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Hepatitis B

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Pegylated Interferon May Be Best Treatment Option in Younger Patients with High Viral Load and Long History of Infection

Two renowned hepatitis B researchers from France and the United States, writing in the February 2008 issue of the *Journal of Hepatology*, recommend pegylated interferon for younger and middle-aged patients who contracted hepatitis B early in life who have high viral loads (HBV DNA).

Their advice counters recommendations promoted by the American Association for the Study of Liver Disease

(AASLD), who recommend interferon if alanine aminotransferase (ALT) levels are above normal. ALT is an enzyme released by dying or damaged liver cells. But normal ALT levels may not reflect the true level of liver disease or fibrosis, they noted.

“Pegylated interferon therapy is often a better choice for young to middle-aged patients with genotype (viral strains) A and B because of the higher rate of HBeAg seroconversion (loss of the “e” antigen and development of “e” antibodies) and a greater chance for HBsAg seroconversion (loss of the hepatitis B surface antigen and development of the surface antibody) in both HBeAg-positive and -negative patients as compared to nucleoside analogs

(antivirals),” the researchers noted.

Antiviral therapy is the current standard of care for many patients. However, long-term antiviral therapy results in viral resistance, and use of more than one antiviral over time can lead to HBV that are resistant to multiple antivirals.

“While great progress has been made in treating hepatitis B, many important issues require further study,” the researchers noted.

Tenofovir Plus Lamivudine Effective in HBeAg-Positive Patients with Adefovir Resistance

Korean researchers treated six cirrhotic, HBeAg-positive patients, who had developed resistance to lami-

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vudine (Epivir-HBV) and in whom adefovir (Hepsera) was ineffective, with a combination of tenofovir (Viread) and lamivudine for at least six months.

After six months of treatment, HBV DNA levels became undetectable in four patients, and after 12 months of treatment, HBV DNA levels were undetectable in all patients and ALT levels normalized in four patients.

According to their reports in the January 2008 issue of the *American Journal of Gastroenterology*, this antiviral combination may be a promising rescue therapy for patients, particularly those with cirrhosis and lamivudine resistance.

A “Weak” HBV Infection May Play Role in Development of Occult Infections

Increasingly, researchers are identifying “occult” HBV infection, when HBsAg has mutated so it is not identified by lab tests, yet there is HBV DNA present, and sometimes signs of liver damage.

Italian researchers studied T-cells, the im-

mune system’s fighter cells, to see what role they played in occult infections.

They examined T-cells in 32 HBsAg-negative individuals, 18 of whom had occult hepatitis B. Six patients with chronic hepatitis B and seven HBsAg-inactive carriers were studied for comparison. Those who had core antibodies (anti-HBc), which shows evidence of past infection, had T-cell responses typical of those who had resolved infections. In contrast, HBV-specific T-cells in those without anti-HBc did not behave aggressively against HBV, which suggests the possibility of “a low-dose” HBV infection that did not elicit the immune response of a regular HBV infection or generate “protective memory” on the part of the T-cells.

“Our results suggest different mechanisms of control of viral replication in seropositive and seronegative occult infections,” the researchers noted in the February 2008 issue of the journal *Gastroenterology*, and they recommended additional studies.

Occult HBV Found in Livers of One-Sixth of People Without Liver Disease

Italian researchers investigated the presence of occult hepatitis B in Italians in the general population who had no signs of liver disease. Writing in the March 2008 issue of the *Journal of Hepatology*, the researchers reported taking liver biopsies and examining them for HBV DNA from 98 liver disease-free individuals who tested negative for HBsAg. Sixteen of them tested negative for the hepatitis B core antibody and the remainder had no signs of past HBV infection.

Occult HBV infection was revealed in 16 of the 98 cases (16.3%). Ten of the 16 with core antibodies (62.5%) versus 7.3% of the HBV-negative were occult carriers.

“This study revealed that about one-sixth of the Italian general population might be carriers of occult HBV infection, and this condition is significantly associated with the core antibody positive status,” they wrote.

New HBV Genotype Identified in Vietnam

Japanese and Vietnamese researchers have identified a new genotype of HBV in Vietnam, according to their report in the March 2008 *Journal of Virology*. The HBV variant, called HBV-VH24, showed similarities to “aberrant strains” that had been identified several years ago by researchers analyzing hepatitis B viruses in Vietnamese people which had unique genetic formations and amino acid residues that were not present in any other identified eight genotypes, labeled genotypes A-H.

The researchers say their findings support the designation of a new HBV genotype I.

Four, Low-Dose Hepatitis Vaccine Injections – Instead of Three – Induces Better Protection

Up to 10% of healthy adults and infants vaccinated with the recommended three hepati-

tis B doses fail to develop adequate levels of protective antibodies against hepatitis B. Revaccination with the same vaccine dose has proved to be effective, but Iranian researchers tried re-vaccinating nonresponders with four – instead of three-lower vaccine doses.

Administration of a single additional dose induced adequate levels of antibody protection against infection in about 83%.

The protection rates obtained after administration of four low doses (ranging from 2.5 to 5 mg) were significantly higher than those obtained after administration of the classical three 10-mg doses. These results indicate that a significant proportion of non-responder infants can achieve protection following revaccination with a single low-dose vaccine. “Thus adaptation of four low-dose (2.5 or 5 mg) vaccination is expected to induce higher seroprotection rate,” in infants, the researchers wrote in the January 2008 issue of *Vaccine*.

Low-Iron Diet May Help Reduce Liver Cancer in People with Viral Hepatitis

Japanese researchers examined 77 patients with hepatitis C and 34 with hepatitis B to see if the amount of iron in their livers played a role in the extent of liver damage caused by “oxidative stress.”

In their report published in the March 2008 issue of the *Journal of Viral Hepatology*, they wrote that the damage they were looking at was higher in patients with greater levels of iron in their livers, confirming other reports that high iron levels enable or enhance liver damage in those with viral hepatitis. These researchers found a higher rate of high iron and liver damage in hepatitis C patients than hepatitis B patients, though it was present in both.

“The strong positive correlation between hepatic DNA damage and iron overload suggests that iron content is one of the most likely mediators

of hepatic oxidative stress and iron reduction may be beneficial to reduce the incidence of hepatic cancer,” they reported.

30-mg Dose of Clevudine Appears Most Effective in Phase II Trials

A multinational team of researchers treated 31 patients with the experimental antiviral clevudine at either 10-, 30- or 50-mg doses for 12 weeks during a phase II clinical trial, with a follow-up of 24 weeks.

At week 12, the average viral load declines at the 10-, 30- or 50-mg doses were 3.2-fold, 3.7-fold, and 4.2-fold respectively.

Clevudine was well-tolerated with no serious adverse side effects. The average half-life of clevudine in the bloodstream was 70 hours. Through modeling, researchers reported in the journal of *Alimentary Pharmacology & Therapeutics*, 97% of the maximum treatment effect was reached with a 30mg daily.

Hepatitis B Declines Continues Due to Immunization in the United States

A U.S. Centers for Disease Control and Prevention surveillance report of new hepatitis infections in the United States in 2006, the most recent year for which data are available, reported that between 1990 and 2006, acute hepatitis B declined 81% to the lowest rate ever recorded – 1.6 cases per 100,000 people.

Declines occurred among all age groups, but were greatest among children, according to a report published in the March 28, 2008, issue of the *Morbidity and Mortality Weekly Report*. The reduced rate was attributed to mandatory immunizations.

Mandatory Immunization Produces Equal Protection Across All Racial Groups

Illinois researchers evaluated the overall effect of Illinois's mandated hepatitis B immunization requirement for fifth grade

school entry on vaccination rates in children, based on racial and ethnic differences, before and after the mandate went into effect.

Researchers reviewed 106,541 students in six Chicago public schools' 12th-grade classes – four entered fifth grade before the mandate went into effect and two entered after the mandated immunization went into effect.

The mandated vaccination group had immunization levels of 38.2% compared to the 4.3% rate among those before the mandate. African-American and Hispanic students were less likely to have received hepatitis B vaccination before the mandate. By the time the mandated students reached 9th grade, vaccination coverage levels for all racial and ethnic groups exceeded 80%.

“School-entry requirements effectively increased hepatitis B vaccination coverage levels regardless of race or ethnicity and should be considered for other recently recommended adolescent vaccines,” researchers reported in the Feb. 29, 2008, online edition of *Pediatrics*.

Dual Hepatitis A and B Vaccine Remains Effective in Children and Adolescents

An international team of researchers followed two groups of children, one aged 1–6 and the second 6–15, who had been vaccinated with the dual hepatitis A and B Twinrix™ vaccine according to the three-injection schedule.

The 1–6 age group was followed for 7.5 years and the 6–15 age group was followed for 10 years, and all were found to have adequate protective levels of hepatitis A antibodies, while 86.5% and 95.5% respectively of the two groups had adequate protective hepatitis B antibodies, according to the report published in the *Journal of Gastroenterology and Hepatology*.

Engineered Molecules Are Able to Stop and Reverse Cirrhosis in Rats

Japanese researchers have designed artificial molecules that, when used in rats with cirrhosis, successfully reverse liver scarring, which can be caused by HBV infection.

In the journal *Nature*

Biotechnology, the researchers reported they designed molecules that could block production of collagen, which causes fibrosis and cirrhosis, by liver stellate cells.

To accomplish this, researchers loaded the molecules into carriers coated with vitamin A, which stellate cells absorb. The liver cells are tricked into absorbing the vitamin A-laden molecules, which then shut down their collagen production capability.

In the study, the researchers induced liver cirrhosis in rats and then injected them with these molecules, which completely cured the rats of cirrhosis. In addition to producing collagen, the cells also secrete enzymes that dissolve collagen. Without new collagen, the enzyme production continued and effectively dissolved the fibrosis.

Researchers hope the molecules would be ready for use in humans in several years.

High Viral Load and High-Normal ALT Levels Should Prompt Treatment in People of Asian Descent

Despite persistently normal ALT levels over two

years or more, many HBV-infected people of Asian descent with detectable viral loads (HBV DNA) are at risk of developing cirrhosis and liver cancer, regardless of their hepatitis B “e” antigen (HBeAg) status, according to an expert commentary by George K. Lau, MD, of the University of Hong Kong, published in a *Projects in Knowledge* continuing education program.

Those at risk of liver cancer include people with high-normal ALT levels of 30 and 40 in women and men respectively, and HBV DNA loads of more than 10,000 copies/mL.

The at-risk patients with high-normal ALT often were older, male, and had developed a viral mutation called the basal core promoter.

Because of this, Lau recommends that doctors check HBV DNA levels regularly, despite the presence of normal ALT levels, and consider treatment if there is a high viral load.

