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Hepatitis B

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Favorable Liver Health Helps HBsAg

A study of 92 adult Chinese patients with chronic hepatitis B found that having a low viral load (HBV DNA), normal alanine aminotransferase (ALT) levels, and genotype B gave one a better chance of completely eradicating the virus (clearing the hepatitis B surface antigen or HBsAg) than not having these favorable factors.

In a report published in the June 2004 issue of *Hepatology*, researchers from Queen Mary Hospital in Hong Kong followed the patients for about 10 years. They studied all aspects of the patients, including their liver health, ALT and antigen and antibody status.

The doctors found no difference in the risk of liver cancer between patients with and without HBsAg clearance. However, they found that liver cancer could still occur in patients who had cirrhosis even though they had cleared the virus at an older age.

“Recombinations” Possible in HBV Genotype A and B

Investigators are beginning to explore what happens when a person is infected with two different hepatitis B viral strains or genotypes. Researchers from Taiwan, writing in the May 2004 issue of the *Journal of Medical Virology*, examined what happened when seven injecting drug users were infected with both genotypes B and C.

When only the pre-S region of the virus was examined, only HBV genotype B was detected. When 10 to 21 “clones” of the pre-S region were cultivated from each coinfecting patient and sequenced, most of the clones were HBV genotype B. However, new “recombinations” of HBV genotype B and genotype C occurred in two patients.

The researchers suggest that HBV genotype B may become the dominant strain when there is a coinfection of genotypes B and C, and that recombinations between different the two genotypes may not be unusual. “The impact of recombination on the evolution of HBV and the clinical significance remains to be studied,” they concluded.

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HBV Genotype C Prone to Core Mutations and Accelerated Liver Disease

Chronic hepatitis B patients with HBV genotype C often experience accelerated liver damage. Japanese researchers, reporting in the May 2004 issue of the *Journal of Gastroenterology and Hepatology*, found that a viral mutation commonly found in genotype C HBV may contribute to this high rate of liver disease.

Researchers compared 42 patients with genotype B and 87 patients with genotype C over four years, continually examining their HBV, their ALT levels and their “e” antigen (HBeAg) status.

Genotype C patients had significantly higher rates of HBeAg (40.2% compared to a rate of 2.4% among genotype B), detectible HBV DNA and elevated ALT levels (71.3% compared to 11.9%) than genotype B patients.

Genotype B patients were more likely to have HBV without mutations. However, among genotype C patients, the core promoter mutation was found in 75.9% of them and the precore mutation was

found in 66.7%.

Of the 67 patients with elevated ALT levels, which indicate liver damage, five had genotype B and 62 had genotype C.

The researchers concluded that genotype C was one of the worst genotypes to have, possibly because of the high rate of viral mutations in the core promoter region.

HBeAg-Negative Hepatitis B Mutations Linked to Infants’ Liver Death

Researchers examined the hepatitis B virus make-up in five infants who died from fulminant hepatitis B (liver death) after their birth to HBV-infected mothers who had HBeAg-negative hepatitis B.

HBeAg-negative hepatitis B is caused by HBV that have the ability to replicate in the liver without producing “e” (HBeAg) antigen.

The Swiss researchers, writing in the June 2004 BioMed Central’s *Gastroenterology*, noted that adults who suffer fulminant hepatitis B often have HBV with mutations. They found that the infants who had fulminant hepatitis B also had viral mutations, the most dominant

were the HBV that did not produce the “e” antigen. However, these were not the dominant HBV in their mothers.

“The data suggest that the selection of a specific HBeAg negative viral strain may be associated with the development of fulminant hepatitis B in children,” they concluded.

Recovery from Hepatitis B and Severe Cirrhosis Possible

Researchers, writing in the April 2004 issue of *Liver International*, followed a 65-year-old patient who had ascites, jaundice, hepatitis B and cirrhosis with a Knodell score of 13 for eight years, beginning in 1995.

The patient spontaneously recovered from hepatitis B and cleared the surface antigen (HBsAg). Except for slight hyperbilirubinemia, his liver health returned to normal from the second year of diagnosis through his eight years of follow-up.

In the last follow-up exam, the markers of liver fibrosis were all normal. The portal vein diameter was decreased and the esophageal varices disap-

peared. An ultrasound and CT-scan of the liver found the liver to be normal.

Two HBV Mutations Persist after HBeAg Seroconversion

Hong Kong researchers, reporting in the June 2004 issue of the *Journal of Hepatology*, found that core-promoter and pre-core mutations in the hepatitis B virus continue, even after patients have cleared the “e” (HBeAg) antigen and developed “e” antibodies.

The researchers examined mutations in the viral core before and after “e” seroconversion. Significant quantities of the core-promoter mutation was found in 65% of patients before and after HBeAg seroconversion, and were significantly changed in only 13% of patients after seroconversion.

Significant quantities of pre-core mutation existed in about 90% of patients before and after HBeAg seroconversion, and were changed in only 16% of patients after seroconversion.

Interferon plus Vaccine Helps Some HBV-Infected Children

In the July issue of the *Journal of Gastroenterology and Hepatology*, researchers reported on a study of 50 HBV-infected children. All were treated with interferon alpha injected three times weekly, but half were also given the hepatitis B vaccine during treatment.

To date, interferon alone has been only moderately effective, helping only 30 to 40% of patients.

The children were treated with interferon for nine months, with half receiving the first vaccine dose at the beginning of treatment and second and final dose at weeks 4 and 24. The children were followed for at least six months after therapy ended.

There was no statistically significant difference in ALT levels or liver tissue health.

However, sustained HBeAg seroconversion with clearance of HBV-DNA was obtained in 13 of 25 children (52%) treated with combination therapy, and in eight of 25 children (32%) treated with just interferon.

Quick Test for Lamivudine-Resistant Viruses Developed

Writing in the June issue of the *Journal of Hepatology*, British researchers reported they have developed a method to quickly detect hepatitis B viruses that have developed resistance to the antiviral lamivudine (brand name Epivir-HBV).

Lamivudine effectively stops most HBV from reproducing, however there are viruses with certain mutations that are able to resist lamivudine's antiviral effect, and they quickly become the dominant HBV after prolonged use of lamivudine. When the mutations develop and become dominant, viral load and liver damage rebound again.

To quickly determine when viral resistance is occurring, before liver damage occurs, the researchers developed a real-time amplification refractory mutation system (ARMS) test that can quickly detect the lamivudine-resistant mutation in the virus's genetic material by analyzing a patient's blood sample.

This new method is more sensitive than the current practice of amplicon se-

quencing, so doctors can detect viral resistance before liver damage occurs.

Look for HBV DNA, Not Surface Antigen, to Safely Screen Blood

Scientists at the University of California San Francisco say testing blood donors for hepatitis B DNA (HBV DNA) should replace current screening practices that test only for the surface antigen (HBsAg) and/or the hepatitis B core antibody (anti-HBc).

Except for some European countries, most countries test donated blood with sensitive HBsAg tests, or a more sensitive core antibody test, which would detect anyone who was infected with HBV but who currently has low or undetectable HBsAg levels.

To date, highly sensitive nucleic amplification tests (NAT) have been used to screen donors for hepatitis C and HIV.

The researchers suggest the more-sensitive and more costly hepatitis B virus NAT test to detect HBV DNA should also be used to screen blood, along with the HIV and hepatitis C NAT tests.

Liver Cancer in HIV-HBV Coinfected Remains a Threat, Despite Therapy

Two researchers, writing in the 2004 *Southern Medical Journal*, examined the threat that resolved and current hepatitis B infections pose to the HIV-HBV-infected. It is estimated that 64 to 84% of HIV-infected individuals have been infected with HBV, and 16% of those with HIV are coinfecting with active hepatitis B infections.

They reported on a coinfecting 44-year-old man who had liver cancer, despite low HBV DNA (viral load). While highly active antiretroviral therapy (HAART) has dramatically improved the outlook of those with HIV, coinfecting populations are still at risk. One report found that chronic viral liver disease represented 45% of in-hospital deaths among HIV-infected individuals.

Reappearance of HBV in newly HIV-infected patients and in patients who developed AIDS has been reported, even in patients who had cleared hepatitis B and developed hepatitis B surface antibodies.

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The case illustrates that despite the advent of HAART, death from underlying chronic, non-HIV-related diseases, such as hepatitis B and liver cancer, “will likely continue to increase in the HIV-infected patient population,” researchers noted.

bility that there is a two-way flow from the machine back to the patient,” she cautioned. “It is entirely possible that a virus such as hepatitis B could stay alive and be able to transmit to another patient within seven to 10 days.”

Patients typically use the machines within 20 minutes of each other. HBV can live in dried blood for several days.

The hepatitis B vaccine contains only the surface antigen (HBsAg) portion of the hepatitis virus, to induce the immune system to produce surface antibodies. Adults who fail to respond to the vaccine and produce enough surface antibodies to guard against infection must receive additional vaccine injections.

which prevents the virus from reproducing, in six women who underwent chemotherapy for breast cancer. The antiviral was administered only during the chemotherapy treatment period.

The doctors monitored the patients’ HBsAg, HBeAg, ALT levels and HBV DNA (viral load) and found no evidence of hepatitis B reactivation.

“Lamivudine can be discontinued safely without emergence of lamivudine-resistant HBV strain or rebound HBV flare-ups,” they concluded.

Hundreds Risk HBV Infections from Faulty Dialysis Machines

About 300 kidney patients in British Columbia will need HIV and hepatitis B and C testing after malfunctions were detected May 26 in dialysis machines at Royal Jubilee Hospital on Vancouver Island. All 40 Baxter Aurora machines at the hospital and those at other Vancouver Island centers were checked, and 10 were found to have blood contamination. Medical microbiologist Dr. Pamela Kibsey said a series of filters and barriers within the machines make the risk for blood contamination slight.

“But, as we have discovered blood in the inside of some of our machines, there is a very small possi-

Newborns Respond Better than Adults to Hepatitis B Vaccine

Hepatitis B immunization produces a greater immune response in newborns, than in adults who are vaccinated.

Researchers from Gambia, writing in *Vaccine*, compared the antibody response in newborns to adults. They found infants produced markedly higher number of surface antibodies, which guard the body against hepatitis B infection should the real virus ever appear, than did adults one year after immunization.

“We conclude the neonatal antibody and T cell responses to hepatitis B vaccine differ from those induced in adults,” they wrote.

Antiviral Recommended to Prevent HBV Reactivation During Chemotherapy

Researchers from Taiwan recommend that breast cancer patients who have resolved or inactive hepatitis B and who are undergoing chemotherapy also take antivirals to prevent reactivation of their hepatitis B.

Chemotherapy weakens the immune system, which allows hepatitis B viruses that have been kept at low levels to re-emerge and increase in number. “Reactivation of hepatitis B after cytotoxic chemotherapy is a serious problem, and it occurred (in) 41% of breast cancer patients carrying HBV,” they wrote.

The doctors administered a “pre-emptive” dose of the antiviral lamivudine,

Wastewater Workers Should Be Vaccinated against Hepatitis A and B

A study of wastewater workers in Greece found a much larger percentage had been infected with hepatitis A and B viruses, than the general population.

Wastewater can carry the hepatitis A virus (HAV), which is found in the feces of infected people, and the hepatitis B virus (HBV), which is found in blood.

Antibodies against HAV (which indicates a past infection) were detected in

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65.7% of wastewater treatment plant workers, compared with 32.6% in a control group. HBV antibodies were found in 32.4% of wastewater plant workers, compared to 5.8% in the control group.

The researchers recommended that all wastewater workers should be immunized against hepatitis A and B.

Tracking and Vaccinating HBV Sexual Partners Recommended

To control hepatitis B in Europe, doctors have focused prevention efforts primarily on pregnant, HBV-infected women to ensure their newborns are immediately vaccinated. In a new approach, Dutch researchers identified and vaccinated the sexual partners of HBV-infected people from 1992 to 1999 in Amsterdam to assess how effective that prevention effort would be.

Writing in the June issue of the *Journal of Hepatology*, researchers said they tested 1,100 contacts of 738 women who were hepatitis B surface antigen positive. Among the contacts, 476 (43%) had cleared the infection, 119 (25%) remained infected with hepatitis B, and 603

contacts showed no signs of HBV infection.

Of the 603 who remained vulnerable to infection, 568 (94%) completed the vaccination series. Of those immunized, 4.5% under the age of 30 did not develop adequate antibodies (or titers) to protect them against HBV infection, and 12.2% over age 30 did not develop immunity against hepatitis B.

The researchers recommended that identifying and immunizing susceptible contacts of people who are HBsAg-positive (similar to many U.S. health departments' approach to identifying and treating sexual partners of those with STDs such as syphilis), should be an integral component of any country's HBV control program.

One-Third of Vietnamese-Americans Not Tested for Hepatitis B

Vietnamese-American men have a liver cancer rate that is 10 times higher than European-American men due to the prevalence of chronic hepatitis B in Southeast Asia.

A lack of early diagnosis and treatment is one reason for the high liver cancer rate.

Researchers, writing in the 2004 issue of *Cancer Detection and Prevention*, surveyed 345 Vietnamese-American men in the Seattle area to find out why some had not been tested for HBV.

They discovered that about one-third (34%) reported they had not been tested for hepatitis B infection. The three leading reasons for lack of HBV testing among the men were:

- They had no regular source of health care.
- Their healthcare providers had never recommended HBV testing.
- They were not aware that HBV can be transmitted during childbirth.

The researchers recommend improved health education about HBV transmission for both Vietnamese-Americans and physicians who serve those communities.

Plant-Made Antibody Targets Hepatitis B Virus

Japanese scientists have successfully used genetically-engineered tobacco plant cells to produce an antibody that targets and destroys the surface antigen (HBsAg) of the hepa-

titis B virus.

Currently, surface antibodies, called immunoglobulin, are collected from blood donors and is very expensive.

“Our plant-derived (antibody) has the potential to be a cheap and effective pharmaceutical,” for the prevention and treatment of HBV infection, said Dr. Akira Yano from the National Institute of Public Health in Tokyo, who wrote about the plant-made antibody in the 2004 *Journal of Medical Virology*.

Yano recommends the use of plant-derived antibodies over blood-derived antibodies to reduce the risk of bloodborne infections.

Yano reported that eventually biopharmaceuticals derived from genetically-modified plants could become “safe and economical for the promotion of global health.”

