

October
2001

Volume 4
Issue 10

HCV Advocate

A monthly newsletter of the Hepatitis C Support Project
www.hcvadvocate.org

Peg-Intron Plus Ribavirin - An Analysis Plus Questions to Ponder

By Alan Franciscus
Editor-in-Chief

Every person affected by hepatitis C, including me, has been waiting for many years for the approval of the pegylated interferons in combination with ribavirin.

There are four reasons which suggest that this new combination will be a major advance over the current standard of care, Rebetron (standard interferon plus ribavirin). First is an increased rate of Sustained Virologic Response (SVR). SVR means that HCV RNA is negative at six months after treatment.

Second, improved liver histology (the health of the liver) and slowed progression to cirrhosis. Third, the new therapy will be easier to tolerate and have fewer side effects.

Finally, pegylated interferon will be more convenient and easier to administer. I have analyzed the Peg-Intron/Rebetol (pegylated interferon (2b 1.5 mcg plus ribavirin 800mg) package insert and can make some educated comments about the first pegylated interferon/ribavirin combination to be approved.

On the positive side, we are getting a drug that only has to be injected once per week, instead of the three times per week injections with Rebetron. However, based on the package insert, I have many concerns about the increased side effect profile.

The cost of the new therapy is another major concern, since we already know that Peg-Intron alone costs approximately \$12000-18000 per year depending on the dose (1.0 mcg/kg to 1.5mcg/kg). If we add the price of Rebetol, we could have a substantial increase in price over Rebetron combination therapy without sufficient benefits that

would warrant that additional expense.

In regards to efficacy or effectiveness, the overall SVR in clinical trials was 52% for Peg-Intron/Rebetol versus 46% for Rebetron, without a p-value listed, which probably means that this improvement in efficacy almost certainly does not meet statistical significance.

In patients with high viral load and HCV genotype 1, the SVR was 30% for Peg-Intron/Rebetol versus 29% for Rebetron. That is only a 1% increase for the majority of people with HCV in the United States. Even more disturbing is that the package insert states that 47% of patients had to have dose reductions due to adverse events.

My next area of concern. Is there a histological improvement from the Peg-Intron component of therapy? This is especially important for those patients who do not clear the virus, but at least could have an improvement in liver health..

The Peg-Intron/Rebetol package insert states that there is no difference in histological improvement between Peg-Intron/Rebetol and Rebetron. That did not come as a surprise, because Peg-Intron monotherapy trials did not show a histological improvement over Intron-A, and the addition of ribavirin is not believed to have any impact on liver histology. When I looked at the side effect profile of

See Peg-Intron & Ribavirin on page 6

In This Issue:

Herbs & Hep C	page 2
Liver Fibrosis & Co-Infection	page 5
Cryoglobulinemia	page 7

Herbs and Hepatitis C

By Lucinda K. Porter, RN

The use of herbs is controversial in the medical community largely because of the lack of evidence-based research supporting efficacy. Couple this fact with the potential harm these substances might inflict, and it's easy to see why physicians are reluctant to endorse the use of herbs. On the other hand, many patients are interested in alternative therapies to use with, or in place of, a standard treatment their doctors have prescribed.

Since many herbs can cause liver damage, this review with list of apparently safe and potentially toxic herbs is to help the hepatitis patient make informed choices. Many herbs can be harmful in other ways, such as by having potentially carcinogenic properties or by causing neurological damage. The list of herbs reviewed below is primarily specific to patients with liver disease and by no means exhaustive. The substances on this list are referred to in their oral form only.

Herbs and supplements can be powerful. As with any medication, be certain your healthcare practitioner is aware of what you are taking or plan to take. Do this even if you feel that your healthcare provider is not supportive of the use of supplements or herbs. Healthcare practitioners are becoming increasingly aware of the use of herbs and the potential for interactions with other drugs and supplements. Herbs and supplements are considered to be dietary supplements. This means that they are virtually unregulated by any federal agency. Since herbs can vary in strength and purity, it is wise to take a standardized and certified form. Certification and standardization is voluntary.

The goal of the United States Pharmacopeia (USP) is to set industry standards for drugs and dietary supplements in the U.S. The label of a supplement that states it meets the standards of the USP is worth considering. If it meets the USP standards, the product is allowed to display a National Formulary (NF) seal. Another standard is that of the world's leading authority on herbs, the German Commission E. This agency is the German equivalent of the Food and Drug Administration (FDA). The American Herbal Pharmacopoeia is also developing standardization guidelines for the American marketplace.

HealthWise

Recently, a company named ConsumerLab.com has provided a much-needed service by testing popular supplements. This company has discovered that many products do not contain the levels of key ingredients that are on the products' labels. A product that passes their inspection may carry the triangular label with the ConsumerLab.com quality of approval. This service is in its infancy and at the time of this article only a few products have been tested. Companies that belong to the American Herbal Products Association and who submit to this organization's code of ethics are another good choice. These are listed at www.ahpa.org/links2.html

Herb Tips

- Tell your doctor all the herbs and supplements you take, even if you think your doctor might disapprove. Drugs and supplements can interact with each other as well as affect other health conditions.
- Follow the label's dosage recommendations; more is not better.
- Know your source; herbs may be contaminated. Before ingesting anything, ask yourself what you know about what you are about to take.
- Buy products that submit to voluntary self-regulation.
- Natural does not equal healthy or safe. Dirt is natural, but would you eat it?
- Do not be swayed by bargain prices; not all herbs are equal.
- Check the expiration date on the container.
- Do not rely on the health food store staff for health care information. Although they may be helpful, remember that they are not licensed to practice medicine. Do not treat your condition on the advice of a salesperson.
- Apply the same commonsense approach to herbs as you would to any drug. Consider that if you are reluctant to take acetaminophen, why would you take an herb?
- Herbs and supplements should not be given to children or taken by pregnant or nursing women without a physician's approval. Older adults and those with various health conditions should also exercise extra caution before taking non-prescribed supplements.

See Herbs on next page

Herbs

Continued from previous page

-Report any suspected adverse reactions to an herb or supplement to the FDA's monitoring program, Medwatch. Call 800-322-1088 or www.fda.gov/medwatch.

Milk Thistle

Milk Thistle (*Silybum marianum*), is the most commonly used herb for liver disease. The use of milk thistle for chronic hepatitis C virus (HCV) infection has not been well researched. Milk thistle may interact with other drugs. If you take milk thistle, look for a standardized dose. A product label that states it meets more stringent manufacturing requirements is even better. Tell your all your doctors you take milk thistle, especially if you are taking other medications. Interferon

Warning: Although Chinese herbs are sometimes used successfully to treat symptoms, these also need to be used with great caution. This article does not cover most of the Chinese herbs. One exception is worth noting.

Xiao Chai Hu Tang (Minor Bupleurum) is a popular herb used in Traditional Chinese Medicine for liver conditions. At least 16 deaths have been reported in Japan for HCV patients being treated simultaneously with alpha interferon and Xiao Chai Hu Tang (Minor Bupleurum).

Herbs with Known Toxicity

Alkanna (*Alkanna tinctoria*) *
 Borage (*Borago officinalis*) *
 Chaparral (*Larrea tridentata*) *
 Colt's Foot (*Tussilago farfara*) *
 Comfrey (*Symphytum officinale* and *S. uplandicum*) *
 Dong Quai (*Angelica polymorpha*) Dusty Miller (*Senecio cineraria*)
 Ephedra aka Ma Huang (*Ephedra Sinica*) Forget-Me-Not (*Myosotis arvensis*) *
 Germander (*Teucrium chamaedrys*) *
 Groundsel (*Senecio vulgaris*) *
 Hemp Agrimony (*Eupatorium cannabinum*) *
 Hops (*Humulus lupulus*)
 Jin Bu Huan (*Lycopodium serratum*)
 Life Root (*Senecio aureus* and *S. nemorensis*) *
 Mistletoe (*Phoradendron leucarpum* and *viscum album*)
 Mormon Tea (*Ephedra nevadensis*)
 Pennyroyal (*Mentha pulegium*) *
 Petasites (*Petasites hybridus*) *
 Pokeroot (*Phytolacca americana*)
 Ragwort (*Senecio jacoboea*) *
 Rue (*Ruta graveolens*)
 Sassafrass (*Sassafrass albidum*)

Skullcap (*Scutellaria lateriflora*) *
 Yohimbe (*Pausinystalia yohimbe*)
 *Signifies Potential Hepatotoxicity

Herbs with Known Toxicity if taken at High Doses (also possibly toxic at low doses)

Alpine Cranberry (*Vaccinium vitis-idaea*)
 Cayenne (*Capiscum annum*)
 Mercury Herb (*Mercurialis annua*)
 Schisandra (*Schisandra chinensis*)
 Sweet Clover (*Melilotus officianalis*)
 Tonka Beans (*Dipteryx odorata*)
 Trailing Arbutus (*Epigae repens*)
 Witch Hazel (*Hamamelis virginiana*)
 Woodruff (*Galium oderata*)
 Uva Ursi (*Uva Ursi srcostaphylos*)

Herbs that May be Safe (Unproven health benefits)

Artichoke (*Cynara scolymus*)
 California Poppy (*Eschcholtzia californica*)
 Chamomile (*Matricaria chamomilla*)
 Dandelion (*Taraxacum officinale*)
 Licorice (*Glycyrrhiza glabra*) (not recommended for long-term use, especially for people with high blood pressure)
 Maitake (*Grifloa frondosa*)
 Milk Thistle (*Silybum marianum*)
 Peppermint (*Mentha piperita*)
 Rosemary (*Rosemarinus officinalis*)
 Soybean (*Glycine soja*)

Resources: The American Pharmaceutical Association
 Practical Guide to Natural Medicines by Andrea Peirce

The Green Pharmacy by James A. Duke

Herbs of Choice by Varro E. Tyler The Honest Herbal by Varro Tyler

PDR for Herbal Medications published by the Medical Economics Company

American Botanical Council 512-926-4900

www.herbalgram.org American Herbal Products Association - www.ahpa.org

ConsumerLab.com - www.consumerlab.com

FDA Dietary Supplement website: vm.cfsan.fda.gov/~dms/supplmnt.html

HerbMed - This is a very comprehensive website that provides a wide variety of information on herbs, including evidence-based information www.herbmed.org

The United States Pharmacopeia 800-822-8772

www.usp.org

**Copyright 2001, Lucinda K. Porter, RN
 All Rights Reserved**

Lucinda K. Porter, RN is a research nurse and patient educator at Stanford in the area of hepatology. She co-facilitates a support group and is active in many aspects of hepatitis C education. In addition to being HCV positive, she has a life which include her husband and teenaged daughter.

Hepatitis C Subtype Determines Interferon Responsiveness Factors

By Alan Franciscus
Editor-in-Chief

In the August 2001 issue of *GUT* it was stated that a factor determining responsiveness of the hepatitis C virus to interferon treatment was the hepatitis C virus subtype. The authors of the article from Nagoya University School of Medicine in Japan state that by accurately predicting a patient's likelihood to obtain a sustained response with viral eradication would spare considerable expense and toxicity for needless interferon therapy. In theory this sounds good, but what about the patients that would benefit from improved liver health and/or reversal of fibrosis (scarring) that would be excluded from therapy based on this theory?

Dr. I. Nakano and colleagues took advantage of a newly identified subtype classification of HCV genotype 1b to explore whether or not predictive factors could be identified for interferon response. What was found was that although genotype 1b patients overall responded more poorly to treatment than patients with genotype 2a, patients genotype 1b with subtype W (distributed worldwide) or subtype J (found mainly in Japan) showed similar viral loads and responses to interferon.

Additional predictors for better interferon responses where women with W-type virus who experienced higher interferon responses than did men with W-type virus, especially if they had low

levels of HCV RNA (viral load). Among patients with J-type virus interferon responsiveness improved if there was a history of blood transfusions, low levels of HCV RNA or mutated amino acid sequence in the region of the hepatitis C virus genome that determines interferon sensitivity.

These results were put through a multivariate analysis that is a type of analysis that looks at multiple factors both for individual as well as combined impact. It was determined that HCV RNA (viral load) was the only significant predictor to interferon responsiveness. The investigators conclude that neither genotype nor virus subtype was a significant independent factor and that "combined analysis with several factors that were associated with interferon response may provide for more precise prediction of interferon response".

Researchers will probably continue to look for predictive factors to viral eradication of HCV to develop protocols for 'ideal treatment candidates'. But as more data becomes available supporting the positive histological improvements with interferon therapy in patients that do not get a virologic response this approach of using predictors for viral eradication and treatment candidates will have its shortcomings. For this reason, as patients with HCV are evaluated for treatment one must not lose sight of a very real goal - liver health.

HCV Advocate

Alan Franciscus.....Founder/Editor-in-Chief
e-mail: sfhepcat@msn.com
Joe Shaw.....Managing Editor
e-mail: joesha@yahoo.com
C.D.Mazoff.....Contributing Editor
Liz Highleyman.....Contributing Editor
Webmaster: Richie Lam

Affiliated with:

Back To Life A group dedicated to providing patient education and support.

Orange County.....Carol Craig 949-654-4250

Santa Barbara.....

You may contact us at:

P.O. Box 427037

San Francisco, CA 94142-7037

The HCV Advocate offers information about various forms of intervention in order to serve our membership at large. By providing information about any form of medication, treatment, therapy or diet we are neither promoting nor recommending use, but simply offering information in the belief that the best decision is an educated one.

Permission to reprint is granted and encouraged with credit to the Hepatitis C Support Project.

Hepatitis C Support Project - A Tides Center Project

HIV and HCV Coinfection: The Effect of Protease Inhibitor (PI) Therapy on Liver Fibrosis Progression.

By Alan Franciscus
Editor-in-Chief

It is clear that hepatitis C virus (HCV) related liver fibrosis progression is accelerated in people infected with human immunodeficiency virus (HIV) and HCV. Fibrosis progression in this population is particularly marked in cases with immunosuppression, heavy alcohol consumption, and old age at time of HCV infection.

Until recently there has been little published data and no conclusions on the affect of protease inhibitors (PIs) on liver fibrosis. In the past couple of months however, a long-term retrospective cohort study (a study based on review of medical records of patients) from Paris looking at the influence of antiretroviral therapy containing PIs on liver fibrosis was published in *Hepatology* 2001; 34:283-287.

The study presents a few limitations because it was a retrospective designed study that did not allow for the control of PI prescriptions. Ideally the assessment would be a prospective study (patients meet specific entry criteria up front, are entered into a protocol and are followed until the end of the study with specific measurable endpoints determined up front). In this study this would include random allocation of PI's and long term histologic evaluation follow up. Obviously this ideal is neither ethical nor

practical.

Contrary to previous findings, this study found that anti HIV therapies that included PIs did not worsen liver damage in people coninfected with HIV/HCV. Certainly, patients who had received PIs had less necroinflammatory and fibrotic lesions than those patients that had never been treated with PIs. Additionally, the actual rate of cirrhosis was much lower in patients who had received PIs compared to people that had not been previously treated with PIs.

Other factors that influenced accelerated progression to cirrhosis in this population were people that acquired HCV infection at an older age, heavy alcohol consumption as well as a CD4 count less than 200. When all the antiretroviral combinations were analyzed, only those combinations including PIs had a significant impact on progression to cirrhosis. Neither the use nor the extent of nucleoside reverse transcriptase inhibitors (NRTIs) had any influence on liver fibrosis.

The authors concluded that PI therapy together with a young age at HCV infection; low alcohol use and high CD4 count were associated with a lower liver fibrosis progression rate. They stated that a HIV/HCV coinfecting patient that was less than 20 years old at time of HCV infection, treated with PIs,

See Protease Inhibitors on page 9

Help Us Reach More People with Hepatitis C! Support us through either a paid subscription or donation.

Yes, I'd like to subscribe.

- \$12 one year—12 issues
 \$6 one year—12 issues
 (for those with fixed incomes)
 Renewal

I'd like to make a tax deductible donation.

- \$10 \$25 \$100 Other

Please make checks payable to:
HCSP/The Tides Center

The Hepatitis C Support Project does not share its mailing list with any individual or organization. All subscribers names and addresses are strictly confidential.

Name _____

Address _____

City _____

State _____ Zip _____

Please mail form to: **HCV ADVOCATE**
P.O. Box 427037
San Francisco, CA
94142-7037

Peg-Intron and Ribavirin

Continued from page 1

Peg-Intron/Rebetol, what I expected from this first pegylated interferon combination was completely the opposite of what I read in the package insert. Across almost every type of side effect, in clinical trials Peg-Intron/Rebetol had a significantly higher percentage of side effects than Rebetron, and some of these are particularly disturbing.

The package insert states that 77% of patients on Peg-Intron/Rebetol had a psychiatric side effect of one type or another. In addition, 75% of patients had an injection site inflammation or reaction.

Other common adverse events in the Peg-Intron/Rebetol patients were myalgia (muscle pain) 56%, a 12% increase over Rebetron; arthralgia (joint pain) 34%, a 21% increase over Rebetron; nausea 43%, a 30% increase over Rebetron; anorexia (loss of appetite) 32%, a 19% increase over Rebetron; weight loss 29%, a 45% increase over Rebetron; fatigue 66%, a 5% increase over Rebetron; headache 62%, a 7% increase over Rebetron; rigors (muscle stiffness) 48%, a 17% increase over Rebetron; and fever 46%, a 40% increase over Rebetron.

It should be noted that side effect profiles in package inserts can be misleading, because there is no severity scale which would record how often a patient experienced a side effect, or how severe it was. Keep in mind, though, that this theory would also hold for reported Rebetron side effects (as it was a head-to-head trial), so the differences in percentages from a trend perspective is accurate.

Notwithstanding this, the side effect profile of Peg-Intron/Rebetol appears much harder to tolerate than that of Rebetron, and is likely to considerably impact a patient's ability to stay on therapy or be compliant with therapy. If that happens, the likelihood of obtaining results even as good as those of Rebetron is questionable.

The last benefit that we had come to expect from the pegylated interferon combination was ease of use and convenient dosing. A benefit that patients will have from Peg-Intron/Rebetol is that they will only have to administer the interferon once per week, versus three times per week for Rebetron.

A disadvantage, though, is the complicated dosing and administration associated with the new combination. In the Peg-Intron/Rebetol package insert

there are six different possible dosages of Peg-Intron, based on a patient's weight. To further complicate the situation, if one follows the recommended dose of Peg Intron (1.5mcg/kg) for combination usage, they will either be under-dosing or over-dosing if they use the table in the package insert.

Additionally, if a patient is not able to tolerate and must discontinue the ribavirin, does that patient then start taking the recommended 1.0mcg/kg of Peg-Intron as recommended for monotherapy, which is a completely different dosing chart? The potential for problems is enormous, and patients will have to be followed very closely during therapy. Up until now this has not been a problem, because patients are followed very closely in clinical trials.

After analysis of the dosing section of the package insert, I feel that the dosing regimen could be problematic for patients if medical professionals are not fully educated on the appropriate dose and if they do not take the time to communicate and demonstrate usage to the patient. Such a demonstration would have to include how to reconstitute the powder and then how to draw up for injection the dose that is correct for the patient's weight.

In summary, the first pegylated interferon combination, Peg-Intron/Rebetol (pegylated interferon (2b 1.5mcg/kg plus ribavirin 800mg), appears to be less than optimal. Can we still hope that Pegasys/ribavirin will provide the benefits we had hoped and waited for when it becomes available next year? From the published data as well as the pivotal Pegasys/ribavirin trial that was presented at DDW this year, it certainly appears to offer significant benefits over the current standard of care, Rebetron.

This is especially true when we look at tolerability, side effects, ease of use, and most importantly, improved histology. However, we will have to wait for FDA approval and then take a closer look at the package insert as we have done with Peg-Intron/Rebetol. Anyone considering Peg-Intron/Rebetol therapy should ask themselves the following important questions: Is this new therapy appropriate based on the data that is emerging? Is the convenience of once weekly dosing worth the increased side effects? Are the costs for a chance at a few percentage points of improvement in efficacy worth it? As you ask

Continued on next page

Cryoglobulinemia and Hepatitis C

By **Liz Highleyman**
Contributing Editor

Chronic hepatitis C virus (HCV) infection is associated with many long-term complications. Among these is cryoglobulinemia (also sometimes called cryoglobulinemia), a condition in which abnormal proteins called cryoglobulins form in the blood. Although many people with hepatitis C have evidence of cryoglobulins in their blood, most do not experience symptoms.

Cryoglobulins are made up of immunoglobulins (antibodies), substances produced by the body to fight infection. When the blood is cooled, the cryoglobulins clump together, or precipitate. This causes the blood to thicken or “gel,” thus restricting blood flow. In the general population, cryoglobulinemia is rare; it occurs most often in people over age 40, and women are twice as likely as men to develop the condition.

The cause of essential cryoglobulinemia is not known, but it is believed to have an autoimmune component. There are three types of cryoglobulinemia (I, II, and III), classified by the makeup of the cryoglobulins; types II and III are mixed, meaning the cryoglobulins are made up of various antibody types.

Secondary cryoglobulinemia is associated with an underlying disease, for example multiple myeloma, lymphoma, rheumatoid arthritis, or systemic lupus erythematosus. Essential mixed cryoglobulinemia types II and III are strongly associated with hepatitis C – so much so that some experts believe the

“essential” should be dropped, since the condition is now known to be secondary to HCV.

Although estimates vary widely, it appears that about half of people with chronic HCV have evidence of cryoglobulins in their blood. However, only an estimated 20% of these experience symptomatic cryoglobulinemia. Conversely, an estimated 80-90% of people with essential mixed cryoglobulinemia types II and III have HCV. For some people, cryoglobulinemia symptoms are their first indication that they have chronic hepatitis C.

Cryoglobulinemia is more likely to develop in people with who have had HCV for longer periods of time and those who have developed cirrhosis (liver scarring). It is not known why hepatitis C is linked with cryoglobulinemia, but researchers increasingly believe that the presence of HCV itself somehow triggers the production of cryoglobulins; this is supported by the fact that cryoglobulin complexes often contain HCV genetic material and anti-HCV antibodies.

Cryoglobulinemia is typically diagnosed by testing the blood for the presence of cryoglobulins. Because cryoglobulins precipitate when the blood is cooled and dissolve again when it is rewarmed, the test should be done immediately after the blood sample is drawn. Some people who show evidence of cryoglobulins on a blood test do not experience any symptoms. Others, however, may develop serious organ or tissue damage. Because cryoglobulinemia can affect almost any part of the body, it can lead to a wide variety of symptoms. The most characteristic signs of essential mixed cryoglobulinemia are generalized weakness, joint pain (arthralgia), and purpura (purplish blotches on the skin).

Cryoglobulinemia can lead to blood vessel, skin, and tissue damage - especially in the extremities - including vasculitis (blood vessel inflammation), Raynaud’s phenomenon (blood vessel spasms), livedo (red or purple marks on the skin due to restricted blood flow), hives, skin ulcers, and gangrene (tissue necrosis or death). Some people experience peripheral neuropathy (nerve damage), signaled by pain, tingling, numbness, or weakness in the

Peg-Intron and Ribavirin

Continued from page 6

yourself these questions, remember that, as we all know, results obtained in clinical trials are difficult to reproduce in the everyday world of treatment. I encourage everyone considering treatment with Peg-Intron/Rebetol to read the package insert and discuss in detail with their medical provider any questions they may have. Please visit our web site <http://www.hcvadvocate.org/> for a link to the FDA web site to review the entire package insert for Peg-Intron/Rebetol.

See Cryoglobulinemia on page 8

Interferon Response Not As Low As Thought In Hemophiliacs with Hepatitis C

By Alan Franciscus
Editor-in-Chief

In a recent article published in the *European Journal of Gastroenterology and Hepatology* 2001;13:859-864 Dr. Isabelle Buerton and colleagues discussed a multi-center study in France looking at alpha interferon therapy in hemophiliac patients with chronic hepatitis C.

To date there has been limited data on the long-term efficacy of alpha interferon in multi-transfused hemophiliacs with chronic hepatitis C that are not coinfecting with HIV. Earlier available data suggested a low rate of response in these patients.

In the recently published data there were 58 hemophiliac participants all of who were dosed 3 million units of alpha interferon 2b three times a week for 12 months. The participants were then followed for at least two years post treatment. The researchers assessed response via HCV RNA (viral load).

What is interesting in this population is the high rate of patients who did not complete the treatment. This seems to be characteristic of this patient population. Of the 58 participants, 24 (41.4%) dropped out of the study.

Dr. Isabelle Buerton and colleagues concluded that except for 7 of the drop out patients, the symptoms leading to interruption of the interferon therapy in the remaining would probably not have resulted in discontinuing therapy if the patients were non-hemophiliacs.

For example one patient developed an inhibitor to the deficient clotting factor without bleeding consequences. In intent to treat analysis (includes all of the data from all of the participants), the sustained virological response (SVR) was 14%. However, if only the 34 patients who received full treatment were analyzed to determine SVR, then the SVR would increase to 23 %.

In summary, it appears that earlier data suggesting lower interferon response in hemophiliacs with hepatitis C is directly related to this patient population having a high treatment drop out rate. In patients that are able to tolerate and complete

therapy, SVR's in the hemophiliac population are very similar to the non-hemophiliac population.

Cryoglobulinemia

Continued from page 7

hands or feet. Restricted blood flow and/or deposition of cryoglobulins can damage organs such as the eyes, liver, and kidneys (deposition of immune complexes in the kidneys is known as glomerulonephritis).

Cryoglobulinemia may also lead to spleen enlargement, abdominal pain, weight loss, and cardiovascular problems such as heart attack or stroke. In some people, exposure to the cold makes cryoglobulinemia symptoms worse. In others, however, symptoms are intermittent, flaring up and subsiding for no apparent reason. In part because it is so uncommon, treatment of cryoglobulinemia is not very advanced. In many cases, doctors recommend ongoing monitoring rather than treatment. Most treatment strategies are intended to limit further tissue or organ damage.

Treatment specifics will depend on the severity of symptoms and which parts of the body are affected. Medications that reduce inflammation or dampen the immune response seem to help control essential mixed cryoglobulinemia. The conditions is often treated with nonsteroidal anti-inflammatory drugs (e.g., acetaminophen, aspirin, ibuprofen, and a variety of prescription medications), corticosteroids (e.g., prednisone), or immunosuppressive drugs (e.g., cyclophosphamide).

Unfortunately, drugs that suppress the immune system make a person more susceptible to infections. In severe cases, plasmapheresis may be done, a procedure in which cryoglobulin-containing blood plasma is removed and replaced with donated plasma or a replacement fluid such as saline solution. If cryoglobulinemia is associated with another disease, treatment of that illness may reduce cryoglobulinemia symptoms. In people with HCV, studies have shown that treatment with interferon-alpha and/or ribavirin can improve cryoglobulinemia.

Continued on next page

Cryoglobulinemia

Continued from previous page

There are steps people can take to minimize cryoglobulinemia symptoms.

Avoid the cold if it makes your symptoms worse.

Wear protective clothing outdoors when it is cold.

Some people wear thermal gloves and socks or boots indoors to keep the hands and feet warm.

Consume a healthy, well-balanced diet, exercise regularly, and get enough rest.

Notify your doctor of any new, unusual, or worsening symptoms.

Ask whether hepatitis C treatment might help to reduce your cryoglobulinemia symptoms and improve your quality of life.

References

Agnello, V. et. al. A role for hepatitis C virus infection in type II cryoglobulinemia. *New England Journal of Medicine* 327:1490-1495. 1992.

Akriviadis, E.A. et. al. Prevalence of cryoglobulinemia in chronic hepatitis C virus infection and response to treatment with interferon. *Journal of Clinical Gastroenterology* 25: 612-618. 1997.

Cacoub, P. et. al. Mixed cryoglobulinemia and hepatitis C virus. *American Journal of Medicine* 96:124-132. 1994.

Casato, M. et. al. Cryoglobulinaemia and hepatitis C virus. *Lancet* 337:1047-1048. 1991.

Lunel, F. et. al. Cryoglobulinemia in chronic liver diseases – role of hepatitis C virus and liver damage. *Gastroenterology* 106:1291-1300. 1994.

Liz Highleyman (liz@black-rose.com) is a freelance medical writer and editor. She has a certificate in public health from the Harvard School of Public Health. She has worked as an editor of the *Bulletin of Experimental Treatments for AIDS (BETA)*, published by the San Francisco AIDS Foundation, and as health editor for the Internet search engine Ask Jeeves

Protease Inhibitors

Continued from page 5

drinking less than 50g of alcohol daily, and with more than 200 CD4 cells had an estimated mean time from HCV infection to cirrhosis of 56.7 years (95%CI, 38.9-71.1), whereas this phase was radically reduced to 18.0 years (95%CI, 13.3-32.4) in a heavy drinker, older than 20 years at time of HCV infection, who had never been treated with PIs, and with less than 200 CD4 cells at liver biopsy.

The correlation between HCV infection, increase of serum ALT levels and the underlying liver disease in patients receiving PIs remains poorly investigated. Both PIs and HCV infection have been recognized as individual cofactors of serum ALT increases.

Ritonavir has been more repeatedly reported to induce hepatotoxicity in HCV coinfecting patients compared with HIV positive/HCV negative patients.

Whether HCV increases the risk of PI induced hepatotoxicity remains inconclusive. The mechanisms involved in the advantageous impact of PI therapy on liver fibrosis remain unknown. Improvement of immune functions assessed by increases in CD4 count related to antiretroviral therapy might reduce the liver fibrosis progression rate. However, in this retrospective study the influence of PI therapy was independent of both the HIV viral load and the CD4 count.

Regardless, many immune adaptations other than the increases in CD4 cell count could influence liver fibrosis progression. For example, changes in intrahepatic cytokine pattern of secretion related to immune restoration should reduce or reverse inflammatory and fibrotic processes and thus improve liver lesions. Another reason might be that PIs may have a direct influence on cytokine expression involved in fibrosis matrix synthesis (the process that forms scar tissue from healthy liver tissue).

The authors concluded that PI therapy does not appear to worsen HCV-induced liver damage. Furthermore, long term use of PIs including antiretroviral therapy together with decrease of alcohol use and preservation of high CD4 count may have a favorable effect on HCV related liver fibrosis progression in people coinfecting with HIV/HCV.

HelpLines:

Southern California
1-888-85LIVER

Northern California
415-978-2400

Clinical Trials

Northern California

University of San Francisco Medical Center

Stephanie Straley, PA (415) 514-2369

VA Hospital-UCSF

(415) 750-2105

California Pacific Medical Center

Linda Brooks (415) 202-1504 or (415) 202-1506

San Francisco General Hospital

Athiana (415) 206-3725

Stanford University Hospital

Stanford Liver Research Clinic (650) 724-7057

Quest Medical Research

Dr. Jay Lalezari (HIV/HCV Co-infection trials)

(415) 353-0800

East Bay Liver Clinic

Oakland, CA 94609

Contact: Grant Young - 510/208-1777

Dr. John J. Jolley - San Rafael

Contact: Lynn Jolley

Monday, Tuesday, & Wednesday

(415) 257-3030

Southern California

USC Hepatitis Research Clinic

Dr. Karen Lindsay, Susan Milstein, RN

(323) 442-5550

UC Irvine Medical Center

Dr. John Hoefs, Barbara Walker, RN

(714) 456-7821

VA Medical Center Long Beach

Dr. Timothy Morgan, Julia Sanborn, RN\

(562) 494-5933

Santa Barbara/Ventura Counties

Dr. Kip Lyche (805) 641-6525

HCSP

P.O. Box 427037

San Francisco, CA

94142-7037