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Hepatitis B

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Researchers Still Searching for the "Best Treatment Strategy" for Hepatitis B

Researchers who assessed the currently available treatments for hepatitis B viral (HBV) infection in the March 2008 issue of *The Lancet Infectious Diseases*, concluded that currently there is no "best strategy" for long-term treatment of hepatitis B.

Pegylated interferon, administered through a weekly injection and intended to boost the immune system to fight infection, may offer long-term beneficial effects after one year of treatment, but most patients fail to respond to interferon.

Antiviral treatment, administered in daily pills, is the only available long-term treatment. Each antiviral disrupts a different "step" in HBV's complicated reproduction cycle, but some antivirals work in similar ways and over time HBV can develop mutations and continue to reproduce despite treatment with one or more antiviral. A patient can develop resistance to one antiviral, which means other antivirals that attack the same reproduction step will also be ineffective. Researchers examined resistance risks posed by each antiviral:

- Lamivudine (Epivir-HBV) has the highest resistance rate of 10-27% after one year, 37-48% after two years, and 60–65% after four years of treatment.
- Adefovir's (Hepsera)'s resistance rate is zero after one year, 3% after two years, and 29% after five years.
- Telbivudine (Tyzeka) has a resistance rate of 3-4% after one year and 9-22% after two years.

Entecavir (Baraclude) resistance is rare in those who have never been treated with an antiviral, remaining less than 1% after one year; however in patients who have already developed lamivudine resistance, entecavir resistance reaches 43% after just four years.

Doctors Should Avoid Antivirals That Set the Stage for Cross-Resistance When Treating HIV-HBV Coinfected

Because of the potential for antiviral resistance and cross-resistance, physicians who treat people coinfected with HBV and HIV are urged to select antivirals carefully when

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they treat only the hepatitis B infection, according to an article in journal of *Antiviral Therapy* because some antivirals impact HIV as well as HBV.

Antivirals that affect only HBV include adefovir, entecavir, telbivudine and pegylated interferon, while lamivudine, emtricitabine and tenofovir affect both viruses. (Emtricitabine and tenofovir have not yet been approved by the U.S. Food and Drug Administration for treatment of hepatitis B.)

If coinfected patients do not require treatment for HIV, clinicians should avoid prescribing tenofovir, entecavir, emtricitabine or lamivudine to avoid compromising future HIV treatment, due to the potential for cross resistance.

Double-Dose of Hepatitis B Revaccination Works in HIV-Infected

Using a double-dose of hepatitis B virus vaccine in HIV-positive patients who don't respond to standard vaccination has a 50% success rate, according to a Dutch study published in the January 2008 edition of the *Journal of Infectious Diseases*.

Many at risk of HIV are also at risk of HBV infection, about 6%-10% of HIV-positive gay men are also chronically infected with HBV. Individuals coinfected with HIV and HBV have an eight-fold increased risk of death compared to those infected with only HIV.

To date, HIV-positive patients have had a poor response to hepatitis B vaccination, with only 40%-76% developing adequate antibody protection against hepatitis B. Researchers tried revaccinating 144 non-responder, HIV-infected people (most men, average age 43) at monthly intervals with double the recommended dose of the vaccine. At the time of revaccination, 96 patients (67%) were receiving antiretroviral therapy and 89 patients (62%) had an undetectable HIV viral load.

Revaccination was successful in 74 of the 144 patients (51%). Female patients were found to have a significantly better response rate, and all younger patients and older patients with undetectable HIV viral load had higher success rates.

People with Chronic Hepatitis B Have Weak T Cells to Fight Infection

Thai researchers, reporting in the February 2008 issue of the *World Journal of Gastroenterology*, found that people with high viral load (HBV DNA) or long-term HBV infections (from birth), have weak levels of peripheral T-lymphocytes (T-cells) that the immune system dispatches to fight and suppress viral infections.

Researchers measured the levels of several types of T-cells – all essential to protect against viral infections – in 206 people with varying HBV viral loads. Generally, they found that the higher the viral load, the weaker the T-cell population was in keeping the infection in check.

Researchers Suggest Sweat May Transmit HBV in Contact Sports

Researchers analyzed blood and sweat samples from 70 male Turkish wrestlers for evidence of HBV infection. One-third of the wrestlers, ages 18 to 30, reported having had bleeding or weeping wounds during training and competition, and half said that they had had an episode of bleeding during other activities. None of the wrestlers appeared to have active HBV infection because all tested negative for the hepatitis B surface antigen (HBsAg), which indicates a current infection.

However, when a more refined test was administered that looked for HBV DNA in their blood, researchers were surprised to detect HBV DNA in nine (13%) of the wrestlers. Eight wrestlers also had HBV DNA in their sweat. The higher the HBV DNA level in blood, the higher the levels of HBV DNA in the wrestlers' sweat. The study showed that the wrestlers had "occult" HBV infections, evidence by a lack of discernable HBsAg, but present HBV DNA.

In addition to contact with blood and body fluids, sweat may be another way of transmitting HBV infections in contact sports, the researchers suggest in a report published in the *British Journal of Sports Medicine*. They advocated requiring HBV tests and vaccinations for all wrestlers.

Kava Linked To Liver Damage, New Evidence Shows

Kava, a plant found in the South Pacific that has been used as a ceremonial beverage and more recently marketed as an herbal treatment for anxiety, has been found to damage the liver, according to a report published in the February 2008 issue of the *World Journal of Gastroenterology*.

Australian researchers focused on kavain, the major ingredient in kava, and studied its effects on the biologic structure of the liver. They found it caused a change in liver tissue, including the narrowing of blood vessels, the constriction of blood vessel passages and the retraction of the cellular lining. Kavain adversely affected immune cells that fight infection.

Patients with Large Liver Cell Dysplasia at Higher Risk of Liver Cancer

Korean researchers studied liver cell dysplasia – when cells appear abnormal but are not cancerous – to see if large or small liver cell dysplasia was an early indicator of liver cancer in people with hepatitis B.

According to their report in the February 2008 issue of the *Journal of Clinical Gastroenterology*, they sampled liver tissue from 181 patients and found large and small liver cell dysplasia in 82 (45%) and 17 (9%) patients, respectively. After about eight to nine years, the patients' livers were biopsied again and doctors found nine (10 percent) of cases of liver cancer, of which 13 (76%) and 3 (17%) cases had large or small liver cell dysplasia respectively. The patients with large liver cell dysplasia (LLCD) showed a threefold higher risk of liver cancer developing. Patients with small cell dysplasia had no increased cancer risk.

Researchers suggest that LLCD in HBV-infected patients should be considered a liver cancer risk factor, and patients with LLCD should receive more intensive liver cancer screening.

Maintaining Lamivudine and Adding Adefovir Yields Best Response

Italian researchers compared the effectiveness of adefovir treatment alone against adding adefovir to ongoing lamivudine treatment after patients develop lamivudine resistance.

Researchers, reporting in the January 2008 issue of the *Journal of Hepatology*, confirm what other researchers have found that maintaining lamivudine treatment and adding adefovir produces the best results.

Fifty-five percent of 29 patients treated with just adefovir experienced a decline in viral load, while 83% of those treated with lamivudine and adefovir responded.

In patients with higher viral load, the antiviral combination was even more effective. The combination of antivirals was also effective in preventing development of adefovir resistance.

Initial Response to Adefovir May Indicate Long-Term Success

Researchers treated 42 people, half of whom had lamivudine resistance, with adefovir for 23 months to see which patients responded rapidly to adefovir and when those who did not respond early during treatment developed resistance to adefovir.

About 88% of people in the study were HBeAg-negative, and 76% had HBV genotype (viral strain) D. Forty percent achieved a four-fold reduction in HBV DNA within six months, and 77% of those early responders also achieved undetectable HBV DNA after 12 months. However, only 5% of those who did not response quickly to adefovir cleared HBV DNA by month 12.

Five (12%) of the patients developed adefovir-resistant mutations and a resurgence in HBV DNA and alanine aminotransferase (ALT) levels, which indicates liver cell damage. The development of adefovir resistance at 12 and 24 months was 5% and 17% respectively.

Spanish researchers, reporting in the January 2008 issue of the *Journal of Viral Hepatitis*, noted that development of adefovir resistance in patients who had never been treated appeared to be higher than previously reported.

Asian- and African-Americans Half as Likely to Get Liver Transplant Than Caucasian Americans

The Surveillance, Epidemiology, and End Re-

sults (SEER) cancer registry collected data on adults with liver cancer who qualified for liver transplants between 1998 to 2002 to see if there were racial disparities in who received and did not receive transplants.

A report in the February 2008 issue of *The American Journal of Gastroenterology* reported that of the study group of 1,156 adults with small (5 cm or less) nonmetastatic liver tumors, about 45% were Caucasian, 29% Asian-American, 17% Hispanic, and 9% African-American.

Only 21% of the patients who qualified received a transplant due to organ shortages. Of those, a recent diagnosis, younger age, and being married and Caucasian increased the chance of receiving a transplant.

African- and Asian-Americans were about half as likely to receive a transplant as compared with Caucasians. Those who underwent liver transplants had 3- and 5-year survival rates of 81% and 75%, respectively.

Researchers concluded that only one-fifth of those with small, liver tumors received a transplant, and African-Americans and Asian-Americans were significantly less likely to receive a transplant after other variables were considered.

Three Years of Lamivudine Therapy Results in a 42% HBeAg Seroconversion Rate in Korean Children

Korean researchers treated 60 children with lamivudine for six years and found 42% lost HBeAg and developed the "e" antibody (called seroconversion), 53% achieved undetectable viral load, and 88% achieved normal ALT levels.

HBeAg seroconversion rates of 60% were higher in patients younger than 6 years, and clearing HBV DNA (68.4%) and achieving normal ALT (94.7%) were highest in patients between 6 and 12 years. Overall, patients age 12 and older had more success. Those with elevated ALT experienced higher rates of HBeAg seroconversion.

Six patients (10%) did not respond to lamivudine and three children developed viral resistance to lamivudine.

"Despite high seroconversion rates in Korean children treated with lamivudine, new therapeutic agents are needed for improved viral suppression and reduction of emergence of resistance," researchers wrote in a recent edition of the *Yonsei Medical Journal*.

Diabetes Much Higher in HCV-Infected Than HBV-Infected Adults

A Japanese study followed 544 people infected with the hepatitis C virus (HCV), 286 infected with HBV, and 122 patients whose HCV had been cleared by interferon treatment to see at what rate insulin resistance (which precedes diabetes) and type 2 diabetes developed in these two populations.

The prevalence of type 2 diabetes in the HBV- and HCV-infected population and the HCV-cleared population was 6.3%, 13.6%, and 9%, respectively. Thee prevalence of insulin resistance in the HCV-infected group (54.3%) was also higher than in the HBV group (36.3%) and the HCV-cleared group (35.7%), according to the report published in the March 2008 issue of *Liver International*.

Liver Transplants More Effective Than Tumor Removal

A team of Italian researchers compared the success of liver transplant to liver resection (removal of a tumor) in terms of recurrence of liver cancer and survival. Forty-eight patients received transplants and 38 had liver resection surgery.

Survival was significantly higher in the liver transplant group, and the rate of cancer recurrence after three and five years was 31% and 76% respectively in the liver resection group and 2% and 2% in the liver transplant group.

Researchers, writing in *Transplant International*, concluded that liver transplantation was superior to liver resection for small tumors in cirrhotic patients.

Arthritis Drug Appears to Cause HBV Reactivation

Texas researchers have found that treatment with tumor necrosis factor-α (TNF-α) inhibitors, used for some medical conditions including rheumatoid arthritis, may lead to resurgence of HBV infection.

The body produces TNF-α and its presence is used by the immune system to combat HBV. The researchers studied 13 patients with HBV, 11 of whom had been treated with the TNF-α inhibitor infliximab, and two were treated with the TNF-α inhibitor etanercept. Some of the patients required antiviral treatment before, during, or after TNF-α inhibitor treatment due to HBV reactivation, which often occurred within a month of the third dose of infliximab. Etanercept, because of its pharmaceutical make-up, apparently did not reactivate the HBV.

"TNF-α inhibitors in general should be used cautiously in chronic hepatitis B viral infection," researchers wrote in *Seminars in Arthritis and Rheumatism*.

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