

B HEPATITIS B

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CAUSE FOR A CURE

We are a national non-profit organization dedicated to finding a cure and improving the quality of life for those affected by hepatitis B worldwide.

INFORMED

HBF Receives NIH Grant \$400,000 Over Three Years

How does a non-profit organization with a small staff and limited budget reach out to a national and international audience? The Hepatitis B Foundation (HBF) turned to the Internet for its answer. In 1997, the HBF launched www.hepb.org and attracted 25,000 visitors in the first year. In 2003, there have been 1,000,000 visits in the past 18 months alone.

With all of its success, however, the website was beginning to show its age: the HBF decided it was time for a major facelift. To fund this electronic initiative, **Chari Cohen, MPH**, HBF program coordinator, submitted a grant proposal to the National Library of Medicine (NLM), a branch of the National Institutes of Health (NIH).

In April 2003, the HBF received notice that its grant would be funded for almost \$400,000 over the next three years. This was great news considering the NLM received over 50 competing applications and less than 10% received funding.

The NLM grant from the NIH provides funding for a total reconstruction of the website, and for the addition of technology-based features that will turn www.hepb.org into a more user-friendly and interactive site. Highlights will include a monthly e-newsletter, electronic bulletin boards, "Ask the Doctor" forums, and more.

In addition, the HBF will develop a tutorial on its website to introduce visitors to the world's largest library, the National Library of Medicine. The tutorial will include how to use the different NLM search engines - MEDLINE, MEDLINEplus,

and www.clinicaltrials.gov - in order to benefit from the wealth of medical information available through these sites.

This is the first grant the HBF has received from the NIH, which is a major achievement for any non-profit organization involved in health education and research.

"The HBF website is a critical source of information for patients, families, healthcare professionals, and researchers in 56 countries worldwide, explains **Molli Conti**, HBF vice-president. "To be effective, the site needs to deliver the latest information. Our new site is ready to meet this challenge and will help us achieve our mission of reaching out to all those across the nation and around the world."

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HBF website re-launches with a new look (April 15, 2003).

HBF Crystal Ball Gala Celebration

After a long winter, the annual Crystal Ball was a welcome relief for 150 people who put on their dancing shoes and enjoyed an evening of fine dining and dancing to the sounds of the Courtney Colletti Orchestra. The black tie event, held on April 12, is the Hepatitis B Foundation's signature fundraising event and is capped by an awards ceremony to publicly recognize individuals who have advanced its *Cause for a Cure*.

This year, the HBF was proud to honor **Jay H. Hoofnagle, MD**, with its *Distinguished Scientist 2003* award. Dr. Hoofnagle is director of the Division of Digestive Diseases and Nutrition, National Institute of Diabetes, Digestive and Kidney Diseases of the National Institutes of Health (NIH). He has made outstanding contributions to the understanding of hepatitis B, advancing therapies for this disease, and providing leadership in the clinical application of these discoveries.

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Message from the President

Timothy M. Block, Ph.D.

HBF is Part of the Solution . . .

In this issue of *B-Informed*, there are personal stories about liver cancer, thoughtful insights from some of the leading authorities, and a clear message of hope.

Fortunately, most people chronically infected with hepatitis B will not suffer from life-shortening liver disease. Serious problems related to chronic hepatitis B infections, however, will occur in as many as 1 out of 4 persons.

Among the most serious complications is primary hepatocellular carcinoma (PHC), which refers to cancer that originates within the liver. This is often referred to as "hepatocellular carcinoma" (HCC) or liver cancer.

Despite the availability of a safe and effective vaccine, the number of deaths due to HCC is expected to rise over the next 20 years. The high mortality associated with HCC is because it is often unresponsive to treatment – it may also be in part because the liver lacks sensory fibers, therefore, symptoms of HCC often occur late in the disease.

As Dr. So writes in his article (page 3), early detection is critical to improving HCC survival rates. Better treatments are needed, such as innovative therapies like radiofrequency ablation that are bringing hope to many (page 9).

Help is on the way. The HBF is dedicated to being a part of the solution and is taking several approaches.

We help by sponsoring research in our labs at The Jefferson Center. We have an active program to develop early detection markers of liver disease and cancer, and the quality of this work is recognized with grant support from the National Cancer Institute.

We help by getting out the message. Our web site is a portal of entry for those seeking information and support. The recently awarded NIH grant is both a tribute to the website's value as well as an opportunity for greater service.

We help by coordinating an annual patient conference. This has created a stronger and more visible hepatitis B community.

Finally, the PA state grant to build a new research facility is a significant contribution to our program, and should also provide hope and promise to all those affected (*B-Informed*, Winter 2003).

In The News



Infections Persist After Recovery from Acute Hepatitis B

Japanese researchers studied the long-term impact of acute hepatitis B on the liver and found that occult HBV infection persists in the liver and is accompanied by abnormal liver histology for a decade after complete clinical recovery from acute hepatitis B. In this study, 14 patients were re-evaluated after recovery from the onset of acute hepatitis B (at a median of 4.2 years after initial infection). All showed clinical and serologic recovery with HBsAg clearance. Antibody to HBsAg (anti-HBs) had developed in 12 patients. Nine underwent liver biopsies at a median of 7.2 years. Results showed that both HBV DNA surface and X regions were found in the liver of all 9 patients examined, including 7 negative for serum HBV DNA. All patients tested positive for cccHBV DNA. [*Hepatology* May 2003;37(5):1172-1179]

New Test May Help Hepatitis B Patients Could Predict Who Will Develop Drug Resistance

Researchers think they've discovered a way to tell if patients infected with a type of hepatitis will eventually fail to respond to a powerful drug. "About half to two-thirds of patients will basically fail therapy after two to three years because they acquire drug resistance," says study co-author **Brent Korba**, professor of microbiology at Georgetown University Medical Center. Korba and his colleagues decided to study the hepatitis B virus genetic makeup in 26 patients who had undergone treatment with lamivudine to see if there were any early warning signs of trouble. They reported their findings at the 16th International Conference for Antiviral Research in Savannah, GA. The researchers found DNA "markers" in the genetic makeup of the virus in the patients who either developed resistance to lamivudine or never responded to it at all. They couldn't find the markers in the virus in patients who responded well to the drug, says study co-author **John Gerin**, professor of microbiology and immunology at Georgetown University Medical Center. The test for the DNA markers is cost-effective, he adds. [*Health Scout News* BB4/29/03, www.healthscoutnews.com]

HBV and Aching Joints

Hepatitis B infection is seldom considered in the differential diagnosis of acute polyarthritis. The onset of hepatitis B-associated arthritis is usually sudden and often severe. The joints of the hands and knees are commonly affected, but other large joints may be involved. Arthralgias occur in 10% to 25% of patients with acute hepatitis B infection, frank arthritis in approximately 5%. Joint symptoms usually persist for no more than 2 weeks and in most cases, the arthritis resolves with the onset of jaundice. In patients who remain without jaundice, joint symptoms may be prolonged. Recognition of hepatitis B as a cause of acute polyarthritis is important to prevent unnecessary treatment with steroids or methotrexate and to avoid further transmission of the virus by a highly infectious patient. [*Lancet* March 2003; 361: 750]

Hepatitis B and Primary Liver Cancer

Samuel So, MD, FACS, Professor of Surgery; Director, Liver Cancer Program; Director, Asian Liver Center at Stanford University School of Medicine, Stanford, CA Visit <http://livercancer.stanford.edu>

Hepatocellular carcinoma (HCC) is the predominant type of malignant primary liver cancer. While the incidence of most types of cancer has dropped or remained unchanged in the recent decade, HCC incidence is increasing, and for example, has climbed by an alarming 40% in California alone. Although survival rates for most types of common cancers have improved over the years due to increased funding, little attention has been paid to HCC. Currently, the 5-year survival rate for HCC is below 10%. The World Health Organization estimates there are 550,000 deaths a year from HCC.

Did you know that hepatitis B is the primary cause of liver cancer? 80% of primary liver cancer worldwide is caused by chronic hepatitis B infections. In other words, if you do not have hepatitis B, your risk for liver cancer is low. Since hepatitis B is a vaccine preventable disease, the hepatitis B vaccine was dubbed the first "anti-cancer vaccine" by the Centers for Disease Control and Prevention (CDC).

Who should be screened for liver cancer? Early detection improves the chances of survival after treatment. Since liver cancer often develops in patients with cirrhosis, patients with cirrhosis due to chronic hepatitis B should undergo regular liver cancer screening. It is important to stress that Asians, who generally develop chronic hepatitis B infections soon after birth, have a high risk of developing liver cancer at an early age *whether they have cirrhosis or not*. The risk is greater in men and those with a positive family history for liver cancer.



Dr. So evaluates a patient with liver cancer in his clinic at Stanford U. School of Medicine. (photo by Katy Raddatz, San Francisco Chronicle).

A reasonable approach is to begin regular liver cancer screening for the Asian hepatitis B carriers starting at 30 years of age. This generally consists of a blood test for alpha-fetoprotein (AFP) level every 6 months and an ultrasound of the liver once a year. Either test alone can miss the diagnosis. Once the patient develops cirrhosis, more frequent screening is generally recommended.

What are the symptoms of liver cancer? Liver cancer is a silent killer because the majority of patients appear to be perfectly healthy and have no early signs or symptoms. Both small and large tumors may be undetected due to the shielded location of the liver underneath the ribs. Pain is uncommon until the tumor is quite large, and some large tumors don't even cause pain or any symptoms. Later stages of liver cancer, when the cancer is very large or when it impairs the functions of the liver, can produce more obvious symptoms such as abdominal pain, weight loss, lack of appetite, and finally the development of jaundice and abdominal swelling.

How is liver cancer treated? Treatment of HCC is particularly challenging when compared with other types of

cancer because in addition to the cancer itself, many patients have livers that have been damaged by chronic hepatitis B infections. Treatment of the liver cancer without regard for the precarious state of the liver itself may hasten the patient's demise. For each individual patient, the potential benefits of the various treatment options must be balanced with the risk of liver failure and how it affects the patient's quality of life.

Surgical Treatment - When the tumor is small or deemed surgically resectable, and the patient's liver condition is deemed fit for the extent of the planned resection, surgical removal offers the best chance for long-term survival. Despite complete removal of the tumor, patients are still at risk for recurrent disease, and they need to be followed closely long-term, especially during the first year when the risk of recurrence is greatest.

Nonsurgical Treatment - For patients who are not suitable resection candidates, a number of treatment options, though limited in effectiveness, are available or being investigated in an attempt to control the disease long-term and with the aim of maintaining normal quality of life. Traditional chemotherapy is generally ineffective, causes many side effects that may severely impair the patient's quality of life, and often does not prolong survival.

Since HCC are hypervascular tumors often fed by one or more blood vessels from the hepatic arteries, they present the unique opportunity to target the therapy directly into the tumor.

Intrahepatic arterial chemoembolization or chemoinfusion (TACE or TAC) has been adopted by the Stanford Multidisciplinary Liver Tumor Clinic in the treatment of selected patients with unresectable lesions. Long-term treatments with TACE or TAC have been associated with prolonged patient survival, and those who have good control or shrinkage of the tumor may even become suitable candidates for surgical resection or transplantation.

Liver Transplantation - Liver transplant is a treatment option for HCC that are surgically or medically unresectable, provided that the tumor is small (less than 5 cm or fewer than 4 lesions), confined to the liver, and without invasion into the blood vessels. More extensive tumors have a high risk for early recurrence after liver transplantation.

Conclusion - Early diagnosis of small tumors is the only effective way of improving the outcome of liver cancer treatment, and that is only possible through screening of the high-risk population. Universal hepatitis B vaccination, unfortunately still far from reality, can ultimately reduce the incidence of this frequently fatal cancer by 80% worldwide.

HBV Drug Watch *HBV Compounds in Development* Spring 2003

FAMILY/DRUG NAME	MECHANISM	COMPANY	WEBSITE	STATUS, USA
INTERFERONS Mimic naturally occurring infection-fighting immune substances produced in the body				
Interferon alpha-2b (Intron A)	Immunomodulator	Schering-Plough, Madison, NJ	www.schering.com	FDA Approved 1991
PegInterferon alfa-2a (Pegasys)	Immunomodulator	Roche, Switzerland	www.roche.com	Phase III, outside USA
NUCLEOSIDE ANALOGUES Interfere with the viral DNA polymerase enzyme used for hepatitis B virus reproduction				
Lamivudine (Epivir-HBV)	Inhibits viral DNA polymerase	GlaxoSmithKline, RTP, NC	www.gsk.com	FDA Approved 1998
Adefovir Dipivoxil (Hepsera)	Inhibits viral DNA polymerase	Gilead Sciences, Foster City, CA	www.gilead.com	FDA Approved 9/20/02
Entecavir	Inhibits viral DNA polymerase	Bristol-Myers Squibb, Princeton, NJ	www.bms.com	Phase III
FTC (Coviracil)	Inhibits viral DNA polymerase	Gilead	www.gilead.com	Phase III / NDA Filed
DAPD (Amdoxovir)	Inhibits viral DNA polymerase	Triangle	www.tripharm.com	Phase II
L-FMAU (Clevudine)	Inhibits viral DNA polymerase	Gilead	www.gilead.com	Phase II
LdT (Telbivudine)	Inhibits viral DNA polymerase	Idenix, Cambridge, MA	www.idenix.com	Phase III
monoval LdC (Valtorcitabine)	Inhibits viral DNA polymerase	Idenix	www.idenix.com	Phase II
ACH-126,443 (Elvucitabine)	Inhibits viral DNA polymerase	Achillion New Haven, CT	www.achillion.com	Phase II (Central & Eastern Europe)
Racivir (RCV)	Inhibits viral DNA polymerase	Pharmasset, Tucker, GA	www.pharmasset.com	Phase II
MCC478	Nucleoside analog "prodrug"	Eli Lilly, Indianapolis, IN	www.lilly.com	Phase I, Germany
MIV-210	Inhibits viral DNA polymerase	Medivir, Sweden	www.medivir.com	Phase I, U.K.
Hepavir B	Inhibits viral DNA polymerase	Ribapharm, Costa Mesa, CA	www.ribapharm.com	Phase I, Europe
Pentacept	Inhibits viral DNA polymerase	Pharmasset	www.pharmasset.com	Preclinical
ALS-920 (Robustaflavone)	Inhibits viral DNA polymerase	Advanced Life Sciences, Woodbridge, IL	www.advancedlifesciences.com	Preclinical
ICN 2001-3	Inhibits viral DNA polymerase	ICN, Costa Mesa, CA	www.icnpharm.com	Preclinical
NON-NUCLEOSIDE ANTI-VIRALS				
BAM 205	"Small Molecule"	Novelos, Newton, MA	http://novelos.com	Phase II/III China
XTL-001 (HepX-B)	Human monoclonal antibodies	XTL Biopharm, Rehovot, Israel	www.xtlbio.com	Phase II, Israel & U.S.A.
Alkovirs *Discovered by HBF scientists	Non-polymerase DNA Inhibitor	United Therapeutics Silver Spring, MD	www.unither.com	Preclinical HBV (Phase II HCV)
HepBzyme	Nuclease resistant ribozyme	Ribozyme, Boulder, Co	www.rpi.com	Preclinical
Bay 41-4109	Inhibits viral nucleocapsid	Bayer AG, Germany	www.bayer.com	Preclinical
NON-INTERFERON IMMUNE ENHANCERS Boost T-cell infection-fighting immune cells and the body's natural interferon production				
HE2000	Hollis-Eden	San Diego, CA	www.holliseden.com	Phase II, Singapore
Theradigm	Immune Stimulator	Epimmune, San Diego, CA	www.epimmune.com	Phase II
EHT899	Oral Viral Protein	Enzo Biochem, NY, NY	www.enzobio.com	Phase II, Israel
Thymosin alpha-1 (Zadaxin)	Immune Stimulator	SciClone, San Mateo, CA	www.sciclone.com	Phase II w/lamivudine Orphan drug approval in US for liver cancer
HBV DNA Vaccine	Immune Stimulator	PowderJect, Oxford, U.K.	www.powderject.com	Phase I
SpecifEx-HepB	Immunological Cell Transfer	CellExSys, Seattle, WA	www.cellexsys.com	Preclinical/Phase I
HBV Antigen	Oral Tolerance	OraGen, Philadelphia, PA	Tel: 215-923-5124	Preclinical
HBV DNA Vaccine	Immune Stimulator	Jefferson Center, Doylestown, PA	Tel: 215-489-4949	Preclinical
POST-EXPOSURE AND/OR POST-LIVER TRANSPLANT TREATMENT				
BayHep B	HBV immunoglobulin	Bayer U.S., Pittsburgh, PA	www.bayer.com	FDA Approved 1977
Nabi-HB	HBV immunoglobulin	Nabi, Boca Raton, FL	www.nabi.com	FDA Approved 1999
Anti-hepatitis B	HBV immunoglobulin	Cangene, Ontario, Canada	www.cangene.com	FDA Filing 2001

NEW

Sincere thanks to Brent Korba, Ph.D. (Georgetown University Medical Center, Rockville, MD) and Raymond Schinazi, Ph.D. (Emory University Medical School, Atlanta, GA) for their regular review of the HBF Drug Watch Update.

Drug Notes

RNA Interference with HBV Replication Hepatitis B virus progression can be contained by inactivating virus-specific RNA in the liver, finds a research team in the June issue of *Nature Biotechnology*. This could be a new strategy for treating hepatitis B infection. In this study, U.S. researchers determined that virus progression in mice can be contained by inactivating virus-specific RNA in the liver using a piece of ribonucleic acid. This research is the first time small interfering ribonucleic acid molecules (siRNAs) have been used to curb a viral infection in an animal. Dr. Mark Kay's team found that by injecting an siRNA that targets hepatitis virus into the tails of mice, they were able to disrupt hepatitis B virus replication and proliferation. The siRNA molecules were designed to specifically bind to 2 hepatitis B virus RNAs in the liver cells, and ultimately interfere with hepatitis B virus replication. The team's approach resulted in an 85% reduction in hepatitis B virus surface antigen (HBsAg) and a >99% reduction in the hepatitis B virus core antigen (HBcAg). This method may hold promise as a therapeutic option, not only for hepatitis B, but also for other types of viral infections. [*www.gastrohep.com* 4/12/03, *Nature Biotechnology* 2003; 21(6)] See *B Informed*, Winter 2002 issue, regarding similar research being done by Drs. Pachuk and Satishchandran at the Jefferson Center.

HepDirect Prodrugs Show Promise Against HBV and Liver Cancer Hepavir B was developed using Metabasis proprietary HepDirect(tm) Technology that results in the production of the active drug specifically in the liver. Adefovir, the active ingredient of Hepavir B, has proven to be an effective drug for the treatment of patients with chronic hepatitis B. However, studies have shown that accumulation of the drug in the kidney results in dose limiting renal toxicity. Preclinical studies show that Hepavir B achieves significantly higher levels of the active form in the liver and lower levels in the kidney resulting in an overall 10- to 50-fold increase in liver targeting. Metabasis believes that this redistribution of the drug will allow for more optimal dosing and therefore a more efficacious drug with improved safety. In addition, Dr. Mark Erion, VP of Research and Development, reported "The second HepDirect prodrug to be recommended for development is MB7133 for treating primary liver cancer. If all goes according to plan, we will begin clinical testing of MB7133 next quarter in the U.S. and Asia." [*Press Release* 4/3/03, *www.mbasis.com*]

T67 in Phase II/III Trials for the Treatment of HCC Tularik Inc. is conducting a two-arm, randomized global study to compare the survival of patients who receive T67 versus those receiving doxorubicin, the current chemotherapy for HCC (hepatocellular carcinoma or liver cancer), although the FDA has not approved it for this indication. Up to 750 first-line HCC patients will be enrolled in Phase II/III trials in 75 centers across the U.S., Europe and Asia. T67 is a small molecule compound that binds irreversibly to beta-tubulin, a proven anti-cancer drug target. T67 is distinguished from other tubulin-binding agents, such as Taxol, because it retains activity against multiple drug resistant tumors in

animal models. There are currently no approved chemotherapeutic agents to treat HCC and surgical resection is feasible in only a small percentage of patients. [*Tularik Press Release* 3/25/03, *www.tularik.com*]

Potential HAPpy Drug for Hepatitis B A new class of compounds, known as heteroaryldihydropyrimidines (HAPs), has been to show inhibit hepatitis B virus replication in the laboratory and in a mouse model. Of the various HAPs tested, Bayer's compound Bay 41-4109 shows the most promise as a monotherapy or in a combination strategy. Currently there are only two drugs that specifically inhibit viral replication – Eпивir-HBV and Hepsera, both HBV polymerase inhibitors. Interferon alpha is also approved, but does not directly inhibit viral replication. New treatments are needed, however, because the hepatitis B virus often develops resistance to polymerase inhibitors and interferon alpha is associated with dose-limiting side effects. Bay 41-4109 shows promise because it works differently. Dr. Karl Deres, Bayer Research Center in Germany, explained in an article published in *Science* (Feb. 7, 2003) the mechanism by which HAPs inhibit hepatitis B infections. He and his colleagues found that the HAPs inhibit formation of the viral core particle, or nucleocapsid, which is required for the completion of HBV replication. [*BioCentury*, Vol. 11(7), 2/20/03]



EASL International Consensus Conference Statement on Hepatitis B

hivandhepatitis.com Report

The European Association for the Study of the Liver (EASL) convened a consensus conference on hepatitis B September 13 - 14, 2002 in Geneva, Switzerland. The purpose of the conference was to define the state of knowledge and to formulate recommendations for the management of patients with hepatitis B.

The outcome of the consensus conference was to be announced at the 38th annual EASL meeting in Istanbul, Turkey in March 2003, but the recent U.S. war with Iraq forced the cancellation of the EASL conference.

Now, however, the EASL Jury, a panel of prominent European liver specialists and one U.S. specialist (Dr. Anna Lok), has formulated and published its consensus statement. The Jury was asked to evaluate the existing scientific data and to write a consensus statement addressing 8 specific questions that included the public health implications of hepatitis B, factors influencing the disease, the best way to diagnose and classify hepatitis B, prevention, who should be treated, optimal treatments, monitoring of untreated patients, and the main unresolved issues in this field.

For the complete article, "EASL International Consensus Conference on Hepatitis B" that was published in the *Journal of Hepatology* (April 2003), visit http://www.hivandhepatitis.com/hep_b/pdf/article.pdf

NAME	TYPE VACCINE	COMPANY	WEBSITE	STATUS
Hepatitis B Vaccines - Recommended for those at risk and patients with chronic HCV				
Engerix B	Recombinant HBV	GlaxoSmithKline Phila, PA	www.gskvaccines.com	Market, USA
Recombivax HB	Recombinant HBV	Merck West Point, PA	www.merck.com	Market, USA
Gen Hevac B	Recombinant HBV	Aventis Pasteur Lyons, France	www.aventispasteur.com	Market, Europe
Hepacare (formerly, Hepagene)	HBV preS1, preS2	PowderJect Oxford, U.K	www.powderject.com	Market, Europe
Bio-Hep B	HBV S, preS1, PreS2	Biotech. Gen. Corp	www.btgc.com	Market, Israel
Hepavax Gene	Recombinant HBV	Berna Biotech, Switzerland	www.bernabiotech.com	Market, Europe
Hepatitis A Vaccines - Recommended for those at risk and patients with chronic HBV and HCV				
Havrix	Inactivated HAV	GlaxoSmithKline	www.gskvaccines.com	Market, USA
VAQTA	Inactivated HAV	Merck	www.merck.com	Market, USA
Avaxim	Inactivated HAV	Aventis Pasteur	www.aventispasteur.com	Market, Europe
Combination Hepatitis Vaccines				
TwinRix (Adult)	HBV and HAV	GlaxoSmithKline	www.gskvaccines.com	Market, USA
Comvax (Pediatric)	HBV and HiB	Merck	www.merck.com	Market, USA
Pediarix (Pediatric)	HBV, Polio, DTP	GlaxoSmithKline	www.gskvaccines.com	Market, USA (12/02)
Hexavac (Pediatric)	HBV, DTP, HiB, Polio	Aventis Pasteur	www.aventispasteur.com	Market, Europe
Hepatitis Vaccines In Development				
Extra Strength Hep B (for poor or nonresponders)	Recombinant	GlaxoSmithKline (with Corixia)	www.gskvaccines.com www.corixia.com	Phase III
Hep B Vaccine	ISS-linked to HBsAg	Dynavax Technology Berkeley, CA	www.dynavax.com	Phase I/II
Hep B DNA Vaccine Px	HBV DNA Vaccine	PowderJect	www.powderject.com	Phase I

Vaccine News

Canadian Public Health Experts Want Vaccination Program Public health officials are urging Ottawa and the provinces to move quickly to set up a national immunization program. Canada has no national immunization plan to protect children from preventable infectious diseases. Each province offers and pays for some childhood vaccinations, but the list isn't the same across the country. It's up to parents to find out what shots they should get for their children, and whether they can afford them. The federal government endorsed the idea of a national immunization strategy, and \$45 million was set aside to set it up in the last budget. It would then cost another billion dollars to actually vaccinate and track the children. [CBC News Online 5/14/03, www.cbc.ca/stories/2003/05/14/immunize030514]

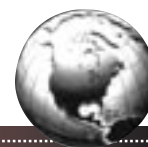
Hepatitis Vaccines Can be Given on Accelerated Schedule Travelers can receive the hepatitis A vaccine on the day before departure, while the hepatitis B vaccine can

be given 21 days before departure, a new study shows. Currently, both vaccines are typically administered 4 weeks before departure. To find out if the vaccines could be administered on an accelerated schedule, Hans D. Nothdurft, MD, a professor of internal and tropical medicine at the University of Munich in Germany conducted an analysis of data from studies evaluating the onset of protection after one dose of the Havrix hepatitis A vaccine and after accelerated schedules of the Engerix-B hepatitis B vaccine and the Twinrix combined hepatitis A and hepatitis B vaccine. If Engerix-B or Twinrix is administered in an accelerated schedule, a fourth dose should be given at 12 months to ensure long-term protection, Dr. Nothdurft added. [HBV Research Archive 5/12/03, <http://archive.mail-list.com>]

Fast Fact

Of the 20 vaccines sold worldwide, 3 include the hepatitis B vaccine.

Hepatitis B Around the World



HBV Vaccine Crucial to Global Cancer Control

Mark A. Kane, MD, MPH
Director, Children's Vaccine Program at PATH

[This article has been excerpted from Dr. Kane's editorial "Global Control of Primary Hepatocellular Carcinoma with Hepatitis B Vaccine" in Cancer Epidemiology Biomarkers & Prevention Vol. 12, 2-3, January 2003]

Health workers and epidemiologists concerned with the prevention of cancer are largely unaware of one of the most significant recent developments in global cancer control, the integration of HB vaccine into the national immunization programs in developing countries, including the poorest. Primary Hepatocellular Carcinoma (PHC) caused by chronic HB infection is the number one or two cause of cancer death in men in most Asian and sub-Saharan African countries and an important cause of cancer death in women.

Chronic HB infection is approximately 90% preventable with proper use of HB vaccine, but until recently, this vaccine has been beyond the budgets of governments in the poorest countries. In addition to the financial constraints, delivery services in the poorest countries were unable to access large parts of their populations with any vaccines. Both of these impediments are being overcome by the creation, in the last 3 years, of GAVI and The Vaccine Fund. It is believed that the comprehensive use of HB vaccine will prevent about 1,000,000 deaths per year from PHC and cirrhosis of the liver (each year) in future birth cohorts.

The report measuring the decline in PHC after immunization in Taiwan, is the latest in a remarkable series of studies in Taiwan dating back to the 1970s, in which much of the epidemiology of chronic HB infection, its link to cancer, and its prevention with HB vaccine were worked out. Before these studies, many researchers thought that aflatoxin from moldy groundnuts (peanuts) was the primary etiologic agent for PHC in developing countries. Whereas aflatoxin may be a cofactor in some countries, the Taiwanese studies showed that chronic HB infection is a necessary and sufficient cause of PHC, and that HB vaccine can prevent the development of chronic infection, strongly suggesting that routine HB immunization would be sufficient to prevent most PHC on a global basis.

It is now generally accepted that prevention of the HB-carrier state with HB vaccine will prevent primary hepatocellular cancer, and the global immunization strategy is based on this assumption.

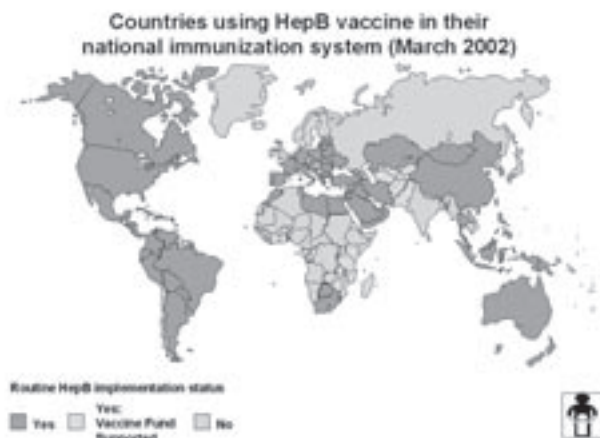
Although safe and effective HB vaccines have been available since 1982, immunization policies, economic constraints, and poor delivery infrastructure (in developing

countries) have been impediments to the introduction of these vaccines. In the 1980s, the cost of a three-dose adult series of HB vaccine was more than \$100, making it impossible to consider for mass use in the developing world.

In developing countries, it was clear that only universal infant immunization could modify disease rates, and the first hurdle was the price of the vaccine. Pioneering work by the International Task Force on Hepatitis B Immunization encouraged the production of HB vaccines in Korea and demonstrated the feasibility and impact of infant immunization programs in Thailand, Indonesia, and China. The price of HB vaccine fell to \$1.00 per pediatric dose, and HB vaccine production technology was transferred to China, India, and Indonesia.

The Chinese Government, GAVI, and The Vaccine Fund have developed an \$80 million dollar project, which will allow Chinese infants to receive HB vaccine free of charge in the 12 poorest western provinces. Previously, although available, HB vaccine was sold to parents and only relatively wealthier families could afford it. If this immunization is sustained, future birth cohorts of Chinese will have very low levels of HBV-related liver cancer that are similar to those of western countries.

In India, where HB vaccine is available on the private market but not through government programs, 30 major demonstration projects are being funded that will lead to routine use of HB vaccine for Indian children in the next 5-year plan, which begins in 2004. In Indonesia, GAVI funding will allow newborns, who already receive free HB vaccine, to receive the first dose of HB vaccine at birth at home. HB vaccine is being prefilled into a unique delivery device that cannot be reused; it allows birth attendants to store the vaccine un-refrigerated in their homes and to deliver it to children at home births. This early dose will increase efficacy against perinatal transmission, the mode most likely to lead to the chronic carrier state and a cancer outcome.



Source: World Health Organization

Life is Meant to be Lived - One Man's Story

A Daughter's Perspective

Cathy Pachuk, Ph.D.
Associate Professor, The Jefferson Center,
Thomas Jefferson University

When my father was diagnosed with primary hepatocellular carcinoma (HCC), or liver cancer, about two years ago he looked to me for help in identifying treatment options. The diagnosis of HCC, difficult for anyone to handle, was extremely devastating to my father, who had already battled numerous life-threatening conditions and diseases.

No Stepping Back from Set Backs

In February 1970, during a routine physical, a massive thoracic/abdominal aneurysm was found on my father's aorta. The odds of surviving surgery were very low and the odds of surviving without serious complications, such as paralysis, were even lower. The only surgeon willing to perform the surgery was the one who pioneered the development of this type of surgery, Dr. Michael DeBakey, of Methodist Hospital in Houston, TX. My father was one of the first patients to undergo this type of surgical procedure. The 12-hour operation was a success. Within three months, my father was back on the golf course.

Due to complications from the aneurysm, however, one of my father's kidneys atrophied, leaving only one functional kidney. In addition, my father developed adult onset diabetes, congestive heart failure and an irregular heart beat that required insertion of a pacemaker. In 1992, my father was diagnosed with prostate cancer and treated successfully. Nine years later, the seemingly impossible happened: the cancer had metastasized and was now in his bones and spinal column. Currently, the cancer is being managed by hormone therapy.

Through it all, my father has been a fighter. He has refused to feel sorry for himself, lose control or break down. He has faced every enemy head-on with a fierce determination to gain the upper hand. My father's philosophy has always been that life is meant to be lived.

A Silent, Deadly Infection

Then one day, almost two years ago, my father was informed that he had liver cancer. Ironically, the same surgery that had saved his life 30 years earlier likely also resulted in his being infected with a deadly hepatitis virus. Silently working behind the scenes, the infection had finally taken its toll. My father had multiple liver tumors. He had about 6 months to live. For the first time, I heard the tiredness in my father's voice. He could only take so much. It wasn't fair. As soon as he surmounted one obstacle, another appeared in its place. But, despite it all, he wanted to lick this one, too, and so the hunt for a treatment began.

Hunt for a Treatment

I spent the next few days speaking with hepatologists and scouring the internet for therapies, treatments and clinical trials. Unfortunately, I was learning that my father was ineligible for many standard treatments, including chemo embolization and surgery, due to his many health problems. His options were growing scarce and time was running out.

Then I spoke with Dr. Jack Wands, director of the Division of Gastroenterology and The Liver Research Center Rhode Island and Miriam Hospital(s). He listened attentively to my story and asked if I had heard of Dr. Damian Dupuy at Rhode Island Hospital, who was doing incredible things with radiofrequency ablation (RFA) therapy, including treating liver cancer.

New Therapy Extends Quality of Life

As soon as I got off the phone, I fired off an e-mail to Dr. Dupuy. Within 24 hours I received a reply – he would be happy to evaluate my father, but cautioned that this treatment was not for everyone. Within a few weeks, my father underwent several tests and was then on his way to Rhode Island for treatment. Dr. Dupuy was able to ablate most of the tumor masses and two months later, my father was back on the golf course. That was eighteen months ago.

Since that time, my father has needed two more RFA treatments. With every treatment, my father has recovered more rapidly. He is currently leading an active life with my mother, spending time with his grandkids, and of course playing golf. We know that the cancer is not gone, but we will control it with ablation therapy for as long as possible. This treatment has not only extended his life; it has allowed him to live it doing the things he most enjoys doing.



My Dad chose this photo because it shows him doing what he loves most. If you happen to be out on the golf course, you may run in to him. Although you won't recognize his face, you'll know him by that "perfect swing" anywhere.

Continued on Page 9

A Doctor's Perspective

Damian Dupuy, M.D., Director of Ultrasound, Rhode Island Hospital and Associate Professor, Diagnostic Imaging, Brown Medical School

In addition to complete tumor eradication, radiofrequency ablation (RFA) can be used to control primary liver cancer in patients with no alternative options due to tumor size, tumor location or associated medical conditions. The daughter of one such patient who greatly benefited from the palliative effects of RFA has written her account of his story. With the patient's permission, I would like to share his case from the physician's perspective.

First Impressions

Mr. Pachuk presented to me with two large hepatocellular carcinomas (>7cm) in the right lobe of his liver approximately 18 months ago. Standard therapy for his disease would have been surgical removal of the right side of his liver. Mr. Pachuk's normal left lobe was sufficiently healthy enough to carry the work load. Unfortunately, Mr. Pachuk had a history of congestive heart failure and chronic renal insufficiency making him a very poor surgical candidate. Despite his medical problems, Mr. Pachuk lives a full life enjoying travel and golf and he is not ready to throw in the towel just yet.

His local physicians as well as specialists at a major cancer center were not aware of the benefits of RFA as a minimally invasive treatment option in cases such as his and he was given no treatment as his only option. This left him with a typical median survival of 4-6 months. Fortunately, his daughter works in the field of hepatology and her connections led her to me at Brown Medical School and Rhode Island Hospital where I had been using RFA as a palliative treatment option in patients with large liver tumors such as Mr. Pachuk's.

Overcoming Medical Complications

The first ultrasound-guided RFA treatment went very well, but I knew upfront that complete tumor eradication was out of the question; nonetheless, I did my best and approximately 80-90% of the tumor was killed. Normally, I follow patients with contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI), but in Mr. Pachuk's case his renal insufficiency precluded use of intravenous CT contrast due to its toxic effects on the kidney. Compounding this management dilemma, Mr. Pachuk developed a cardiac arrhythmia requiring a permanent pacemaker. This now prevented him from being followed with MRI since the magnetic fields interfere with pacemaker function.

Fortunately, Mr. Pachuk's tumor made a protein, which approximately 50% of primary liver tumors make, called alpha fetoprotein (AFP). Therefore, I have been following Mr. Pachuk's disease status with the AFP blood test. He has had two additional RFA treatments using CT guidance, whereby his tumor has been retreated to keep it from growing into the vital part of his liver where the major blood

vessels and bile ducts are located. Walking the fine line between killing enough tumor without hurting the overall health status of Mr. Pachuk has been challenging enough, but compounding the inability to clearly see the areas of viable tumor has made it even more challenging.

A Physician's Reward

Despite the complexities of his disease and overall health status, Mr. Pachuk continues to live a normal life probably more active than most people in their 80's. This desire to live life to its fullest is most refreshing and as a physician, I find it very rewarding to be able to apply state-of-the-art technology in a clinical situation where no other hope exists.

I thank Mr. Pachuk and his family for their bravery and open-mindedness during the course of his RFA treatment. I will continue to do my best at keeping his quality and quantity of life the main goal of therapy. Hopefully, those who hear this story may share this knowledge so that others in similar situations may benefit from this truly remarkable treatment option.

Radiofrequency Ablation

For decades, direct injection of absolute ethanol had been used to treat small primary liver cancers with success rivaling surgery. Recently, radiofrequency ablation (RFA) a heat-mediated therapy has replaced alcohol due to its ability to treat larger lesions with fewer treatments.

RFA is a technique whereby an alternating current in the frequency of radio waves is emitted from the tip of an electrode or needle placed directly into a tumor. The alternating current flowing back and forth through the tissue causes frictional heating and coagulation of tumor. For the treatment of primary liver cancer, RFA has achieved complete cell death in over 85-90% of cases in lesions smaller than 5 cm, with less than a 10% local recurrence rate. Unlike surgery and many other treatments, RFA can be performed many times in the same patient. This is very important in the hepatitis B population because these patients are prone to develop tumors in more than one site in the liver over time.

The RFA procedure is a very safe and non-toxic treatment. The procedure is almost exclusively performed on an outpatient basis with the administration of intravenous medication to alleviate pain during the procedure. After the procedure, patients are given a small bandage and sent home with narcotics for a few days to reduce discomfort at the treatment site.

Until modern medicine can prevent the formation or stop the growth of primary liver cancer at the gene level, focal ablative therapies such as RFA will be mainstays in the treatment of primary liver cancer for years to come.

Foundation at the Forefront

HBF Partnership is CHIC

The HBF has become involved with the Jefferson University Hospital **Chinese Health Information Center (CHIC)**, which serves as a bridge between Philadelphia's Chinese community and the hospital's services by offering referrals, translation, counseling, and educational assistance. "Jefferson recognized that Chinatown is in its backyard, and that a large percentage of the approximately 30,000 Chinese residents do not speak English," says **Philip T. Siu, MD**, director of the Center. Staff members are fluent in Mandarin, Cantonese and Vietnamese as well as English. Dr. Siu has established an aggressive hepatitis B program that includes free health screenings for adults and free immunizations for children. The HBF will provide its Chinese translated materials and assist with research and data analysis for the project. For more information about this organization, visit www.JeffersonHealth.org/CHIC.

O'Liver Brings Good Fortune to Chinatown

Molli Conti, HBF vice president of outreach, and **Sarah Bergin**, HBF outreach associate, joined the Chinese Health Information Center (CHIC) for health screening in Philadelphia's Chinatown.



O'Liver gives a hug of congratulations to **Dr. Phillip Sui** director of CHIC (on right) and **Mr. Kin Lam**, program manager, at Chinatown health screening (3/29/03).

on Saturday March 29. The HBF's liver mascot, **O'Liver**, made a guest appearance to the delight of the many families and children. More than 250 people showed up for the free hepatitis B screenings, which far exceeded CHIC's expectations. The large turnout provides strong evidence that hepatitis B programs and services are very much needed in this underserved Chinese community. Media attention from a local Chinese TV station and several articles in the Philadelphia City Paper (April 24 – May 1, 2003 issue) also helped to raise awareness about this important health initiative.

HBF Joins National Viral Hepatitis Roundtable

Viral hepatitis currently affects millions of Americans. To address this growing public health concern, the Centers for Disease Control and Prevention (CDC), in partnership with Hepatitis Foundation International, co-founded the new National Viral Hepatitis Roundtable (NVHR). The Hepatitis B Foundation was invited to join the organizing committee, which is comprised of 28 public, private and non-profit organizations. On April 23, **Molli Conti**, HBF vice-president, attended the planning committee held in Wash-

ington, DC. HBF board member, **Steve Bingham**, has been invited to join as a patient advocate for hepatitis B. The goal of the group is to develop a national strategy for the prevention and treatment of viral hepatitis. **Dr. Harold Margolis**, director of the Division of Viral Hepatitis, CDC described "gap areas" in the prevention, transmission and risk of chronic infections. Other important concerns include both access to and lack of funding for testing and counseling, immunization of adults, medical management, and treatment. A national meeting of the NVHR is planned for early 2004.

YOU ARE INVITED!

Hepatitis B Foundation Sponsors

B-Informed 2003: A Gathering of Friends
July 20-22, Doylestown, PA

The Hepatitis B Foundation (HBF), in partnership with the Hepatitis B Information and Support List (HB-L), is sponsoring the 3rd annual patient conference this summer. This is the only national conference geared towards patients, parents and families of those affected by chronic hepatitis B. A \$50 per-person registration fee includes lodging and meals for participants during their stay on the beautiful campus of Delaware Valley College in Doylestown, PA.

Keynote Speaker Samuel So, M.D., Director, Asian Liver Center at Stanford University
"Eliminating the Voodoo from Hepatitis B"

Guest Speakers

Minh Nguyen, M.D. - *"Hepatitis B: Precore Mutants, Genotypes and Difficult Questions"*

Cosme Manzarbeitia, M.D. and Ken Rothstein, M.D. - *"Transplant Basics & Politics: How Do You Get On the Transplant List?"*

Parents of Kids with Infectious Diseases (PKIDs) - *"Hep B and Kids"*

Cynthia Weaver, MSW - *"Psych Issues"*

Timothy Block, Ph.D. - *"Research and Drug Watch Update"*

Pharmaceutical Updates on *Hepsera, Entecavir and Peg-Interferon*

Registration

Visit www.hepb.org or call (215) 489-4900.

Registration deadline is July 10.

Dr. Jay Hoofnagle Receives Distinguished Scientist 2003 Award



Jay H. Hoofnagle, M.D. Director, Division of Digestive Diseases and Nutrition, National Institute of Diabetes, Digestive and Kidney Diseases, National Institutes of Health

The Hepatitis B Foundation is proud to publicly recognize the professional accomplishments and contributions of Dr. Jay Hoofnagle to advancing our *Cause for a Cure*.

Dr. Jay Hoofnagle represents the very best as an outstanding clinician and scientist. He has been a pioneer in advancing hepatitis B therapeutics and is an internationally respected leader in the field. His findings have provided the scientific underpinnings of the current practice guidelines for individuals infected with hepatitis B.

In the 1980s, Dr. Hoofnagle and his NIH colleagues began evaluating interferon alpha for its antiviral potential in hepatitis B and hepatitis C (formerly known as non-A, non-B hepatitis). At the time, few people believed that viral hepatitis could be treated.

His definitive work regarding the efficacy of interferon and mechanism of therapeutic action for viral hepatitis was instrumental in leading it to be the first licensed therapy for hepatitis B in 1991. Now there are three approved drugs and many more on the way.

In 1988, Dr. Hoofnagle was appointed Director of the Division of Digestive Diseases and Nutrition at the NIDDK, NIH. He is Board Certified in Gastroenterology and Internal Medicine, and continues to conduct clinical trials to improve the treatment of hepatitis patients.

From 1991-1992, he served as President of the American Association for the Study of Liver Diseases (AASLD). He is a member of every national medical association for liver diseases, as well as the International and European associations for liver diseases. Numerous organizations have presented him with awards for his outstanding work. In 2001, he was selected to receive the "AASLD Distinguished Achievement Award" for lifetime achievement in liver disease research.

HBF Crystal Ball Gala - continued from front page

Dr. Hoofnagle wrote in his acceptance letter, "I am particularly pleased to receive this award from the Hepatitis B Foundation because I join a fellowship of outstanding scientists whose work and contributions have been very important and an inspiration to many. **Baruch Blumberg, Harvey Alter, Tom London, Jesse Summers and Bill Mason** are individuals with whom I have been proud to share

this important field of research. To have been a part of this story of scientific discovery has been an honor; to receive this award for participating in this story is a pleasure indeed."

Dr. Timothy Block, HBF president, thanked all those who attended the Crystal Ball for their support. With his usual exuberance, he went on to say, "We have a lot of good news to celebrate this evening and it's wonderful to share this excitement with all of our friends."

Dr. Block spoke about the new discoveries in the HBF labs and then asked all of the scientists at the gala to stand for much deserved applause. He talked about the HBF's ambitious plan to build a new Science Center in partnership with Delaware Valley College, which was made possible through a generous state grant of \$7.9 million. Finally, he announced that the HBF had just been awarded a three-year NIH grant to expand its award-winning website www.hepb.org.

To top off the awards ceremony, **Molli Conti**, HBF vice-president, gave special recognition to four dedicated volunteers from RSVP of Bucks County, **Terry Grundman, Paul Radosza, Les DeFonso, and Kathryn Graham**, who have touched every newsletter and every piece of mail that the HBF has sent out over the past five years!



HBF Receives NIH Grant - continued from front page

To redesign and expand the site, the HBF selected Refinery, a leading interactive professional services company that is headquartered in Huntingdon Valley, PA.

Visit the HBF's newly expanded award-winning website, recognized as having the best hepatitis B information on the Internet by the American Social Health Association. Bookmark www.hepb.org to make use of the exciting new features that will be coming soon.



PKIDs Fights Hepatitis B in China

Christine Kukka



PKIDs team teaches Chinese village doctors how to give injections safely. (Photo by Christine Kukka, March 2003)

PKIDs is a national nonprofit organization that is dedicated to creating broad-based support for families whose children are chronically infected with hepatitis B, hepatitis C or HIV. In the past, year, PKIDs decided to step onto the international stage to combat hepatitis B and other infectious diseases in China due to its successful infectious disease prevention program in the U.S. This first step has been made possible by grants from the Children's Vaccine Program at PATH and PKIDs USA.

High Price of Hepatitis B in China

Hepatitis B is widespread in China – an estimated 60% of Chinese have been exposed to the virus. The virus is spread primarily from infected mother to child at birth.

Unsafe injections are another major source of infection. UNICEF officials estimate 1 out of 4 hepatitis B infections in China resulted from the reuse of needles. During the Cultural Revolution of the 1960s and 1970s, "barefoot doctors," who received minimal medical training before they were sent into the countryside, may also have unwittingly helped spread the virus when they re-used improperly sterilized needles.

A recent study by Dr. Zhuo Jiatong, deputy director of the Guangxi Centers for Disease Control and Prevention, found evidence of past or current HBV infection in 76% of residents, ages 1 to 59, in Guangxi Province. The chronic infection rate (HBsAg-positive) was 23% in males and 14% percent in females.

According to Dr. Zhuo, it is not surprising that males experienced a higher chronic infection rate in this study. Boys are culturally preferred in China, hence, they are much more likely to have received injections as part of their medical care – and consequently HBV infections – than girls.

Today, injections continue to be used heavily for dispensing antibiotics, vitamins and other medications. Doctors promote injections to make money since they are losing their government subsidies as socialized medicine breaks down in this emerging capitalist society.

PKIDs China Goes to Work

The first goal of PKIDs China was to develop a Chinese-language infectious disease prevention training program that could be easily adapted for use by families, orphanages, schools, health centers, government health departments, community groups and others.

In October 2002, a team made up of **Christine Kukka**, PKIDs Director of Communications and Training, **Maureen Kamischke**, PKIDs Medical Advisory Board Member, and **Dr. Laura Robertson**, a pediatrician at Columbia-Presbyterian Hospital, traveled to China to present and test the effectiveness of their pilot training before doctors, provincial health officials, orphanage workers and foster parents.

The PKIDs team also met with groups of adults infected with hepatitis B in Shanghai and Nanjing to learn what their needs were. Many of these adults, who are parents or newly-married, require more information about the effectiveness of immunization to halt perinatal transmission of hepatitis B.

The PKIDs team found the Chinese had many misconceptions about how hepatitis B is transmitted, which results in chronically infected children and adults suffering stigma and discrimination. PKIDs revised its presentation and expanded the hepatitis B information in their training program.

Village Doctors Recruited to Help

In March 2003, Kukka, Kamischke, and PKIDs Advisory Board members **Dr. Karen Steingart**, a Washington public health official and **Dr. Heidi Schwarzwald**, a pediatrician at Baylor College of Medicine's Department of Pediatrics and director of the Texas Children's Health Center for International Adoption, returned to China to present a pilot training program to teach doctors and health workers about safe medical practices and to encourage them to teach their patients about effective disease prevention. 35 different schools sent instructors, who also serve as village doctors throughout China, to attend the PKIDs presentation.

The newly translated training program is now available to health departments, orphanages and other organizations to promote awareness and prevention against infectious diseases. **To learn more about PKIDs China, contact Executive Director Trish Parnell at pkids@pkids.org or call 360-695-0293. Be sure to visit www.pkids.org**

Fast Fact

UNICEF estimates 1 out of 4 hepatitis B infections in China resulted from the reuse of needles.



Speaking Personally

Steve Bingham

Co-Owner of the Internet Hepatitis B Information and Support List (HB-L)

Our Toughest Questions ...

May 12, 2003, was the 5th anniversary of the Hepatitis B Information and Support Listserv (HB-L). In those five years, thousands of anxious "hepBers" have made their way through cyberspace to ask us their difficult questions. With the help of our resident health professionals who participate on the list, we do our best to help out, but some of the questions are difficult to answer and are asked again and again:

1. What's a good diet for people with hep B?

There seem to be as many diet theories as there are people who eat, and the diet advice that we get from our government is wavering, too. We try to get our subscribers to back up their diet theories with sound research.

2. What pain reliever would be safe for me?

NSAID painkillers have troublesome side effects for those of us with hepatitis B. Acetaminophen (i.e. Tylenol) can send you for a liver transplant if you overdose on it or if you take it while consuming alcohol. The narcotic painkillers seem to be easier on our systems, but they might lead to another set of problems, such as addiction.

3. If there are really 400 million people in the world with chronic hep B, where are they all?

We hear and read a lot about HIV and HCV, but not HBV. Related questions include, "Why aren't there any local support groups for hepatitis B patients?" "How come I'm the only hep B patient that my doctor sees?" Well, some of these folks will be attending the annual "B-Informed" patient conference this summer (see page 10), so join us and meet a great group of new friends.

4. I read about new hepatitis B drugs on the Internet. Why aren't they available?

Over the past five years, I have accumulated a list of "85 Possible Treatments for HBV" (visit www.pub.nxs.net/bit.cruncher/hbv/index.htm). I only add treatments to my list that have had at least one promising research abstract written about them. Presently there are only a handful of HBV treatments available to us in the USA, and I can't help but believe that lost on my list there is something big that might potentially help my HBV friends.

5. I can't afford treatment, and I don't have insurance. So what do I do?

Many of our subscribers can't afford medical insurance. Others slip through the cracks somewhere between Medicare and Medicaid. We American subscribers

sometimes find ourselves envying our friends in the UK and other countries where health care is more equitable.

6. I have this weird pain in my right side. What's that all about?

What we on the listserv have come to call "liver pain" seems like a small thing, but it can really cause a lot of worry. It comes from the liver area, but we're told that the liver itself has no nerves and feels no pain. We could use more research to help us understand and control this and other liver-disease symptoms.

7. Can I drink alcohol and, if so, how much?

We have doctors who preach complete abstinence and others who allow their patients a glass of wine or two. Half of our subscribers can't figure out why on earth anyone would want to take the risk of drinking alcohol, and the other half insist that alcohol is important to their quality of life.

8. Is it safe for me to kiss?

We veterans find ourselves advising the "newbies" on their love life and just how athletic they can be with their kissing. But the truth is that there is a degree of risk for anyone who has sex, safe or unsafe.

9. What are hepatitis B viral mutants and are they a problem?

One prominent HBV scientist proclaimed that the two most serious obstacles to future HBV research would be a) controlling HBV resistance (mutations), and b) the lack of agreement on HBV terminology. Both of these topics make hepatitis B even more confusing.

10. Are we ever really cured?

It's been reported that some people who thought they were cured of hepatitis B had relapsed after being put on immunosuppressant treatments for other illnesses. Some professionals tell us that it's not important to be cured, as long as our hepatitis B is under control, like diabetes.

But myself, I'd rather be cured.

Best Wishes, Steve

Internet Support Groups



Hep B Information and Support List

<http://www.geocities.com/Heartland/Estates/9350/hblist.html> (case sensitive)

Well-supervised list with useful information and lively exchanges between supportive members.

HBV Adoption Support List

<http://www.onelist.com/community/hbv-adoption>

For adoptive or biological parents of children with HBV. This is a restricted list and requires pre-approval.

PKIDS Support List

<http://www.pkids.org/>

For adoptive and biological parents of children with chronic viral infectious diseases, including HBV, HCV, and HIV.

Hepatitis B Clinical Trials

Hepatitis B Foundation HBV Clinical Trials Watch
www.hepb.org

National Institutes of Health Clinical Trials
www.clinicaltrials.gov

Centerwatch Clinical Trials
www.centerwatch.com/studies/cat79.html

Open Enrollment for Phase III Trial of LdT (telbivudine)

Idenix Pharmaceuticals Inc. is sponsoring a phase III clinical trial of LdT for treatment of chronic hepatitis B, conducted at over 100 sites in North America, Asia, Europe, Australia, and New Zealand. Adults with chronic hepatitis B who have never been treated with lamivudine or other nucleoside or nucleotide analogues are eligible and will be randomized to receive either LdT or lamivudine for 2 years. Neither the patient nor the doctor will know which treatment has been administered until the end of the study. Contact: Barbara Fielman, RN at 617-250-3100, ext. 145 or email fielman.barbara@idenix.com.

Open Enrollment for Phase II Trial of Clevudine

The purpose of the study is to evaluate the safety and effectiveness of 12 weeks of treatment with clevudine, at one of three doses (10 mg, 30 mg, or 50 mg), in patients chronically infected with hepatitis B virus. Trials are being conducted in the U.S., Canada, China, France and Singapore. Visit the HBF at www.hepb.org for a complete listing of clinical trial sites.

Open Enrollment for Phase III Trials of Entecavir

Bristol-Myers Squibb (BMS) is conducting studies of this once daily oral drug in approximately 130 sites in more than 30 countries worldwide. Three different studies are being conducted based on the results of patients' serological status (hepatitis B e-antigen positive or negative), and whether the patient is currently on lamivudine therapy and has evidence of resistance to lamivudine. Patients will be randomized to receive either entecavir or standard therapy with lamivudine. Neither the patient nor the doctor will be aware of which treatment the patient is receiving. After completing the study, all participants will be monitored for up to 5 years for survival and incidence of HBV-related complications. Contact: BMS toll-free at 1-866-892-1BMS.

Columbia-Presbyterian Medical Center Entecavir Study

The safety of Entecavir (BMS 200,475) will be evaluated in adults with chronic HBV. Those co-infected with HIV are not eligible to participate. Contact: Ms. Cabilia Gomez at 212-305-3839 (New York, NY).

NEW A Randomized, Double Blind Trial of LdT (Telbivudine) versus Lamivudine

This is a trial for adults with compensated chronic hepatitis B who have never been treated. Contact: Debora Goldman, RN, clinical trials coordinator for Dr. Douglas Dieterich at 212 241-7270 (Mt. Sinai School of Medicine, NY, NY).

NEW Phase II Comparison of Adefovir and Tenofovir for the Treatment of Lamivudine-Resistant HBV

This NIAID study will compare the combination of adefovir

and lamivudine with the combination of tenofovir and lamivudine to determine which drug combination is most effective in people who are infected with both HBV and HIV. Contact: NIH Patient Recruitment at 1-800-411-1222 or email prpl@mail.cc.nih.gov. Visit the HBF website at www.hepb.org for the locations and contact information in 12 states.

Pilot Study of Telbivudine Treatment for HBV Prior to Starting Anti-HIV Drugs in Co-infected Patients

This NIAID study will evaluate telbivudine (LdT) for the treatment of hepatitis B in HIV infected patients. Patients will take telbivudine alone for 24 weeks, add anti-HIV drugs for 24 weeks, then stop taking telbivudine while continuing their anti-HIV drugs. The primary aim of this study is to assess the safety of telbivudine alone and in combination with a lamivudine-based highly active antiretroviral therapy (HAART) regimen in patients coinfecting with HBV and HIV. Contact: Karen Savage, RN, CCRC, at 205-975-7925 (kgsavage@uab.edu) at the Univ. of Alabama.

Prevention of Recurrent HBV After Liver Transplantation

Eligible patients for this study MUST be on a liver transplant waiting list or have already received a liver transplant for hepatitis B. The aim of this NIDDK study is to establish the most cost-effective preventive therapy for recurrent hepatitis B after liver transplantation. HBIG, Epivir-HBV and Hepsera will be evaluated. Contact: Doug Armstrong at darms@umich.edu or call 734-936-1712 at the Univ. of Michigan Medical Center.

Treatment of Hepatitis in Patients Who are Triple-Infected With HIV, HBV and HCV

This NIAID phase II study will investigate the safety and effectiveness of using adefovir, pegylated interferon, and ribavirin in patients with HBV, HIV, and HCV. All patients in this study must be taking lamivudine. The overall rate of HBV and HCV infection in HIV infected persons is 5 to 10%. The study will evaluate the effect of HBV and HBV therapy on HCV and HIV disease progression. Contact: Karen Savage, RN, CCRC, at 205-975-7925 (kgsavage@uab.edu) at the Univ. of Alabama or M. Ray at 303-372-5535 (graham.ray@uchsc.edu) at the Univ. of Colorado Health Sciences Center.

Pegylated Interferon to Treat Chronic Hepatitis D

This NIDDK study will evaluate the safety and effectiveness of pegylated-interferon in treating hepatitis D virus (HDV). HDV only infects people who are already chronically infected with hepatitis B. HDV is often severe and progressive. Patients with HDV over 6 years old may be eligible for this study, conducted by the NIDDK of the NIH, Bethesda, MD. Contact: NIH Patient Recruitment at 1-800-411-1222 or email prpl@mail.cc.nih.gov.

Fast Fact

The current worldwide market for HBV drugs is estimated at \$650 million annually.

Resource Roundup



Hepatitis B Foundation

215-489-4900

www.hepb.org

info@hepb.org

Comprehensive website dedicated to hepatitis B. Facts, useful advice, Drug Watch, liver specialist directory, and a responsive email service. Includes *Chinese, Vietnamese and Korean Language Chapters*.

American Liver Foundation

1-800-GO-LIVER

www.liverfoundation.org

webmail@liverfoundation.org

Information about all liver diseases, including viral hepatitis. Fact sheets, legislative advocacy, research funding.

Asian Liver Center at Stanford University

650-725-4837

<http://livercancer.stanford.edu>

This website informs, updates, and educates people about hepatitis B and liver cancer among Asians and Asian-Americans. Information is available in English, Chinese and Korean.

Centers for Disease Control, Hepatitis Division

1-888-443-7232

www.cdc.gov/ncidod/diseases/hepatitis

The national authority for viral hepatitis information: epidemiology, disease facts, prevention, scientific studies, national recommendations, and more.

CDC Hepatitis Immunization Hotline

1-800-232-2522 (English)

www.cdc.gov/nip

1-800-232-0233 (Spanish)

nipinfo@nip1.em.cdc.gov

Hepatitis B Research List

To subscribe, send a blank email to:

HBV_Research-on@mail-list.com

A free electronic research list maintained by Sheree Martin that provides abstracts, reports and notices.

Hepatitis B Research Archive Website

http://dispatch.mail-list.com/archives/hbv_research

Archived research bulletins posted on the Hepatitis B Research List, from 1998 until current year.

Hepatitis B Virus Page

<http://www.globalserve.net/~harlequin/HBV/index.html>

Maintained by Robert Garces, Ph.D. Candidate in Virology, at the University of Toronto.

Hep C Connection

1-800-522-4372

www.hepc-connection.org

info@hepc-connection.org

Comprehensive information to assist Hep C-challenged individuals and their families.

Hepatitis Foundation International

1-800-891-0707

www.hepfi.org

mail@hepfi.org

Information about viral hepatitis, support groups, research articles, and education programs.

Hepatitis Magazine

1-800-310-7047

www.hepatitismag.com

editor@hepatitismag.com

The only print magazine published bi-monthly for those affected by viral hepatitis.

Hepatitis Neighborhood

www.hepatitisneighborhood.com

info@HepatitisNeighborhood.com

Features a Town Hall with a Live Speakers Forum. Sponsored by Priority Healthcare Corporation.

HepTrec

1-866-HEPTREC

www.heptrec.org

The Delaware Valley Hepatitis Treatment, Research and Education Center (HepTREC) provides support group information, training and prevention programs in the greater Philadelphia area.

HCV Advocate

sfhepcat@pacbell.net

<http://www.hcvadvocate.org>

Excellent research, education and support information for the HCV community. One of the few HCV websites that also includes information about hepatitis B.

HIV and Hepatitis Treatment Advocates

www.hivandhepatitis.com

Professional online publication with updates, conference reviews, free teleconferences, and an e-mail service.

Immunization Action Coalition

651-647-9009

www.immunize.org

www.vaccineinformation.org

Comprehensive resource of immunization information. "IAC Express" is a free email announcement service. "Vaccine Information" is a new complementary website launched by IAC and is specifically written for the general public.

MEDLINEplus Health Information

www.medlineplus.gov

A goldmine of reliable health information from the world's biggest medical library of medicine, the National Library of Medicine. This database is maintained in collaboration with the NIH.

Memorial Sloan Kettering "About Herbs"

aboutherbs@mskcc.org

www.mskcc.org/aboutherbs

Objective information about herbs, their side effects, drug interactions, and links to scientific research. This site is maintained by experts at Memorial Sloan Kettering.

National Center for Complementary and Alternative Medicine

1-888-644-6226

www.nccam.nih.gov

Sponsored by the National Institutes of Health (NIH), this site contains databases galore and research articles.

Parents of Kids with Infectious Diseases

1-877-55-PKIDS (toll-free)

www.pkids.org

pkids@pkids.org

An excellent resource for parents and professionals. Pediatric clinical trials, research list and support listserv.

Calendar of Events



- June 30 - July 1** **VII International Symposium on Viral Hepatitis**
 Accion Medica S.A.
 Hospital Universitari Vall d'Hebron,
 Barcelona, Spain
congresosbarcelona@accionmedical.es
- July 11** **4th Annual Joseph Nagy Golf Tournament**
 To Benefit the Hepatitis B Foundation
 Bunker Hill Golf Course, Princeton, NJ
www.hepb.org
- July 20 - 22** **3rd Annual "B Informed Conference"**
 Hepatitis B Foundation and Hepatitis B Support List (HB-L)
 Delaware Valley College, Doylestown, PA
 Contact info@hepb.org
- Sept. 7 - 10** **International Meeting of the Molecular Biology of HBV**
 Centro Congressi Giovanni XXIII
 Bergamo, Italy
 Co-chairs: Drs. A. Bertolotti & J. Travis
 Contact: a.bertolotti@ucl.ac.uk
- Sept. 14 - 17** **43rd ICAAC**
 American Society for Microbiologists
 McCormick Place, Chicago, IL
 Chair: Dr. Barbara Murray
 Contact: icaac@asmusa.org
www.icaac.org/procom.asp

- Oct. 24 - 28** **Annual AASLD Meeting**
 American Association for the Study of Liver Diseases
 Hynes Convention Center, Boston, MA
 Contact: jdeal@asld.org
www.aasld.org
- Nov. 9 - 12** **IX International Antiviral Symposium**
 Organizasyon DIAS
 Renaissance Antalya Resort
 Beldibi, Antalya, Turkey
 Co-Chairs: Drs. Yung-Chi Cheng, Raymond Schinazi, and A. Bozdaya
www.antiviral.dias.com.tr
- Dec. 14 - 18** **HepDART: Frontiers in Drug Development for Viral Hepatitis**
 Kauai Marriott Resort, Kauai, Hawaii
 Chair: Dr. Raymond Schinazi
 Contact: info@informedhorizons.com
<http://www.informedhorizons.com/hepdart2003/>
- 2004**
- Feb. 14 - 17** **Hong Kong - Shanghai International Liver Congress**
 Hepatitis Research Foundation and The Shanghai Organizing Committee
 Hong Kong Convention and Exhibition Centre, Hong Kong SAR, China
 U.S. Speakers: Yung-Chi Chen, Mark Kane, Anna Lok, Jack Wands, and others
 Contact: info@hepa2004.org
www.hepa2004.org
 Abstract deadline: October, 15, 2003



HB FOUNDATION
 700 East Butler Avenue
 Doylestown, PA 18901-2697

We are a national non-profit organization dedicated to finding a cure and improving the quality of life for those affected by hepatitis B worldwide.

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