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Hepatitis B

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Liver Cancer Rates Continue to Climb in the United States

A report published jointly in the *Journal of the American Medical Association* and the U.S. Centers for Disease Control and Prevention's *Morbidity and Mortality Weekly Report* exploring trends and changes in liver cancer rates in the United States revealed that cancer rates have increased 3.5% between 2001 and 2006, primarily due to viral hepatitis infections.

Liver cancer is the third leading cause of death from cancer worldwide and the ninth leading cause of cancer deaths in the United States. Infection with the hepatitis B virus (HBV) and hepatitis C virus (HCV) account for an estimated 78% of liver cancers worldwide.

Researchers reported that liver cancer rates in the U.S. increased from 2.7 per 100,000 in 2001 to 3.2 per 100,000 in 2006. The largest increases in HCC incidence rates were among whites, African-Americans, and people aged 50-59 years.

Liver cancer rates ranged from 1.4 per 100,000 in South Dakota to 5.5 per 100,000 in Hawaii. "The results demonstrate a continuation of long-term increases in (liver cancer) incidence and persistent racial/ethnic disparities," researchers noted. Development of viral hepatitis services, including screening with care referral for persons chronically infected with HBV or HCV, comprehensive immunization programs, and improved public health surveillance are recommended to reverse the growing trend.

The average age of liver

cancer diagnosis was 64 years—62 years for males and 69 year for females. The highest incidence rate was among persons aged 70-79 years.

The incidence rate for men was approximately three times higher than that of women. The cancer rate was highest among Asians-Pacific Islanders (7.8 per 100,000 persons), followed by African-Americans, American Indians-Alaska Natives, and whites.

Cancer Risk Remains Even After HBsAg Clearance in Older Patients

Korean researchers followed 96 patients who cleared the hepatitis B surface antigen (HBsAg) for an average of 166 months to see if they were at lower risk of developing liver cancer. The average age of the patients at

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the start of the study was 40 years.

During a 4.5-year follow-up period after HBsAg seroclearance, 6 (6.5%) developed liver cancer. The average age at the time of developing cancer was age 56.

The presence of cirrhosis at the time of clearing HBsAg and age older than 45 at time of clearance increased the risk of liver cancer.

Writing in June 2010 issue of the *Journal of Clinical Gastroenterology*, researchers cautioned that even patients who clear HBsAg can develop liver cancer if they have cirrhosis, and cancer monitoring should continue.

HBV Genotype D Responds Poorly to Interferon Treatment

There is little information about how hepatitis B patients with strain or genotype D fare when treated with pegylated interferon. In a study based in Turkey, where genotype D is prevalent, doctors followed 71 hepatitis B e antigen (HBeAg)-positive patients for 10 years after they were treated with interferon.

Twenty-eight (39%) patients of the patients cleared HBeAg and developed “e” antibodies—

called HBeAg seroconversion. Twenty-five seroconverted during treatment and 3 seroconverted 12 months after treatment ended.

The responders were followed for an average of 10 years, and during this longer follow-up period 21 of the 25 (84%) initial responders relapsed. But, 3 patients who did not respond at the end of therapy responded during follow-up.

In total, 21 of 28 responders relapsed (75%), either with HBeAg reversion (14.3%) or HBV-DNA elevation over 2,000 international units per milliliter (IU/ml) and elevation above normal of alanine aminotransferase (ALT) (85.7% of patients), which indicates liver damage.

The response was sustained in only 7 patients (9.8%). Researchers, writing in a recent issue of the *Journal of Digestive Diseases and Sciences*, concluded that sustained response to interferon treatment is low in HBeAg-positive patients with genotype D.

Researchers Suggest Saliva of Children with High HBV DNA Levels Could Be Infectious

Can saliva transmit

hepatitis B?

Danish researchers investigated HBV DNA levels in saliva of children, with high viral loads, who were positive for HBeAg to explore if saliva could transmit the infection.

In their study published in a recent issue of the *Pediatric Infectious Diseases Journal*, the researchers reported they “found high levels of HBV DNA in saliva of HBeAg-positive children, suggesting saliva as a vehicle for horizontal transmission of HBV among children.”

Entecavir Proven Highly-Effective in Korean and Japanese Patients

Korean and Japanese researchers treated 167 patients with the antiviral entecavir (Baraclude) at doses of 0.01 mg, 0.1 mg or 0.5 mg for between 24 and 52 weeks in a Phase II study, and then treated them with a dose of 0.5 mg daily for another 44 weeks to assess the long-term effects of the antiviral treatment, which works by disabling the virus’ replication process.

After 148 weeks of treatment, 88% of patients had undetectable HBV-DNA levels, 90.1% of those who previously had elevated ALT levels

achieved normal ALT levels, and 26% of those who were HBeAg-positive achieved HBeAg seroconversion.

Twenty-one patients in the group, who had liver biopsies before treatment and another biopsy during treatment, achieved improvement in liver health, and 57% demonstrated improvement in fibrosis over three years.

The 3-year risk of developing drug resistance to entecavir was 3.3% for all patients. Researchers, writing in the June 2010 issue of the *Journal of Hepatology*, concluded that long-term use of entecavir in previously-untreated patients was highly effective and caused minimal drug resistance.

Vitamin E Reduces Liver Damage

A double-blind, randomized trial of nondiabetic adults with liver damage from nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) found that vitamin E improved liver health and led to a decline in inflammation.

Currently there is no established treatment for NASH, which causes liver damage similar to what can be caused by

HBV, so researchers conducted clinical trials that tested either insulin-resistance reduction (pioglitazone) or oxidative stress reduction therapy (using vitamin E) against placebo in 247 patients with NAFLD.

Only vitamin E treatment produced a significant improvement in the health of the patients' livers. "In the future, vitamin E treatment should also be evaluated in diabetic NAFLD-affected patients, taking into account that the use of this antioxidant therapy may ameliorate the disease progression," researchers wrote in a commentary published in the May 2010 issue of the *New England Journal of Medicine*.

"Further trials are needed, but this study highlights the role of vitamin E in NAFLD, which is becoming the most common hepatic disease worldwide," they wrote. "This trial is large enough to give all clinicians the opportunity to begin immediate use of vitamin E in non-diabetic adult patients affected by NAFLD/NASH and should also be used as the reference drug in future clinical trials when new drugs are investigated."

Reuse of Syringes Linked to HBV and HCV Infections in 13 Patients

A team of U.S. researchers, including experts from the CDC, explored the outbreak of hepatitis B and hepatitis C virus (HCV) infections related to one anesthesiologist.

HBV and HCV can be transmitted during administration of intravenous anesthesia when medication vials are used for multiple patients, which allows body fluids from one patient to be transferred to another.

Researchers investigated outbreaks of acute HBV and HCV infections among endoscopy patients who received anesthesia from the same anesthesiologist who worked at two different gastroenterology clinics. Chart reviews, patient interviews, clinic site visits and infection control assessments, and molecular sequencing of HBV and HCV were performed.

Writing in the July 2010 issue of the journal *Gastroenterology*, researchers identified 6 cases of HCV and 6 cases of HBV infection related to one clinic, and one HCV infection related to the second clinic. HCV from the

patients were nearly identical to that of a "source" patient with hepatitis C who was treated at the clinic.

The anesthesiologist inappropriately used a single-patient-use vial of propofol for multiple patients. Re-use of syringes to re-dose patients, with resulting contamination of medication vials, likely resulted in viral transmission, according to the researchers.

"Gastroenterologists are urged to review carefully the injection, medication handling, and other infection control practices of all staff under their supervision, including providers of anesthesia services," researchers wrote.

Antivirals Dramatically Improve Survival after Liver Cancer Diagnosis

Past studies have proven that antiviral treatment—which keeps viral load low—reduces the risk of liver cancer in hepatitis B patients. Recently, researchers from Thomas Jefferson University in Philadelphia reported in the *International Journal of Cancer* that antivirals also prevent recurrence of liver cancer.

Surgery to remove liver tumors is successful if the tumor is small, but often

liver tumors and lesions redevelop in these patients. Researchers compared survival in post-liver cancer patients who received antivirals to those who did not.

Experts reported that the median survival in patients who received antiviral therapy after liver cancer diagnosis was 60 months. Survival in patients who did not receive treatment averaged 12.5 months.

Before the antiviral drugs were developed, patients would often develop new lesions within a few months of tumor removal because the underlying virus that was causing the cancer was not suppressed, experts explained. Once suppressed by antivirals, survival increased markedly.

The small study included 15 patients who had a single tumor, which was less than 4 cm, removed by surgery. The first six patients were diagnosed between 1991 and 1997, prior to development of antivirals and were considered a control group.

The other nine patients, diagnosed between 2000 and 2004, were treated with the antiviral lamivudine (Epivir-HBV) immediately after their cancer diagnosis, and with other antivirals, such as

tenofovir (Viread) and adefovir (Hepsera), when lamivudine resistance developed.

All patients who received the antivirals maintained undetectable viral load. Seven of the 9 patients have not had recurrence of liver cancer.

Commonly-used Cholesterol Drugs May Damage Liver

Statins, commonly prescribed drugs used to treat heart disease by lowering cholesterol levels, may lead to liver damage, according to a report by British researchers published in the May 2010 issue of the *BMJ*.

The type and dosage of statin drugs given to patients to treat heart disease should be proactively monitored as they can have unintended adverse effects, concludes a new study published on bmj.com.

Researchers collected data from 368 general practices that contributed data on more than 2 million patients, aged 30-84, including 225,922 patients who were new statin users. The patients' response to statins, including the type, dose and duration of statin use, was studied from January 2002 to June 2008.

They found an increased

risk with using statins for moderate or serious liver dysfunction, acute renal failure, moderate to serious myopathy (nerve damage), and cataracts. They also found the higher the dose, the greater the risk of liver damage.

The highest risk of liver damage occurred when the statin fluvastatin (Lescol) was prescribed, and the risk was highest during the first year of use.

Overall, for every 10,000 high-risk women treated with statins, there would be approximately 271 fewer cases of cardiovascular disease, but 74 additional cases of liver dysfunction, 23 extra patients with acute renal failure, 307 extra patients with cataracts, and 39 extra patients with myopathy. Similar figures were found for men except rates of myopathy were higher.

As a result, patients with pre-existing liver damage from hepatitis B should monitor for any liver damage worsening as a result of statin use.

Coffee Decreases the Risk of Cirrhosis in Heavy Drinkers

Italian researchers monitored the alcohol and coffee consumption of 749

patients with chronic liver disease, including HBV and HCV infections, over a six-month period to see what impact the two drinks had on patients with cirrhosis (severe scarring of the liver).

They found that alcohol intake of more than 3 units (drinks) per day resulted in increased risk of cirrhosis in males and an even higher risk of cirrhosis in females. The alcohol intake dramatically increased the risk of cirrhosis in those infected with HBV or HCV.

However, there was a reduced risk of cirrhosis when these heavy drinkers also drank coffee, and the more coffee they drank, the lower their risk of cirrhosis. The risk of cirrhosis decreased from 2.3-fold in subjects drinking zero to two cups of coffee daily, to 1.4-fold more in those drinking more than two cups per day.

Significant Decline in HBV DNA by Week 24 Indicates Interferon Treatment Successful

Dutch researchers treated 136 patients with pegylated interferon and carefully followed their HBeAg and HBV DNA levels during the first 26 weeks of treatment to search for early indicators

that the treatment was working.

Interferon is an expensive drug that causes major side effects, and works in less than one-third of patients treated. Doctors are hoping to find a model that they can use to determine within a few weeks if the treatment will work.

Researchers found that a 100-fold decline in patients' HBV DNA levels by week 24 of treatment—or earlier—was strongly associated with achieving low viral load and even HBeAg seroconversion after 32 weeks of treatment.

Writing in the July 2010 issue of the *Journal of Medical Virology*, researchers recommend that interferon treatment be stopped if patients haven't achieved a 100-fold decline in HBV DNA by week 24.

