

B HEPATITIS B

INFORMED

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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.

A Gathering of Friends Second Annual HBF Patient Conference

Almost 80 people traveled to the Hepatitis B Foundation (HBF) in Doylestown, PA, the weekend of June 28 - 30 for the "B Informed 2002" patient conference. Attendees came from all across the nation, and some as far away as India and the United Kingdom to join this annual event, which is the only one of its kind. Despite the fact that hepatitis B affects 1 out of 20 Americans, until recently there had never been a national meeting dedicated to those living with HBV.

Historically, those affected by hepatitis B have been a very silent group. The HBF decided it was time to break down the wall of silence. The first-ever patient conference, "B Informed 2001", was hosted last summer by the HBF in partnership with the Hepatitis B Information and Support Listserv (HB-List), the only online hepatitis B support group. People were finally able to meet face-to-face, exchange stories and information, and share their laughter and tears in a supportive environment. Everyone agreed they wanted to gather again the next year.

"B Informed 2002" started with an official welcome from **Molli Conti**, HBF associate director, and **Steve Bingham** and **Sheree Martin**, HB-List co-owners. In a surprise ceremony, attendees from the HB-List presented HBF co-founders **Paul and Janine Witte** and **Tim and Joan Block** with gifts baskets as a token of their appreciation. Both couples were visibly moved and expressed heartfelt gratitude for this recognition.

For two days, the schedule was packed with information from medical and legal experts, research scientists, and pharmaceutical rep-

resentatives. Considering how well informed and motivated the audience was, all of the discussions were very lively and ran overtime. Fortunately, the guest speakers were flexible and eager to share their expertise with this friendly but determined audience.

In addition to research and clinical updates, special features included a panel of "four mothers" who raised awareness about issues faced by parents of children with hepatitis B; personal stories of liver transplantation; an ad hoc "hepper helpers" support group organized by family members; a lunch session with four "hepatitis B ambassadors" to Asian communities in the U.S.; and a celebratory book signing by the author of "The First Year: Hepatitis B".

This year's "B Informed" conference continued the successful blending of the intellectual, the practical and the emotional. As participants soak up the information from experts and share their personal stories, they begin to feel less alone in their daily struggle with this chronic disease. As those in the medical and scientific fields hear the patients' stories, they gain new insight and renew their own professional commitment to the problem of hepatitis B. Clearly, the HBF patient conference is providing a highly visible focus for the emerging hepatitis B community of friends.



Old and new friends meet at "B Informed 2002".

Patient Conference Highlights on Pg. 9



Message from the President

Timothy M. Block, Ph.D.

Giving for the Future

I hope that supporters of the HBF, after reading this issue of B-Informed, will take pride in both the quantity and quality of our accomplishments. Moreover, perhaps those most affected by hepatitis B will see what we have done and be encouraged.

Consider our activities in outreach. On pages 9 and 10, the "B-Informed 2002" patient conference is reviewed by one of the attendees. This conference is not only a great experience for the participants, but it is also highly motivational for us because it puts faces on the people most important to our cause and represents the kind of unique personal style of outreach that has come to characterize the HBF.

On page 3, there is an update of the discovery research being advanced by HBF scientists. This is cutting-edge stuff, highly focused on either developing specific drugs ourselves or enabling their development elsewhere. Our scientists are at a critical point in the development of a new family of drugs and detection of possible markers of liver disease. Often times this kind of work is unpopular because of its degree of uncertainty. Yet, this is the kind of research upon which we are most dependent. Therefore, it needs and deserves our support.

In light of these accomplishments, the HBF is embarking on a major campaign to reinforce our existing strengths and to enable our growth for the future. The outreach efforts need to be provided with stable support so that our constituents can be assured there will continue to be a voice for them. The research must be nurtured and expanded in order to bring hope to all those affected by hepatitis B.

Although charitable giving is being challenged in this time of economic stress, it is during these times that the need is the greatest. *We ask our readers to make the HBF a priority this year . . . please take a moment to respond generously to our annual holiday appeal. Thank you!*



"The cheerful and obvious commitment from the good people at the Hepatitis B Foundation is a shining example to us all. To them we owe so much, and in whatever small way I can, I hope to help, to support, and above all to encourage you all to continue." John K. (June 2002)



In The News

Chinese Herbal Medicine Shows Promise in Treatment of Chronic HBV

Chinese herbal medicine combined with interferon alfa was 1.5 to 2 times as effective as interferon alone in reducing hepatitis B viral load to undetectable levels in HBV patients, according to University of California, Berkeley, researchers who conducted a meta-analysis of 27 clinical trials. The ingredients in the herbal treatments included mixtures of plant and root extracts. Two of the 27 studies specifically looked at bufotoxin, an extract from the skin of the toad *Bufo gargarizans*. Another two studied kurorinone, an extract from the root of the plant *Sophorae flavescens*. In particular, bufotoxin combined with interferon was significantly more effective than interferon alone in measures of HBeAg and HBV DNA, but not for measures of the surface antigen. Kurorinone was nearly as effective as interferon in the two studies that tested it. "We cannot make firm conclusions about the use of Chinese herbal medicines based upon these results," said Dr. Jack Colford, senior researcher for the study, "But the findings certainly justify additional investigation of these herbal therapies in more rigorous trials." [Am. J. Public Health (vol.92, No.10), Oct. 2002]

Hepatitis B e-Antigen Important Marker For Liver Cancer

Researchers at National Taiwan University followed almost 12,000 men from 1991-2000 for the development of liver cancer, and their findings confirm that the presence of hepatitis B e-antigen (HBeAg), in addition to hepatitis B surface antigen (HBsAg), may be an important marker of the risk of liver cancer. Compared with men who were negative for both HBeAg and HBsAg at enrollment, men who were HBsAg+ were almost 10 times more likely to develop liver cancer. Men with both positive HBsAg and HBeAg were 60 times more likely to develop liver cancer. "Our key message is that HBeAg is important for the prediction of liver cancer risk, so it should be regularly monitored among those who are chronically infected with HBV," according to study author, Chien-Jen Chen. [Lancet Infectious Diseases (vol. 2), Sept. 2002]

Doctor Held Responsible for HBV Outbreak -

A Toronto neurologist whose clinics used dirty needles on patients and caused a major hepatitis B outbreak in Ontario was found guilty of incompetence by the College of Physicians and Surgeons of Ontario in August 2002. Ronald Wilson, MD, was held directly responsible for this outbreak, even though his technician, who was later tested for hepatitis B and found to be the source of the infections, carried out the EEG tests. The ruling comes more than six years after public health officials first discovered that 14,000 people had been exposed to the hepatitis B virus in this neurology clinic. Patients testified they never saw the technician use surgical gloves when he inserted needle electrodes into their scalp. Some left the office with blood running down their face or neck after he removed the needles. Later, several were hospitalized with complications from the hepatitis B infections and one person died. [Toronto Star, Aug. 23, 2002]

HBF Lab - A Research Update

The HBF Lab, which is located in The Jefferson Center of Thomas Jefferson University (TJU) in Doylestown, PA, continue to make impressive progress in the area of therapeutics and the early detection of liver cancer caused by viral hepatitis.

Drug Discovery - Alkovirs

The "alkovirs" are a new class of anti-hepatitis drugs discovered by **Timothy Block, PhD**, HBF president, and director and professor of The Jefferson Center (TJU), and **Anand Mehta, D.Phil**, HBF's Bruce Witte Scholar, in collaboration with the labs of **Prof. Raymond Dwek, FRS**, HBF scientific advisor and chair of Biochemistry at Oxford University. This new class of compounds is described in the recent issue of *Antiviral Chemistry and Chemotherapy* (TM Block & R. Jordan, 2002: 317-325).



Anand Mehta, D.Phil, the HBF Bruce Witte Scholar

The alkovir, called UT231, recently entered Phase I human trials and is in development for the treatment of HCV by United Therapeutics, Inc. (Silver Springs, MD). UT231 is being tested for HCV first because the data from Prof. Dwek's lab suggested that its activity was best against this virus. However, tissue culture studies suggest that the alkovir strategy should also be effective against HBV, and design of a modified compound with enhanced HBV activity is being developed. There is evidence that alkovirs work by activating an "innate cellular" antiviral defense. Some of these results will be reported in the December 2002 issue of *Antimicrobial Agents and Chemotherapy*. **Xuanyong Lu, PhD**, HBF scientist, has shown that these compounds prevent HBV nucleocapsid formation, reinforcing the notion that they will be active against HBV.

Glucovirs

HBF scientists, with Prof. Dwek's group, have also developed new "glucovirs", the protein folding inhibitors previously described (Block et al, 1998, *Nature Medicine*, 4: 610-614) that are 10 times more active, and 100 times less toxic than the initial lead glucovir, NN-DNJ. These new compounds are called "methoxys". With the development of the methoxy class, it is hoped that the glucovir family will get a fair testing for their value in the management of HBV since they have been shown to be active against HBV in animal studies and thus hold great promise.

Early Detection of Liver Cancer and Other Liver Disease Markers

Better methods to determine who will get sick and who will not are certainly needed for those chronically infected with viral hepatitis. HBF sponsored scientists, in collaboration with **W. Thomas London, MD**, HBF board member and senior scientist at Fox Chase Cancer Center, have been

developing proteomic and genetic (DNA) tests for discovery of early detection markers of cancer and liver disease in HBV infected people.

To date, HBF sponsored research by TJU faculty at The Jefferson Center have found the following: **Ying Su, PhD**, has found that human urine can be used as a source of "cancer" DNA. Thus, it may be possible to develop a test that uses urine for monitoring liver disease. In addition, Dr. Mehta and **Laura Steel, PhD**, and **MaryAnne Communale, MS**, have used proteomics (the comprehensive and electronically-assisted analysis of protein profiles) to help identify several proteins that appear in the blood of HBV carriers that may be useful in predicting the onset of disease.

The early detection work is preliminary, but shows that the genetic and proteomic approaches are feasible. The hope is that simple urine or blood-based tests will be developed to help a doctor predict who may need intervention and identify the onset of disease in HBV carriers early enough for treatment to be successful.

FDA Approves Adefovir for Chronic Hepatitis B

The Food and Drug Administration (FDA) announced September 20, 2002, the approval of adefovir dipivoxil tablets (marketed as "Hepsera") for the treatment of chronic hepatitis B in adults with evidence of active viral replication and either elevations in serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST), or histologically active disease. Hepsera slows the progression of chronic hepatitis B by interfering with viral replication and causing DNA chain termination after its incorporation into viral DNA.

FDA based its approval of Hepsera on the results of two randomized, double-blind, placebo-controlled studies. A statistically significant improvement in the degree of liver fibrosis (scarring) was observed in the patients who received Hepsera. Moreover, Hepsera has been shown to be effective in treating patients with clinical evidence of HBV that is resistant to another approved antiviral therapy called lamivudine.

The major adverse events associated with the use of Hepsera include severe, acute exacerbation of hepatitis B after discontinuation of Hepsera and kidney toxicity. The labeling for Hepsera states that patients who discontinue Hepsera should be monitored at repeated intervals over a period of time for hepatic function. Kidney toxicity was reported in patients at risk of or having underlying kidney dysfunction.

In addition, HIV testing prior to initiating Hepsera therapy should be offered to all patients to avoid the potential risk that HIV resistance could emerge in chronic hepatitis B patients with unrecognized or untreated HIV infection. (Reprinted from *FDA Talk Paper*, Sept. 20, 2002, www.fda.gov)

HBF Drug Watch

Compounds in Development For Chronic Hepatitis B

Update October 2002

Links to the pharmaceutical companies are provided for your information only and are not intended as an endorsement for the therapies or the manufacturers listed below.

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
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
REVISED 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	Triangle, RTP, NC	www.tripharm.com	Phase III
DAPD (DXG)	Inhibits viral DNA polymerase	Triangle	www.tripharm.com	Phase II
L-FMAU (Clevudine)	Inhibits viral DNA polymerase	Triangle	www.tripharm.com	Phase II
REVISED AM365	Inhibits viral DNA polymerase	Amrad, Victoria, Australia	www.amrad.com.au	Stopped July 2002
LdT (Telbivudine)	Inhibits viral DNA polymerase	Idenix, Cambridge, MA	www.idenix.com	Phase III
REVISED monoval LdC (Valtorcitabine)	Inhibits viral DNA polymerase	Idenix	www.idenix.com	Phase II
ACH-126,443 (L-Fd4C)	Inhibits viral DNA polymerase	Achillion New Haven, CT	www.achillion.com	Phase II (Central & Eastern Europe)
MCC478	Nucleoside analog "prodrug"	Eli Lilly, Indianapolis, IN	www.lilly.com	Phase I, Germany
Racivir (RCV)	Inhibits viral DNA polymerase	Pharmasset, Tucker, GA	www.pharmasset.com	IND Filed, May 2002
Fluoro-L and D nucleosides	Inhibits viral DNA polymerase	Pharmasset	www.pharmasset.com	Preclinical
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	Human monoclonal antibodies	XTL Biopharm, Rehovot, Israel	www.xtlbio.com	Phase II, Israel & U.S.A.
Imino-Sugars (Nonyl-DNJ) *Discovered by HBF scientists	Protein folding inhibitor	Synergy, Edison, NJ	Tel: 732-302-1111	Preclinical
HepBzyme	Nuclease resistant ribozyme	Ribozyme, Boulder, Co	www.rpi.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.enzo.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
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

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

Drug Watch Correction

"Valtorcitabine", a new drug in development for HBV was incorrectly spelled in the summer 2002 Drug Watch. The manufacturer of this drug is Idenix Pharmaceuticals (formerly Novirio) located in Cambridge, MA.

LdT (Telbivudine) Moves Into Phase III Trials

In a phase II clinical trial, LdT has shown marked viral suppression after 6 months of therapy in adult patients with chronic hepatitis B. Interim results of this study will be presented at the AASLD annual meeting in Boston, November 1-5, 2002. Idenix is now sponsoring a phase III clinical trial of LdT, in which LdT will be compared with lamivudine over a treatment period of two years. [Idenix 9/25/02, www.idenix.com]

Amrad Ceases Development of AM365 for Hepatitis B

Amrad announced in July 2002 the completion of a Phase IIa trial of AM365 that was well tolerated without side effects in chronic HBV patients and conducted at several hospital sites in Australia, New Zealand and Asia. "Amrad is committed to moving projects forward efficiently and cost-effectively", said managing director Dr. Sandra Webb, and "despite showing good antiviral activity in the gold-standard animal model and successfully completing Phase I trials in healthy volunteers, AM365 did not demonstrate sufficient antiviral activity in HBV-infected patients to warrant further development of this compound." [Amrad 7/11/02, www.amrad.com.au]

FDA Hearing: The Patient Element

Brett Grodeck

I'm sitting in a meeting - actually the FDA hearing on adefovir held this past August - where I'm serving on a panel as the patient representative to speak on behalf of people with chronic hepatitis B. This particular panel of the FDA's Antiviral Drugs Advisory Committee is composed of 17 doctors and me. I'm hardly a medical expert, just a regular guy with chronic HBV. However, I am expected to make comment for public record.

The other attendees at the meeting are liver specialists, researchers, Gilead executives, and people from the FDA. We're all at this hearing to discuss whether the drug adefovir is safe and effective for treating chronic hepatitis B.

The FDA invited me to serve on this advisory panel because I spoke at a similar FDA meeting a few months earlier. Having tracked the clinical trials of the drug for several years, I was already quite familiar with adefovir. In terms of potency, the drug was a slam-dunk since the committee basically all agreed that adefovir works - what surfaced were questions about its safety.



Brett Grodeck is a writer in Santa Monica, CA

Continued on Page 12

HBF Participates in FDA Hearings on Adefovir (August 2002)

Timothy Block, PhD, HBF president, and W. Thomas London, MD, HBF board member and chief medical advisor, were invited by the FDA to serve as expert consultants for the FDA Antiviral Drugs Advisory Committee for the two-day hearing on adefovir dipivoxil, August 6 - 7, 2002. The 10 member advisory committee and panel of experts met in Bethesda, MD, to discuss the new drug application of adefovir, manufactured by Gilead Sciences. On the second day, the committee discussed future clinical trial design issues in the treatment of chronic hepatitis B.

The hearing included presentations from Gilead Sciences and the FDA, followed by committee discussions on the safety, efficacy and risk/benefit profile of adefovir. In addition, there were public sessions where individuals had the opportunity to speak directly to the committee. Several patients told moving stories about their lifesaving experiences with adefovir, including Lee C., a liver transplant recipient from Florida, who had also shared his story at the HBF's summer patient conference. Molli Conti, HBF associate director, and Joan Block, RN, HBF co-founder, attended the hearing as well.

Although the FDA Advisory Panel unanimously voted to recommend adefovir for the treatment of chronic HBV, there was vigorous discussion about adefovir's uncertain long-term renal toxicity and adverse effect on liver enzymes when the drug was stopped (25% of patients developed serious liver enzyme elevations when taken off the drug). The fact that data was limited to 48 weeks also raised questions: What will happen to patients after 48 weeks? When can patients be safely taken off the drug?

The pivotal issues in any drug review are safety and effectiveness, and benefit vs. risk. The data must show that the drug works for its intended use and that it is safe. Although no drug is considered absolutely safe (there is always some risk), the FDA considers a drug safe enough to approve when a proposed drug's benefits outweigh known risk.

Adefovir will be marketed as "Hepsera" in the U.S. and abroad. In anticipation of FDA approval, Gilead and GlaxoSmithKline (GSK) signed a licensing agreement in April 2002 for the rights to commercialize Hepsera. Under the agreement, Gilead will retain rights to Hepsera in the United States, Canada, Eastern and Western Europe, Australia and New Zealand. GSK will receive exclusive rights to Hepsera for all countries outside of the Gilead territories, the most significant of which include China, Korea, Japan and Taiwan.

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
GenHevac 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 Iselin, NJ	www.btgc.com	Market, Israel
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
Hexavac (Pediatric)	HBV, DTP, HiB, Polio	Aventis Pasteur	www.aventispasteur.com	Market, Europe
Hepatitis Vaccines In Development				
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

HBV Vaccine Marks 20th Anniversary (1982 - 2002)

This year marks the 20th anniversary of the world's first anti-cancer vaccine, the hepatitis B vaccine. The Centers for Disease Control and Prevention (CDC) issued a special report regarding the progress made in eliminating hepatitis B and the future challenges that lie ahead.

Since 1982, 40 million infants and 20 million adults in the U.S. have received the HBV vaccine. Transmission has declined from 200,000 - 300,000 new infections each year, to only 79,000 new infections in 2001. This decline is due in large part to universal vaccination recommendations published by the Advisory Committee on Immunization Practices (ACIP) in 1991. Before these recommendations, the strategy was to vaccinate only high-risk adults, such as IV drug users and men having sex with men.

Following the introduction of the ACIP recommendations, overall HBV immunization coverage rose to 90% by the year 2000. The coverage rates of adolescents were boosted from near zero in 1993 to 67% in 2000. With the help of school entry laws, acute cases of hepatitis B in children ages 1 to 9 years old has dropped more than 80%.

The rate among health care workers fell 95% between 1983 and 1995. In addition, the recommendation to screen all pregnant women for hepatitis B helped to reduce mother-to-child transmission by over 75%.

With all of the strides made over the past 20 years, there have been some bumps in the road. Critics have suggested that the vaccine was linked with neurologic disorders (such as MS) and that the preservative, thimerosal, used in the vaccine could exceed safe mercury exposure levels for children (it was removed from the vaccine last year). The National Academy of Sciences' Institute of Medicine recently issued a report stating there was no evidence that the vaccine could lead to neurologic damage and reaffirmed the safety of the hepatitis B vaccine.

In marking the public health achievements of the HBV vaccine, the CDC concluded its special report with three main challenges that lie ahead in the battle to eliminate hepatitis B: 1) maintaining a high screening rate of pregnant women, 2) ensuring vaccination for all infants, and 3) immunizing high-risk adults. [CDC, MMWR 6/28/02]



Hepatitis B Around the World

Hepatitis B in India

Sharat C. Misra, MD, DM, FACG

Talwar Medical Center, New Delhi, India

Dr. Sharat Misra was the keynote speaker of the Hepatitis B Foundation's "B Informed 2002" conference this past June (see page 9). He is a Fellow of the American College of



Dr. Misra (left) with Steve Bingham and Sheree Martin at "B Informed 2002".

Gastroenterology and has a thriving private practice as a gastroenterologist and hepatologist in India. The dialogue that was started in response to his excellent presentation on the differences between

hepatitis B in the east and west at the patient conference is continued here with more answers from Dr. Misra.

1. How many people are estimated to live with chronic HBV in India? India has the largest number of chronic hepatitis B infections after China. There are more than 40 million people infected with hepatitis B, of which 4 million have chronic liver disease. Hepatitis B is the 5th most frequent cause of death in India for those who are 15-45 years.

2. Why is HBV so prevalent in India? There are four major reasons: (a) lack of public awareness of hepatitis B, (b) no measures for national control of hepatitis B, (c) inadequate control of the blood supply (i.e. tainted blood transfusions and blood products), and (d) lethargic vaccine programs.

3. Are there universal infant HBV vaccination requirements? HBV vaccination has now been incorporated into the EPI (expanded programme of immunisation) in Delhi and in another 9-10 states (out of 29 states). These newborns receive free HBV vaccine at birth along with other vaccines. This is still not implemented all over India because of the cost involved. Currently, an estimated 15-20% of newborns are being vaccinated through EPI. Another 20% are probably vaccinated by their doctors.

4. To what extent is the medical community in India screening for HBV?

Screening specifically for HBV is usually done for the following conditions: major surgery, blood donation, pregnancy, blood and blood product transfusions. Otherwise, there is no screening being done. Most chronic hepatitis B is detected by default: routine health check ups, at the time of surgery, blood donors. Otherwise, only patients with suspected liver disease are referred to gastroenterologists for further investigation. There are not many qualified gastroenterologists in India, probably not more than 1,500 (in a population of one billion). However, many do practice as liver specialists even without a qualification. Since medical investigations are expensive, not all doctors may be ordering all of the needed tests or treating patients appropriately.

5. Speaking of treatments, what is available in India and approximately how much does it cost? The drugs available to us for treating chronic HBV are interferon (approx. \$50/week), lamivudine (\$5/week), thymosin (\$300/week) and an herbal drug called phyllanthus. Liver tonics are also quite popular and inexpensive. Most people resist treatment but more are now accepting it. Unfortunately, there continues to be a lack of knowledge about hepatitis B in the general public and also among the medical community, which hampers in screening, vaccinating and treating hepatitis B.

HEPATITIS B	INDIA	U.S.A.
No. of chronic carriers	40 - 45 million	1.25 million
Primary age of infection	infant/child	adult
Primary mode of transmission	mother to infant (vertical)	sexual (horizontal)
Type of hepatitis B virus	precore mutant (HBeAg-) and wild type	wild type ("normal" virus)
Prevalence of e-antigen (among chronic HBV patients)	24% HBeAg+	68% HBeAg+
Incidence of liver cancer	high (184,000/year)	low

Dr. Sharat Misra's References:

- Hepatitis B in India - Problems & Prevention. Sarin SK, Singal AK, Editors. New Delhi: CBS Publishers (1996).
- Proceedings of the 2nd National Single Theme Symposium on Hepatitis B Infection in India. Indian J. Gastroenterology 2000;19 (suppl. 3).
- Profile, Spectrum and Significance of HBV Genotypes in Chronic Liver Disease Patients in the Indian Subcontinent. Thakur V, Guptan RC, Kazim SN, Malhotra V, Sarin SK. J. Gastroenterol Hepatol 2002; Feb. 17;165-70.

Foundation at the Forefront

"Vietnamese Language Chapter" Launched On HBF Website

A Vietnamese "language chapter" is now available on the HBF website at www.hepb.org/v. The website also includes Chinese and Korean language chapters. This information is provided to reach out to those in high-risk ethnic communities. An English version of each chapter is available as well as PDF versions of all chapters for easy printing. "At less than 40 pages in length, these chapters are more than a brochure and less than a book, touching on many important points about hepatitis B in a single document that can be read in a single sitting."

HBF Provides Expert Testimony in Support of HBV Vaccine Bill

On August 5, 2002, New Jersey Governor McGreevey signed Assembly Bill 1888 into law. The statute requires that beginning in September 2003, all 444,000 high school students in NJ, grades 9-12th, are required to be immunized against hepatitis B. An HBV immunization requirement for college students will be effective September 2008. This past spring, **Molli Conti**, HBF associate director, and **Joan Block**, co-founder, provided expert testimony before the NJ Assembly and Senate in support of hepatitis B prevention, as legislators considered this important public health initiative.

HBF Welcomes New Board Members!

Mr. Stanley Broadbent is a senior vice-president and director of sales for The Glenmede Trust in Philadelphia, PA, which is a wealth management firm providing services to 1400 clients in 46 states. He joined Glenmede in 1991 with 30 years of diversified experience in the financial services field. Mr. Broadbent has already been a generous contributor to the HBF as both a donor and valued advisor to the Planning and Development Committee. His experience in the senior management of Glenmede will provide important financial, marketing, and networking resources to the HBF. **Ms. Patricia David, Esq.**, has been a practicing attorney for the past 12 years, specializing in the financial and estate planning field. In 2001, she joined the law firm of Souder, Rosenberger, et al, located in Souderton, PA. Her professional background also includes having served as vice-president of human resources at The Travelers Co., and establishing her own business. Ms. David's entrepreneurial experience and knowledge of estate/trust/planned giving and new business development will be a valuable asset to the HBF.

HBF Summer Internship Program Sparks Students' Research Interest

Each year the HBF offers summer internships to college juniors and seniors to spark their interest in research. This past summer, the HBF sponsored eight students. During the ten-week program, students learn valuable research skills in

the HBF labs at The Jefferson Center of Thomas Jefferson University. In addition, the HBF seeks to raise the students' awareness about the importance of hepatitis B and how research can bring hope to those who are affected by this chronic disease. Senior faculty scientists at The Jefferson Center supervise the students and design research projects that will contribute to advancing the work in viral hepatitis. For more information about this exciting summer program in Doylestown, PA, please contact the HBF at info@hepb.org or call 215-489-4900.

"Fore" a Good Cause! Joseph Nagy Golf Tournament Benefits the HBF

Each year, the Drake and Nagy families generously host the Joseph Nagy Golf Tournament, which raises funds for the HBF. The 3rd annual golf outing, which was held on July 12th at the Bunker Hill golf course in Princeton, NJ, had the greatest turnout ever. This year, there were 95 golfers at tee off (an increase from 75 golfers last year) and a total of \$3,200 was raised, which included a \$1,000 matching gift from **MetLife Insurance**.



Kevin Drake (right) at the Nagy golf tournament.

The first-place prize went to a local Doylestown, PA, foursome Keith Armstrong, Rich Cherichello, Thaddeus Budzinski and Mike Colangelo. New Hope attorney Al Ceparrulo hosted a foursome that included **Joe and Molli Conti**, and Paul Cohen and they came in an honorable 4th place. HBF board member **Bob Goldberg** also polished up his clubs and sponsored a foursome.

The Nagy family established the annual Joseph Nagy Golf Tournament in memory of a wonderful husband, father, and grandfather who passed away due to complications from a hepatitis B infection acquired through a tainted blood transfusion. The HBF extends sincere thanks to son-in-law **Kevin Drake** and the entire **Nagy family** for planning another successful golf benefit. We truly appreciate their hard work and commitment on behalf of the HBF and are looking forward to next year's golfing event!

Fast Fact

More than one billion doses of the hepatitis B vaccine have been given worldwide.

The Best of "B Informed 2002" Patient Conference in Review

Pam Ladds, CQSW, SRN, HV Cert.



Pam Ladds is a psychotherapist, writer, and health activist.

"B Informed 2002" was a wonderfully unique conference. The schedule was designed to maximize learning and to respect our need for frequent breaks, but as usual, the cry was that we didn't have enough time for everything. All sessions ran well beyond their allotted time and discussions continued into the breaks, the cafeteria, dorm rooms, and sleeping hours!

DAY ONE

On the first day, we gathered for breakfast to exchange hugs with those we hadn't seen since last year and put faces with screen names of the new folks. Ed demonstrated Tai Chi with grace and then guided the rest of us, wobbling precariously, through some of the basic movements before the sessions started.

Drug Watch of New HBV Compounds - Tim Block, PhD, C. Satishchandran, PhD, Cathy Pachuk, PhD, and Tom London, MD

Virology is a foreign language for most of us, so any session that can demystify the hepatitis B virus (HBV) is very popular with non-scientist attendees! Discussion focused initially on the two main treatment strategies - targeting the virus or targeting the host. Targeting the virus is the approach that is most usually discussed, and it involves looking at the structure of the virus for "windows of opportunity" to interrupt the cycle of replication. Most of the drugs currently in use attempt to interfere with the DNA/RNA switch, one of several points of entry. The downside of this approach is that a virus is hard-wired for survival and that interruption of its cycle eventually leads to mutation.

The other approach focuses on targeting the host, the person living with hepatitis B. It attempts to get the body's own defenses to do the right thing. Approaches so far have involved stimulating the immune system with interferon to encourage natural recovery. The nature of our immune response means that there is always some damage to the liver cells as our own body attempts to deal with the invading virus. Therefore, it is always a balancing act. The challenge for vaccine therapies of the future will be to boost the immune system enough to clear the virus without causing further damage or liver failure. Interferon treatment has shown just how delicate this balance is.

Other strategies such as working on the cell itself instead of the RNA/DNA switch and vaccine/antiviral combinations were also discussed. We learned about future techniques including "smart particles", gene silencing techniques that

could prevent mutation and DNA vaccines that had a great response in animals but have been unsuccessful so far in humans.

HBV and Civil Rights - Amanda Maisels, Esq, U.S. Dept. of Justice

This was an animated discussion on the rights of those living with HBV and how the Americans with Disabilities Act (ADA) applies. The good news is that this Act exists; the bad news is that its application will be litigated forever! Although in theory HBV fits into the scope and intention of the ADA, this is a relatively new piece of legislation and still has to be "test driven" to find out what fits and what doesn't. Reasonable accommodation, confidentiality, who has the right or need to know, and employment concerns in general were all covered. There was particular interest from the group about children with HBV, confidentiality and disclosure issues, and liability concerns. However, one size does not fit all and definitive answers were not possible. This area is really challenging. Many of the same questions are currently being asked and litigated in the HIV arena.

Four Mothers' Stories - Maureen, Christine, Melinda, and Bambi

The title for this session should probably be changed to "four mothers and one son" since Melinda's 19 year-old son, Travis, was co-opted to the panel at the last minute and spoke eloquently about his experience living with hepatitis, secondary to hemophilia, and the implications both diseases have on his daily life. This workshop was fascinating and raised many issues including disclosure, sexual activity and liability, the pros and cons of "poster" children, disease progression and treatment options for children. In the future, more time is certainly needed for parents' concerns.

Chronic Hepatitis B: East Meets West - Sharat Misra MD, DM, FACG

The keynote presenter, Dr. Sharat Misra traveled from New Delhi, India, for this conference. He is an internationally known HBV expert and active participant on the HB-List. Although it is easy to assume that a viral disease is treated and prevented in the same way throughout the world, Dr. Misra's informative presentation clarified that recognizing the differences in viral type, age of infection, and ethnicity is vital. *He has made his entire talk, with slides, available on his website at http://in.geocities.com/gihepworld/ch_hep_b.htm (see page 7, "A Conversation with Dr. Misra" for more information).*

DAY TWO

All participants were raring to go the second day. There was some complaining about sleep deprivation, but that was only because no one had wanted to go to bed the night before! After breakfast, lots of caffeine and a few stretching exercises, it was back to the meeting.

Continued on Page 10

HBV Variations, Mutations and Co-Infection - Tim Block, PhD and Ken Rothstein, MD

HB-List discussions frequently focus on these issues. Members wonder what is better or worse, to be a precore mutant, to seroconvert the e-antigen, to know the meaning of a flare and other imponderables. Although most attendees knew that the risk of developing liver cancer was greater for HBeAg(+) carriers, it was a surprise to learn that the "gold standard" of seroconversion to HBeAg(-) did not mean all troubles were over! Yes, it is the indicator of current treatment efficacy to convert the e-antigen from positive to negative, and it does mean that viral load drops. Serious liver disease complications may also be less frequent in those who have seroconverted, but the risk is still present and there are fewer treatment options. A conclusion of this session was that cancer screening every six months by ultrasound and blood test (AFP levels) is very important, even for those who have seroconverted to HBeAg(-).



Clinical Treatment Updates - Gilead and Bristol-Myers Squibb (Drs. Tim Block and Ken Rothstein moderated)

Session 1: Gilead Sciences - Jonathan Zalk

Adefovir has been out for a while, initially in the HIV community, where it has been associated with serious kidney damage at high doses. Those with HBV taking a lower dose of adefovir (10 mg compared with doses of up to 120 mg for HIV) do not appear to have kidney problems, according to Gilead. They claimed that their studies were across the board, meaning there were clinical trials on every HBV permutation, and that adefovir's efficacy was comparable with "other first line drugs". [The FDA approved adefovir (Hepsera) for HBV Sept. 20, 2002]

Tenofovir (aka Viread), is another Gilead drug that is a close relative of adefovir with apparently less (not none) kidney toxicity. It is currently being marketed as an HIV "salvage" drug, although it also appears to be active against HBV. Since tenofovir is an FDA approved drug with anti-HBV activity and has no history of kidney toxicity, it is unclear why Gilead didn't develop it for HBV? Despite clinical trials in progress for people co-infected with HIV and HBV, Gilead states that tenofovir will not be developed for HBV.

Session 2: Bristol-Myers Squibb - Bruce Kreter, MD

Entecavir is in development by Bristol-Myers Squibb and is currently in phase 3 clinical trials. They are gearing this drug for the accelerated FDA approval track based on "need" and early trial information, which has the advantage of making medications available sooner for those who need them; the downside is that it is impossible to know all the side effects and longer term risks. The phase 3 study, we

were assured, is worldwide and inclusive of all populations. We were also assured that entecavir has a high safety rating and that it has the advantage of getting into the cccDNA of the hepatitis B virus, an essential component of the viral life cycle.

Immunization Issues - Patrick Fineis, HBV Case Manager, Michigan Department of Community Health

We were reminded that sticking to the vaccine schedule is important and that those particularly at risk should check antibody levels after the complete series is given. Parents raised the issue of how to handle HBV vaccine requirements without disclosing their children have HBV. Disclosure is a very complicated, emotionally charged topic and the only agreement is that there is no correct answer! Vaccine therapy is a potential new treatment approach for

HBV and although it is considered experimental, it is attracting interest.

Personal Transplant Stories - Christopher and Lee

Christopher had attended last year's B Informed conference, four months before his liver transplant. The difference in his appearance and energy was amazing. Lee, seven years post-liver transplant, and living a full life, was inspirational as well. Transplantation as a topic at a patient conference is controversial. Is it failure? Is it too heavy a topic for attendees? The group clearly found this issue of great interest. Both Christopher and Lee talked about living as the steward of a "previously owned" organ and their candor was refreshing.

Conclusion

The conference finale was a presentation from Will Green, author of "The First Year: Hepatitis B". Will had attended last year's conference, which coincided with the beginning of his book; so many of us were eager to have our copies signed. He shared what he learned about himself in the process of writing his story, which was a wonderful way to end the conference.

After adjourning for one last meal (we fed our bodies and minds equally), some of us left reluctantly to go back to our homes. Others stayed another day for a relaxing trip on the Delaware River. All of us are certainly planning to attend next year's conference!

"I hope that like me, those who attended will also have come away with more hope, more determination, and above all a sense that I felt, more love and compassion than we may have felt before we met."

In The Spotlight



The Asian Liver Center at Stanford University is the only non-profit organization in the United States dedicated to addressing the high incidence of hepatitis B and liver cancer in Asians and Asian-Americans. It was founded in 1996 by **Samuel So, MD, FACS**, associate professor of surgery at Stanford, who serves as director of the Center. Dr. So is a tireless advocate for hepatitis B education and research who has also been a long-time supporter of the Hepatitis B Foundation. It is a privilege to spotlight this excellent organization and the HBF looks forward to working together on future projects to meet the needs of the Asian community, here in the U.S. and abroad.

According to the Asian Liver Center, liver cancer is the most common malignant cancer and the main cause of cancer-related deaths in Asia. Approximately 200 million people in Asia are chronic carriers of HBV. In the U.S., Asian-Americans comprise over half of the total of 1.25 million chronic HBV carriers. The greatest health disparity between Asian-Americans and Caucasians is liver cancer (80% of liver cancer in Asian-Americans is caused by chronic hepatitis B virus infection). Liver cancer rates among males are 13 times higher in Vietnamese-Americans, 8 times higher in Korean-Americans, and 6 times higher in Chinese-Americans than Caucasian-Americans.

To help address this serious health problem, the Asian Liver Center spearheads education outreach and advocacy efforts in the area of hepatitis B and liver cancer prevention and treatment; serves as a resource for the general public and health practitioners; and implements clinical trials and basic science research programs for liver disease through its clinic facilities.

In addition, the Center has launched the national **Jade Ribbon Campaign** in the San Francisco Bay Area in May 2001. The objective of the campaign is to increase awareness and provide ethnic-sensitive health information to the Asian community and health professionals in an effort to reduce hepatitis B and liver cancer. It is a multi-media campaign that includes television public service announcements, radio shows, bus ads, lectures in the community, and more.

The Jade Ribbon was selected as the emblem of the campaign because jade is considered by Asians to be the essence of heaven and earth. In many Asian cultures, it is believed to bring good luck and longevity while deflecting negativity. The Jade Ribbon is also symbolic of the spirit of the campaign in bringing people in the Asian community together to help each other eliminate this liver disease. Ribbons can be ordered directly from the Asian Liver Center.

Asian Liver Center at Stanford University
Tel: (650) 72-LIVER or (650) 725-4837
<http://liver.stanford.edu>

New Books About Hepatitis B

Understanding Hepatitis

James L. Achord, MD
University Press of Mississippi
Available Directly from the Publisher!

Hepatitis has many causes, including viruses, a host of chemicals and drugs, bacteria, diseases of the immune system, inherited factors, and herbs. For more information, visit www.upress.state.ms.us or call 1-800-737-7788.

Hepatitis B: The Quiet Killer

Robert Peshek, DDS
International Foundation for Nutrition and Health
Available Directly from the Publisher!

Dr. Peshek writes about his personal experience with hepatitis B and his journey to France where he was treated with an experimental HBV DNA vaccine. He writes extensively about nutrition and hepatitis B. For more information, visit the International Foundation for Nutrition and Health at <http://www.ifnh.org/hepatitis.html> or call 858-488-8932.

Visit the HBF Bookstore at www.hepb.org this Holiday Season!

Be sure to stock up on copies for yourself, family, friends and your favorite doctors and nurses this holiday season.

Remember, making a donation to the Hepatitis B Foundation is as easy as ordering a book. For every book that you purchase, half of the cover price is a direct donation to us! Thank you.

First Year: Hepatitis B

William F. Green
Paperback Available NOW! (\$20, includes S/H)



Drawing upon his own personal experience of living with chronic hepatitis B, Will Green provides insight for both the newly diagnosed and the experienced veteran.

Living with Hepatitis B: A Survivor's Guide

Gregory T. Everson, MD, and Hedy Weinberg
Paperback Available NOW! (\$20, includes S/H)



This patient guide walks readers through the process of diagnosis, ongoing care and treatment. Hedy Weinberg offers practical advice about living with a chronic disease.

Hepatitis B: The Hunt for a Killer Virus

Baruch S. Blumberg, MD, PhD
Hardcover Available Now! (\$32, includes S/H)



This scientific memoir is a fascinating chronicle of Dr. Blumberg's discovery of the hepatitis B virus and the vaccine against it, which was one of the great triumphs of 20th century medicine.

Speaking Personally

Steve Bingham & Sheree Martin
Co-Owners of the Internet Hepatitis B
Information and Support List (HB-L)

More Friends, More Knowledge Gives Patients More Power



"B Informed" is the name of this top-notch newsletter, and "B Informed" is also the name of the annual gathering of friends sponsored jointly by the HBF and HB-List. It's ironic how so many people can be brought together in a positive way by such a crummy disease as hepatitis B (Steve).

I didn't think it was possible, but this year's B Informed conference was just as good as last year's!" I heard this several times, from folks who attended our first conference and again this year (Sheree).

The interesting thing about an online support group is that you become good friends with people you've never met. So, imagine how it feels to meet for the first time dozens of your best friends all at once! That's what happened to me at B Informed 2002.

These were my very thoughts too! Meeting people face to face whom you've communicated with for years, and become dear friends, is a wonderful and fun experience.

In planning the program, we found that we had so many capable "experts" among our own list members to call upon - each one of you has expertise and stories to share. There was lots of audience participation during the presentations, and I think the experts were impressed with the depth of our knowledge. I think we even stopped the doctors and pharmaceutical reps in their tracks a few times.

The folks from our support list are a "rare breed" indeed. I'm so proud of them! They are very knowledgeable about HBV, eager to learn everything that they can. We all share a common bond; we are either infected with hepatitis B, or someone we know and love is infected. As a result, we're a caring and close-knit group, even though many of us just met for the very first time this summer. We've supported each other for years, and finally being able to see each other, and give them a real hug, was just more than I can describe!

Some of the best memories come from outside the "sessions" as people get to know one another and make lasting friendships. We even had at least two participants acknowledge their hepatitis B for the first time - this was one place where we didn't have to worry about people "finding out".

Together, we've battled this disease for four years, and now we have an annual gathering place where we can finally share our stories in person. The happiness of meeting and sharing our joys and sorrows for an entire weekend, accented with up-to-date information, was a winning combination.

I, for one, had a great time at B Informed 2002. When I think back to the conference, my first thoughts are about the smiling faces. For a few days this summer, we were all able to forget our problems and get together to laugh, learn, and participate in a true gathering of friends.

We are forever in debt to the HBF for their unwavering support of us and their commitment to research. I'm no sooner back home, than my mind is thinking about next year... more friends, more knowledge, which is power for a patient. Who knows, together we may even be able to help move the scientists closer to a cure!

Best Wishes and Hugs, Steve & Sheree

FDA Hearing: The Patient Element
Brett Grodeck continued from page 5

At the meeting, the doctors focused on kidney issues, which certainly merits discussion. What mattered to me, as a patient, was not so much the potential for kidney problems, which are preventable; what unnerved me was what can happen when the drug is stopped. According to the data, about one in four patients experienced an ALT flare five to ten times normal. This flare can occur with any drug for HBV; it's not limited to adefovir. Still, having experienced a flare of the same magnitude just months earlier, I was concerned because my life was not fun during the three or four months this carried on.

Despite my initial reluctance to say anything, I figured my fear of public speaking was less important than calling attention to this potential adverse effect. I spoke up. At first, I felt like I made no sense, but the other panelists listened. In fact, it sparked a good deal of discussion. Although the meeting ended with a unanimous vote in favor of recommending the drug for approval, I later learned that the FDA takes committee discussions into serious consideration before they make a final decision.

Thus, I believe I had an impact on the process, that my comments during the hearing were important to the FDA. Sometimes I hear people complain about pharmaceutical companies or the FDA, saying the "patient element" has been lost amongst the bureaucratic medical industry. I don't agree. For people willing to speak up, I believe the role of the patient in health care is becoming more important every day.

Hepatitis B Clinical Trials

Hepatitis B Foundation Clinical Trials Watch
www.hepb.org/clinicalinfo.html

National Institutes of Health Clinical Trials
www.clinicaltrials.gov

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

NEW 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. This trial will be conducted at over 100 sites in North America, Asia, Europe, Australia, and New Zealand. Patients must be adults with chronic hepatitis B who have never have been treated with lamivudine or other nucleoside or nucleotide analogues. Patients will be randomized to receive either LdT or lamivudine for 2 years, and neither the patient nor the doctor will know which treatment the patient has received until the end of the study. *Contact: Barbara Fielman at 617-250-3100.*

NEW 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. U.S. studies are being conducted in Philadelphia, PA and Chicago, IL. Additional countries include 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 periodically for up to 5 years for survival and incidence of HBV-related complications. *Contact: HBF at info@hepb.org or call 215-489-4900.*

Phase II Comparison of Treatments of Co-Infected HIV/HBV Subjects

The purpose of this study is to find out if adding adefovir (ADV) or tenofovir (TDF) with lamivudine (3TC) has an effect on HBV infection, and to study the tolerability and safety of the drugs. The National Institute of Allergy and Infectious Diseases (NIAID) is sponsoring this study at 11 sites across the country. *Contact: NIH Patient Recruitment and Public Liaison Office at: 1-800-411-1222 or e-mail at prpl@mail.cc.nih.gov, or visit the HBF website at www.hepb.org for a complete listing of trial sites.*

NIH Sponsors Adefovir plus Lamivudine HBV Trials: With or Without HIV

Patients 18 years of age or older with active HBV despite treatment with lamivudine for at least 1 year may be eligible for this 48-week study. Patients with or without HIV infection may participate. *Contact: NIH Patient Recruitment and Public Liaison Office at: 1-800-411-1222 or prpl@mail.cc.nih.gov*

Open Enrollment for Phase II Trial Of ACH-126, 443 for Lamivudine-Resistant HBV

The purpose of this study is to evaluate the safety and antiviral activity of 3-dose levels of ACH-126, 443 over a twelve-week treatment of adults with lamivudine-resistant chronic HBV. Patients 18 years and older with chronic HBV longer than six months may be eligible to participate. Studies are being conducted in the U.S., Canada, and China. *Contact: John Pottage, MD, at: 203-624-7000 (jpottage@achillion.com)*

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).*

Columbia-Presbyterian Medical Center Adefovir Study

Comparison of adefovir dipivoxil to placebo for the treatment of adults with eAg+ chronic HBV. Those treated within 6 months or involved in an investigational drug trial two months prior to this study will be ineligible to participate. *Contact: Ms. Cabilia Gomez at 212-305-3839 (New York, NY).*



SPECIAL NOTICE!

Patient Assistance for Hepsera (adefovir dipivoxil)

Gilead has established a U.S. Patient Assistance Program for people who do not have insurance or cannot afford to pay for treatment with Hepsera.

For more information about the Patient Assistance Program in the U.S., call **1-800-GILEAD-5** or 1-650-574-3000

Fast Fact

On average, it costs a company \$802 million to get one new medicine from the laboratory to U.S. patients

Calendar of Events



- Oct. 29 - 31 Therapies for Viral Hepatitis**
International Medical Press
Boston, MA
www.intemedpress.com/hepatitis
- Nov. 1 - 5 Annual AASLD Meeting**
American Assoc. for the Study of Liver Diseases
Hynes Convention Center, Boston, MA
Contact: 703-299-9766 or jdeal@asld.org
www.aasld.org
- Nov. 7 - 8 Annual Princeton Workshop**
Hepatitis B Foundation
Nassau Inn, Princeton, NJ
- Nov. 8 - 9 Hepatitis Magazine Conference**
Houston Marriott North, Houston, TX
Contact: Barbara Veres at 1-800-792-6397
www.hepatitismag.com

YEAR 2003

- Jan. 27 - 30 National Hepatitis Coordinators Conference**
Centers for Disease Control and Prevention
Hyatt Regency, San Antonio, Texas
Contact: Valerie Curry at vcc0@cdc.gov
www.cdc.gov/hepatitis
- Mar. 17-20 37th Annual National Immunization Conference**
Centers for Disease Control and Prevention
Sheraton Chicago Hotel, Chicago, Illinois
www.cdc.gov/nip/nic
- March 29 - April 1 38th Annual European Association for the Study of the Liver (EASL)**
Istanbul, Turkey
Contact: easl2003@easl.ch
www.easl.ch/easl2003
- April 6 - 10 International Symposium on Viral Hepatitis and Liver Disease 2003**
Convention Centre, Sydney, Australia
Contact: isvhld@tourhosts.com.au
www.tourhosts.com.au/isvhld
- April 12 Annual Crystal Ball**
Hepatitis B Foundation
Doylestown Country Club, Doylestown, PA
Contact: info@hepb.org or 215-489-4900
- April 27 - May 1 International Conference on Antiviral Research**
International Society for Antiviral Research
Savannah Marriott, Savannah, GA
Contact: isar@courtesyassoc.com
www.isar-icar.com



Save this Date!

Saturday April 12, 2003

You're invited to the
Hepatitis B Foundation

Crystal Ball

*Please join us
for an elegant evening
of fine dining and dancing.*

*Doylestown Country Club
Doylestown, PA*



OLiver, the HBF liver mascot, joins in at the Liver Walk sponsored by the American Liver Foundation (Oct. 5, 2002).

Internet Support Groups



Hep B Information and Support List
<http://www.geocities.com/Heartland/Estates/9350/hblist.html> (case sensitive)

To subscribe, send a blank email to:
hepatitis-b-on@mail-list.com

Well-supervised list with useful information and lively exchanges between supportive members. For those with HBV, their caregivers, and anyone interested in or affected by HBV are invited to participate.

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 to protect the privacy of parents and children, and requires pre-approval by the list owner to join.

PKIDS Support List
<http://www.pkids.org/>
For adoptive and biological parents of children with chronic viral infectious diseases, including HBV, HCV, and HIV.

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 new Vietnamese, Chinese 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://liver.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 Branch

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:

http://archive.mail-list.com/hbv_research/

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

Hepatitis B Research Archive Website

http://archive.mail-list.com/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.

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

admin@immunize.org

Comprehensive resource of immunization information. "IAC Express" is a free email announcement service.

MEDLINE Plus 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.

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.


PKIDS Legislative Action Center Website

<http://capwiz.com/pkids/>

This website makes it easy to contact your legislators and keep current about the latest legislation online! Just enter your zipcode and you're on the way to the Capitol.



Nonprofit Organization
U.S. POSTAGE PAID
Permit No. 38
Doylestown, PA


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

Giving Hope to Millions Is As Easy As Giving...

... and we've Just Made It Easier!
Credit Card Donations Can Be Made On-Line.

The growing number of people seeking information and support each year continues to affirm the importance of the HBF's *Cause for A Cure* since we rely on the generosity of individual donations, we need your help to continue our work. Thank you!

Yes! I wish to join the *Cause for A Cure*. Enclosed is my tax deductible gift.

Name _____ \$40 Donor
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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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