection among unvaccinated, high-risk people, and many suspect the prevalence of hepatitis B and C is much higher in the U.S. than reported by the CDC because many infected individuals may not be included in surveys that do not count the homeless, incarcerated, or illegal immigrants.

Also contributing to the spread of viral hepatitis are inconsistent recommendations about whom to screen for infection. The U.S. Preventive Services Task Force in 2004 recommended against routine screening of asymptomatic indi-

viduals for hepatitis B.” The USPSTF does, however, recommend routine screening of pregnant women for HBV, but some of its screening recommendations conflict with current, more aggressive CDC guidelines.

Once patients with viral hepatitis infection are identified, the next challenge is providing them access to treatment and regular monitoring because many in these high-risk groups are 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.

Green Tea Continues to Prove Beneficial in Preventing Fibrosis

Green tea has been shown to benefit liver health by conferring protection against toxic carbon tetrachloride, cholestasis, and alcohol abuse. South Korean researchers studied whether the tea could also protect the liver against the known cancer-causing agent dimethylnitrosamine (DMN).

Their report, published in the November 2009 issue of the *World Journal of Gastroenterology*, found that green tea extract prevented the development of fibrosis in DMN-exposed animal liver cells. The researchers concluded that green tea may protect liver cells by reducing the levels of collagen fibers in the liver, which contribute to fibrosis. The information may be helpful to HBV-infected patients who suffer fibrosis.

Careful Monitoring Urged for Children and Young Adults with Chronic Hepatitis B

Writing in the November 2009 issue of the journal *Pediatrics*, a team of U.S. pediatric hepatologists, who specialize in treating children and teens with hepatitis B, urged doctors to regularly monitor young patients, even if they appear to have no signs of liver damage during early childhood.

“In a study of Asian subjects, 20% to 25% of individuals with chronic hepatitis B developed severe hepatic fibrosis before the age of 25 years. These individuals most likely acquired their disease in childhood and may have experienced a prolonged period in the immune-active phase,” when viral load and ALT levels are high, they wrote.

New adult guidelines, which recommend more frequent monitoring to quickly identify liver damage, has led to a heightened awareness among pediatric liver specialists that treatment during a prolonged immune-active phase is important to decrease a child’s risk of developing cirrhosis and/or cancer later in life.

“In addition, a strict linkage of ALT level

with progression of liver disease is not always apparent, especially in children,” they added. “Practitioners need to rigorously monitor HBV-infected patients at regular intervals (every 6 to 12 months) and refer to a pediatric liver specialist any patient who has elevated ALT and HBV DNA levels.”

What are “Healthy” ALT Levels in Children?

Recently, the “healthy” levels for ALT in adults have been revised and are at 30 IU/L for adult men and 19 IU/L for women. However, healthy ALT levels for children have not been established. Therefore, the experts recommended that doctors apply adult ALT levels to older teens. For younger children, upper healthy ALT levels can vary according to each laboratory and age, they noted. “In the absence of guidelines for children, the panel recommends that the ALT level be considered elevated if it is greater than the testing laboratory’s ULN or 40 IU/L, whichever is lower,” they wrote.

When determining whom to treat, the panel recommended that, “any child with an elevated ALT and/or AFP level and/or a positive family history for liver disease, especially liver cancer, be referred to a pediatric liver specialist who will advise on opportunities to treat and/or the need for further evaluation,” they wrote. “The specialist will also recommend a strategy for long-term monitoring.”

In more urban areas, a local pediatric liver specialist often manages an infected child’s care while in more rural areas, it may be primary care practitioners who continue to monitor and treat in consultation with the specialist.

Entecavir plus HBIG Effective in Preventing Reinfection in Liver Transplant Patients

To date, lamivudine (Epivir-HBV) has been used in combination with hepatitis B immunoglobulin (HBIG) to prevent HBV reinfection following liver transplantation. However, doctors are concerned about lamivudine’s high drug re-

sistance rate, so Chinese researchers tried treating 30 previously HBV-infected transplant patients with the antiviral entecavir (Baraclude) (0.5 mg daily) along with HBIG.

Their findings, published in the October 2009 issue of the *Journal of Digestive Diseases*, revealed that none of the entecavir-treated patients became reinfected with HBV, and their hepatitis B surface antigen quickly disappeared one week after surgery.

“This study shows that entecavir combined with low dosages of HBIG is effective and safe in preventing hepatitis B recurrence after liver transplantation, but its long-term effect is still under investigation and a large-sample study will be carried out in the future,” they wrote.

In a separate study, published in the October 2009 issue of *Digestion*, researchers reported that immediate treatment with entecavir was highly effective when six patients experienced acute hepatitis B, which often occurs after initial infection with HBV.

Text Messaging Effective in Achieving Medication Compliance among Teens Who Undergo Liver Transplantations

Liver transplant patients must take one or more types of immunosuppressant drugs for several years, which can be challenging for children and teens. New York researchers tried using text messaging to send medication reminders to 41 teens in a 12-month study to see if it improved their medication compliance.

According to their findings, reported in the October 2009 issue of *Pediatrics*, the strategy was effective for most participants, whose average age was 15. The number of acute cellular rejection episodes decreased from 12 to 2 during the study. Risk factors for rejection were older age (17.6 years of age vs. 13 years) and use of more than one immunosuppressant medication.

However, 13 patients (37%) stopped the study after 4 months.

HBV Infection Does Not Increase Risk of Pancreatic Cancer

A U.S. study using data from the Henry Ford Health System found that HBV infection does not increase the risk for pancreatic cancer—which contradicts an earlier study that suggested a link between the two. Researchers determined that only advanced age increases pancreatic cancer risk.

The study results were presented at the American Association for the Study of Liver Diseases' Annual Meeting in Boston. Physicians looked at more than 74,000 patients who were tested for hepatitis B between 1995 and 2008 and watched for pancreatic cancer among hepatitis B patients over a 13-year period.

When factors such as age, race, sex, HIV or HBV status, and the presence of diabetes were considered, only older age and the presence of diabetes proved to be significant risk factors.

Study Shows Doctors Do Poorly at Screening Hepatitis B Patients for Liver Cancer

U.S. researchers assessed how well patients who were at high risk of liver cancer—because they had HBV infection, were older, or had cirrhosis—were screened for liver cancer. They followed 557 patients treated at two community gastroenterology clinics in northern California. Cancer screening was categorized into four groups based on the combined frequency of alpha fetoprotein (AFP) tests (high levels indicate the presence of tumors) and ultrasound imaging: optimal, suboptimal, poor, and no screening.

About 40.6% of patients received poor or no screening. Non-cirrhotic patients had worse screening than cirrhotic patients. Patients who had a greater number of clinic visits per year were 3.4-times more likely to have regular screening than patients who made fewer clinic visits.

“Since more frequent clinic visits is a strong independent predictor of improved screening

adherence, regular routine clinic visits may help improve adherence to (liver cancer) screening, which may also lead to improved clinical outcomes,” researchers wrote in the November issue of the *Journal of Digestive Diseases and Sciences*.

HCV-HBV Coinfection Causes Less Liver Damage

Italian researchers followed 27 patients coinfecting with HCV and HBV and 27 similar patients infected with just HBV over 23 years to see what impact a single viral hepatitis infection vs. a coinfection had on the progress of liver disease.

They determined that coinfecting patients with HBV and HCV, and HBV-only-infected patients who acquired the infection in youth showed a lower rate of fibrosis, no liver failure, and low development of liver cancer over the 23-year study period, according to their report in the October 2009 issue of the *Journal of Medical Virology*.

Diabetes and Obesity May Contribute to Liver Damage in Those Infected with HBV

Taiwanese researchers followed 934 patients to see what impact obesity and diabetes (with elevated blood-glucose levels) played in the progression of liver damage, indicated by elevated ALT levels.

About 25% of the patients had elevated ALT levels (greater than 40 IU/L). Those with elevated ALTs were more likely to be obese and have unhealthy, elevated blood-sugar levels.

“In conclusion, a body mass index greater than or equal to 25 kg/m² (indicating obesity) and a fasting blood glucose level greater than or equal to 126 mg/dL were risk factors for increased ALT activity in subjects with hepatitis B infection,” researchers wrote in the *Journal of Clinical and Experimental Metabolism*. They suggested that obesity and diabetes may aggravate or accelerate liver injury in the HBV-infected.

Earlier HBeAg Seroconversion Linked to Better Long-Term Health

Patients who achieve HBeAg seroconversion—losing the hepatitis B “e” antigen (HBeAg) and gaining the “e” antibody—before age 30 have a far lower risk of developing HBeAg-negative hepatitis B, cirrhosis, and liver cancer, according to a report in the October 2009 issue of *Hepatology* by Taiwanese researchers.

The researchers carefully monitored 508 patients over 15 who had spontaneously—without treatment—achieved HBeAg seroconversion. They compared the rate of HBeAg-negative hepatitis (when viral load remains elevated despite the loss of HBeAg due to a viral mutation), cirrhosis, and liver cancer among patients based on their age at HBeAg seroconversion.

Of the 483 patients who had no evidence of cirrhosis or liver cancer, HBeAg seroconversion had occurred:

- Before age 30 in 218 patients (group A),
- Between age 31

and 40 in 199 patients (group B),

- And after age 40 in 66 patients (group C).

The 15-year incidences of HBeAg-negative hepatitis, cirrhosis, and liver cancer increased as those undergoing HBeAg seroconversion aged. The lowest rates for HBeAg-negative hepatitis, cirrhosis and liver cancer respectively were in group A (31.2%, 3.7%, and 2.1%) and the highest incidence was in group C (66.7%, 42.9%, and 7.7%).

