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Hepatitis B

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More Proof that Coffee May Prevent Severe Liver Fibrosis and Scarring

A study published in the June 12, 2006, *Archives of Internal Medicine* suggests that an ingredient in coffee may help prevent severe liver fibrosis and scarring (cirrhosis) in people with liver disease caused by alcoholism or viral hepatitis.

Researchers studied 125,580 people without known liver disease enrolled in a healthcare plan between 1978 and 1985, and then followed them through 2001.

During the follow-up period, 330 people developed liver cirrhosis – 199 had alcoholic-related cir-

rhosis and 131 had cirrhosis from viral hepatitis and other causes. Participants who drank coffee had a lower rate of cirrhosis, and the more cups of coffee they drank each day, the lower their risk of cirrhosis.

Among the 131 with nonalcoholic cirrhosis, the risk for severe liver damage was 1.2 if they drank only one cup per day, and 0.7 if they drank four or more cups of coffee each day. Those who refrained from coffee had higher alanine aminotransferase (ALT) levels, a substance released when liver cells are damaged or die

In contrast, tea drinking did not lower people's risk

of cirrhosis, so the ingredient that prevents cirrhosis may not be caffeine, researchers suggested.

Non-Invasive Liver Tests that Work in Hepatitis C Patients Don't Work in Hepatitis B Patients

Researchers continue to look for a non-invasive way – one which will not require the withdrawal of a sample of liver tissue, as in a liver biopsy – to assess liver health in people infected with the hepatitis B virus (HBV).

In hepatitis C patients, doctors use ALT, ratios between platelets and aspartate aminotransferase (AST), and other means. Doc-

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tors, reporting in the August 2006 issue of *Liver International*, decided to see if the non-invasive diagnostic procedures used in hepatitis C patients would work in 218 hepatitis B patients. Most were male, and most were Chinese.

They tried them out and compared the results with a liver biopsy that revealed the true health of the liver. They found that platelets were the only factor significantly associated with predicting fibrosis and cirrhosis, but by and large none of the other non-invasive practices used in hepatitis C patients successfully predicted cirrhosis and fibrosis in hepatitis B patients.

Viral Mutation Concerns Shadow Availability of New Antivirals

A variety of experts addressed the pros and cons of the latest hepatitis B antiviral treatments at the Digestive Disease Week 2006 Conference. Several researchers ex-

pressed concern about the accumulating viral resistance that HBV develop over time when exposed to one or more antivirals.

Currently, doctors try a new antiviral medication when viral resistance occurs – indicated by a resurgence in viral load (HBV-DNA) and elevated ALT levels. But doctors are finding that HBV can develop resistance to lamivudine (Epivir-HBV) quickly, and then go on to develop resistance to a second or even third antiviral, which in the long run may limit the choice and availability of treatment. Here is a summary of findings and reports about treatment options.

Lamivudine (Epivir-HBV): This antiviral, the first to be approved by the U.S. Food and Drug Administration (FDA), causes viral resistance quite rapidly, though it is still used by many doctors as a first choice for treatment. Lamivudine, which meddles with the genetic material of the virus,

makes it difficult for HBV to replicate. But over time, the lamivudine-resistant HBV multiply and become the dominant virus, and the viral load begins to increase and ALT levels start to climb. When lamivudine is used, patients should be followed closely so any viral resistance is diagnosed quickly.

Adefovir (Hepsera): Doctors often prescribe the antiviral adefovir when a patient begins to develop viral resistance to lamivudine, which is often still the first antiviral used. Conference participants agree that adefovir resistance does not appear to cause a significant problem when it's used after lamivudine resistance has developed. The HBV with mutations that can resist lamivudine cannot resist adefovir. Adefovir mutations take place in a different area of the virus than lamivudine mutations.

Five-year data on patients who do not have the hepatitis B “e” antigen (called HBeAg-negative

hepatitis B) found that adefovir by itself produces a viral mutation rate of 29% over five years, with 11% of patients experiencing mutations that were accompanied by viral rebound and elevated ALT level.

Doctors also found that in order for an antiviral to be effective in causing long-term seroconversion (loss of HBeAg and gaining of the “e” antibody), a patient should be kept on adefovir and other antiviral agents for six months or more after HBeAg seroconversion to achieve sustained response.

Entecavir (Baraclude): This drug, the most recently-approved FDA antiviral, was given to HBeAg-negative patients for 96 weeks; 96% of the entecavir-treated patients achieved or maintained undetectable HBV DNA.

In another study, 77 HBeAg-positive patients who had developed lamivudine resistance were given entecavir. Entecavir increased the number of patients with undetectable

HBV DNA, there was a 21% clearance rate at week 48 and 40% at week 96, and the proportion of patients with normal ALT ranged from 65% to 81%. However, viral resistance with entecavir-resistant HBV occurred in 9% of patients by week 96.

In conclusion, patients with lamivudine resistance may experience some benefits from taking entecavir a second year, even though 9% of them may develop entecavir resistance.

Telbivudine: This antiviral, not yet approved by FDA for treatment of hepatitis B, is under investigation. One study followed 921 HBeAg-positive and 446 HBeAg-negative chronic HBV patients treated with telbivudine. In the HBeAg-positive group, HBeAg loss occurred in 26% and 60% had undetectable HBV DNA. In the HBeAg-negative groups, better viral suppression was seen in the telbivudine-treated patients than those treated with lamivudine. Viral

resistance was reported at a rate of 2% to 3% in patients after one year.

Another study compared telbivudine with adefovir. In 133 patients with HBeAg-positive hepatitis B, telbivudine achieved a significantly greater decrease in HBV DNA levels than adefovir, but there were similar rates of ALT normalization.

Tenofovir: This antiviral, used to treat HIV, has not yet been approved by the FDA for hepatitis B treatment. In a study of 109 lamivudine-resistant hepatitis B patients, tenofovir achieved quicker suppression of HBV DNA than adefovir within the first six to 12 months, however the two antivirals had similar rates of HBeAg seroconversion and ALT normalization.

Entecavir Better than Lamivudine in Achieving Low or Undetectable Viral Load

Bristol-Myers Squibb Company, in

a report presented to the Digestive Disease Week conference, showed that 96 weeks of entecavir treatment produced undetectable HBV DNA in 94% of HBeAg-negative patients, compared to 77% of patients treated with lamivudine.

No evidence of viral resistance was seen in entecavir-treated patients during the 96-week period.

Thirty percent of patients who were switched to entecavir after they developed lamivudine resistance achieved an undetectable viral load. Viral resistance to entecavir, among the lamivudine-resistant patients, occurred in 9% of patients through week 96.

HBV-Infected Donor Livers May Be Useable and Increase Survival

Due to the severe shortage of donor livers needed for transplantation, doctors are considering using donor organs that have been in-

fectured with HBV. Writing in the June 2006 issue of the journal *Liver Transplantation*, South Korean doctors offered a report on a hepatitis B patient who had received an HBsAg-infected liver five years ago.

The recipient recovered slowly after liver transplantation and he continued to test positive for HBsAg despite high-dose hepatitis B immunoglobulin (HBIG) and lamivudine treatment. The patient was also treated with the experimental antiviral famciclovir and interferon. To date, combination treatment with lamivudine and adefovir has kept the patient's liver healthy for the past 20 months.

"In conclusion, our result impli[es] that a recipient of liver graft from an HBsAg-positive carrier may survive for a long period following antiviral therapy with lamivudine and adefovir," the researchers wrote. "Considering this living donor case and previously re-

ported cases, the use of an HBsAg-positive cadaveric liver graft may deserve attention when no other donor is available.”

Dr. Rosenthal Describes Hepatitis B Monitoring and Treatment Options for Children

Philip Rosenthal, director of the Pediatric Liver Transplant Program at the University of California San Francisco Children’s Hospital, described his recommended treatment and monitoring options for children with hepatitis B at the Sixth Annual B Informed Patient Conference 2006.

While there are no “official” guidelines for children, Rosenthal is currently serving on a panel to help the Pediatric Gastroenterology Society develop general recommendations.

Based on his own experience, Dr. Rosenthal suggests the following guidelines, along with checking for liver

cancer with regular AFP testing:

- If a child has HBeAg, moderate viral load, and normal ALT, doctors should check the child’s ALT every 3-6 months
- If a child has HBeAg, moderately high viral load, and ALT that is elevated, check ALT every 1-3 months.
- If a child has HBeAg, high viral load, and ALT that is more than twice upper normal limits, consider performing a liver biopsy and treating the child.

If a child has “e” antibodies, normal ALT and low HBV DNA levels, check ALT levels every six to 12 months.

There are currently only two FDA-approved drugs available to children with hepatitis B.

Interferon alpha (Intron A) – Is an interferon that requires three injections each week. Children with HBeAg and elevated ALT should receive the drug for 4-6 months, according to Rosenthal,

children who have the “e” antibody should receive interferon for one year. Most children tolerate interferon’s side effects better than adults.

Lamivudine – Children should take the oral antiviral daily for one year, however, 20% of children will develop lamivudine-resistance at year 1, and 70% will experience resistance at year 5.

“Long term use of any drug in children is a thorny issue – what is the potential impact on a child’s future growth and development? With the current oral HBV drugs, what will happen if a 9 year-old child develops resistance? What will be his or her treatment options?” Rosenthal asked.

There are currently ongoing pediatric clinical trials for adefovir, which has already been approved for adults. Currently, there are no pediatric clinical trials in the works for either entecavir or pegylated interferon.

Hepatitis C, Not Hepatitis B, Is Causing a Spike in Liver Cancer Deaths in Taiwan

Doctors in Taiwan have assumed a recent increase in liver cancer cases were due to hepatitis B, which is endemic in the region despite an aggressive immunization campaign. However, a study by Taiwanese hospitals found the culprit to be hepatitis C.

The doctors reviewed 18,423 liver cases in the country between 1981 and 2001, focusing on Yunlin and Tainan counties, and Chiayi City, where the cancer rate is high. They found that while the overall death rate in patients with liver cancer caused by hepatitis B had dropped, hepatitis C deaths increased 66 percent in Taiwanese males, and deaths doubled for Taiwanese females. The study is scheduled to be published in the *International Journal of Cancer*.

Hepatitis C is transmitted primarily through tainted

blood products, unsafe injections and shared drug injecting equipment.

Shared Rinse Water and Filters Linked to HBV Infection in Methamphetamine Users

Researchers, studying an outbreak of acute HBV infection among methamphetamine injectors in Natrona County in Wyoming, found that users who shared rinse water and cotton, used to filter the drug, were at far higher risk of acute hepatitis B, according to a report in the May issue of *Addiction*.

Researchers studied 18 meth users who were acutely infected with HBV from January to August, 2003, and 49 uninfected meth users who had never been immunized against hepatitis B. Researchers found that sharing water, used to prepare injections and/or rinse syringes, was associated with HBV infection (94% of the infected, versus 44%

of the control group). Sharing cotton filters, also used in drug preparation, also put meth users at high risk.

Sharing syringes did not present as high a risk as sharing water and filters.

“Methamphetamine use has become increasingly prevalent in the United States, the researchers wrote, “Our findings highlight the need for awareness of risks associated with injection drug use and sharing behaviors. Enhanced hepatitis B vaccination programs and educational campaigns that target methamphetamine injectors specifically, including those living in rural areas, should be developed and implemented.”



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