

HCV ADVOCATE

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HealthWise

Liver Labs: Part Two

Lucinda K. Porter, RN

In last month's Healthwise, there was a basic description of common tests used for monitoring the condition of the liver. One issue that can be very frustrating for hepatitis C patients is that they often hear "do not worry about the ALT and AST results". An understandable response to this is, "then why order the test?" Simply put, the physician is looking at the bigger picture. When someone has elevated ALTs, it is perhaps more significant at that point to look at other indicators. If nothing else is abnormal, then this is a much better condition than if there are abnormalities. Furthermore, looking at trends and specific ranges of lab abnormalities is more important than just looking at a single abnormality.

Treatment Advocate

Joe Shaw

Before we get started with this month's treatment advocate column, I wanted to share a little about myself.

I was diagnosed in January '98. Had a biopsy, PCR, etc. The biopsy showed the beginnings of fibrosis, the PCR was 1,400,000. My liver enzymes have been consistently high (over 100), since January '98.

My HMO doctor wanted to put me on Intron A, but I rejected that because I believed that if I was going to subject myself to interferon therapy, I might as well go for one that has a better chance of success such as the interferon-ribavirin combo therapy.

I was accepted into a clinical trial in October '98, and I am on the standard 3 MU dose of interferon with 1200 mg. of ribavirin.

One of the ironies of this study is that they tested my genotype and it turned out to be 2b, which responds to therapy better, so it may have been an okay decision to have gone with the monotherapy back in July, like the doctor wanted, since there was a better chance for success. But knowing my genotype strengthened my decision to participate in this trial as I may have an even better chance of responding to treatment.

I have really been through the ringer--changed jobs, now I have a much better one, but with that comes more responsibility and stress--I moved to a new place at the beach (which should help with the stress some), and I've been distressed and taking it out on myself by eating constantly and I virtually stopped exercising which I used to do four-five times a week. I've gained about 25 pounds since January.

When I first began the combo therapy, the side effects were muscle aches and headaches, you know, the flu-like symptoms they tell you about. But after several weeks, it was depression. I didn't really want to do anything. Just watched TV and sat around the house, when I was home from work. After two months, I saw a psychiatrist and began taking anti-depressants. The nurse in my clinical trial said that they were going to start recommending that all people who do interferon therapy start their anti-depressants right away. I would highly

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HCV ADVOCATE

Alan Franciscus – Founder / Editor
Russell Keimer – Co-editor
Hepatitis C Support Project
P.O. Box 427037
San Francisco, CA 94142-7037
Helpline: (415) 834-4100
Email: SFHEPCAT@MSN.COM

suggest that if you are beginning therapy, to go ahead and start on anti-depressants. I'm on 50 mg. of Zoloft daily.

After only two weeks of treatment, my liver enzymes went down by half and two weeks later they were normalized. They remained normal since then, and because I'm in a PCR-blind study, I won't know my PCR until the end of the study. I'm really happy that my enzymes are normal, because to me that means this crazy virus "ain't working no more." So my liver's getting better.

I'm also lucky in that I've been able to continue to work, and the sides have been relatively mild. After nearly five months on treatment, though, new sides have popped up: dry skin and itching. I've switched all my soaps and shampoos to Nutragena products and am taking Aveeno bath treatments to relieve the itching. But it's worth it to me to suffer a little now for the positive results for my liver.

Now, here are some selected studies, news briefs and other items that may be of interest to people living with Hep C. Remember, these are compiled from the internet, come from various sources which I cannot absolutely 100 percent vouch for their accuracy. The purpose of this column is to give you information so you can be your own treatment advocate.

Info about Genotypes and Genetic Variation of Hepatitis C Virus from The Hep C Review, December 1998

Hepatitis C virus is not a single organism but is a range of viruses, similar enough to be called hepatitis C virus, yet different enough to be classified into subgroups.

Genotype patterns

It is believed that the hepatitis C virus has evolved over a period of several thousand years. This would explain the current general global patterns of genotypes and subtypes:

1a - mostly found in North & South America; also common in Australia

1b - mostly found in Europe and Asia.

2a - is the most common genotype 2 in Japan and China.

2b - is the most common genotype 2 in the US and Northern Europe.

2c - the most common genotype 2 in Western and Southern Europe.

3a - highly prevalent in Australia (40% of cases) and South Asia.

4a - highly prevalent in Egypt

4c - highly prevalent in Central Africa

5a - highly prevalent only in South Africa

6a - restricted to Hong Kong, Macao and Vietnam

7a and 7b - common in Thailand

8a, 8b & 9a - prevalent in Vietnam

10a & 11a - found in Indonesia

From The Hep C Review, December 1998.

Regression Of Cirrhosis, Hepatic Fibrosis In Hepatitis C Patients Possible With Interferon Therapy

Early-stage cirrhosis and fibrosis may be reversible in some hepatitis C patients who respond to long-term interferon therapy, according to researchers from the New England Medical Center in Boston.

Two patients had early-stage (class A) cirrhosis and/or extensive fibrosis. After 23 and 30 months of treatment with interferon-alpha, liver biopsies in both patients revealed no evidence of cirrhosis or liver fibrosis. Both patients also demonstrated complete responses to interferon therapy, with "...normalization of all liver function tests and disappearance of hepatitis C viral RNA."

Based on this evidence and that of other investigators, the Boston researchers concluded that "...the presence of cirrhosis on a liver biopsy in a patient with chronic hepatitis C and conserved hepatic synthetic function should not be a contraindication for treatment with [interferon-alpha]."

From: Digestive Diseases and Sciences, December 1998.

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(Condensed consensus statement. The full version can be obtained by contacting the PWA Health Group: (212) 255-0520 or email: james@aidsinfo NYC.org. Please return endorsed statements to the PWA Health Group, 150 West 26th Street, Suite 201, New York, NY 10001 or by fax: (212) 255-2080.

HEALTH CARE COMMUNITY ALERT

Consensus Statement to Schering-Plough Pharmaceuticals

Re: Rebetron Development and Marketing Practices

The initial creators and sponsors of this consensus statement are: The Hepatitis C Action & Advocacy Coalition (HAAC), a national, grassroots, all-volunteer group of individuals committed to non-violent direct action to end the Hepatitis C crisis; the PWA Health Group, a New York City-based national HIV/AIDS treatment information, education and advocacy organization; and Project Inform, a national organization located in San Francisco dedicated to HIV/AIDS treatment information, education and advocacy.

UNBUNDLING OF REBETRON: Ribavirin must be unbundled from Intron-A and made available as a separate anti-viral agent to be used in combination with other interferon formulations. It is to be clearly labeled so that the drug is not used as a single agent for HCV, but only in combination with another HCV treatment. In addition, clinical trials comparing the efficacy of Rebetron with combinations of ribavirin and other interferon formulations must be developed immediately through inter-company cooperation and access of ribavirin to private researchers.

We know that the FDA is prepared to work with Schering on the unbundling process. People with Hepatitis C must have a choice of the available interferons in order to have the best shot at ribavirin/interferon combination treatment. This is a matter of individual patient choice!

PRICING: Ribavirin is to be cut in price by 75% from the current estimated price of \$1,020/month (1,200 mg/day dosing) to \$255/month, near its 1995 price and in line with current drugs in its class.

Ribavirin is available as a single agent in Mexico and Western Europe. However, because Schering-Plough does not own the rights to the drug there, the price is at least 265% lower than in the United States, if you could get it alone here. Ribavirin is easy to manufacture compared with most other anti-viral agents, yet it is priced 346% higher than the next highest priced drug in the same nucleoside analogue anti-viral class (Ziagen, abacavir). Schering has ample opportunity to continue to make substantial profits with a lower-priced, unbundled ribavirin product since it is in high demand to be used with other companies' interferons.

UNBLINDING OF VIRAL LOAD RESULTS IN CLINICAL TRIALS: Schering-Plough must immediately unblind the results of clinical trial participants' HCV viral load tests. Rather than advising doctors to explain the reasons for blinding to their patients, Schering-Plough should initiate and finance an education campaign, implemented by the primary care physicians treating people with Hepatitis C, which will endeavor to explain the importance of viral load test results in assessing the full clinical picture of the individual's response to his/her treatment regimen. With such education, people enrolled in the clinical trials can make thoughtful, well-informed choices about whether or not to continue in the trial if their viral loads are increasing.

THE CREATION OF ETHICAL PATIENT ASSISTANCE PROGRAMS: Schering-Plough must develop two truly comprehensive, ethical drug assistance programs:

1) an expanded access/compassionate use program to help individuals gain access to ribavirin alone in order to create viable personal treatment regimens with other available interferons, and 2) a more conventional program to assist individuals access Rebetron free-of-charge who have no other means to do so. Until the products are unbundled, the expanded access/ compassionate use program must allow individuals, through their doctors, to obtain ribavirin alone and free of charge for use with other interferons or different doses of Intron-A-without having to jump through hoops and undergo substandard therapy first.

In the interest of public health, we the undersigned demand that Schering-Plough respond immediately to the concerns set forth in this statement.

Print Name

Signature

Date

Organization

Contact Info (Names, phone, fax, email)

MY BIOPSY

Alan Franciscus

There is a lot of fear surrounding a liver biopsy. When I had a liver biopsy 3 years ago I was very nervous and asked for some pain medication. The experience was relatively pain free but I didn't know if it was pain free due to the pain medication or the procedure itself. Lately, I have been thinking about being re-treated and a liver biopsy would help in my decision making process. Besides I wanted to see if the pesky little virus had done any further damage to my liver. Due to the feedback I had received from so many people, I decided to have the procedure without any pain medication.

I woke up at 7:00AM but could not drink any liquids (coffee!) or eat anything solid. This is not a good way for me to start my day – cranky!

I arrived at the hospital around 9:00AM to register. I was told to go to the radiology department where they located my liver via an ultrasound and marked the spot where the doctor would insert the biopsy needle.

Next it was up to the GI Department where I was shown into a room and told to get into bed. There were two of us in the room with only a curtain separating us. The doctor came in and started the biopsy procedure on my hospital roommate. I listened with interest as he instructed his patient on exactly what the procedure involved. I was starting to get a little nervous! Hmmm...no sounds (screams) were coming from my roommate. That was very reassuring. The patient even said “that was painless.” That one statement reassured me more than all the people I had ever talked with about a biopsy.

My turn was next! The doctor came in and proceeded to explain the procedure and had me practice my breathing. First he gave me a shot to numb the skin around the needle insertion site. This felt like a little pinch - good so far. Next I was told to breathe in - breathe out and hold my breath. The doctor then inserted the biopsy needle. Whew - I felt a little pressure but **NO PAIN!** It was done. The doctor took out a very, very tiny piece of liver and the procedure was over before I knew it. I was then told to roll over on the side where the needle had been inserted. Next came the worse part... lying on your side for 2 hours to monitor you for possible complications. Shortly after rolling over on my side I experienced a little pain and nausea but it was over in approximately 20 minutes. Thirty minutes later I was given some juice and crackers, which were extremely tasty – guess I was hungry!

A couple of hours later a friend picked me up and we went out for coffee and pastries. I think the worst part of the whole procedure was missing my morning coffee!! Now, when I have patient education sessions and people ask about a liver biopsy with fear in their eyes and a slight tremble in their voice - I will be able to say it was practically painless and will really enjoy seeing some of their fears disappear.

Biopsy results: In the three years since my original biopsy, HCV has not produced further recognizable damage to my liver. I attribute this to a year on interferon therapy as well as lifestyle changes. This information will further help me in my decision making process for re-treatment with high daily dosing of Infergen.

For more information about hepatitis C, please contact the following organizations:

- American Liver Foundation 800-223-0179 <http://www.liverfoundation.org/>
- Hepatitis Foundation International 800-891-0707 <http://www.hepfi.org/>
- Hep C Connection 800-522-4372 <http://www.hepc-connection.org>

VA to Offer New Hepatitis C Drugs

The Department of Veterans Affairs announced on January 27 plans to offer a combo therapy--interferon and ribavirin--treatment to former military personnel suffering from hepatitis C. The costs of the HCV initiative--\$250 million to \$300 million this year alone--have provoked questions outside the VA about the necessity of the effort. The costs likely will rise sharply as more veterans are tested. Those veterans who test positive will have the option of taking the new drug treatment. VA officials say that a six-week study at the veterans hospital in Northwest Washington found 20 percent of the patients tested positive for HCV. A study at the San Francisco VA hospital found 18.9 percent of the patients undergoing routine blood work tested positive and the department said more than half of all its liver transplant patients have HCV.

From The Washington Post.

Life After the Combo

by Darlene Morrow

Today is January 3rd and I am 45 years old. It seems like a good time for reflection; a time to consider what this life is all about.

Exactly five years ago I was attacked by a mysterious illness. In a matter of months I was struck down from a vibrant, healthy and active life to one teetering on the brink of disaster and uncertainty. Slowly I began to lose my life as I knew it.

My health quickly deteriorated. In addition to dealing with that, I was forced to battle a medical system that I thought existed to protect and help me. I had to give up my job. I almost lost my faith. I almost lost my hope. But without hope, what are we?

Everyday was a struggle. I would often think- when did life get to be so hard? How do I go on? How can I drag my family down like this? Why must they live this life too?

And then it was more for them than for me that I found the courage to go on the interferon and ribavirin therapy. I just wanted OUR life back.

For 21 months my life was indescribable. I won't try to soft sell you- I reacted badly to the drugs. At times I thought I was crazy! The response rate is only 42 percent-it's not even half. What chance was there? At times my husband would beg me to stop. And that's really what I wanted to do. But I couldn't stop hoping. I just wanted my LIFE back.

In September the therapy was finished. I wanted to feel life again NOW. Immediately I had a surge of energy, easily explainable as my hemoglobin rose from 97 to 125. And then it stopped. I was still tired. Very tired. Was this as good as it would get? 3 months went by. I was desperate. I didn't want this to be my life. But then something happened. I began to feel a little more energetic. I didn't want to get excited- this disease waxes and wanes- it could just be a part of the cycle. But I kept on feeling better. I kept on getting more energy.

I joined the gym. I started doing cardiovascular conditioning-the bicycle, then the treadmill, and yes-even the Stairmaster! I started lifting weights. And I kept on feeling better.

I am afraid to say it out loud- I don't want to tempt the gods. BUT I FEEL BETTER!!!! I am about 75% of normal! I HAVE my life back. I feel as though I am blessed. I don't know how long this will last but I am going to enjoy every single second. Every day of that therapy was worth having my life back. And this could be you. You might get your life back. How will you know if you never try?

42% respond. How many will relapse? We need to continue to push for the research to find a cure, to help those people that can't take the combo, to help those people that don't have a sustained response.

Post script February 9, 1999: There is more to the story. Unfortunately 2 1/2 months post treatment I am PCR positive again. But I had a repeat biopsy and it showed a reduction in the scarring from Stage 2 to Stage 1 and the inflammation from Grade 2 to grade 1!!!! There is NO piecemeal necrosis present! The therapy stopped the HCV in its track and the liver is powerful enough to destroy the scar tissue and regenerate new healthy tissue. The official biopsy report read SUSPENDED HCV.

I still feel great. I am now discussing the option of going on low dosage maintenance therapy interferon. The combination therapy bought me time - time to find a cure. Time to live my life. :-)

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Gene treatment shows promise in reversing liver cirrhosis

Scientists wiped out liver cirrhosis in rats by injecting their muscles with a human gene, raising early hopes for a new treatment for people. The gene made the rats pump out high quantities of a protein that promotes liver regeneration while reducing cell death. That cleared up serious cirrhosis in the animals, researchers reported. A liver expert called the work exciting and said such treatment might someday be able to prevent cirrhosis in people at risk for it, and possibly reverse the damage in patients who already have it.

There's no guarantee the treatment would work in people. The treatment was based on a protein called hepatocyte growth factor, or HGF. Previous work has shown HGF can promote liver regeneration and suppress cell death, while blocking a second protein that encourages scar formation. *From The Associated Press.*

INFO UPDATES

Is Ibuprofen Harmful to the Liver? A Small Study Raises The Question

By Lynn Shawn - The Hepatitis Place

<http://www.hepplace.com>

The pain-reliever, ibuprofen, is one of the nonsteroidal anti-inflammatory drugs (NSAIDs) effective in treating a variety of aches and pains, and reducing fevers. Ibuprofen is easily obtained over-the-counter or by prescription, and many individuals believe that ibuprofen offers better pain relief. But is this NSAID drug safe for individuals with chronic hepatitis C? Could ibuprofen be harmful for the liver, or cause drug-induced hepatitis?

Inflammation is characteristic of liver injury. Typically, liver injury is estimated by increased activity of several liver enzymes. These enzymes are known as alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gamma-glutamyltransferase (GGT).

Few studies have been conducted on the potential hepatic danger of ibuprofen. A recent article entitled "Ibuprofen-Induced Hepatotoxicity in Patients With Chronic Hepatitis C: A Case Study" by Thomas R. Riley, III, MD and Jill P. Smith, MD from the Hershey Medical Center at the Pennsylvania State University (American Journal of Gastroenterology 1998; 93:1563-1565) offered the findings of three case reports. In this article, the case studies reported elevations in liver transaminases during the use of ibuprofen. Upon discontinuation of ibuprofen, liver transaminases returned to baseline. Based upon the findings of these three case reports, the authors of this study recommended the use of acetaminophen over nonsteroidal antiinflammatory drugs.

This report monitored 3 adult male Caucasian HCV-positive patients presenting with neck, shoulder, and/or wrist pain. Ibuprofen was prescribed for pain relief, in each case. Each patient's liver enzymes were measured prior to ibuprofen therapy, as well as during and after therapy. Each case showed a marked increase in liver enzymes during ibuprofen therapy. Each case showed a resolution to baseline after ibuprofen was discontinued.

The results from this small study are interesting to note, and raise valid questions concerning the safety of ibuprofen for those with HCV. However, drawing medical conclusions using study data of only 3 individuals would be premature. Perhaps future studies will provide more conclusive data with which to base sound, medical judgements upon when choosing over-the-counter ibuprofen.

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Sometimes the ALT and AST are called liver function tests. In reality, these are not measurements of liver function, rather than an indicator of an inflammatory process occurring in the liver. True liver function can be more accurately gauged by a group of tests commonly referred to as synthetic function tests. These include total bilirubin, creatinine, and albumin. In addition to these, platelets and prothrombin time are monitored. Your physician will be monitoring these, looking for trends as well as for the particular numbers. Keep in mind that if any one of these is abnormal, this does not automatically signify a dire situation.

In addition to liver function panels and complete blood counts, your doctor might monitor your iron levels. Hemochromatosis, or iron overload, is a fairly common condition. Those with cirrhosis should be monitored for cancer (hepatomas). In addition to an ultrasound test, a blood test called an AFP (Alpha-fetoprotein) can be useful. This test can be abnormal without cause for concern. Again, the key here is to look for trends and high abnormal.

In addition to tests that monitor our condition, there are tests that reveal specific information about the actual HCV virus. These tests are not particularly useful for anything except to monitor a patient's response to treatment. One test is called a viral load test. It is sometimes called a viral count, PCR, or HCV RNA. This test counts the actual viral particles. This test is not standardized and there can be wide variations from lab to lab. Sometimes patients think their viral count is worsening when in fact the difference is nothing more than variations in testing capabilities. Furthermore, the actual number does not correlate to HCV progression. In other words, a high viral load is no reason to lose sleep. Another test is to determine the genotype. This test is much like blood typing – we all have blood, but some of us are A, B, AB or O. Well, among those with the hepatitis C virus, some are 1's, 2's, 3's, etc. In this country, most people with HCV are genotype 1 (1a or 1b). Again, the genotype can give the clinician some descriptive information about the HCV virus, but its usefulness is very narrowly defined.

This article covers a lot of ground using a very brief format. This information is intended to help you build tools. However, tools are useless without the knowledge of how to apply them. That knowledge will come in time. If this information serves to reduce anxiety while broadening your base of knowledge, then it has served its purpose. If this article raises your anxiety, please look for other tools.

Treatment Advocate - continued from page 2 -

Heterosexual transmission of hepatitis C in Italy.

An Italian study evaluated the risk of heterosexual transmission of hepatitis C virus (HCV) associated with sexual activity with multiple partners in subjects over 15 years of age. After factoring out transfusions and IV drug use, the risk of hepatitis C was 2.0 times higher for subjects with two sexual partners and 2.8 times higher for subjects with three or more sexual partners, as compared to subjects with less than two sexual partners. These findings suggest that heterosexual transmission may play an important role in the spread of hepatitis C in Italy. *From: J Med Virol Feb 1999.*

Liver Transplant Waiting Times by Region

A list of liver transplant waiting times around the country. Waiting times are given by region. Listed is the region, the states it includes and the median number of days a patient with blood type O (the most common) waited in 1994-96 for a liver transplant. Half the people waited longer than the median and half waited for fewer days. Nationwide, the median wait was 374 days.

Region 1: Maine, Vermont, New Hampshire, Massachusetts, Connecticut, Rhode Island -958 days.

Region 2: Pennsylvania, New Jersey, Delaware, Maryland, West Virginia, District of Columbia -- 572 days.

Region 3: Arkansas, Louisiana, Mississippi, Alabama, Georgia, Florida -- 123 days.

Region 4: Texas, Oklahoma -- 213 days.

Region 5: California, Nevada, Utah, Arizona, New Mexico, Hawaii -- 723 days.

Region 6: Washington, Oregon, Idaho, Montana, Alaska -- 344 days.

Region 7: North Dakota, South Dakota, Minnesota, Wisconsin, Illinois -- 393 days.

Region 8: Wyoming, Colorado, Nebraska, Kansas, Iowa, Missouri -- 384 days.

Region 9: New York -- 496 days.

Region 10: Michigan, Indiana, Ohio -- 475 days.

Region 11: Kentucky, Tennessee, Virginia, North Carolina, South Carolina -- 208 days. *From The Associated Press.*

If you would like more information on any of these items, or would like copies of particular studies or articles, please e-mail me at joeesha@yahoo.com