

The Battle against HBV **The Evolution of a Cure**

As any good army general knows, the more you know about your enemy-how it operates, its invasion strategies for getting a stronghold, how it reinforces itself—the better your chances are to thwart its power and to achieve victory. What scientists are learning about the hepatitis B virus (HBV) is opening up whole new ways about how best

to attack it. And the more we learn, the more we can wipe out this disease that every year, afflicts an estimated 200,000 new people in this country. While most people may shed the virus, ten percent of those infected become chronic carriers and vulnerable to progressive liver disease. Currently, 1.25 million Americans are chronically infected with hepatitis B.

It's inside the liver cells where the HBV is headquartered and conducts its destructive operation on the body. Approximately 5,000 people in the U.S. die every year of liver failure related to HBV; another 1,500 die of HBV-related liver cancer.

Scientists who have been working on methods to eradicate this virus have learned that this formidable foe is programmed to survive for years, even decades and that "it replicates faster than we had appreciated," according to Raymond Schinazi, Ph.D., director of the Laboratory of Biochemical Pharmacology at Emory University and Senior Research Career Scientist at the V.A. Medical Center at Emory University. Dr. Schinazi is one of the generals working in the labs at the front lines against HBV and is credited with co-discovering lamivudine, the first oral anti-HBV therapy.

"If you look at all the hepatitis viruses, HBV has the highest viral load in the body," says Dr. Schinazi. "This means it's a bigger challenge to wipe out." While we have some useful drugs now, he says, we need more potent drugs, 'bigger guns' so to speak.

It All Started with HIV Research

The ammo in the current arsenal includes interferon alpha-2b (marketed under the name Intron A for HBV). This is an injected drug that became FDA-approved in 1991 and was, in fact, initially developed to fight HIV, the virus that causes AIDS.

"Research on HBV therapies actually grew out of research that began nearly three decades ago with Thomas Merigan of Stanford University who was searching uses for interferon," says Dr. Schinazi. "At that point, interferon was a drug looking for a disease."

Interferon, he explains, occurs naturally in the body in response to a virus. It's believed that interferon alters the immune system and can prevent the spread of the infection to surrounding cells. When it was discovered that the interferon response was deficient in some people and that interferon alpha 2-b could effectively fight viruses, including HIV and HBV, this immunomodulator drug became the gold standard for treatment of the diseases caused by these viruses.

Unfortunately, interferon alpha2-b has proved it may not be the silver bullet needed to wipe out HBV. For one thing, the drug, which is administered through injection and causes flu-like side effects, is only effective in about 20 to 40 percent of a subpopulation of chronic HBV carriers. Another problem: HBV rebounds in half of the people who initially respond to it after the 3-6 month course of treatment.

Nevertheless, studying HIV led to some revealing information. Dr. Schinazi began to look at ways to attack the virus itself, specifically how to dismantle it. This was an entirely different approach than bolstering the immune response.

"We've learned that the virus reproduces much more rapidly than we expected – the equivalent to a hundred billion particles a day. That's more of a viral load than hepatitis C or HIV", says Dr. Schinazi. It also means HBV is a bigger challenge to wipe out.

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CAUSE FOR A CURE

"The only non-profit organization dedicated solely to the cause and cure of chronic Hepatitis B"

From the Desk of the President....

Joan M. Block, R.N.

Finding the Cure Takes a Team Effort

Finding a cure for chronic hepatitis B has never been more exciting than right now. It's incredible to realize that in only nine years, we have moved from having no available treatments to several treatment options. With two FDA-approved drugs for HBV, three drugs in clinical trials and at least eight compounds in the pipeline, the promise of research is finally bearing fruit.

With a cure so close at hand, however, this is also a time of great frustration for those who have chronic HBV. As more is learned about this virus, more questions are raised. How can we prevent mutations? Which drugs should be given to whom, and for how long? What clinical outcomes are the most significant? Because HBV may manifest differently in people, it is clear that many approaches must be pursued in order to find appropriate solutions.

Finding the solutions-and moving the *Cause for a Cure* along requires a team effort. Government grants, biotech investment, and major pharmaceutical R & D (research and development) programs are all needed to fund the cure. And non-profit organizations like ours can help increase disease awareness, keep you up-to-date about drug developments and serve as patient advocates.

But it's also critically important for those who are affected to become an active part of this team. Individuals and families can make a difference and in numbers we can create change.

Get involved. Share your stories to help eliminate the stigma of the disease. Volunteer for clinical trials if it's medically appropriate. Urge industry and government leaders to respond by increasing research dollars.

Help us keep the fire of progress burning brightly towards a cure.

OOPS...

A Belated Thank You to our Generous Donors

In our last issue of B Informed, we inadvertently omitted the following donors who have supported our mission through gifts, memorial donations and attendance at our benefit events. We apologize for this oversight and wish to express our gratitude now for your kind generosity.

Ms. Angela C. Frey	Ms. Faith G. Byrd
Ms. Diane Dambach	Ms. Teena C. Riley
Ms. Mary Jo Sweeney	ICN Pharmaceuticals
Mr. and Mrs. Russell Brown	Ms. Kathleen Sundquit

In The News

New Two-dose Hepatitis B Vaccine for Adolescents Reduces Office Visits

In September 1999, the FDA approved Merck's adult two-dose of Recombivax HBV vaccine (10 mcg) for adolescents, aged 11 to 15. The effectiveness measured by the production of HBV antibodies for the two-dose vaccine is similar to the traditional three dose (5 mcg) vaccine. The two-dose vaccine should be administered 4-6 months apart and can be used instead of the three-dose schedule. However, adolescents who have already begun the traditional three-dose schedule should not switch to the two-dose schedule. The two-dose vaccine supplied through the Vaccines for Children (VFC) resolution will not be available until the CDC negotiates a vaccine contract for this alternative dosing schedule.

For more information, contact: the Immunization Action Coalition, (651) 647-9009; www.immunize.org.



Testing Trials Begin for First HBV Cocktail

In January, SciClone Pharmaceuticals announced the start of a U.S. Phase II drug trial at Loyola University in Chicago to assess Zadaxin (thymosin alpha-1), an immune enhancer drug in combination with lamivudine, the FDA-approved nucleoside analogue drug. The study will assess the safety and efficacy of the combination which boosts the patient's immune system while suppressing the hepatitis B virus reproduction rate in treatment of chronic carriers. Contact: SciClone.com or 1-800-724-2566.



FDA Approves Immunotherapy for Liver Cancer

In March, the FDA granted orphan drug status to Zadaxin for the treatment of hepatocellular carcinoma, the most common form of liver cancer worldwide and often the fatal endpoint in the progression of hepatitis B. Orphan drug status provides for U.S. marketing exclusivity for seven years once it's been approved for marketing. Phase II trials testing Zadaxin on liver cancer will begin in the U.S. in the fall 2000. Contact: SciClone.com or 1-800-724-2566.

Thus, around 1989, 3TC (lamivudine) was discovered. It's a type of drug called a nucleoside analogue indicating that it's aimed at the cell's nucleus – the virus headquarters. "We basically stumbled on 3TC and related molecules – they worked and we got excited."

Even more exciting, says Dr. Schinazi, is that 3TC worked on HIV and also on HBV. "We realized that this cousin of HIV had a similar enzyme and uses it to make the viral DNA. By destroying the virus and preventing its spread, the disease would go away."

Understanding How the Virus Operates

Once inside the body, the hepatitis virus makes a bee-line for the liver cell's nucleus. Inside the nucleus, the virus produces messenger RNA, the basic building block needed for the virus to reproduce. The messenger RNA then moves outside the nucleus and is used by the DNA polymerase, the enzyme that helps the RNA build viral DNA. In a nutshell, this is how the virus copies itself and continues to grow in numbers.

What Dr. Schinazi discovered was that viral reproduction could be halted by introducing nucleoside analogue drugs aimed at inhibiting the DNA polymerase. "Basically, the drug throws a wrench into the works," says Dr. Schinazi. Inhibiting the polymerase shuts down the virus reproduction factory, stopping HBV in its tracks.

This may be only a short-lived victory, as revealed by further research. "We've learned that the virus reproduces much more rapidly than we expected—the equivalent to a hundred billion particles a day," says Dr. Schinazi. "That's more of a viral load than hepatitis C or HIV. We're now realizing that this viral burden is a bigger challenge to eliminate than lamivudine alone can handle."

Resistance is a Major Factor in Drug Development

Research has revealed that when the hepatitis virus is reproducing, mistakes may be made in copying the viral DNA. This may result in different "mutant" strains of HBV that are resistant to lamivudine.

Indeed, the resistance rate seen in lamivudine is significant. Lamivudine is initially effective in almost all HBV-infected people, however, more than a third will develop resistance over a period of two years. Also, HBV usually rebounds after withdrawal of the prescribed therapy.

The resistance problem has caused many experts to view lamivudine with caution. They worry that, as in the case of antibiotics, there may be a danger of overusing this drug and that we may have controlled one problem, only to trigger another in the form of resistance.

Other experts have voiced concern as to whether any patients with HBV should be treated with a single agent. Jenny Heathcote, M.D., professor of medicine at the University of Toronto put it this way: "It's like many years ago, when we were trying to treat HIV with just AZT. In retrospect, we realized that we should have been using cocktails (of several agents) because the virus becomes resistant so quickly to just one drug."

Dr. Schinazi echoes the argument for combination therapy. He also believes that, despite its limitations, lamivudine (prescribed as



Raymond Schinazi, Ph.D.

Epivir-HBV) should definitely remain a part of the anti-HBV cocktail and perhaps even be the lead compound in the cocktail.

"Lamivudine is useful in the hepatitis B patient requiring a liver transplant," he points out. It has been shown to reduce the incidence of post-transplant hepatitis B infection. Long-term studies are required in this population but current results are most promising. Some patients treated with lamivudine while waiting for a liver transplant improved so much they were taken off the transplant waiting list.

"Drug companies should definitely join in our fight against HBV," he says. "Lamivudine can substantially decrease the virus load, while, admittedly, it works best in patients who begin treatment with low viral loads."

The main focus should not be targeting the immune system solely, he adds. "You need to first bring down the virus levels, reduce the replication, then you can use immunological weapons."

A reasonable approach, he believes, is to use lamivudine backed with other drugs. "What we need are drugs that are complementary to lamivudine."

Promising Drugs in the War Against HBV

The flare-up of HBV in people with dual infection of HIV and HBV infections was predicable, says Dr. Schinazi. When the immunosuppression of interferon quashed HIV, the HBV—which was below the radar before—flared up.

At this point, research is advancing for drugs that work against both viruses as well as for those that work specifically against HBV.

One of these HBV-specific drugs is L-FMAU, a nucleoside analogue that showed promise in studies conducted by Brent Korba, Ph.D., professor of microbiology at Georgetown University. In experiments on the woodchuck, L-FMAU showed anti-HBV activity and helped reduce the abundance of cccDNA, considered one of the goals of therapy. cccDNA is the template the virus forms to replicate itself and is known to stay dormant for years – even decades – in the body until activated by various triggers. De-activating the cccDNA appears to be another way to close down the virus replicating factory.

Several other nucleoside analogues with similarities to lamivudine are being investigated in both lab animals and humans. Adefovir dipivoxil (GS890) – now in Phase III clinical trials – produced significant and sustained antiviral activity in early tests in patients with chronic hepatitis B after one month with only mild to moderate side effects. In other studies, two-thirds of the patients who took adefovir pills for 12 weeks showed depleted levels of HBV by 99.99 percent – from several billion copies to just a few hundred. Another plus: adefovir appears to be effective against the lamivudine-resistant virus strains.

Other research aimed at destroying the RNA molecules involved in reproducing the virus is being conducted by Timothy Block, Ph.D., director of the Jefferson Center for Biomedical Research in collaboration with Raymond Dwek, D.Phil. and FRS, professor at the University of Oxford and Baruch Blumberg, M.D., Ph.D., Nobel Laureate. These scientists discovered that certain plant sugars called imino sugars could alter a small percentage of proteins

CONTINUED ON PAGE 4

within the cell – just enough to keep the HBV from using them to replicate as shown in tissue cultures from infected woodchucks. Their sugar-based nonyl-DNJ drug also appears to work against the lamivudine-resistant virus. Testing on humans is expected to begin within the year.

Advancing research also continues on non-interferon immune enhancers. Thymosin alpha-1, for example, which recently gained FDA-approval for the treatment of liver cancer, appears to give a general boost to T-cell immune fighters that attack infected liver cells and to prompt natural interferon production. Six months of twice weekly injections reduced the virus to undetectable levels in 40 percent of the Taiwanese patients who received it—an effect that lasted 18 months. Thymosin's results were not as striking as with lamivudine, however, the drug has low toxicity.

Vaccines such as theradigm, now in Phase II trials, also boost the helper T-cell activity against infection. In lab animal studies, vaccinating mice with epitope-based vaccines such as theradigm, helped suppress the effect of HBV.

A Combination Approach Is Likely

An increasing number of experts agree that a two-pronged attack on HBV—attacking the viral replication factory and then reinforcing the immune system—is the best hope for victory. “Neither one approach alone is likely to be the answer,” says Dr. Schinazi.

But a combination therapy raises many issues. Should the drugs be started together or staggered? If staggered, which drug should come first? How long should each be given? And which patients are the best candidates for these therapies?

Despite the many unanswered questions, chronic HBV carriers have reason to hope, according to Dr. Schinazi. “There may be a lull right now in effective therapies, but be assured that scientists are working behind the scenes at new plans of attack and corresponding weapons to add to the artillery. It may appear to be slow, but we are moving in the right direction.”

Currently, he says, three drugs are now in clinical trials. “Within two years, another drug will be on the market.” In order for this to happen, however, “we need patients to volunteer for clinical trials.” (See this issue for more information about clinical trials.)

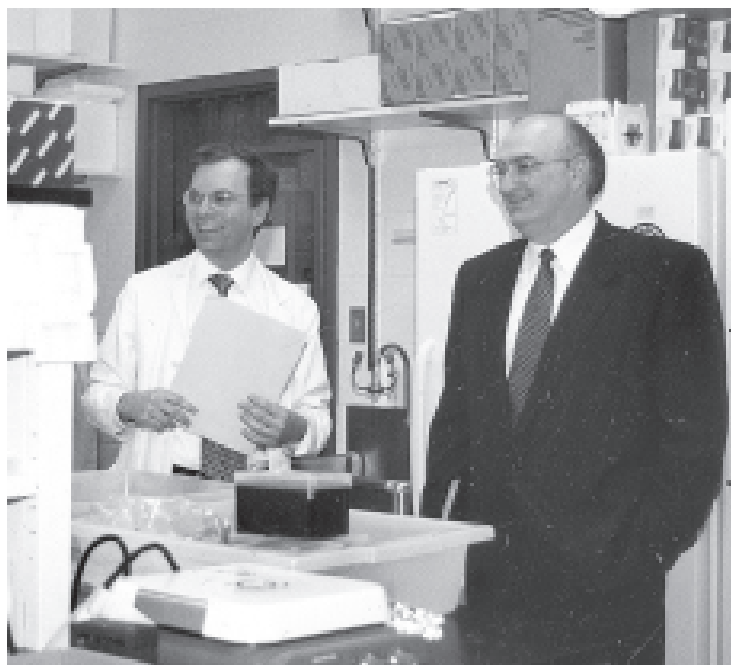
Only through research are we going to get to the cure, experts say. And yes, we said *cure*. Consider that a percentage of people spontaneously recover from HBV after periods of chronicity. “Cure through drugs should not be abandoned,” says Dr. Schinazi. “We have the opportunity to help patients with powerful new drugs on the horizon.”

Although delay in disease progression is the only possibility with the current drugs in development, suppressing viral replication by even ten years represents a huge step forward in turning the tide against this dreaded disease.

Foundation At The Forefront



Raymond Schinazi, Ph.D., (center) is honored with the first Bruce Witte Distinguished Lecturer Award on March 13. Pictured (left to right) are Timothy Block, Ph.D. and Paul and Janine Witte, co-founders of the Hepatitis B Foundation.



The Hepatitis B Foundation and the Jefferson Center announced a grant award from the state of Pennsylvania on February 23. Timothy Block, Ph.D., director of the Jefferson Center (left) shows Robert Zimmerman, secretary of health, Pennsylvania Department of Health, the HBF labs.

Fast Fact!

Currently, there are 2 FDA-approved drugs for HBV, 3 drugs in clinical trials, and at least 8 drugs in the pipeline.

Speaking Personally....

Living with Hepatitis B

Our daughter Maren is a beautiful, engaging, two-year-old. We adopted her when she was ten months old from Hunan province in China. A number of health issues prompted blood tests and Maren tested positive for Hepatitis B.

Despite being home only three months with her new family, Maren's pediatric gastroenterologist at Johns Hopkins urged us to have her biopsied and started on alpha-interferon treatment. When we asked the doctor (who directs Hopkins pediatric transplant program) why we should consider this treatment, given that the odds for sero-conversion are so low and the difficulty of the treatment protocol so high, she replied, "Because you have to try anything that you can to prevent her from needing a liver transplant later in life."

This statement had a profound effect on our decision. Even though the odds for success were low, we had to at least try the interferon.

At fourteen months of age, Maren had her first liver biopsy and began interferon injections at Johns Hopkins. One week later my husband and I were giving her injections three times a week. The shots were tolerable, but the monthly blood draws were very hard on Maren.

Fortunately, the side effects from interferon seemed less significant than what I had expected. Maren had limited muscle/joint pain, although she was certainly more fatigued than the average toddler. Despite all this, her personality continued to blossom.

Sadly, as we approach the one year anniversary of the completion of Maren's six-month protocol, we are told that she is considered a "non-responder." Worse, her liver is 20% on the way to cirrhosis. That seems like a lot for a two-year old baby.

I anxiously await the discovery of some new treatment protocol and live in fear that Maren's liver will not hold out long enough for a 'cure.'

We now are only beginning to consider some alternative therapies for Maren. She has been on milk thistle supplements for the last four months, despite her doctor's concerns about the purity of supplements. We would be interested in pursuing other alternative medicine options for Maren, but we're leery about "experimenting" on our two-year-old. I truly wish that there were some form of regulation on supplements.

Currently, the options for children with Hepatitis B are limited. Alpha-interferon is the only approved treatment. The current clinical trials testing lamivudine on children now underway are closed and FDA approval for this drug is not expected for two years. Our next opportunity to participate in a clinical trial will probably not occur until the summer of 2001 when Johns Hopkins hopes to conduct a combination trial involving two drugs, lamivudine and adefovir.

I find the lack of options for children with Hepatitis B frustrating. At this time, we're seriously considering putting Maren back on interferon because we understand the odds of sero-conversion on the second go-around are higher. Meanwhile, I anxiously await the discovery of some new treatment protocol that will eradicate the virus completely. Until then, I live in fear that Maren's liver will not hold out long enough for a "cure." My goal is to keep her liver in the best shape possible, so that we can delay such drastic measures as a liver transplant or progression to liver cancer down the road.

From this experience with Maren, I've learned about the importance of life and living it to the fullest. I can't begin to express the amount of respect I have for my little one. She is tough and courageous and sweet all at the same time. I admire all that she endures and will continue to endure as she grows up living with this terrible virus.

—Maren's Mom

**Have a question? Comment?
Personal story to share?**

We want to hear from you!
Contact us at:

**Hepatitis B Foundation,
700 East Butler Avenue,
Doylestown, PA. 18901-2697
Phone us at (215) 489-4900**

Visit Us On The Worldwide Web:
www.hepb.org

E-mail: info@hepb.org

Hepatitis B Foundation 4th Annual Awards Celebration

CAUSE FOR A CURE 2000
Friday June 23, 2000
Doylestown Country Club
Country Club Drive, Doylestown, PA

FOUNDERS' AWARD
Timothy M. Block, Ph.D.
Professor of Biochemistry and Director,
Jefferson Center for Biomedical Research
Jefferson Medical College
Co-Founder, Hepatitis B Foundation

DISTINGUISHED SCIENTIST
Harvey J. Alter, M.D.
Chief, Infectious Disease Section and
Associate Director, Research Department
of Transfusion Medicine National
Institutes of Health

DISTINGUISHED LEADERSHIP
Deborah L. Wexler, M.D.
Founder and Executive Director
Immunization Action Coalition

VOLUNTEER OF THE YEAR
Richard A. Rosenberger, Esq.
Partner, Souder, Rosenberger,
Bricker, Maza & Landis
Board Director, Hepatitis B Foundation
(1994 - present)

DISTINGUISHED PUBLIC SERVICE
Honorable Richard A. Tilghman
Pennsylvania State Senator
17th Senatorial District, Montgomery
& Delaware Counties

HBV DRUG WATCH: COMPOUNDS IN DEVELOPMENT FOR CHRONIC HEPATITIS B

Update: May 2000

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

FAMILY/DRUG NAME	MECHANISM	COMPANY	WEBSITE	STATUS, USA
Interferons Mimics naturally-occurring infection-fighting immune substance produced in the body				
Interferon alpha2-b (Intron A®)	Immunomodulator	Schering-Plough Madison, NJ	www.schering.com	FDA Approved 1991
<i>There are other brands of interferon approved for HCV treatment, but they have not been FDA-approved for HBV: Wellferon® (Glaxo), Roferon® (Hoffman-La Roche), and Infergen® (Amgen)</i>				
Nucleoside Analogues Interfere with the polymerase enzyme used to make the DNA involved in viral reproduction				
Lamivudine (Epivir-HBV®)	Inhibits viral DNA polymerase	GlaxoWellcome Research Triangle Park, NC	www.glaxowellcome.com	FDA Approved 1998
Adefovir Dipivoxil	Inhibits viral DNA polymerase	Gilead Sciences Foster City, CA	www.gilead.com	Phase III
DAPD	Inhibits viral DNA polymerase	Triangle Research Triangle Park, NC	www.tripharm.com	Preclinical
L-FMAU	Inhibits viral DNA polymerase	Triangle Research Triangle Park, NC	www.tripharm.com	Phase I
FTC (Coviracil®)	Inhibits viral DNA polymerase	Triangle Research Triangle Park, NC	www.tripharm.com	Phase II
Entecavir (BMS 275,400)	Inhibits viral DNA polymerase	Bristol-Myers Squibb	www.bms.com	Preclinical
Racivir	Inhibits viral DNA polymerase	Pharmasset	www.pharmasset.com	Preclinical
Fluoro-L and nucleosides	Inhibits viral DNA polymerase	Pharmasset	www.pharmasset.com	Preclinical
Non-Nucleoside Anti-virals Interfere with proteins involved in viral reproduction				
Nonyl-DNJ	Protein folding inhibitor	Synergy, Edison, NJ		Preclinical
Non-Interferon Immune Enhancers Boost T-cell infection-fighting immune cells and natural interferon production				
Theradigm	Immune stimulator	Epimmune, San Diego, CA		Phase II
Thymosin alpha-1 (Zadaxin®)	Immune stimulator	SciClone San Mateo, CA	www.sciclone.com	FDA Approved 2000
HBV DNA Vaccine (Genevax®)	Immune stimulator	Wyeth-Lederle Products London, U.K.	www.ahp.com	Preclinical
PreS1/S2 vaccine (Hepagene®)	Immune stimulator	Medeva PLC, London, U.K.	www.medeva.com	Preclinical
HBV Antigen	Oral Tolerance	Oragene, Alexandria, VA		Preclinical
Post-Exposure and/or Post-Liver Transplant Treatment				
HBV Immune globulin (Nabi-HBV®)	HBV Immune globulin	Nabi, Boca Raton, FL	www.nabi.com	FDA Approved (1999)
HBV Immune globulin (BayHep B®)	HBV Immune globulin	Bayer U.S., Pittsburgh, PA	www.bayer.com	FDA Approved

Thanks to Brent Korba, Ph.D. (Georgetown Univ. Medical Center, Rockville, MD) and Raymond Schinazi, Ph.D. (Emory University Medical School, Atlanta, GA) for their review of this Drug Watch Update.

How Do I Enroll in Clinical Trials?

Recently, the government opened a comprehensive database (www.clinicaltrials.gov) listing the thousands of clinical trials on experimental drugs and therapies targeting a range of diseases—including hepatitis B—to help link up sick patients with study centers throughout the country. The site joins the growing list of Internet sites such as www.centerwatch.com, a commercial site listing both NIH and pharmaceutical/biotech-sponsored trials around the world.

These easy-to-use sites should help widen the pool of eligible candidates and bring us a step closer to a cure, according to Robert Brown, M.D., medical director of the Center for Liver Disease and Transplantation at Columbia-Presbyterian University in New York City. "If we are to move forward on finding a cure for Hepatitis B, we need patients to move forward and become part of the testing of experimental drugs," he says.

Advantages to participating in a study include access to the latest advancements and "close monitoring by an expert specializing in liver diseases at a leading health care facility," says Dr. Brown. Expensive blood work and clinical monitoring are normally free of charge. Some trials even pay you to participate.

Whether you log onto the web sites above or contact the resources listed on page 9 be sure you understand the who, what, where, when and how of clinical trials.

For starters, you should know that **Phase I** clinical trials test new treatments in small groups of people (20-80) to evaluate safety, determine dosage and identify side effects. **Phase II** trials test the drug on 100-300 people to further evaluate its safety and effectiveness. **Phase III** studies test the drug on 1000-3000 people to confirm its effectiveness, monitor side effects and compare it to

commonly used treatments. **Phase IV** studies are done after the drug or treatment has been marketed to collect information about its effect in various populations and any side effect associated with long-term use.

A blinded or masked study means the participants do not know whether they are in the experimental or control group (the group given an inactive placebo). In a double-blind study, neither the participants nor the study staff know which participants are in the experimental or control group.

Testing sites for HBV treatments now in various stages of clinical trials include Stanford University in Palo Alto, California. At this writing, investigators there are recruiting participants to test antibodies. Dr. Brown's Columbia center recently closed its enrollment for testing the drug adefovir, but he expects to begin recruiting for FTC – another anti-viral nucleoside analogue drug – within the next few months.

Enlist your doctor to help you sift through all the information about trials and weigh the pros and cons. "Make sure you are clear about whether the drug being tested is better – or riskier – for you than no or existing treatment," says Dr. Brown. Remember that you'll continue to work with your primary health care provider if you participate in a trial and you can drop out of a trial at any time, he adds. Find out who is financing the study (i.e., the NIH, pharmaceutical companies, individual physician-investigators, or HMOs). Keep in mind that major medical centers that test drugs have the primary goal of research on the disease rather than the drug, says Dr. Brown.

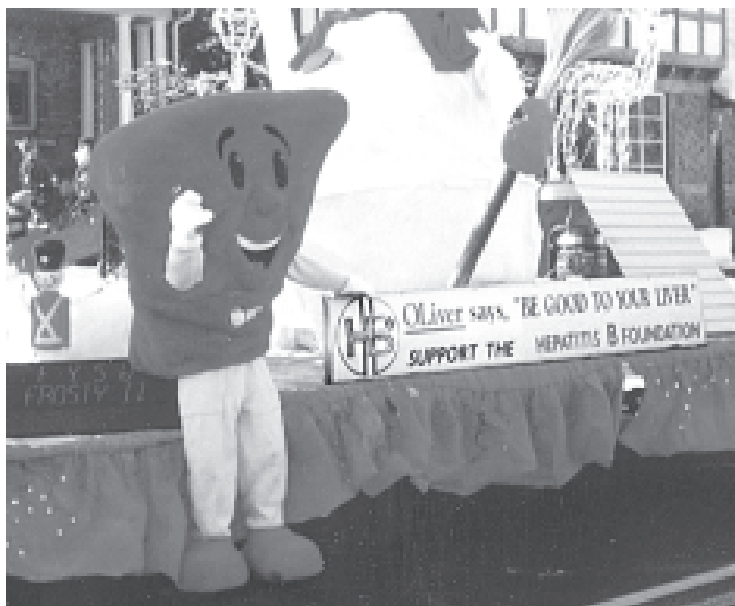
Take along a friend or family member when you meet the researchers as they go over the information in the box below.

Make sure you are clear about whether the drug being tested is better, or riskier, for you than no or existing treatment

Eight questions to ask before enrolling in a clinical trial:

1. Where is the site located (i.e., hospital, university, doctor's office or community clinic)? How often will I need to go there?
2. Will I be charged for any part of the trial? Will this be covered by my insurance?
3. Why do researchers think the treatment will work better than standard (FDA-approved) treatment?
4. What tests or procedures are involved?
5. How many people have tested it and what happened to them?
6. What are the possible short and long-term side effects? How are patients safely monitored while on the treatment?
7. What happens to my HBV when I stop the drug?

Foundation At The Forefront



O'Liver brings sunshine to the Lambertville/New Hope Winter Carnival Parade in Pennsylvania held on February 5.



The White House invited nonprofit leaders to Washington, D.C. to discuss the serious health threat of hepatitis B and C in America. This was also an opportunity for the groups to discuss how to work together to raise the national profile of viral hepatitis (May 10, 2000).

Left to Right: Mr. Francis Clark, Board Member, Hepatitis Foundation International; Dr. Elizabeth Fagan, Hepatologist, Rush-Presbyterian Medical Center; Ms. Trish Parnell, Executive Director, Parents of Kids with Infectious Diseases; Mr Alan Brownstein, President & CEO, American Liver Foundation; Ms. Joan Block, President, Hepatitis B Foundation; and Dr. Mark Kane, Executive Director, Bill and Melinda Gates Children's Vaccine Program.

Y2k Calendar Of Events

June 23, 2000

HBF Annual Awards Dinner to honor individuals who have helped the Cause for a Cure

Doylestown Country Club, Doylestown, PA.
Contact: HBF at (215) 489-4900

July 5 - 8, 2000

The 34th National Immunization Conference
Washington, D.C.

Sponsor: CDC National Immunization Program
Contact: (404) 639-8225
www.cdc.gov.nip/NIC

September 8-10, 2000

NIH workshop - Management of Hepatitis B: 2000
Bethesda, MD

Sponsor: National Institutes of Health
Contact: (301) 493-9674
Chun@computercraft-usa.com
www.ep.niddk.nih.gov/epconferences.htm

September 17-21, 2000

Molecular Biology of Hepatitis B Viruses Annual Meeting
Institut Pasteur, Paris, France

Contact: Marie Annick Buendia,
Institut Pasteur, Paris and
John Taylor, Fox Chase Cancer Center,
Philadelphia, PA.
www.pasteur.fr/infosci/conf/hbv2000.html

October 27-31, 2000

50th Anniversary Meeting of the American Association
for the Study of Liver Diseases,
Dallas, TX

Contact: AASLD (703) 299-9766
www.aasld.org

November 9-10, 2000

Viral Hepatitis Update
Philadelphia, PA.

Sponsor: American Society for Microbiologists
(Eastern PA.) in collaboration with the HBF
Contact: Karen Hartwig at (610) 280-3464
email: khartwig@state.pa.us
Or, HBF at (215) 489-4900 email: info@hepb.org

December 3-7, 2000

7th International Meeting on Hepatitis C
and Related Viruses

South Brisbane, Queensland, Australia
Contact: Drs. Graham Cooksley and Eric Gowans
www.icms.com.au/hepcv

Fast Fact!

Chronic HBV is the 9th most common cause of death worldwide.

Resource Roundup

Hepatitis B Foundation
215-489-4900 www.hepb.org
info@hepb.org

A website dedicated solely to hepatitis B. Facts, useful advice, Drug Watch, liver specialist directory, and a responsive email "info-line".

Centers for Disease Control, Hepatitis Branch
1-888-443-7232 www.cdc.gov/ncidod/diseases/hepatitis

The national authority for 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

American Liver Foundation
1-800-Go-Liver www.liverfoundation.org
webmail@liverfoundation.org
Information about all liver diseases, including viral hepatitis. Patient support, legislative advocacy, research funding, and chapter reports from across the nation.

Hep C Connection
1-800-522-4372 www.hepc-connection.org
hepc-connection@worldnet.att.net

Hepatitis C Foundation
215-672-2606 www.hepcfoundation.org
hepatitis_c_foundation@msn.com

Hepatitis Control Report
www.hepatitiscontrolreport.com
A quarterly publication on-line (and hardcopy) with thoughtful and timely news articles on the control of viral hepatitis.

Hepatitis Foundation International
1-800-891-0707 www.hepfi.org
mail@hepfi.org
Information about viral hepatitis, support groups, research articles, and education programs.

HIV and Hepatitis Treatment Advocates
www.hivandhepatitis.com
Professional On-line publication focusing on treatment updates with a free email announcement service.

Immunization Action Coalition
651-647-9009 www.immunize.org
medinfo@immunize.org
Comprehensive resource of practical immunization and hepatitis information health care providers can use. "IAC Express" is a free email announcement service.

Parents of Kids with Infectious Diseases
1-877-55-PKIDS (toll-free) www.pkids.org
pkids@pkids.org
An excellent resource for parents who need information and support. Pediatric clinical trials, ask "Dr. Jane", Listserve, and useful articles.

On-Line HBV Support Groups

...Important Links

Hep B Information and Support List
<http://www.geocities.com/heartland/estates/9350/hblist.html>

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

A well-supervised list with useful information and lively exchanges between supportive members. Primarily adults with HBV, but parents are welcome to join.

PKIDS Support List
<http://www.pkids.org/>

For parents of children with chronic viral infectious diseases, including HBV. Kids are also encouraged to join, and if there's enough interest, a separate list will be developed by PKIDS.

HBV Adoption Support List
<http://www.onelist.com/community/hbv-adoption>

For parents of adopted 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 Publications

Viral Hepatitis: A Handbook for Clinicians and Scientists
by Dr. Elizabeth Ann Fagan, Rush Medical Center (Chicago, IL) and Dr. Tim J. Harrison, University College London (London, U.K.). Springer-Verlag (Secaucus, NJ).

This book bridges the gap between the clinical and molecular aspects of viral hepatitis. It provides a practical guide to the application of molecular virology in clinical practice and the scientific rationale behind managing and treating patients with viral hepatitis.

For information, visit www.bios.co.uk, email: efagan@rush.edu, or call 1-800-SPRINGER.

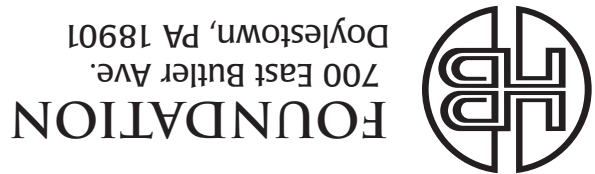
Vaccines: What Every Parent Should Know (revised edition)
by Paul A. Offit, M.D., Children's Hospital of Philadelphia (Phila, PA) and Louis M. Bell, M.D., Children's Hospital of Philadelphia. IDG Books (NY, NY)

An essential reference on vaccines for parents (and doctors!). With the many vaccine choices and all the vaccine controversy in the media, this book helps sort out the confusing information in an accessible and easy-to-understand format. For more information, call Rebecca Baumgold @ 215-590-4172

Hepatitis Magazine

Published 6 times yearly by Quality Publishing Inc. as a resource for individuals and families affected by viral hepatitis. Although primarily geared towards hepatitis C, the articles frequently include information that is also relevant for those chronically infected with HBV.

For more information, email: editor@hepatitismag.com or call 1-800-310-7047.



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HEPATITIS B FOUNDATION

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