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Hepatitis B

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Expert Opinion: How to Treat Patients with HBV Precore Viral Mutations

William F. Balistreri, MD, director of the Liver Transplantation Program at Cincinnati Children's Hospital Medical Center, addressed how patients infected with the hepatitis B virus (HBV) with precore mutations should be treated in a recent "Ask the Experts about Liver Disease" column published in *Medscape Gastroenterology*.

Patients with precore mutations tend to have moderate or high levels of HBV DNA (viral load) circulating in their blood, and they usually test negative for the hepatitis B "e" antigen (HBeAg). The precore mutation in HBV enables it to replicate without producing the "e" antigen.

According to guidelines from the American Association for the Study of Liver Diseases, patients with HBeAg-negative hepatitis B, moderate HBV DNA levels (less than 20,000 IU/mL) and elevated alanine aminotransferase (ALT) levels (twice normal, which shows liver cell damage) should be considered for treatment. Treatment is recommended if a liver biopsy reveals moderate to severe inflammation.

However, HBV with precore mutations tends not to respond well to interferon, even with prolonged therapy. Antivirals, which meddle with the viral genetic material and hinder replication, are safe; however, prolonged antiviral treatment is required.

"Thus, pegylated interferon, adefovir (Hepsera), telbivudine (Tyzeka), or entecavir (Baraclude) is preferred

in view of the need for long-term treatment," Dr. Balistreri suggested. "The endpoints of treatment are not well defined, but presumably are based on viral elimination (reduction in HBV DNA levels) and resolution of liver injury (reduction in ALT levels)."

Balistreri did not recommend the antiviral lamivudine (Epivir-HBV) because long-term use of this antiviral results in rapid development of viral resistance.

New Hepatitis A, B and C Cases Decline By 88%, 79% and 90% Respectively in the U.S. During 1995-2005

Rates of infection with HBV, hepatitis C (HCV) or the hepatitis A virus (HAV) have fallen to historic lows between

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1995 and 2005, according to a report published in the March 16, 2007, issue of the U.S. Centers for Disease Control and Prevention (CDC)'s *Morbidity and Mortality Weekly Report*.

The rates of HAV and HBV are currently at their lowest levels since the federal government began collecting data more than 40 years ago, according to the CDC report, "Surveillance for Acute Viral Hepatitis -- United States, 2005."

Since 1995, there has been an 88% decline in the reports of new hepatitis A cases and a 79% decline in hepatitis B. Since the early 1990s, there has been a 90% decline in new reports of hepatitis C cases. Much of the decline in hepatitis A was attributed to vaccination of children, recommended in many Western states since 1999. For hepatitis B, the greatest decline was among children and teens age 15 and younger due to a high vaccination rate in this age group.

While there is no vaccine for hepatitis C, CDC officials attributed the decline to changing behaviors among injecting drug users, and better screening of blood donations.

Important Plasmacytoid Dendritic Cells, Which Target Viral Infections, Are Few in HBV-Infected Patients

Researchers still don't know why HBV can so effectively infect the liver without facing tough opposition from the immune system in people with chronic infections. A group of Chinese researchers examined the number and function of plasmacytoid dendritic cells (pDCs) that normally produce interferon and promote immunity against viral infections.

Writing in the April 2007 issue of the *Journal of Viral Hepatitis*, the researchers compared pDCs levels in 56 people with chronic HBV infections and 19 healthy subjects.

They found the frequency and interferon-producing capacity of pDCs was dramatically reduced in HBV-infected patients with elevated ALT levels.

Additionally, patients with the HBV strain or genotype C had lower levels of pDCs and interferon than HBV-infected patients with genotype B, and may therefore be at higher risk of progressive liver disease.

Hepatitis B Infection from HBsAg-Positive Bone Marrow Can Be Prevented

Thai researchers successfully transplanted bone marrow from a hepatitis B surface antigen (HBsAg)-positive patient into an uninfected patient with leukemia without transmission of HBV to the patient.

The researchers lowered the viral load (HBV DNA) of the bone marrow donor to undetectable levels through antiviral therapy. Then, after the transplant, hepatitis B immunoglobulin (HBIG/hepatitis B antibodies) was administered for one week to the patient who received the bone marrow and the antiviral drug lamivudine was also administered long-term.

One year after discontinuation of lamivudine, the patient who received the transplant remained free of HBV infection, according to their report published in the February 2007 *World Journal of Gastroenterology*.

Higher HBeAg Seroconversion Rates in HBV Genotype B Patients Linked to Higher T Cell Levels

A group of Chinese researchers tackled the question of why people infected with HBV genotype B often seroconvert – lose HBeAg and developed "e" antibodies – more frequently than patients infected with HBV genotype C.

Writing in the April 2007 *Journal of Viral Hepatitis*, they reported examining the role of T helper cells. They studied the response of T cells, which fight infection, in 10 patients with HBV genotype B and 10 patients with genotype C who experienced a "flare," marked by an increase in ALT.

There was no difference in the HBV DNA levels during hepatitis flares between patients with genotypes B and C. But patients with genotype B had a significantly higher number of interferon-producing cells, which spur the immune system to fight infection, compared to genotype C patients.

They found patients that with genotype B had a higher rate of HBeAg seroconversion. Patients with precore mutations in their HBV also had a significantly higher number of interferon-producing cells compared to patients without precore mutations. This could

indicate that the immune system had successfully eradicated HBV without precore mutations.

The researchers suggested the higher number of interferon-producing cells and resulting T cells triggered the higher seroconversion rate in genotype B patients.

HBV-Infected Liver Transplant Patients with Cancer and Cirrhosis Have Similar Survival Rates

Liver transplant patients infected with HBV-related liver cancer have similar survival rates as those with HBV-related cirrhosis, according to a recent report in the March 2007 issue of *Liver Transplantation*.

Liver cancer patients often get higher priority for transplants than those with cirrhosis (severe liver scarring), resulting in earlier transplantation. However, survival following transplantation may be reduced in liver cancer patients because of the high risk of cancer recurrence.

To compare survival, researchers from the University of Michigan in Ann Arbor reviewed data from 279 patients enrolled in the U.S. Hepatitis B Virus-Orthotopic

Liver Transplantation study. The median follow-up period was 30.2 months from first appearance on the transplant list.

The transplantation rate in cancer patients was higher than in cirrhotics (78.1% vs. 51.4%). Following transplantation, the survival rate in the cancer group was 83% -- not significantly different from the 90% survival rate noted in the cirrhotic group.

The HBV recurrence rate was also similar in each group, roughly 10%. Disease recurrence, by contrast, was significantly higher in the cancer group -- 19% vs. 10%.

High Viral Loads Linked to Liver Damage

A group of Brazilian researchers investigated the link between HBV-DNA levels and liver health in 78 HBsAg-positive blood donors whose ALT, HBeAg and HBV DNA were studied, along with tissue samples collected during liver biopsies.

Among the 78, HBV-DNA was detected in 47 (60%) patients; 39 (83%) were males with an average age of 37. The researchers, writing in the February 2007 issue of

the *Journal of Clinical Gastroenterology*, reported that 31 (66%) were HBeAg-negative, and ALT was elevated in 26 (55%).

They reported that HBV-DNA levels were significantly higher in patients with liver inflammation or cirrhosis, compared to patients without signs of liver damage.

Researchers concluded there was a significant association between viral replication and liver damage, however low viral loads did not necessarily exclude signs of liver damage.

Most People Who Get Only the First Two HBV Vaccine Doses Are Protected from Infection

How protected from HBV infection are people who receive only the first two doses of the three-dose hepatitis B vaccine?

Swiss researchers, writing in the January 2007 issue of *Vaccine*, assessed the amount of antibodies to the hepatitis B surface antigen (only the surface antigen is administered in the vaccine) in 86 travelers who postponed getting their third dose vaccine more than one year after getting the

first two doses.

Eighty-two travelers (95.3%) had evidence of antibody protection against hepatitis B, including 16 of 17 travelers who were tested five years after receiving only two vaccine doses.

Most Patients Expect Pain, But Experience Little, During Liver Biopsies

How much pain and discomfort do liver biopsies cause? Researchers polled 118 patients (ages 19-68) who were undergoing a liver biopsy for the first time about how much pain they expected before the procedure, compared to the actual pain they experienced.

While the expected pain scores of female patients were significantly higher than male patients, there was no difference between female and male patients in the actual experienced pain scores. Both genders reported little pain from the procedure.

“Calming the patients by informing them about the procedure and their diseases will probably diminish the expected pain,” researchers suggested in their report published in the February 2007 issue of *Digestive Diseases and Sciences*.

Doctors Fail to Follow Hepatitis B Status in HIV-HBV Co-infected Patients Treated with Antivirals

Researchers followed 357 HIV and HBV co-infected patients to see how well health care providers managed the HIV infection as well as the HBV infection in co-infected patients when they were treated with antivirals.

According to their report published in the journal of *Clinical Infectious Diseases*, HBV information (HBeAg and HBV DNA status) was obtained for only 16% of patients before antiviral therapy began, while doctors evaluated HIV viral status in 99% of patients.

Once antiviral therapy began, there were 497 HIV evaluations compared to 85 HBV evaluations.

The percentage of patients who received any level of HBV monitoring (HBeAg and viral load) after treatment began increased from 7% in 1999 to 52% in 2001 while the percentage of patients who underwent HIV load testing remained at 80%-90% during the same period.

In conclusion, health care providers who treated co-infected pa-

tients during 1999-2003 infrequently monitored HBV but systematically monitored HIV.

“Improved physician adherence to guidelines that better delineate HBV treatment and monitoring for patients with HIV-HBV co-infection is needed,” researchers urged.

Researchers Suggest Sweat Could Transmit HBV

Turkish researchers say sweat from HBV-infected wrestlers could potentially transmit infection, according to their report of 70 Olympic wrestlers published in the March 2007 issue of the *British Journal of Sports Medicine*.

Researchers from Celal Bayar University in Izmir, Turkey, identified nine HBV-infected wrestlers, eight of whom reportedly had HBV DNA in their sweat.

“The results proposed that other than bleeding wounds and mucous membranes, sweating could be another way of transmitting HBV infections in contact sports,” the researchers suggested.

However, the athletes reported that they frequently had bleeding or weeping wounds during training or competitions,

which offers an undisputed method for transmission of this blood-borne virus.

Some sporting organizations already require HIV testing among athletes taking part in contact sports, but the researchers say HBV infection may be a bigger issue, given there are higher concentrations of HBV in blood, than HIV, making it easier to transmit infection.

Livers from Older Organ Donors Associated with Lower Survival Rate

A team of South Korean researchers investigated what role age played when older people donated livers to patients with HBV-related liver damage.

The researchers, reporting in the March 2007 issue of *Liver International*, followed 136 hepatitis B patients who underwent liver transplants from 1999 to 2004. All received partial livers from living donors. They monitored survival in those who received livers from donors who were age 40 and older, and those who received livers from donors younger than 40.

There were more females in the older donor

group, and more donors with antibodies to the hepatitis B core antigen. The frequency of immediate organ rejection and early death was similar in both groups, but the long-term survival rates for the older donor group were significantly lower (1-, 3- and 5-year survival was 84%, 75%, 46% for the older group versus. 92%, 86% and 83% for the younger donor group.)

“Our study suggests that older donor allografts (livers) would be associated with poor patient survival after (transplant) for HBV-related liver diseases,” the researchers wrote.

Hepatitis B Patients Should Be Screened with Ultrasound Every Six Months

A Baylor College of Medicine researcher, writing in the March 2007 issue of the *American Journal of Medicine*, recommends that inter-nists should screen patients at high risk of liver cancer by ultrasound every six months.

High-risk patients include those infected with HBV and/or HCV or consume large quantities of alcohol.

