

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.

Crystal Ball Celebration Returning to New Hope

"Returning to New Hope, home of the Hepatitis B Foundation, is a wonderful reminder of our beginning and a reflection of how much we have grown," enthused **Molli Conti**, vice president, during her welcome at the annual Crystal Ball. "The foundation was started to help one family and today, we all carry on the legacy of making a difference for thousands of families."

The Crystal Ball, held at Occasions in New Hope, PA on April 30, was an evening to remember! More than 175 distinguished guests sparkled; brilliant, soaring floral arrangements added glamour; and lively music kept people dancing until almost midnight.

"This is an exciting time for the Hepatitis B Foundation," reported **Dr. Timothy Block**, HBF president, in his opening statements. "We have made tremendous progress the past year towards expanding our research and increasing our outreach to those affected by hepatitis B." He also announced a major advocacy triumph of the HBF. The first *National Hepatitis B Awareness Week* was officially designated May 9-16, 2005 in a unique bi-partisan resolution passed by the U.S. Congress.

The HBF's *Distinguished Founders' Award* was presented to **Dr. Bill Stephenson**, vice provost for Research and dean for Graduate Policy, and **Drexel University** in recognition of their extraordinary commitment to the foundation. "Dr. Stephenson and his colleagues have transformed Drexel with their energy, vision and enterprise. We are fortunate they have brought these same qualities to the new partnership with HBF," said Block. "By partnering with a major research university, we will increase exponentially the

hope that a cure for hepatitis B will be found," he added.

In accepting his award, Dr. Stephenson expressed being overwhelmed and grateful to the HBF. "We have exciting plans for direct involvement with the foundation in its research efforts, arguably one of the best hepatitis B research programs in the world." He also spoke about his commitment to creating an atmosphere "where researchers can do what researchers do, unfettered by bureaucratic concerns."

Drexel is very research encouraging, Stephenson explained with enthusiasm, and requires a team effort. He invited **Ken Blank, Peggy Vigiolto, Donna Jones, Kate Donohue, and Jim Cavan** to the podium to accept the *Founders' Award* on behalf of the University.

This is "the group that makes things work," he said proudly.

The ceremony concluded with a moving personal story shared by **Joel Rosen**, HBF board member. He told of his family's experience with hepatitis B that motivated him to get involved with helping others and has a happy ending. He helped everyone at the gala realize that hepatitis B can strike anyone, and that the Hepatitis B Foundation continually works to bring new hope to thousands of families each year; one family at a time.



Dr. Bill Stephenson (right) receives award from Dr. Block.

**First National Hepatitis B
Awareness Week!**

May 9-16, 2005

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Message from the President

Timothy M. Block, Ph.D.

The Future of Nonprofits

Can we write the history of the 21st century nonprofit organization, today, in the first five years of the century? Thomas Friedman of The New York Times implies as much for political affairs. So perhaps it is possible.

We think the future of nonprofits is all about partnerships. The Hepatitis B Foundation has a history of making some important friends, and lately, we've been getting some big help.

After being launched from a store front office and small lab, with the help of Thomas Jefferson University (our first big partner) and under the leadership of its Dean, **Dr. Joe Gonnella**, we grew into a professional outreach and research organization.

In 2004, the HBF and Drexel University entered into an historic agreement in which HBF/IHVR and Drexel scientists and staff work together, greatly amplifying what we are able to accomplish. After just six months, the results of our partnership are already exceeding expectations and we are both thriving. This should make our goal of improving the quality of lives of those affected by hepatitis B, through research and outreach, attainable all the sooner.

This new partnership, which we believe represents an innovative model for nonprofits, was made possible by the vision of **Dr. Bill Stephenson**, vice provost, and other leaders from Drexel University such as its president **Constantine Papadakas**, provost **Ali Houshmond**, vice president **Jim Archibald**, and microbiology chair **Brian Wigdahl**. This is why the Hepatitis B Foundation is honoring Dr. Stephenson and Drexel University with our *Distinguished Founders' Award 2005*, which is given to individuals and/or organizations who have helped, in an extraordinary way, to advance our *Cause for a Cure*.

We expect to create some medical history with Drexel and make hepatitis B a thing of the past!



Dr. Stephenson (center) and Drexel leaders (to his left) receive awards from the Hepatitis B Foundation (to his right) on April 30, 2005.

In The News



Coffee Consumption Reduces Risk of Liver Cancer

Results of a study by Gelatti et al, published in the *Journal of Hepatology*, provide more evidence that drinking coffee can reduce the risk of hepatocellular carcinoma [HCC, or primary liver cancer]. Coffee consumption by the study group in the decade prior to the comprehensive survey was associated with a decreasing risk of HCC with a clear dose-effect relation. Compared with non-coffee drinkers, the relative risks were 0.8 for drinkers of 1-2 cups per day, 0.4 for those of 3-4 cups, and 0.3 for drinkers of five or more cups per day. More important, the study by Gelatti provides original information on the independent effect of coffee from the major recognized risk factors for primary liver cancer. The inverse relation with coffee, in fact, was of similar magnitude in subjects negative or positive for HBV or HCV...Coffee appears to have a real, but moderate effect in reducing the risk of HCC. *J. of Hepatology 42(4): 444-446; April 2005.*

Stepping Out of Line

Faced with a widening gap between supply and demand, people desperate for an organ transplant are increasingly turning to the Internet. There are almost 88,000 people in the U.S. on the waiting list for a transplant and on average, every 90 minutes someone dies waiting for a kidney, liver, lung or heart. MatchingDonors.com is the first commercial Web site pairing living organ donors and recipients. Critics charge the Web site encourages schemers to prey on the sick, and the sick to take cuts in line, bypassing a national waiting list. "Access to organ transplantation isn't meant to be a popularity contest," says Dr. Mark Fox, co-chairman of the ethics committee of UNOS. While bioethicists, doctors and patients debate whether medical maladies should read like the personals, pairings from MatchingDonors.com have resulted in six successful surgeries. Clients pay up to \$295 a month or nothing at all if they can't afford the fees. Dr. Richard Howard, president of the American Society of Transplant Surgeons, worries that billboards and Web sites give the physically attractive, the technologically adept, the financially flush, first dibs on an organ that another person may need more urgently. *St. Petersburg Times Floridian, April 17, 2005.*

Cancer Now the Leading Killer of Americans

Cancer has displaced heart disease as the leading killer of Americans under the age of 85 since 1999, according to a report in the *Cancer Journal for Clinicians*. It is estimated there will be 1.4 million new cases of cancer in the U.S. this year, and 570,280 deaths. Currently, one in four deaths in the U.S. is due to cancer, the annual report found. In American children between the ages of 1-14 years, cancer is the second leading cause of death (following accidents). Cancers linked to infectious diseases, many of which are preventable, were also highlighted. The report estimates that worldwide, 17 percent of new cancers will be attributable to infection...[such as] liver cancer caused by the hepatitis B and C viruses. *Cancer J. Clinicians 55:10-30; Jan/Feb 2005.*

More Antivirals Provide Choices, But Force Harder Decisions

In March, both patients and physicians cheered when the federal Food and Drug Administration approved the Bristol-Myers Squibb drug entecavir (Baraclude) as the latest addition to the anti-HBV drug arsenal.

Entecavir, the third oral "nucleoside analog" and the fourth approved drug overall promises to be the most powerful antiviral drug to date, with a lower rate of resistance and a more potent antiviral effect than the other two FDA-approved antivirals, lamivudine and adefovir. The drugs prevent HBV from making more copies of itself, reducing the amount of virus in the blood to extremely low levels.

"Having three oral drugs gives us so many options," said **Adrian Di Bisceglie, MD**, chief of Hepatology at the Saint Louis University School of Medicine. Less than a decade ago, interferon was the only game in town, he said.

"It's great news," said **Hie-Won Hann, MD**, professor of medicine at Jefferson Medical College of Thomas Jefferson University in Philadelphia. "Now, doctors don't have to depend on only one drug. We have several choices, and might be able to offer such medicines in combination or in sequence."

But at the same time, having so many choices complicates an increasingly difficult decision-making process. How do doctors and patients choose which drug to use, and when?

"No one is really sure how to best use the oral nucleoside analogs," said **Jenny Heathcote, MD**, professor of medicine at Toronto Western Hospital. "We have guidelines, but there's no consensus in treatment and there's not even a consensus on whom to treat. It's very complicated and we have and continue to make many mistakes with this kind of therapy."

One problem, Heathcote noted, is that no one knows which chronically infected individuals will develop cirrhosis and liver cancer. "We need to be able to assess how severe the liver inflammation and damage from the disease is and weigh the benefit of suppressing the virus with the likelihood of developing resistance."

"It's difficult to know when to start a medication, when to stop, when to add and we don't have enough information about the current drugs," said **Ray Schinazi, PhD**, professor of pediatrics at Emory University in Atlanta.

Many physicians prefer to use interferon, the fourth approved drug given by injection and thought to work by boosting the immune system. "For young patients without cirrhosis or contraindications to use of interferon, it is reasonable to try interferon first," said **Anna Lok, MD**, professor of internal medicine at the University of Michigan. "Oral medicine is great but once we start, very few patients can get off, and the benefits versus risks of committing young patients to life-long medication with risk of drug resistance, side effects and cost must be carefully weighed."

Interferon is effective in only about 30 percent to 40 percent of HBe-antigen positive patients, but the response is frequently long-lasting, even permanent, Lok added. Patients typically take it for 4 to 6 months, but it is expensive and has several side effects.

In contrast, antivirals work to some degree in nearly every individual, albeit not indefinitely. Some 15 to 20 percent of those taking lamivudine develop resistance in the first year, and 30 percent in the first two years. In three to four years, two-thirds are resistant. About 30 percent respond long-term. Adefovir is a little better: it works on lamivudine-resistant virus, with only 18 percent resistant after 4 years. But adefovir works slowly, and about a quarter of individuals have little virus suppression.

"Adefovir and entecavir, in my opinion, are now the drugs of choice," Di Bisceglie said. "Lamivudine resistance is just too great."

Perhaps. Yet, for many, lamivudine is the best choice because it is the least expensive of the three, said Dr. Hann. In Hann's case, many of her patients are Asian immigrants who own small businesses and lack health insurance. While the chance of developing resistance to lamivudine is a very real concern, she has to weigh this against the ability of her patients to pay for medication. Adefovir costs more than lamivudine, and now entecavir may cost 30 percent more than that.

Drugs in the pipeline

Schinazi, who created lamivudine and another antiviral used against HIV and in trials for HBV called FTC, is extremely bullish on the new agents in clinical trials. "Within the next decade, he said, one or more of the drugs still being tested, such as telbivudine or clevudine, will become the main HBV drug. We'll have better drugs, clinically better that reduce viral load quicker and further, cut liver enzymes and prevent liver fibrosis," he noted.

"We need controlled trials of combinations of drugs," said **Brent Korba, PhD**, professor of microbiology and immunology at Georgetown University. "As the data comes in, we'll have a better idea of what works and then eventually we'll have powerful combinations to offer patients."

Korba said the new group of drugs in clinical trials will be far superior to those on the market today. Telbivudine and clevudine are likely to make the discussion of other agents moot, he said. If these two drugs pan out, short-term therapy may be a real possibility.

Steve Benowitz, science writer in Philadelphia, PA

Entecavir Approved for Hepatitis B
On March 29, 2005, the FDA approved entecavir, which will be sold as Baraclude.

Visit www.baraclude.com

HBV Drug Watch *HBV Compounds in Development* Spring 2005

FAMILY/DRUG NAME	MECHANISM	COMPANY	WEBSITE	STATUS, USA
INTERFERONS Mimic naturally occurring infection-fighting immune substances produced in the body				
Intron A (Interferon alpha-2b)	Immunomodulator	Schering-Plough, Madison, NJ	www.schering.com	FDA Approved 1991
Pegasys (PegInterferon alfa-2a)	Immunomodulator	Roche, Switzerland	www.roche.com	Phase III / NDA Filed
NUCLEOSIDE ANALOGUES Interfere with the viral DNA polymerase enzyme used for hepatitis B virus reproduction				
Epivir-HBV (Lamivudine)	Inhibits viral DNA polymerase	GlaxoSmithKline, Phila., PA	www.gsk.com	FDA Approved 1998
Hepsera (Adefovir Dipivoxil)	Inhibits viral DNA polymerase	Gilead Sciences, Foster City, CA	www.gilead.com	FDA Approved 2002
Baraclude (Entecavir)	Inhibits viral DNA polymerase	Bristol-Myers Squibb, Princeton, NJ	www.bms.com	FDA Approved 2005
Emtricitabine (FTC)	Inhibits viral DNA polymerase	Gilead Sciences, Foster City, CA	www.gilead.com	Phase III
Clevudine (L-FMAU)	Inhibits viral DNA polymerase	Bukwang, Seoul, Korea	www.bukwang.co.kr	Phase III, South Korea Phase II, U.S.
Telbivudine (LdT)	Inhibits viral DNA polymerase	Idenix, Cambridge, MA	www.idenix.com	Phase III
Viread (Tenofovir)	Inhibits viral DNA polymerase	Gilead Sciences, Foster City, CA	www.gilead.com	Phase III
Valtorcitabine (monoval LdC)	Inhibits viral DNA polymerase	Idenix, Cambridge, MA	www.idenix.com	Phase II
Amdoxovir (DAPD)	Inhibits viral DNA polymerase	RFS Pharma LLC	under construction	Phase II
ANA 380 (LB80380)	Inhibits viral DNA polymerase	Anadys, San Diego, CA	www.anadyspharma.com	Phase II
Pradefovir (Remofovir)	Inhibits viral DNA polymerase	Metabasis, San Diego, CA	www.mbasis.com	Phase II
Elvicitabine (ACH-126,443)	Inhibits viral DNA polymerase	Achillion New Haven, CT	www.achillion.com	Phase II (Central & Eastern Europe)
RCV (Racivir)	Inhibits viral DNA polymerase	Pharmasset, Tucker, GA	www.pharmasset.com	Phase II
Pentacept (L-3'-FD4C)	Inhibits viral DNA polymerase	Pharmasset, Tucker, GA	www.pharmasset.com	Preclinical
NON-NUCLEOSIDE ANTI-VIRALS				
NOV-205 (Bam 205)	"Small Molecule"	Novelos, Newton, MA	http://novelos.com	Phase II/III China Approved in Russia
HepeX-B (XTL-001)	Human monoclonal antibodies	XTL Biopharm, Rehovot, Israel and Cambridge, MA	www.xtlbio.com/	Phase II, Israel & U.S.A. Orphan drug approval in US for liver transplants
UT 231 - B *Discovered by HBF scientists	Small Molecule	United Therapeutics Silver Spring, MD	www.unither.com	Preclinical HBV (Phase II HCV)
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				
EHT899	Oral Viral Protein	Enzo Biochem, NY, NY	www.enzobio.com	Phase II, Israel
Zadaxin (Thymosin alpha-1)	Immune Stimulator	SciClone, San Mateo, CA	www.sciclone.com	Phase II w/lamivudine Orphan drug approval in US for liver cancer
EP-HBS (HBV Therapeutic Vaccine)	Immune Stimulator	Epimmune, San Diego, CA	www.epimmune.com	Phase I
HBV Core Antigen Vaccine	Immune Stimulator	Microscience, U.K.	www.microscience.com	Phase I
SpecifEx-HepB	Immunological Cell Transfer	Chromos, Burnaby, BC	www.chromos.com	Preclinical/Phase I
HepX (eiRNA Technology)	Expressed Interfering RNA	Nucleonics, Horsham, PA	www.nucleonicsinc.com	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

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.

Therapies for Hepatocellular Carcinoma

A Significant Unmet Need

By Drs. Robert Gish and Yehuda Patt



Robert Gish, MD

Robert Gish, MD, Medical Director of the Liver Transplant Program, California Pacific Medical Center, San Francisco, CA

Yehuda Patt, MD, Chief of Gastrointestinal Medical Oncology at the Greenebaum Cancer Center of the University of Maryland, Baltimore, MD

The HBF thanks Drs. Gish and Patt for writing the following article for our newsletter.

Hepatocellular carcinoma (HCC), a common malignancy globally, has been increasing in incidence in the United States, mostly due to the maturation of hepatitis C viral (HCV) and hepatitis B viral (HBV) infections, the high frequency of alcohol consumption and due to an increasing incidence of obesity and the associated non-alcoholic fatty liver disease.

The prognosis of patients with this cancer has been poor and even tumor resection has rarely been curative. However, orthotopic liver transplantation has been associated with long-term survival benefit and cure, provided rigorous patient-selection criteria take place. Liver cirrhosis is the most common precursor for HCC, and attempts have been made to prevent the progression from HBV and HCV associated liver cirrhosis to HCC.

Management of patients with HCC requires a multi-disciplinary approach and a team following an algorithm that sorts through the appropriateness of surgical resection, liver transplantation, thermal or other ablative procedures and those should be combined with systemic or regional chemotherapy, including chemoembolization and potentially biological therapy. The identification of effective staging systemic to evaluate regional therapies for HCC, especially among cirrhotic patients who are not candidates for surgery, transplantation or ablative techniques, should be used for screening new non-surgical treatment modalities. Current therapeutic approaches have not resulted in dramatic improvements in patients' overall survivals.

Finding effective systemic treatments for non-resectable HCC has been challenging and quite frustrating. The presence of liver cirrhosis and its associated complications often prevents the application of aggressive therapies and patients may die from complications of cirrhosis or have complication of cirrhosis exacerbated by the presence of HCC. Additionally, staging of HCC using the Tumor Node Metastases (TNM) system, but ignoring the underlying liver disease makes it extremely difficult to compare results of different trials. For that reason, newer staging systems for HCC take into account the severity of the cirrhosis when assessing a patient with HCC (Okuda CLIP Barcelona).

When HCC is detected, if there is no evidence of extrahepatic spread, metastases, or major portal vein involvement, and the tumor is confined to one liver lobe that can be completely resected with a curative intent, it should be resected. However, by and large it seems that more aggressive chemotherapy agents and combinations are associated with increases in median survival times of 3-5 months.

Considering the vascular nature of HCC it may be reasonable to combine tolerable chemotherapy and newly released agents with angiogenesis inhibiting properties.

Key concepts

Orthotopic liver transplantation (OLT), achieves the best outcome in HCC patients with decompensated cirrhosis who meet eligibility criteria. Surgical resection seems most appropriate in patients without cirrhosis whose liver function is preserved. It may be followed by OLT at a later point.

Local ablative techniques such as Radio Frequency Ablation (RFA) may be employed for small solitary liver nodules and for those patients who are not surgical candidates. RFA may also be employed in combination with surgical resection to handle multi-lobe disease. Trans-arterial chemoembolization (sub-selective) may improve survival in intermediately advanced HCC in properly selected patients without evidence of significant portal hypertension.

Systemic chemotherapy and biological agents such as interferon may be tolerated by cirrhotic patients and have very modest activity in Phase II trials. They should continue to be the focus of therapeutic research. Promising agents identified in Phase II and III trials, such as Thymitaq (nolatrexed), among patients with advanced disease may be later employed for adjuvant or neo-adjuvant therapy in combination with surgery, ablation or OLT.

Summary

The numerous agents and combinations that have been studied in the treatment of HCC attests to the inadequacy of our current approach and indicates the need for more research into the understanding of molecular carcinogenesis that leads to the development of HCC.

Such an understanding may help with the implementation of trials preventing the progression from liver cirrhosis to HCC. For advanced disease one must consider orthotopic liver transplantation, possibly in combination with neo-adjuvant chemotherapy. For early disease loco-regional therapies will be most useful to delay progression until tumor targeted therapies are refined.

The need for varied interventions including resection, ablation and transplantation as well as chemotherapy and biologic agents and the need for prevention studies mandates that patients be managed in a multi-disciplinary fashion by teams capable of providing such care. Clinical trials that are pursued in the near future will focus on therapies that are less toxic and likely to be tolerated by patients with complex medical problems including decompensated liver disease.

Editor's Note: Over the past decade, there has been a three-fold increase in the incidence of hepatocellular carcinoma (HCC), or primary liver cancer in the U.S. Liver cancer is now considered to be the fastest growing cancer. Currently, there are no FDA approved treatments, which represents a significant unmet need for effective drug therapy to improve both prognosis and survival rates from this deadly cancer.

Liver Cancer Drug Chart, continued on page 6

LIVER CANCER DRUG WATCH: POTENTIAL THERAPIES FOR HEPATOCELLULAR CARCINOMA

The list of potential therapies for the management and treatment of hepatocellular carcinoma (HCC or, primary liver cancer) was compiled by Drs. Robert Gish and Yehuda Patt. Currently, there are no FDA approved therapies for primary liver cancer.

Adjuvant and Neo-Adjuvant Therapy - In addition to surgery (resection or transplantation) drug therapies are considered in an attempt to improve outcomes.

- Retinoids
- Interferon
- Cytotoxic agents
- Topoisomerase I inhibitors
- Ursodiol
- Glycyrrhizin (Stronger-Neo-Minophagen)
- Sho-saiko-to
- Adoptive immunotherapy with autologous lymphocytes
- Activated ex vivo with Interleukin-2
- Dendritic cells pulsed with an HCC lysate
- Autologous formalin-fixed tumor vaccine (AFTV)
- Pravastatin (3-hydroxy-3-methylglutaryl coenzyme A inhibitor)

Hormonal Therapy - This type of therapy is based on the belief that the growth of HCC is promoted by endogenous estrogen via a receptor-mediated process. Characterization of the estrogen receptor will be a pre-requisite to any further studies of hormonal treatments of HCC.

Systemic Therapy for Unresectable Disease; Drug therapy for patients with inoperable HCC and for whom surgery is not an option. Oral fluoropyrimidines, such as capecitabine and UFT (tegafur and uracil)

- Gemcitabine combined with amifostine and cisplatin (GAP)
- Gemcitabine combined with oxaliplatin
- T67- Phase II, Bayer
- Thymitaq (nolatrexed) - Phase III, Eximias

Angiogenesis Inhibition

These drugs reduce new blood vessel formation, and given the highly vascular nature of HCC, could help reduce tumor growth and metastasis.

- Bevacizumab
- TNP 470
- Thalidomide

Epidermal growth factor receptor antagonists - The epidermal growth factor receptor (EGFR) is highly expressed in many human tumors and provides a new target for anticancer drug development.

- Cetuximab

April 2005

Dreams Can Come True A Young Guatemalan Woman's Story



My life completely changed on November 16, 1997. I still remember that Sunday morning. I was going to have my breakfast when, suddenly, I fainted. Two weeks later, I had a rash over my whole body and my eyes and

skin were yellow. I went to a doctor who ordered an ultrasound and blood tests. He recommended that I stay one week at the hospital.

My diagnosis: hepatitis A with a co-infection of hepatitis B. At the time I did not understand what my doctor said, but I remember him saying, "You will recover from hepatitis A, but what concerns me is your hepatitis B because it does not have a cure. Many people die from liver cancer and cirrhosis as a consequence of hepatitis B."

I was only 21 years old and can express in three words my feelings - I was shocked! I was also very frustrated because for the second time in 18 months, I had to interrupt my university studies in Chemical Engineering. Several doctors stopped by my hospital room to ask me questions about my personal life. They asked if I was a drug-addict and how many sex partners I had. The truth is, I was not a drug addict and I had never had sex. It is very important to mention this because it is wrongly assumed that you can only get hepatitis B through drugs and unprotected sex.

I spent many years crying, complaining, blaming and playing the role of victim, until I realized that there are just two solutions for situations like this: you sit and cry or, you en-

joy the beauty of being alive and make every day count. I decided on the second choice.

Last year I needed to get a liver biopsy and I promised that if the results were negative for cirrhosis, I would live to make two of my dreams come true: to study a specialization in hepatitis B and to create a foundation in my country. The day I can help to make sure that my country can provide free hepatitis B screenings, vaccines, and affordable treatments, I will feel that I did not pass through a couple of inconveniences in my life for nothing.

After receiving good news about my biopsy results, I happened to read the foundation's *B-Informed* newsletter and was suddenly inspired to send an email to Dr. Block telling him about my dreams. Honestly, I never imagined that he was going to answer my email! I still remember how happy I felt when he answered my email almost immediately.

My dreams are coming true with the support and motivation of Dr. Block and his wife Joan, co-founders of the Hepatitis B Foundation. For years this foundation has been not only a source of information about hepatitis B, but a place and group of people who really care about those living with chronic hepatitis B. This makes me feel that I am not alone.

Finally, I am healthy enough to continue my normal life. I have been working as a science teacher for five years and just completed my Bachelor's degree this past November. I think that now is the moment to start my voyage to the world of hepatitis B research.

Editor's note: The HBF is pleased to sponsor this young woman for a two-week internship this summer.

HBV Around the World: Guatemala



The ghost of a silent killer - the hepatitis B virus - is walking around the streets of Latin America and the people don't even know it.

Each year it is estimated there are between 140,000 and 400,000 new cases of hepatitis B in the Americas. Two-thirds of these cases occur in South America, mainly in the Pacific

Coast of Colombia and the Amazon area (Brazil, Colombia and Peru).

Based on information from the National Health Institute of Lima (NHI), in 2002 the population in Latin America was 410 million with an estimated 6.6 million people chronically infected with hepatitis B. The NHI also predicted that 33,000 of the 13.5 million babies born in 1985 will die as consequence of cirrhosis or liver cancer due to chronic hepatitis B.

Central America, including Guatemala, are listed at "intermediate levels" for hepatitis B by the World Health Organization, which means an estimated 2-7% of the population is chronically infected. Dr. Julio Cesar Argueta, a well-known Guatemalan infectious disease specialist, believes the rate of chronic infections is much higher. Based on his research, up to 20% of the population in Guatemala City and rural areas such as Escuintla, Suchitepequez, and Zacapa are chronically infected with hepatitis B.

In 1994-1995, the Roosevelt Hospital reported three cases of teenagers with primary liver cancer from the southwest region of Guatemala, Patulul Suchitepequez. This caught the attention of doctors who decided to identify the number of people with chronic hepatitis B in Patulul, an indig-

enous area with 310 habitants. The results of the research showed that 13% of children between 1-5 years were chronically infected with hepatitis B and 92% between 6-15 years.

The fact that so many young children are chronically infected with hepatitis B in this one area is a serious problem since 80% of all cases of primary liver cancer worldwide are due to hepatitis B. The Guatemalan Cancer Institute (INCAN) reported that the incidence of liver and intrahepatic cancer has been increasing since 1999. In 2002, liver and intrahepatic cancer represented almost 30% of all new cancers in men and women.

In 2001, Guatemala spent 5.4% on health care expenses. Neither the hepatitis B vaccines nor antiviral drugs are provided by the Guatemalan public health ministry. In recent years, a national immunization campaign for hepatitis B and other diseases was approved for babies born since January 1, 2005. Although doctors recommend the hepatitis B vaccine, each shot costs approximately \$10. In Guatemala, where the monthly salary per capita is \$150, vaccines are a luxury.

It wasn't until last year that the Guatemalan Institute for Social Security finally acquired the necessary equipment to perform the HBV DNA test, an important blood test used to decide whether to start treatment or not. If treatment is indicated, however, the cost is exorbitant. For example, lamivudine therapy costs \$200 per month. In a country where the annual salary per capita is \$1,833, treatment is basically unavailable to most patients.

This raises a difficult question. If by chance someone in Guatemala finds out they have chronic hepatitis B, what then will be their future?

Editor's Note: This article was researched and written by the same young Guatemalan woman who shared her personal story on page six.

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Frontiers in Nucleosides and Nucleic Acids

Edited by RF Schinazi and DC Liotta (March 2005)

A compilation of the latest advances in nucleic acid research that encompass the clinical development of nucleosides as antiviral agents.

Frontiers in Viral Hepatitis

Edited by RF Schinazi, JP Sommadossi and C Rice

A compilation of research from over 40 key opinion leaders in the field of hepatitis with a focus on the latest advances in the search for new, more effective therapeutic options and related topics.

Register Now for the 2005 International HBV Meeting!



This year marks the 20th anniversary of the *International Meeting on the Molecular Biology of Hepatitis B Viruses*, co-chaired by Dr. Timothy Block and Dr. Stephan Urban. Abstract submission deadline is July 18, 2005. A limited number of travel grants for graduate students and post docs are available.

For more information or to register, www.hbvmeeting.org

Foundation at the Forefront



Distinguished Bruce Witte Lecturer, Dr. Ben Yen (second from left) with Janine and Paul Witte, HBF Co-Founders, with Mollie Conti (far left), and Joan and Tim Block (at right).

Hepatitis B Scores Almost "9" on the Richter Scale of Viral Diseases

Hepatitis B scores nearly as high as HIV on the "Richter Scale of Viral Diseases", based on the total number of deaths from acute and chronic viral infections, but scores very low on the public health radar screen, according to **Ben Yen, MD, PhD**, vice chair, Dept. of Pathology, University of California San Francisco, and the HBF's 6th Annual Distinguished Bruce Witte Lecturer. With this dramatic introduction, Dr. Yen discussed "ER Stress and Hepatitis B" on February 23 and how his research is demystifying hepatitis B disease one protein at a time. Although it is known that the hepatitis B virus itself doesn't damage liver cells (rather, it's the infected person's immune response to the virus that damages the liver), complete understanding of how hepatitis B causes disease remains a mystery. Dr. Yen's research has led him to an important molecular explanation for a rare but lethal consequence of hepatitis B infections most commonly seen in highly immunosuppressed patients - fibrosing cholestatic hepatitis (FCH). He has discovered that hepatitis B large protein surface proteins are a significant factor in causing FCH that can rapidly progress to life-threatening hepatic fibrosis and liver failure (usually within one year). The discovery of how a hepatitis B viral protein is involved in disease progression could contribute to the discovery of targeted drug therapy to eradicate this disease.

HBF "Train the Trainers" Workshop

The Hepatitis B Foundation and HepTREC co-sponsored a "Train-the-Trainer" workshop on March 23 at Temple University, Philadelphia, PA. The workshop provided an overview of hepatitis B and viral hepatitis for social service providers, including substance abuse counselors, STD/HIV and family planning counselors, public health professionals, and corrections workers. **Chari Cohen, MPH**, HBF program coordinator, spoke about hepatitis B and **Amy Jessop, PhD, MPH**, director of Research and Education at HepTREC, spoke about hepatitis A and C. Social service providers interact with thousands of clients who are infected or are at high risk for infection, thus, need education in order to protect themselves and educate others.

Alphabet Letters Left Behind at Annual Meeting of the NVHR

The National Viral Hepatitis Roundtable (NVHR), during its second national meeting on April 11-12 in Washington, D.C., was led by **Dr. John Ward**, the new head of the Hepatitis Division of the Centers for Disease Control, who told participants to "leave their alphabet letters behind" and focus on the problem of viral hepatitis as a whole. He stressed that if all the viral hepatitis numbers are consolidated, a stronger message could be conveyed to Congress in order to help increase federal funds to support prevention, education and treatment initiatives.

Molli Conti, HBF vice president for community outreach and a member of the NVHR steering committee, and **Peggy Farley**, HBF community relations coordinator, attended the meeting. Ms. Conti was invited to join the panel of experts during sessions with hepatitis C advocates who were interested in learning more about hepatitis B. "This was certainly a step in the right direction and very reflective of the engaging environment at the conference to put aside our differences and try to better understand the common ground of viral hepatitis," she said.

The NVHR has been working on a national strategy for the elimination of viral hepatitis in the U.S. that will be released in June 2005.

MAY IS NATIONAL HEPATITIS AWARENESS MONTH!

First National Hepatitis B Awareness Week May 9-16, 2005

Through the educational efforts of the HBF, *National Hepatitis B Awareness Week* has officially been designated for the week of May 9-16, 2005, in a bi-partisan resolution co-sponsored by **U.S. Senators Dianne Feinstein** and **Rick Santorum**, and **Representatives Tim Murphy** and **Mike Honda**. It calls for a comprehensive public education and awareness campaign for both physicians and patients, with the goal of extending and improving the quality of life for all those living with chronic hepatitis B.

HBF Launches "Aim for the B"

A nationwide education campaign, *AIM for the B: Awareness, Involvement and Mobilization for Chronic Hepatitis B*, will be launched during *National Hepatitis B Awareness Week* to raise the profile of hepatitis B as an urgent health issue. This initiative is co-sponsored by HBF and Bristol-Myers Squibb to highlight the impact of hepatitis B through testimonies from patients, doctors and nonprofit groups. Local events will be held in four cities where there is a high incidence of hepatitis B. In Philadelphia, **Dr. Hie-Won Hann**, HBF medical advisor, and in San Jose, **Dr. Huy Trinh**, will meet with hepatitis B patients who will be encouraged to share their personal experiences at roundtable gatherings. In New York City, **Mayor Michael Bloomberg** will issue a proclamation designating May 11 as "Hepatitis Awareness Day" with **Molli Conti**, HBF vice president for Community Outreach, **Dr. Thomas Tsang**, **Dr. Ira Jacobson** and patients who will make supporting statements. In San Francisco, **Congressman Mike Honda** will issue a similar proclamation on May 13 with **Joan Block**, HBF co-founder, **Dr. Teresa Wright**, **Jeffrey Caballero** and patients also making additional statements.



Speaking Personally

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

My Favorite Charity

Hey, I'm NOT cheap! I'm not sure how I got that reputation, but it's totally undeserved. It's just that I like to get the "most for my bucks", even when it comes to donating to charity. So I do the research before I hand over my dough to total strangers.

Having been diagnosed with hepatitis B in 1981, I've been researching the Hepatitis B Foundation (HBF) for about as many years as it has existed, and I've come to the conclusion... (drum roll)...that the HBF is my favorite charity!

In 1991, two couples, Paul and Janine Witte and Tim and Joan Block, responded to a personal story in their community and decided to invest their time and money in an important cause. They could have chosen a more glamorous disease, but fortunately for all of us, they settled on hepatitis B. Their choosing hepatitis B was a minor miracle, in my opinion, and in effect, saved hepatitis B from becoming an orphan disease.

Fast forward to 2005, and we have a highly respected foundation that stands out among the other hepatitis and liver charities. I invite you to visit the HBF facilities in Doylestown, PA, and I promise that you will be impressed.

Three words that I'd use to describe these folks: friendly, visionary, and ethical.

Not only does the foundation promote hepatitis B research, but they and the new research institute they just created, the Institute for Hepatitis and Virus Research (IHVR), actually DO the research. HBF has one of the few research centers in this country that focuses exclusively on hepatitis B.

In addition, another outstanding feature of the HBF is that they help all of us. They encourage Sheree Martin and me in our online support and research efforts. And every year, they co-host our unique patient conference.

I've been involved with other organizations, but they never just ask the patients directly what they need. HBF, on the other hand, is eager to listen. They've even invited this patient, me, to write a column in their always impressive *B Informed* newsletter.

2005 is the 50th anniversary of the discovery of the polio vaccine. I'm sure that 50 years ago, few thought that we'd actually be able to eliminate polio in the USA, but that's pretty much what has happened.

The Hepatitis B Foundation knows there is the same potential for hepatitis B. Just read their mission motto, "Cause for a Cure". There's nothing wishy-washy about the word "cure", and I commend HBF for having as their goal to find a cure for hepatitis B and to eliminate the suffering it causes worldwide.

Do your own research or take my word for it, and I know you'll want to join HBF and support my favorite charity!

Crystal Ball



HBF Distinguished Founders' Award 2005

Dr. Bill Stephenson & Drexel University

The Hepatitis B Foundation (HBF) is proud to present the 2005 *Distinguished Founders' Award* to **Dr. Bill Stephenson**, Vice Provost for Research and Dean for Graduate Policy, and **Drexel University**. Thanks to Dr. Stephenson's vision and commitment, hepatitis B research will increase tremendously at the foundation.

In July 2004, Drexel University created the Drexel Institute for Biotechnology and Virology that will help extend the resources and number of scientists working on hepatitis B at the HBF and its new research institute, the Institute for Hepatitis and Virus Research (IHVR).

At Drexel University, Dr. Stephenson oversees a research portfolio with current expenses in the \$100 million range with plans for doubling this number in the next several years. He is also responsible for advancing Drexel's mission as a research intensive, Ph.D.-granting institution. Today, with an enrollment of more than 1000 medical and over 300 graduate students, Drexel University College of Medicine is the largest private medical school in the country.

Prior to joining Drexel University College of Medicine, Dr. Stephenson served as Vice President for Research at the University of Medicine and Dentistry of New Jersey. He received a B.S. in chemistry from the University of North Carolina and a Ph.D. in chemistry from the California Institute of Technology, followed by a research year at Harvard University.

In the academic arena, Dr. Stephenson has held professorial appointments at Stanford University, Case Western Reserve, and the University of Southern California. In the business world, he has been Vice President for Research at two Fortune 500 companies and has formed, managed, run and sold a biotech instrument company.



Hepatitis B Foundation HBV Clinical Trials
www.hepb.org/clinicaltrials

National Institutes of Health Clinical Trials
www.clinicaltrials.gov

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

NEW **Comparison of Entecavir to Adefovir in Nucleoside-Naive Chronic Hepatitis B Patients**

A new clinical trial for nucleoside-naive chronic hepatitis B patients opened in January 2005. This is a Phase IIb comparative study of entecavir versus adefovir in patients with chronic hepatitis B. The treatment period is for up to 96 weeks. Trial sites are located throughout the U.S. and Canada. *Contact Bristol Myers Squibb at 1-866-892-1267, ext. 150.*

Entecavir for Chronic HBV: An Early Access Program

The purpose of this research study is to provide entecavir to subjects with chronic hepatitis B infection who have failed or who have demonstrated intolerance of marketed therapies or for those in whom use of these agents is contraindicated and have no other available treatment options. Patients 16 years or older are eligible to apply. *Contact: Bristol-Myers Squibb tollfree at 1-866-892-1BMS, ext. 127.*

Adefovir Dipivoxil in Children and Adolescents with Chronic Hepatitis B

The purpose of this study is to investigate the efficacy and safety of adefovir for the treatment of chronic hepatitis B in children and adolescents (age 2 to 17 years) compared to placebo following 48 weeks of treatment. Additional goals include - to evaluate the number of eAg and sAg seroconversion following 48 weeks of adefovir or placebo; to evaluate the development of resistance to adefovir; and to evaluate the long-term safety and efficacy in children and adolescents over an additional 4-year follow-up period including assessment of growth and renal function. Study started June 2004 and will enroll approximately 150 individuals. *Contact: Anant Jain, Gilead Sciences at 650-522-5523 or ajain@gilead.com.*

Safety of and Immune Response to a HBV Vaccine Given with a Booster (CpG7909 ODN) in HIV Infected and HIV Uninfected People

The purpose of the study is to determine the safety of and immune response to a hepatitis B virus vaccine series given with a boosting agent, CpG7909 oligodeoxynucleotides (ODN), in HIV infected and HIV uninfected individuals who previously failed to develop a response to hepatitis B vaccine. Healthy volunteers accepted, too. Study started Dec. 2004 and will enroll 30 individuals. Study is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID). *Contact: Kathy M. Burgner, BSN, at 216-844-8136 or burgner.kathy@clevelandactu.org, Cleveland AIDS Clinical Trials Unit.*

Lamivudine and Adefovir to Treat Chronic Hepatitis B

This NIH study will evaluate the safety and effectiveness of lamivudine plus adefovir versus adefovir alone to treat chronic hepatitis B infection. Candidates may not have received lamivudine treatment in the past 6 months or prior treatment with adefovir and must not be taking other anti-viral treatments for their hepatitis. *Contact: NIH Patient Recruitment at 1-800-411-1222 or email prpl@mail.cc.nih.gov*

Telbivudine versus Lamivudine in Adults with Decompensated Chronic Hepatitis B and Evidence of Cirrhosis

Idenix Pharmaceuticals is conducting this research study to see if the investigational medication, LdT (Telbivudine), is safe and effective in the treatment of decompensated hepatitis B infection over two years. The results for patients taking LdT will be compared to results for patients taking lamivudine (EpiVir-HBV). *Contact: Gloria Dubuc at 617-995-9814 or email dubuc.gloria@idenix.com*

Evaluate Efficacy, Safety and PK of Adefovir Dipivoxil Liquid Suspension in Patients with Chronic Hepatitis B

Gilead Sciences is sponsoring a multi-center phase 3, open-label, parallel-group study designed to evaluate the efficacy, safety and pharmacokinetics of adefovir dipivoxil liquid suspension in patients with chronic hepatitis B and varying degrees of renal impairment. *Contact: Anant Jain at 650-522-5523 or email ajain@gilead.com*

Comparison of Entecavir to Adefovir in Chronic HBV Patients with Hepatic Decompensation

A Phase IIIb comparative study of entecavir vs. adefovir in patients who have chronic hepatitis B and hepatic decompensation for up to 96 weeks. *Contact: Bristol-Myers Squibb toll-free at 1-866-892-1BMS.*

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. 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.*

Pegylated Interferon to Treat Chronic Hepatitis D

This NIH study will evaluate the effects of pegylated interferon, given once weekly, on hepatitis D (HDV) and hepatitis B. HDV is often severe and progressive and only infects people who already have hepatitis B infection. Patients with chronic hepatitis D over 6 years old may be eligible for this study. Patients who improve with treatment may continue therapy long-term. *Contact: NIH Patient Recruitment Office at 1-800-411-1222 or email prpl@mail.cc.nih.gov*

Fast Fact

Liver cancer is the fastest growing cancer in the U.S and the fifth most common cancer worldwide.

Resource Roundup



Spring 2005

Hepatitis B Foundation 215-489-4900

info@hepb.org

Comprehensive website dedicated to hepatitis B. Facts, Drug Watch, clinical trials, liver specialist directory, and responsive email. Includes *Chinese, Vietnamese, Korean, and Spanish Language Chapters*. Subscribe to our free e-newsletter *B News You Can Use*.

www.hepb.org

Institute of Hepatitis and Virus Research info@ihvr.org

This research institute, also known as the Pennsylvania Commonwealth Institute, was established by the HBF in 2004 to search for hepatitis B and C therapies.

www.ihvr.org

American Liver Foundation

1-800-GO-LIVER

www.liverfoundation.org

Information about all liver diseases, including viral hepatitis.

Asian Liver Center at Stanford University

650-725-4837

<http://livercancer.stanford.edu>

Educates people about hepatitis B and liver cancer among Asians and Asian-Americans.

Centers for Disease Control, Hepatitis Division

1-888-443-7232

www.cdc.gov/ncidod/diseases/hepatitis

The national authority for viral hepatitis information.

CDC Hepatitis Immunization Hotline

1-800-232-2522 (English)

1-800-232-0233 (Spanish)

www.cdc.gov/nip

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.

Hepatitis B Research Archive Website

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

Archived research bulletins from the Hepatitis B Research List.

HCV Advocate

www.hcvadvocate.org

HCV website that also includes hepatitis B information.

Hep C Connection

1-800-522-4372

www.hepc-connection.org

Comprehensive information about hepatitis C.

Hepatitis Foundation International

1-800-891-0707

www.hepatitisfoundation.org

Information about viral hepatitis, support groups and research.

Hepatitis Magazine

1-800-310-7047

www.hepatitismag.com

The only print magazine about hepatitis published bi-monthly.

HepLink

www.heplink.org

A search engine that gathers viral hepatitis information.

HepTrec

1-866-HEPTREC

www.heptrec.org

The Delaware Valley Hepatitis Treatment, Research and Education Center (HepTREC) in the greater Philadelphia area.

HIV and Hepatitis Treatment Advocates

www.hivandhepatitis.com

Professional online publication with free e-mail updates.

Immunization Action Coalition

651-647-9009

www.immunize.org

www.vaccineinformation.org

www.hepprograms.org

Comprehensive source of immunization information. The first website is for health professionals, the second is for the general public and the third highlights preventive programs. "IAC Express" and "HEP Express" are free e-mail announcement services.

Memorial Sloan Kettering "About Herbs"

www.mskcc.org/aboutherbs

Scientific information about herbs, their side effects and drug interactions. Maintained by experts at Memorial Sloan Kettering.

Nat'l Center for Complementary and Alternative Medicine

1-888-644-6226

www.nccam.nih.gov

Sponsored by the National Institutes of Health (NIH).

Parents of Kids with Infectious Diseases

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

www.pkids.org

An excellent resource for parents and professionals.

Internet Support Groups



Hepatitis B Information and Support List

www.hblist.org

To subscribe: 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 other concerned individuals.

HBV Adoption Support List

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.

New! PKIDs Lists for Children and Teens

www.pkids.org/listserve

Children (8-12 years) and teens (13-19 years) living with hepatitis B or C can now talk with each other on two separate lists that are well supervised.

