

May
2002

HCV Advocate

Volume 5
Issue 5

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

New Pegasys Results Offer Renewed Hope For Patients With Hepatitis C

Data on Pegasys in Combination with Ribavirin from EASL Brings Treatment Hope for Patients with Chronic HCV

By Alan Franciscus
Editor-in-Chief

The results from the second pivotal phase III combination Pegasys and ribavirin global trial were recently released for the first time at the European Association for the Study of the Liver Conference (EASL) in Madrid, Spain. The results are very impressive and give much needed hope for people with hepatitis C. What is especially striking are the reported results for those patients with hepatitis C genotype 1, which accounts for about 70-75% of the people with HCV in the United States.

There has been over the last few years much excitement and anticipation for the introduction of the pegylated interferons. The hope has not only been that these medications would be more effective than the current standard of care, Rebetron, but also that they would show improved histology (health of the liver), be better tolerated as well as more convenient to use. The first pegylated interferon to market, Peg Intron has been very disappointing because the efficacy, in combination with Rebetol (ribavirin), is no better than Rebetron in the great majority of patients. In addition there is no histological improvement over standard interferon, plus Peg Intron has many more side effects, is difficult to use and is very expensive for just the convenience of once weekly injections. For this reason Rebetron still remains the

standard of care in the treatment of hepatitis C which is witnessed by the recently released National VA Hepatitis C Treatment Guidelines that only recommends Peg Intron in combination with ribavirin over Rebetron in a small percentage of patients infected with hepatitis C, genotype 1 low viral load (<2 million copies ml).

The poor results of the first pegylated interferon to market and the fact that Schering Plough has done a very good job confusing the HCV marketplace that a "peg is a peg" has left many skeptics believing that all the fan fare that has surrounded the pegylated interferons for the last few years has been nothing but pharmaceutical company marketing hype.

A Peg is not a Peg

The news on Pegasys in combination with ribavirin from EASL will hopefully give the skeptics reason to take another look and certainly refutes the "peg is a peg" mind-set. This new data adds to the mounds of other excellent data on Pegasys suggesting that by all accounts Pegasys is without doubt the superior pegylated interferon. For Roche, who developed Pegasys there was a price to pay for all the research that they did on pegylation to find the ultimate sized peg and pegylation process which ultimately would achieve these results in even challeng-

See Pegasys on page 6

In This Issue:

Healthwise: Managing Symptoms....page 2
Arthritis and HCV.....page 3
Transmission Update.....page 5

Living with Hepatitis C: Managing Common Symptoms Part One

By Lucinda K. Porter, RN, CCRC

Chronic hepatitis C virus (HCV) infection is often referred to as a silent disease. This reputation for silence is based largely on the fact that the liver is considered to be a “non-complaining” organ. In short, the liver can suffer considerable damage and still function quite well.

However, when talking to patients chronically infected with HCV, common symptoms are frequently reported. Results of a study published in *Hepatology* stated that more than 70% of HCV positive patients reported at least one complaint.¹

The following article identifies some of the most common symptoms reported by patients with chronic HCV infection, along with some tips for managing symptoms. These tips are aimed for the average non-cirrhotic HCV patient. Before employing any of these techniques, talk to your doctor or other licensed care provider. Self-diagnosis can prevent one from obtaining health care; it can also be a prescription for disaster.

Fatigue

* Rule out other causes of fatigue, such as thyroid abnormalities, diabetes, anemia, depression, sleep disorders, dehydration, etc.

* Make sure you are getting sufficient sleep. The National Sleep Foundation states that the average adult needs 7 to 9 hours of sleep per night.

* Drink sufficient water and other nutritional liquids (10 to 16 glasses per day) that do not contain sugar or caffeine.

* Use moderate exercise to reenergize. A ten-minute walk can work wonders, particularly a walk in a scenic area. Stretching, especially for those confined to a desk for hours, can be helpful.

* Consider an integrated movement program such as Pilates, Qigong, Tai Chi, or Yoga.

* Avoid excess stress. Use stress-reduction techniques, such as meditation, massage, watching the sun rise and set.

* Keep your life simple. Establish priorities and cut back on responsibilities.

* Look for short cuts. All meals do not have to be

made from scratch. A car can be cleaned at a car wash rather than by hand.

* Ask for help. As much as they would have you believe, it is not considered slave labor to ask children to empty the dishwasher. It is not gauche to ask friends over for a

potluck dinner and ask them to help with the dishes.

Muscle and Joint Aches

* Get a proper diagnosis for the cause of pain before beginning a self-help regimen.

* Ask your physician about the use of prescription and non-prescription medications to help with these symptoms. It is a common myth the HCV patients cannot take acetaminophen (Tylenol). In most cases, acetaminophen is considered to be safe if taken occasionally and within the recommended dose. Never mix acetaminophen and alcohol. If you take other prescription or over the counter medications, ask your doctor about the safety of taking these along with acetaminophen.

* Try gentle stretching exercises.

* Avoid prolonged periods of inactivity.

* Try warm or hot baths. Spoil yourself with a bubble bath.

* Massage and acupuncture may be helpful. These techniques can be learned and applied by you or by a trained practitioner.

Headaches

* Discuss this complaint with your health care provider.

* Ask your physician about the use of prescription and non-prescription medications to help with these symptoms.

* Avoid stress.

* Try relaxation techniques.

* Learn acupuncture points for headache relieve.

Dryness

* This includes dry skin, mouth, nose and eyes.

* Drink sufficient water.

* Hypoallergenic lotions applied immediately following bathing can reduce dry skin. Add a couple of drops of lightweight oil to the lotion for extra

HealthWise

Arthritis and Hepatitis C

By Liz Highleyman
Contributing Editor

A variety of different extrahepatic (outside the liver) conditions are associated with chronic hepatitis C. Several HCV-related manifestations are autoimmune conditions, in which the immune system attacks the body's own tissues.

Autoimmune conditions sometimes seen in people with chronic HCV include lichen planus, Sjogren's syndrome (a disorder in which immune cells damage moisture-secreting glands including those that produce tears, saliva, and sweat), scleroderma (hardening of the skin and connective tissue), autoimmune thyroiditis, and rheumatoid arthritis. Most serious conditions occur during late-stage HCV disease after the liver has sustained significant damage. A majority of people with HCV never experience serious associated conditions.

Arthritis in general refers to inflammation of the joints. There are several different types of arthritis, but the one most often associated with HCV is rheumatoid arthritis (RA). RA is one of the most common types of arthritis. It is characterized by inflammation of the linings of the joints (synovial membranes) and internal organs such as the heart, lungs, and spleen; nerves, skin, and connective tissue may also be affected.

While it is known to be an autoimmune condition, researchers do not know the exact cause of RA, although genetic factors appear to be involved. Like most autoimmune diseases, RA is more common in women than in men. Some experts believe that infectious organisms such as HCV can trigger RA in susceptible individuals, although this has not been well studied. RA may involve several different joints, usually symmetrically on both sides of the body. The small joints of the hands, feet, wrists, and ankles are most often affected.

Symptoms include pain, stiffness, swelling, heat, and redness. As RA progresses, synovial cells multiply abnormally and inflammatory proteins may invade and damage surrounding tendons, cartilage, and bone. Over time, affected joints may become misshapen and lose their normal range of motion.

RA is usually chronic, although many people experience a recurring cycle of flares (worsening) and remission (improvement). In addition to joint-specific symptoms, people with RA may also experience fever, fatigue, loss of appetite, and anemia. Some also develop rheumatoid nodules, or lumps under the skin.

RA is diagnosed on the basis of symptoms, X-rays, and the presence of an antibody called rheumatoid factor. Rheumatoid factor is found in as many as 80% of people with RA, but may also be detected in people who do not have RA. Some HCV positive people have elevated levels of rheumatoid factor.

A study by Dr. Nicole Leone from Molinette Hospital in Turin, Italy, and colleagues revealed that people with chronic HCV often also have rheumatological symptoms. Among the 114 patients studied, 44.7% had rheumatologic symptoms (often including arthritis in large or medium-sized joints) and 9.6% met the American College of Rheumatology definition of RA.

Rheumatological symptoms and RA were seen more often in people with cirrhosis (scarring) of the liver than in those with minimal or no liver damage. The researchers recommended that HCV infection should be considered in patients with rheumatological symptoms of unknown origin.

Dr. Leonard Calabrese of the Cleveland Clinic in Ohio agreed, saying, "[W]e believe that hepatitis C represents a major cause of undetected rheumatological symptomatology, and is now a major focus of education for rheumatologists" (*Journal of Medical Virology* 66 (2): 200-203, February 2002). Dr. Eli Zuckerman of B'nai Zion Medical Center in Haifa, Israel, believes that in some cases, the presence of arthritis symptoms may be the only indication that a person has HCV.

Other types of arthritis that may occur in people with HCV include osteoarthritis (degenerative joint disease, typically seen in older people), reactive arthritis (Reiter's syndrome), and psoriatic arthritis. Arthritis in people with HCV may occur in conjunction with other conditions such as mixed cryoglobulinemia and Sjogren's syndrome. While there is no cure for

See Arthritis on page 4

Arthritis

Continued from page 3

RA, several different treatments are available, and are often used in combination. Symptomatic arthritis treatments include drugs that reduce pain and inflammation. These include both over-the-counter medications such as aspirin and ibuprofen (Advil), and prescription drugs such as celecoxib (Celebrex) and rofecoxib (Vioxx). Corticosteroids may also be used to reduce inflammation. Disease-modifying anti-rheumatic drugs (DMARDs) that can reduce joint damage due to RA include methotrexate (Rheumatrex, Folex), leflunomide (Arava), cyclosporine (Sandimmune, Neoral), penicillamine, sulfasalazine (Azulfidine), hydroxychloroquine (Plaquenil), and even gold.

Unfortunately, some anti-inflammatory drugs used to treat autoimmune diseases suppress the immune system and may lead to increased HCV replication. Biological response modifiers such as etanercept (Enbrel), infliximab (Remicade), and anakinra (Kineret) that affect the action of cytokines (chemicals released by immune system cells) may also have an impact on HCV disease progression, although this is not well studied.

In addition, Dr. Calabrese notes that HCV positive people with arthritis “pose a particular challenge for therapy since so many of the drugs used to treat the arthritis are metabolized by the liver.” In people with damaged livers, such drugs may build up in the body, leading to increased toxicity and side effects.

Some studies indicate that hepatitis C treatment that succeeds in reducing HCV viral load appears to

improve arthritis symptoms.

For example, Dr. Zuckerman and colleagues reported at the 1998 American Association for the Study of Liver Disease conference that interferon-alpha therapy led to a complete or partial resolution of arthritis symptoms in 78% of the 25 people he treated; a majority of these patients had responded poorly to anti-inflammatory drugs and were described by Dr. Zuckerman as “actually crippled” by their arthritis. However, interferon therapy itself may cause arthritis-like symptoms.

Alternative therapies such as acupuncture or the application of heat or cold can help manage arthritis pain. Although rest, stress reduction, and limiting strenuous activities are beneficial, regular moderate exercise can help preserve joint flexibility and strength; focus on low impact activities such as swimming and other water exercises. In severe cases, surgery may be done to repair or replace damaged joints.

People with HCV who experience joint pain or other RA symptoms should consult their doctors promptly. Early treatment can help prevent long-term joint damage and loss of function.

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

HCV Advocate

Alan Franciscus.....Founder/Editor-in-Chief
e-mail: sfhepcat@msn.com
Joe Shaw.....Managing Editor
e-mail: joeesha@yahoo.com
Jayna H. Maxwell..Contributing Editor
C.D.Mazoff.....Contributing Editor
Liz Highleyman.....Contributing Editor
Webmaster: C.D. Mazoff

Affiliated with:

Back To Life A group dedicated to providing patient education and support.
Orange County.....Carol Craig 949-654-4250

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 community. 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

A New Look At Hepatitis C Transmission

By Liz Highleyman
Contributing Editor

Many people with hepatitis C and their advocates are well informed about the transmission and prevention of HCV. Most are aware that the virus may be transmitted by blood-to-blood contact and, more rarely, by sexual activity or from mother to child. However, recent studies and news reports have suggested that HCV may be transmitted in some unexpected ways.

Shared drug injection equipment remains the most common method of HCV transmission. In fact, studies have shown that as many as 60% of new HCV infections may be associated with injection drug use, and that 50% or more of people who have injected drugs are infected with HCV.

Any equipment that comes into contact with blood can transmit HCV; this can happen when a small amount of HCV-containing blood stays in the needle or on the equipment after it is used by one person, and then comes into contact with the bloodstream or mucous membranes of the next person who uses the equipment. Even tiny amounts of blood that are too small to be seen can still transmit HCV. People can contract HCV through sharing not only needles and syringes, but also potentially cookers, cotton filters, ties, and water

used to dissolve drugs or rinse syringes.

A recently published study by Dr. Lorna Thompson of the University of Illinois at Chicago and colleagues found that among young injection drug users in Chicago, the risk of contracting HCV was highest among those who shared cookers and cottons. After controlling for syringe sharing, the sharing of cookers quadrupled the risk of HCV seroconversion, while the sharing of cottons more than doubled the risk; sharing rinse water was associated with a marginally increased risk.

According to the researchers, "Prevention messages and campaigns should be revised to alert active injection drug users to the importance of reducing or eliminating all equipment-sharing practices." (American Journal of Epidemiology 155 (7): 645-653, April 1, 2002). Shared non-injection drug equipment such as cocaine straws and crack pipes is also a possible transmission route.

A recent study by Dr. Kimberly Page-Shafer of the University of San Francisco at California and colleagues found that young, low-income women in the San Francisco Bay Area have a high rate of HCV infection that appears to be associated with inhaled cocaine use ("snorting"). Among the HCV positive women studied, 17.5% had snorted cocaine; they were also more likely than HCV negative women to

See Transmission on page 8

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

Yes, I'd like to subscribe.

- \$18 one year—12 issues
- \$9 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**

Pegasys

Continued from page 1

ing patient populations which they have studied extensively; the price is that they are way behind Schering Plough to market. That price though has certainly resulted in a huge gain for people with HCV that are awaiting an effective treatment regimen.

In the prospective intent-to-treat analysis of Roche's Phase III Global 942 study of Pegasys (pegylated interferon alpha 2a) plus ribavirin, the highest ever sustained virologic response (SVR) in hepatitis C patients in history was reported - 61%. This news is not only very exciting but the genotype breakdown analysis as well as the design of the study will teach us about how to effectively manage hepatitis C patients based upon genotype with the introduction of Pegasys to the United States marketplace.

The aim of the 942 Pegasys and ribavirin study was to compare the efficacy and safety of the combination given for 24 weeks versus 48 weeks as well as compare the efficacy and safety of two different daily doses of ribavirin (low dose 800mg versus 'standard' dose of 1000/1200mg). There were 1284 patients in the study enrolled from all over the world. The patients were stratified by HCV genotype (1 versus non-1) and viral titer (low versus high defined as equal/below or above 2 million copies/ml respectively) in a pre-planned distribution of genotypes randomized to 4 arms.

The arms of the study were as follows:

A: Pegasys 180 mcg sc plus ribavirin 800mg qd, 24 weeks

B: Pegasys 180 mcg sc plus ribavirin 1000/1200mg qd, 24 weeks

C: Pegasys 180 mcg sc plus ribavirin 800mg qd, 48 weeks

D: Pegasys 180 mcg sc plus ribavirin 1000/1200mg qd, 48 weeks

Patient characteristics in the study were very well balanced across groups for age, weight, gender and viral titer and there was a high level of patients with bridging fibrosis/cirrhosis (approximately 25%).

The top line results are as follows:

* The Pegasys plus ribavirin phase 3 trials yielded:

* All Patients Overall SVR - 61%

* Non-Cirrhotics Overall SVR - 65%

* Cirrhotic Overall SVR - 50%

* Genotype 1 Overall SVR - 51%

* Genotype 1 - high viral load - SVR 46%

* Genotype 1 - low viral load - SVR 61%

* Genotype Non-1 Overall SVR - 78%

Genotype 1 - Important Points:

It was found that for patients with genotype 1, 48 weeks of treatment is needed with standard ribavirin doses of 1000/1200mg. In genotype 1 efficacy falls if either the duration of therapy is reduced or the ribavirin dose is reduced.

Genotype Non- 1 - Important Points:

In genotype non-1 patients, only 24 weeks of treatment is needed with a low dose of ribavirin (800mg). The study design was able to show that there was not a benefit in efficacy by increasing either the duration of therapy or the ribavirin dose for non-genotype 1. For this reason with Pegasys and ribavirin only 24 weeks of therapy is needed for non-genotype 1 and low dose ribavirin is adequate to achieve maximum results. This is in contrast to the Peg-Intron plus ribavirin FDA label, which requires 48 weeks of treatment for all genotypes.

This news is extremely exciting because for the first time in history an overall SVR of 61% in a prospective intent to treat trial for the treatment of hepatitis C has been reported. What prospective means is that the ground rules for reporting the efficacy were established prior to the trial and that these results have been achieved on real people actually taking and tolerating the medications. These results take into account patients that had to modify their dose or discontinue treatment due to side effects. Additionally this data is reported by intent-to-treat analysis, which is a strict and conservative analysis that includes in the results patients that only took one dose of the treatment. In medicine, often retrospective analysis of data is done. Retrospective analysis evaluates data in a way that the original study design did not plan for it to be evaluated. When studies are designed there are end points set and the trial is then designed to be able to evaluate those endpoints with a degree of statistical signifi-

Continued on page 7

Pegasys

Continued from page 6

cance. Retrospective analysis tries to find answers after the fact. This type of analysis is very helpful in determining possible trends of response or for making theoretical deductions that then must be prospectively studied for validity and should never be used to mislead people by making them believe that they are able to get results that in fact have never been studied and are more theoretical and unproven. A good example of this is the Michael Mann's article that was published in the Lancet last year (Lancet 2001:358, 958-65). This article includes a retrospective analysis of the Peg Intron/RBV pivotal phase III trial using optimized weight based dosing of ribavirin (>10.6mg/kg/day) reporting an SVR far higher than what was achieved in the trial. What is so misleading about this retrospective analysis is that the likelihood of ever getting such results is close to impossible. Here's why – according to the retrospective analysis, all of the patients would have to take 1.5 mcg of Peg Intron plus >10.6mg/kg/day of ribavirin to achieve an overall SVR of 61%. But the data from the original trial shows that 49% of patients taking the 1.5 mcg dose of Peg Intron and getting optimized weight based dosing of ribavirin (>10.6mg/kg/day) required a dose reduction! Patients need to be critical of the information that they are being quoted. If what is being quoted wasn't prospectively studied and was a predetermined endpoint for evaluation there are no guarantees! The FDA agrees and has required that Peg Intron and optimized weight based dosing of ribavirin be studied prospectively before it will be considered for marketing approval.

Of course not everyone needs to be treated, but for those that are waiting for better treatment options, the news from EASL is very promising. It is anticipated that Roche will receive marketing approval by the FDA in the fourth quarter of this year and at that time a label will be released that will be a result of the FDA's analysis of the data submitted.

The Advocate analyzed the Peg Intron/RBV label when it was released last year and published the thoughts in the October 2001 newsletter in an article titled "Peg-Intron plus Ribavirin - An Analysis plus Questions to Ponder". A similar analysis of the Pegasys label will be done when it is approved by the

FDA and will be published in the Advocate. Until that time, the two pivotal phase 3 trials, one presented at DDW last year and the other just presented at EASL look very promising not only from an efficacy standpoint but also for improved histology, better tolerability and ease of use. The side effect profile for Pegasys in combination with ribavirin in both trials showed results that suggest that Pegasys plus ribavirin is much better tolerated than the current standard of care, Rebetron or Peg-Intron plus ribavirin.

Symptoms

Continued from page 2

protection. (Neutrogena sells excellent body oil. Baby oil is another choice.)

- * Do not forget to use sun protection.

- * For occasional dry eyes, use over-the counter artificial tear drops. If regular use is necessary, use a preservative-free type.

- * Saline nose sprays can help with dry nasal passages.

Gastrointestinal (GI) Complaints

- * Intermittent pain in the liver area is common.

Discuss any GI complaint with your health care provider.

- * Eat small, frequent meals.

- * Choose low-fat, nutritional foods when at all possible.

- * Avoid acidic food.

- * Consult a nutritionist for further advice.

This is part one of a two-part article. Next month's HealthWise column will address common psychosocial issues that sometimes accompany chronic hepatitis C infection. I would like to give a special thanks to Alan Fransicus and Emmet Keeffe, M.D. for their input on this article.

1 Patrice Cacoub, Thierry Poynard, Pascale Ghillani, Frederic Charlotte, Martine Olivi, Jean Charles Piette, Pierre Opolon October 1999. Extra Hepatic Manifestations in 1614 Patients with Chronic Hepatitis C. Hepatology Vol. 30, No. 4 (Supplement) (Abstract No. 805)

**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.

Transmission

Continued from page 5

have used injection drugs, to have exchanged sex for money or drugs, and to have genital herpes. Dr. Page-Shafer said, "I think the study shows that hepatitis C prevention needs to extend beyond just blood-to-blood transmission." (*American Journal of Public Health* 92 (4):670-676, April 1, 2002). It is important to avoid sharing needles, syringes, and other equipment for drug preparation and injection, as well as equipment for non-injection drugs such as crack and inhaled cocaine or speed.

Needle exchange programs are increasingly recognized as an effective means of disease prevention and are available in many cities. If using a clean needle is not possible, some experts believe that cleaning needles with bleach may provide some protection against HCV transmission, although this has not been proven. Use regular household bleach. Draw bleach into the syringe and flush it out, then draw up new bleach and let it stand in the syringe for ten minutes; finally, rinse the bleach out of the syringe using cold water.

Many people know that tattooing and body piercing can potentially transmit HCV, but there is a growing awareness that other cosmetic and personal care procedures may also present some risk. HCV can potentially be transmitted by manicure and pedicure tools such as cuticle scissors, files, and nail clippers, and by barber tools such as razors and hair clippers. As with drug equipment, this can happen when tools come into contact with HCV-infected blood that is then transmitted to a second person.

The California Department of Health Services recently released a report about a Bay Area woman who contracted HCV and whose only apparent risk factor was regular visits to a nail salon. The San Mateo County Health Department is developing methods to educate nail salon owners, employees, and customers about the need for proper infection control procedures. Some tattooing, manicure, pedicure, and barber tools should be used only on a single person. Most professional tattooists use new needles and ink pots for each client. Some people prefer to bring their own razors with them to the barber.

Manicurists should not use soaking water for more than one person. If tools are to be shared, they should be carefully cleaned and sterilized between customers.

Similarly, personal health and beauty items used in the home, including nail files, razors, toothbrushes, and pierced earrings and other jewelry, should not be shared or should be sterilized between users.

Another potential method of blood-borne HCV transmission is through contact with blood or body fluids in a health-care setting. This may happen when a health-care provider accidentally sticks themselves with a used needle or other sharp object. Although such cases are rare, it was recently reported in the news that a surgeon may have infected some of his patients with HCV.

Health-care workers should always use universal precautions while performing medical procedures, including the use of gloves, face masks, and eye protection when appropriate. All needles, scalpels, and other equipment should be disposed of in a "sharps" container after each use, or should be carefully sterilized between uses. Bandages should be properly discarded, and infected blood and body fluids should be immediately cleaned up and disinfected.

Transmission of HCV from mothers to babies before or during birth (perinatal or vertical transmission) is uncommon, occurring in an estimated 5% of cases. Perinatal transmission is most likely when the mother has a high level of HCV in her blood. According to a recent multicenter Italian study, among HCV positive women without HIV coinfection (widely considered a risk factor for HCV perinatal transmission), the risk of mother-to-child HCV transmission was significantly higher in women who had used injection drugs; this was true whether or not she was still using injection drugs during pregnancy.

The researchers concluded that injection drug use, but not HIV coinfection, is an important risk factor for perinatal HCV infection. In this study, breast-feeding and delivery method (vaginal versus Cesarean) had no effect on mother-to-child transmission. (*Journal of Infectious Diseases* 185:567-572. March 1, 2002). HCV positive women should discuss with their health-care provider the possibility of HCV transmission if they are thinking about becoming pregnant.

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

How Does Interferon Work?

By Alan Franciscus
Editor-in-Chief

Interferon works against HCV by protecting healthy uninfected cells from being attacked by the virus. Our immune system naturally produces a variety of different interferons to help defend the body against invaders. By supplementing interferon as treatment for HCV this further boosts what our own interferon can do. Interferons also work in other ways, such as promoting the body's immune response against viruses such as the virus that causes the flu. The interferon used for treatment of HCV has been genetically engineered in large quantities to mimic how our body's natural interferons work to fight diseases like viruses.

Interferon has the following actions:

Antiviral action - Interferons prevent the entry of viruses into cells, thereby limiting new cellular infection. They also inhibit the uncoating of viruses within cells and interfere with viral protein synthesis.

Immunomodulatory effect - Interferons stimulate the production of cytokines (chemical messengers) that activate macrophages, natural killer (NK) cells, and cytotoxic T-lymphocytes (CTLs, or killer T-cells).

Antitumor effects - Interferons reduce the proliferation of both normal and malignant (cancerous) cells and inhibit oncogene expression. Interferons also enhance direct T-cell-mediated cytotoxicity against tumor cells.

Enhanced cell surface expression of MHC - Interferons enhance the expression of class 1 major histocompatibility (MHC) antigens on the surface of infected cells. Expression of these proteins on the cell surface allows cells infected with viruses to be targeted and destroyed by CTLs.

Sometimes the body does not make enough natural interferon to defeat an infection, and giving additional genetically engineered interferon can make a difference.

There are various types of interferon and produced by different companies: Among the most common are:

* interferon-alpha-2a (Roferon-A, produced by

Roche Laboratories)

* interferon-alpha-2b (Intron-A, produced by Schering-Plough)

* interferon-alpha-n1, lymphoblastoid (Wellferon, produced by GlaxoSmithKline)

* interferon-alpha-n3, human leukocyte derived (Alferon N, produced by ISI Pharmaceuticals)

* consensus interferon, or interferon alfacon 1 (Infergen, produced by Amgen, recently acquired by InterMune)

* pegylated interferon-alpha-2b (Peg-Intron, produced by Schering-Plough)

* pegylated interferon-alpha-2a (Pegasys, produced by Roche Laboratories) - not yet FDA-approved

Interferon-alpha-2a and interferon-alpha-2b are referred to as standard interferon. Consensus interferon is a combination of different types of interferon. Some studies suggest that consensus interferon may work better than a single type of interferon (e.g., 2a or 2b). Pegylated interferon is a recently developed, long-acting formulation of interferon that can be injected less often. Pegylation is a process in which polyethylene glycol is attached to a protein in order to extend its activity in the body. Schering-Plough's Peg-Intron was approved in August 2001; Roche Laboratories' Pegasys is awaiting approval.

Interferon is injected subcutaneously (under the skin). Standard interferon and Pegasys are premixed solutions. Peg-Intron is a powder that must be reconstituted before use. Typically people with HCV learn how to reconstitute, measure, and inject interferon themselves or with assistance from a family member.

Typically, the side effects of the genetically engineered interferon is similar to the side effects of natural interferon flu like symptoms, but can be more pronounced since it is injected in such large quantities.

HelpLines:

Southern California

1-888-85LIVER

Northern California

415-978-2400

Clinical Trials

National Trials

ROCHE - 866-GO-WINGS
NIH - HALT-C (Cirrhosis)
800-411-1222

Quest Medical Research (HIV/HCV Coinfection)
Dr. Lalezari (415) 353-0800
East Bay Liver Clinic
Oakland , CA - Grant Young (510) 208-1777

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) 600-1100 or (415) 600-1106
San Francisco General Hospital
Athiana (415) 206-3725
San Francisco
Dr. Cazen (415) 565-6288
Stanford University Hospital
Stanford Liver Research Clinic (650) 724-7057

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