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Hepatitis B

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Hepatitis B Grossly Under-Diagnosed and Untreated in the United States

A group of hepatitis B experts, including researchers from the U.S. Centers for Disease Control and Prevention, the Hepatitis B Foundation, and leading medical centers, have published a report in the *Journal of Viral Hepatitis* that indicts the medical community for its flawed screening and under-treatment of people infected with the hepatitis B virus (HBV).

An estimated 2 million people in the U.S. have chronic or long-term hepatitis B infections and are at high risk of developing liver damage and cancer.

There are seven U.S. Food and Drug Administration-approved antiviral medications available that effectively treat the infection by suppressing viral reproduction, and there are two interferon medications available that strengthen the immune system to fight HBV infection.

Despite those available treatments, fewer than 50,000 people nationwide per year receive prescriptions for HBV antiviral medications.

The experts lay the blame for the low rates of screening and treatment at the feet of a health care system that remains inaccessible to many of those infected, including recent immigrants, Asian-Americans, and other high-risk groups. Compounding this problem is lack of insurance coverage for screening and treatment, inadequate education of medical providers, and poor referral of infected patients to liver specialists.

San Francisco Program Offers a Successful National Model for Screening At-Risk Populations for Hepatitis B

As a gateway for many Asian immigrants and home to many Asian-Americans, the San Francisco area has one of the highest rates of hepatitis B and related liver cancer in the country. In 2007, a consortium of community, cultural, medical, and academic organizations formed the Hep B Free Campaign to screen everyone in the area for hepatitis B, and then refer them for treatment or vaccinate them against hepatitis B as needed.

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According to a report published in the December 2010 issue of the *Journal of Viral Hepatitis*, that program has become a successful, national model for outreach and screening of under-served populations at risk of HBV infection.

Today the campaign involves more than 50 public and private health care organizations, businesses, and educational institutions, and has created seven low-cost public access hepatitis B screening and vaccination sites. It integrates culturally-targeted HBV screening, vaccination, treatment, and disease management initiatives. The model is now being replicated in other California communities and is considered a blueprint for similar programs nationwide.

The program is lauded for saving lives—as well as health care dollars—by its early detection, effective treatment, and prevention through immunization.

Tenofovir Effective When Liver Failure Occurs and a Transplant Is Not Possible

Because of the shortage of available organs for liver transplants, researchers have been searching for new methods to save patients when they experience liver failure due to a spontaneous reactivation of their hepatitis B.

Writing in the journal *Hepatology*, researchers described using the antiviral tenofovir (Viread) in 14 HBV-infected patients with high viral loads (HBV DNA) who experienced liver failure to see if this treatment prolonged their lives.

After three months of treatment, 57% of those receiving tenofovir survived, compared to only 15% of HBV-infected patients who did not receive tenofovir, nor any other antiviral medication.

In the surviving patients, there was significant improvement in liver health and a significant decline in the HBV-DNA levels.

Those who survived were found to experience a significant reduction in HBV DNA after just two weeks of treatment.

Antiviral Combination May Replace Costly HBIG to Prevent HBV Reactivation

Traditionally, hepatitis B immunoglobulin (HBIG-hepatitis B antibodies) is used after a liver transplant to prevent re-infection of hepatitis B in patients. It is costly, and it is not clear how long it should be administered after transplant surgery to prevent re-infection.

A team of doctors replaced long-term HBIG with a combination of the antivirals tenofovir and entecavir (Baraclude) in a male transplant patient, who had liver failure. Before the transplant, the patient had developed drug resistance to the antiviral lamivudine (Epivir-HBV), and was receiving the tenofovir and entecavir combination before surgery.

HBIG was administered for three days after the transplant surgery and then the patient received the combination tenofovir-entecavir therapy only.

Twenty-one months after the transplant, the patient continued to have undetectable HBV DNA and remained negative for the hepatitis B surface antigen (HBsAg), which indicates infection, according to the report published in the December 2010 issue of the *Transplant Infectious Disease* journal.

"This case illustrates that combination oral antiviral therapy might substitute for HBIG as indefinite [treatment] due to [its] profound antiviral efficacy and low risk of viral resistance," they wrote.

Getting Just Two - of the Three-Dose Hepatitis B Vaccine Appears Effective

Current medical recommendations call for newborns and adolescents to receive three doses of hepatitis B vaccine over a six-month period. But many, especially adolescents, do not receive the full three doses.

Doctors screened adolescents (aged 11-15), who had received just two doses, to see if the two doses conferred adequate protection against the infection five years later. They measured the quantity of hepatitis B surface antibodies in their blood to see if they were adequate to prevent infection.

After five years, 79.5% of adolescents who received only the two doses had adequate surface antibodies (greater than 10mIU/mL) in their bloodstream; in comparison 91.4% who received the full three doses had adequate antibodies.

The adolescents who received only two doses were given one more vaccine dose and they quickly developed higher rates of surface antibodies, according to the re-

port published in the journal *BMC Infectious Diseases*.

F141L Mutation in the Surface Antigen Be Trigger That Causes Liver Cancer

Researchers continue to search for the mutation or viral trigger that causes some people with hepatitis B to develop liver cancer. South Korean researchers reported in the January 2011 issue of the *Journal of Virology* that they may have found a mutation in the surface covering of the virus, called HBsAg, that may play a role in causing liver cancer.

They identified a mutation called F141L and looked for that in the surface antigen of 241 Korean patients with liver diseases at different stages.

They found F141L mutants were present in a significant number of liver cancer cases. The mutation was present in cancer cases more often than was cirrhosis—severe liver scarring—which is often considered a precursor to liver cancer.

"Our results suggest that (F141L) may contribute importantly to the [development] of liver cancer by inducing cell proliferation and transformation," they wrote. They suggest that the F141L mutation could serve as a diagnostic test for liver cancer.

New, More Accurate Cause of Fibrosis Identified

A multinational research team, including scientists from the University of California, San Diego School of Medicine, have for the first time accurately identified how fibrosis forms in the liver, and how these fibrotic cells multiply and produce cirrhosis.

Their findings, published in the *Proceedings of the National Academy of Sciences*, identify a previously unknown kind of inflammatory white blood cell as the culprit behind liver fibrosis. Their report completely changes current beliefs about how fibrosis develops in livers infected by the hepatitis B virus (HBV).

When the liver is diseased, healthy liver tissue is progressively replaced by fibrous scarring, which impairs liver functioning. Ultimately, severe fibrosis results in cirrhosis and contributes to liver cancer and failure, the 12th leading cause of death by disease in the United States.

For years, scientists did not understand how these fibroblast cells were created and assumed they were simply transformed "epithelial" cells. Based on that assumption, they measured fibroblast-specific protein 1 (FSP1) to determine if fibrosis was present in a patient.

However, this new research shows that FSP1 is not a reliable marker for fibrosis. Instead, endogenous stellate cells appear to be the culprit in the development of fibrosis. However, scientists did find that FSP1 was a consistent marker for a previously unknown subset of inflammatory white blood cells or macrophages found in injured livers.

Neuromuscular Problems Common Among Patients Taking Telbivudine

With increased, long-term use of antivirals, researchers are increasingly identifying nerve and muscle damage as side effects from this treatment. In a recent issue of the *Journal of Viral Hepatitis*, researchers reported on their findings into neuromuscular and nerve damage from the antiviral telbivudine (Tyzeka).

The scientists measured creatine kinase (CK), an enzyme that is released into the blood when muscle tissue is damaged, and they monitored patients for myopathy, a disease of the skeletal muscles.

They measured CK levels in 200 patients treated with telbivudine for hepatitis B between January 2007 and July 2010. The 3-year cumulative incidence of CK elevations and myopathy was 84.3% and 5%, respectively. CK elevations occurred more frequently in men than in women, and in patients aged 45 and older who tested negative for the hepatitis B "e" antigen (HBeAg-negative). Viral load did not appear to have an impact on CK elevations.

CK elevations usually occurred 21 months after starting the antiviral, and most patients stopped having CK elevations spontaneously without having to stop telbivudine treatment. However, three patients had to switch to other antiviral agents.

"In conclusion, CK elevations are common adverse reactions associated with telbivudine therapy, while myopathy is rare," researchers wrote.

Conventional Lab Tests Miss HBV Genotype G Infections

Dutch researchers have discovered that HBV genotype (or viral strain)

G, found in Europe and the United States, has a mutation that allows it to be missed by conventional blood tests, according to a report in the *Journal of Hepatology*.

Blood tests to identify the presence of HBV infection often look for HBsAg, the most common antigen present in blood when a hepatitis B infection is present.

Researchers found that infection with HBV genotype G resulted in a decreased production of HBsAg, and "e" antigens and antibodies, which makes it difficult for lab tests to find those infection indicators.

Researchers took a series of blood samples from a blood donor with HBV genotype G infection. Even though they found HBV DNA and hepatitis B core antibodies in the donor's blood, they found no signs of HBsAg or HBeAg, and during follow-up, they found no evidence of "e" antibodies.

The HBV from the donor had lamivudine-resistant mutations, indicating the person had become infected by an HBV-resistant strain.

"Our findings demonstrate that HBV genotype G mono-infection occurs and that routine serology [the common blood test] is unsuitable for its detection," the researchers wrote.

U.S. Health Care Workers Still Re-using Syringes and Vials

While medical guidelines clearly prohibit re-use of syringes and single-dose vials, some providers still re-use this equipment, according to an article in the December issue of the *American Journal of Infection Control*.

More than 50 outbreaks of hepatitis B and C and bacterial infections have caused hundreds of infections, and 100,000 people have potentially been exposed to infections. The researchers surveyed 5,500 health care providers to understand injection practice patterns and to draft appropriate education and prevention initiatives. Results showed that:

- 6% (318) "sometimes or always" used single-dose/single-use vials on more than one patient.
- Nearly 1% (45) sometimes or always reuse a syringe, only changing the needle for use on a second patient; and
- 15% (797) reported reuse of a syringe to enter a multi-dose vial. Of this group, 6.5% (51) reported saving vials for use on another patient, representing about 1% of all respondents.

Half of the 51 worked in hospitals, and the other half worked in surgical centers and physician offices. Researchers noted that the survey "revealed that a dangerous minority of providers engage in unsafe practices such as syringe re-use."

CDC guidelines recommend syringes and needles should be used only once and never reused for another patient or to access a medication or solution that might be used for a subsequent patient.

For example, when a syringe is reused to draw up additional medication for a single patient, the medication vial becomes contaminated. Any subsequent use of either the syringe or the vial put that patient at risk of infection.

The authors recommend reducing risks through partnerships among professional, governmental and non-governmental organizations with a focus on the redesign of devices, products and processes.

Tenofovir Effective Against Hepatitis B in HBV-HIV Coinfected

Dutch researchers studied the effectiveness of tenofovir in patients coinfected with HBV and HIV over a five-year period to assess the success of the antiviral treatment on hepatitis B, and to see if the drug caused any kidney problems.

They followed 102 patients, 80% of whom had detectable HBV DNA at start of treatment, and 67 of whom tested positive for HBeAg.

Over the course of the treatment, 46% lost HBeAg and 12% cleared HBsAg. Among 15 HBeAg-negative patients with detectable viral loads at the start of treatment, 100% responded to the treatment and 2 (13%) lost HBsAg.

Twenty subjects (all HBeAg-negative) had undetectable HBV DNA at the start of the study. Over nearly five years, 19 (95%) responded to treatment and 2 (10%) lost HBsAg.

Only one patient developed drug resistance and experienced a resurgence of HBV DNA.

Three (3%) of the patients discontinued tenofovir because of increased creatinine levels, which indicates kidney problems, according to the report in the December issue of *Gastroenterology*. Some minor kidney problems were identified at the start of treatment, but they decreased over time.