

## June 2000's Advocate:

### Chronic HCV in Children and Adolescents

Many questions about Hepatitis C in children remain unanswered.

### At Two Conferences, Experts Urge Comprehensive Approach to HCV, HIV and Drug, Alcohol Abuse

Conferences explore strategies for dealing with complex treatment problems.

### Healthwise: Navigating the Vitamin Maze

What vitamins and supplements are safe for people with HCV.

### Impact of the Closing of a Needle Exchange Program

Study finds needle exchanges provide scientific means for reducing the spread of HIV

### A Teenager's Story

An 18-year-old tells of coming to terms with Hepatitis C and how she's now working to inform others.

### Treatment Advocate: Preliminary Report from Digestive Diseases Week 2000: Pegasys, Pegasys, Pegasys

Hoffmann-LaRoche's Pegylated Interferon makes wave in San Diego.

## Chronic HCV in Children and Adolescents

By Philip Rosenthal, MD  
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Hepatitis C in children has many similarities but also differences as compared to adults with this infection.

As in adults, parenteral transmission is the primary mode of spread. This may result from contaminated needles used for intravenous drug abuse, tattoos, or body piercings; intranasal cocaine; high risk sexual activity; exposure in hemodialysis units; and blood and blood product exposure. In particular, high risk for hepatitis C acquisition are patients who received blood transfusions before 1992, coagulation factor concentrates before 1987, or intravenous immune globulin (Gammagard) between April 1993 to February 1994.

Thus, the risk groups for hepatitis C infection in children include:

- ◆ Blood or blood product recipients
- ◆ Hematologic disorders
- ◆ Major surgery (e.g., scoliosis, congenital heart disease)
- ◆ Trauma
- ◆ Premature birth
- ◆ Immune deficiency disorders
- ◆ Hemodialysis patients
- ◆ Infants of HCV-infected mothers

Much anxiety and concern has been raised regarding the perinatal transmission of hepatitis C. Maternal to neonatal transmission of hepatitis C in newborns occurs in less than 5% of children of infected mothers. It is more likely to occur when maternal HCV RNA levels are high such as in HIV co-infected mothers. Our current knowledge of the disease indicates that perinatal transmission of hepatitis C is not related to breast feeding.

Like adults, up to 50% of children with chronic HCV will be asymptomatic. Symptoms in children may be similar as in adults with malaise, right upper quadrant discomfort, fatigue, polyarthralgia and pruritus the most common symptoms. There are often no physical signs of chronic hepatitis C infection in children. Progressive disease may result in hepatomegaly, signs of cirrhosis, ascites, encephalopathy, jaundice or peripheral edema.

When liver biopsies are performed in children with chronic hepatitis C infection, a wide spectrum from mild to severe is observed. As in adults, it is impossible to predict the histology based upon clinical and laboratory findings in children.

Recently, a German study found that after a 20-year follow-up, nearly half of all children who contracted hepatitis C from a blood transfusion during heart surgery were free of the infection. Prior to 1991, reliable blood donor screening for hepatitis C was unavailable in Germany. Of those patients who still had the infection present, few had developed liver disease, although they had other risk factors. The German researchers are careful to point out that they do not know if more serious liver conditions will appear 30 to 40 years after initial infection. These results contrast markedly with adults. Only 20% of adults rid themselves spontaneously of the disease (80% have chronicity) and 30% develop cirrhosis and liver cancer.

Is there a difference in children who acquire hepatitis C from blood or blood transfusions as opposed to children who acquire the infection from their mother at birth? We do not currently have the answer to this important question. Yet, hepatitis C is not a benign disease in all children. There are children only several

years of age with significant liver disease as the result of hepatitis C infection who have required liver transplantation. Many other questions remain unanswered. What are the host, virologic and environmental factors that make chronic HCV infection so aggressive in a minority of young children? Are short duration of infection and mildness of disease good prognostic factors for treatment in children? Is treatment of HCV in children unwarranted or should it be delayed?

Currently, there is no approved therapy for the treatment of chronic hepatitis C in children.

Neither interferon nor combination therapy with ribavirin are approved by the FDA for children with HCV < 18 years of age. Limited experience with interferon use in children suggests the efficacy of interferon is similar in children and adults. Unfortunately, interferon use alone is not very effective for the treatment of chronic hepatitis C infection. Interferon side effects can be troublesome including three times a week injections, growth failure and seizures amongst more concerning side effects in children. A clinical trial utilizing a long-acting interferon (pegylated interferon) is soon to begin in children.

In summary, children are at risk for chronic hepatitis C virus infection. Hepatitis C viral infection can range from mild to severe in children. The various factors responsible for the progression of the disease in children are unknown. Currently, there is no approved nor effective therapy for chronic hepatitis C viral infection in children. Identification and research are the keys to combating chronic HCV in children.

Dr. Rosenthal is the Director of Pediatric Hepatology, Medical Director of the Pediatric Liver Transplant Program and a Professor of Pediatrics and Surgery at the University of California, San Francisco (UCSF). He is board certified in Pediatrics and Pediatric Gastroenterology. Dr. Rosenthal completed his medical training at Downstate Medical Center and the Albert Einstein Medical Center in New York. He then completed a fellowship in pediatric gastroenterology at UCSF. He joined the UCSF faculty in 1995 after serving as Professor of Pediatrics at University of California, Los Angeles (UCLA).

Currently, Dr. Rosenthal is pursuing research on the pharmaceutical treatment of hepatitis B and C, genetics and immunology of biliary disease, use of bioartificial liver support utilizing porcine hepatocytes for patients with fulminant liver failure, as well as researching the quality of life following liver transplantation in children.

## **At Two Conferences, Experts Urge Comprehensive Approach to HCV, HIV and Drug, Alcohol Abuse**

By Alan Franciscus

Two recent conferences shed light on the interrelated issues of hepatitis C, drug use, HIV infection and other forms of viral hepatitis. The American Methadone Treatment Association Conference held in April and the Drug Use, HIV and Hepatitis Conference held in May both offered insight into these complex issues.

The American Methadone Treatment Association Conference held in San Francisco focused on the latest science-based information correlating drug use and chemical addiction. Presentations on how chemical reactions in the brain change with drug use, emphasized the importance of treating drug use as a chronic medical condition with social and economic consequences.

Hepatitis C affects a majority of methadone users. Several presentations involved developing effective treatment strategies along with support and advocacy for HCV-positive individuals on methadone. Many HCV-positive methadone users are now successfully treated with interferon or the combination of interferon and ribavirin. Studies show that a comprehensive approach combining medical and social support dramatically increases the potential for success. Visit their website at [www.assnmethworks.org](http://www.assnmethworks.org) for more information.

The Center for Substance Abuse Treatment, National Institute of Drug Abuse (NIDA), CDC and the Center for HIV, Hepatitis, and Addiction Training and Technology sponsored the Drug Use, HIV and Hepatitis Conference held in Baltimore in May. The goal of this conference was also to focus on the complex and inter-related issues of drug use, HIV and hepatitis.

During the conference NIDA and the Center for Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment (CSAT) issued two new publications. The Makings of a Public Health Epidemic: Drug Use, HIV/AIDS and hepatitis C. NIDA'S a Community Drug Abuse Bulletin on Hepatitis C provides basic information on hepatitis C. CSAT's publication Substance Abuse Treatment for Persons With HIV/AIDS, providing information on HIV/AIDS and drug abuse was also released.

The importance of integrating hepatitis C into existing HIV/AIDS, TB and STD services was a main theme throughout the conference. The need for developing specific HCV prevention and support strategies that enhance the HIV model was highlighted. For more information visit NIDA's home page - [www.drugabuse.gov](http://www.drugabuse.gov) and CSAT's home page - [www.samhsa.gov/csat/csat.htm](http://www.samhsa.gov/csat/csat.htm)

These two conferences provided a wealth of information on HCV. Future articles in the HCV Advocate will focus on some of the information presented.

A special acknowledgement for providing information, support and access to various organizations and speakers should go to Mark Parrino, M.P.A. President - American Methadone Treatment Association, Dan Magill and the conference staff of the American Methadone Treatment Conference. And to Jeffrey A. Hoffman, Ph.D., Kathleen Hauck and the conference staff for the Drug Use, HIV and Hepatitis Conference.

## Healthwise: Navigating the Vitamin Maze

By Lucinda K. Porter, RN

Are you curious about vitamins and supplements? Do you wonder which to take and which to avoid? Do you have questions about which brands to buy? If so, you are in good company. I am frequently asked questions about vitamins and supplements by patients with chronic hepatitis C virus (HCV) infection. This article discusses some aspects of supplementation. One caveat-the perspective I offer is exactly that-a perspective. My views are not a substitute for medical care. You are strongly advised to speak to your physician or other health care provider about any vitamins, minerals, or herbal supplementation you are taking. If your physician is disinterested about this topic, consider exercising your right to a second opinion or asking for a referral to a nutritionist.

What, if any supplements should you consider? In a recent article published in Health magazine (March 2000), there were a few sensible suggestions. I have modified these recommendations for patients with liver disease. Keep in mind that supplements are not a substitute for good nutrition.

### Multivitamins

This is the one supplement that most experts recommend. Unless your doctor advises you otherwise, look for a multivitamin without iron. These can be found in the "over 50" versions of most major brands. As for which brands, there are many to choose from. High price does not correlate with high quality. Most manufacturers buy the ingredients from the same sources. If you are paying more money for your multivitamin, it is probably for advertising or unnecessary fillers. These fillers are often herbs in doses too low to offer any benefit. Here are a few suggestions for multivitamins without iron:

- o Safeway Select OmniSource Senior
- o Rite Aid Whole Source Mature Adult
- o Dr. Art Ulene Nutrition Boost Formula (Senior version)

### Vitamin C

This vitamin is best obtained from food. A minimum of 5 servings of most fruits and vegetables will cover most of your vitamin C requirements. If you do supplement, look for small dose pills, such as 100 or 250 milligrams (mg). You can also break a 500 mg pill in half. A government advisory panel has recently recommended that women consume 75 mg daily. The recommendation for men is 95 mg. Smokers need an additional 35 mg daily. Do not exceed 2000 mg per day. If you eat a high iron meal, postpone taking your vitamin C supplement. Vitamin C can bind with iron, putting extra load on the liver. As for specific brand, your body cannot tell the difference between an inexpensive or expensive version.

### Vitamin E

This vitamin is constantly making news. It has been the subject of research in liver disease as well as a host of other conditions. The optimum levels appear to be between 400 and 800 International Units (IU) daily. Vitamin E is available in natural and synthetic forms. Natural E is absorbed by the body better than the synthetic form. It is also more expensive. However, most of the clinical trials that show the benefits of vitamin E use the synthetic form. All in all, this may be the better choice. If you use the natural form, the dosage may be closer to 200 - 400 IU daily. Do not exceed 800 IU per day. At high doses, vitamin E can act as an anticoagulant, or anticlotting agent. Consult your doctor if you have low platelets, are taking Coumadin or have a clotting disorder.

### Selenium

This mineral is found in most multivitamins, but it may be worth it to add this in as a supplement. The

recommended daily doses for men is 70 micrograms (mcg) and 55 mcg for women. In a recent article in the Nutrition Action Newsletter, the Center for Science in the Public Interest (CSPI) suggested a daily dose of 200 mcg. Do not exceed 400 mcg daily. Selenium can be toxic at higher levels. Selenium can be purchased in its most inexpensive form.

## Calcium

The daily doses for this are 1000 mg (ages 19-50), 1200 mg (51-70), and 1500 mg if you are over 70 years old. Each serving of low fat milk, yogurt, or cheese has roughly 300 mg of calcium. Add in a supplement for each one you miss. Talk to your doctor about calcium supplementation if you have kidney or gall stones. Any brand that can dissolve in a glass of warm water in 30 minutes should be the guiding factor, rather than price. Most brands of calcium are acceptable although lately there has been some evidence that the most expensive form, calcium citrate, has the most bioavailability. Avoid calcium from oyster shell or dolomite sources.

## Milk Thistle

The jury is still debating the milk thistle (or silymarin or thisilyn) issue. Milk thistle has been used for hundreds of years as a folk remedy for liver disease. The European medical community has done some promising research using milk thistle for liver diseases, but as for HCV, the evidence is just not solid. The good news is that milk thistle does not appear to do any harm and may provide some benefit. The recommended dose is 200 mg three times daily. Only buy brands that use standardized amounts of at least 80% silymarin. Try to find a brand that states it complies with standards of the American Herbal Pharmacopoeia, the German Commission E, or any of the organizations that are striving to maintain standards in a market that is completely unregulated. This is the one supplement in which I spare no expense. I use Nature's Way Thisilyn or Eclectic Institute's Milk Thistle, but there are other fine brands.

What supplements should you avoid?

The Information Packet published by the Hepatitis C Support Project has a list of herbs that should be avoided, especially for those with liver disease. This list can be obtained either by contacting the Project (see address and phone number on this newsletter) or through their web site at [www.hcvadvocate.org](http://www.hcvadvocate.org). In addition to the herbs listed, avoid supplementation with vitamin A, D and iron. One can usually get sufficient vitamin D in a multivitamin, diet, and sun. Unless these are not available to you, supplementing with extra D is not recommended. Large doses of any supplements are strongly discouraged. Vitamin A in doses above those recommended can cause liver injury.

Certain foods and medications interfere with vitamin and mineral absorbency. Consult with a nutritionist if you want individual counseling about your particular situation. For more general information, the following magazines are good sources of up to date information:

o Health (800) 274-2522

o Nutrition Action Newsletter, published by the Center for Science in the Public Interest  
CSPI, 1875 Connecticut Ave., NW, Suite 300, Washington, D.C. 20009

[www.cspinet.org](http://www.cspinet.org)

o Prevention (800) 813-8070

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## Impact of the Closing of a Needle Exchange Program

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### Synopsis

A wealth of scientific findings demonstrate that unsafe injection practices are the direct or indirect cause of one third of new HIV infections in the United States and that needle exchange programs are effective in reducing drug-related risks. While previous studies have analyzed the impact of needle-exchange programs in operation, we analyzed the impact of an established needle exchange's closure on its clients' risk behaviors, and on the community-at-large.

**Background:** After operating with state-sponsorship for four years, the Windham, Connecticut needle exchange was closed after becoming embroiled in a public controversy in which it was blamed for causing the city's 'drug problem,' 'discarded needle problem,' and even the economic decline of the city itself.

**Methods:** From March 1994 through February 1997, as part of a larger AIDS prevention research project funded by the National Institute on Drug Abuse (RO1 DA08014), risk-assessment interviews were administered to 330 injection drug users in Windham, the majority of whom were clients of the needle exchange. After the exchange was closed in March 1997, for the next eleven months, we re-recruited former respondents who remained in the area and were still active injectors. This produced 111 'post-closure initial' interviews and 78 'post-closure follow-up' interviews three months later. Based on the interviews administered before and after the closure of the needle exchange, and surveys of public drug-using sites, an impact analysis is offered of the exchange's closure.

**Results:** Following the closure of the needle exchange, a statistically significant increase in drug injectors' procurement of syringes from street and other 'unreliable sources' was found, as well as in their re-use of syringes and the sharing of injection equipment. Surveys of outdoor drug-use areas found that the closure of the needle exchange did not reduce the volume of discarded syringes and other drug-injection debris, or reduce the robustness of Windham's illicit drug scene.

**Conclusions:** The problems in Windham that led to the closure of the exchange still remain, and the city's drug injectors are engaging in higher levels of HIV risk-behavior. In closing the needle exchange, Windham has deprived itself of one of the few scientifically proven means for reducing the spread of HIV and for reducing other drug-related problems within the community.

## **A Teenager's Story: An 18-year-old tells of coming to terms with Hepatitis C and how she's now working to inform others**

By Casia Freitas

I am a teenager living with chronic Hepatitis C.

Early last spring, after donating blood at a school blood drive, the letter from the Blood Bank of the Redwoods arrived as I headed out the door. Expecting to find a confirmation of my blood type, I found no such thing. Confused, it took awhile to comprehend the contents of the notice, and when I did, I was shocked. Surely I could not have the virus they told me of, a virus I had never even heard of. Without any compassion the letter stated: "Your blood tested positive for the screening for a newly discovered virus, called Hepatitis C."

After an agonizing wait following more tests, the positive screening was confirmed. I was another victim of the "silent killer," Hepatitis C. A blood transfusion I received at birth after an amazing recovery from a diaphragmatic hernia is the only possible explanation for my contracting the virus. This discovery has changed almost every aspect of my life, especially the way I view life itself.

Returning to school the following week, suddenly everything seemed pointless- all the activities I crammed into my already too-full life-how significant were they? Easy classes became even more mundane. An urge to quit school and focus on my passions for writing, music and community service constantly occupied my thoughts, distracting me from the lessons I was supposed to be absorbing.

Having the virus also filled me a great deal of cynicism. Looking at my peers, I felt I was no longer a part of them; I had this virus which separated us, which they couldn't relate to, or even begin to comprehend. Their actions became foreign to me, seemingly superficial. How could they be so consumed with problems such as who to ask to the school dance, which seemed truly insignificant to me in the scheme of things?

After a liver biopsy a month later, my ability to concentrate was even farther from my grasp. Perhaps through faith alone, a realization came: maybe this is what I was supposed to be doing. As difficult as it was to carry on in the same way as I had before, these classes and leadership roles were my future. I realized I could get nowhere without an education.

One mission for the future is now clear: I must spread awareness about Hepatitis C. Having eclectic interests, deciding on a profession has, until now, always instilled some fear in my heart. While striving to devour as much information about this disease as I can, I have applied my obsession for writing to hopefully produce something worthy of my efforts. Through my words, I hope to bring comfort to others who may have experienced the same fear, frustration and feeling of isolation that I have encountered from having Hepatitis C. I never expected this, but I will make of it what I can. My brain is swirling with ideas of ways to create awareness in such an unknown subject: my chief goal is to educate my peers about hepatitis C and encourage getting tested, especially since it took me almost seventeen years to learn that I have it. In creating awareness, I have already begun by teaching myself how to construct an informative web site and email support group, which seemed to be the most tangible starting point. On my web site, I have supplied the basics about hepatitis C, told of my experiences, included the most up-to-date information I can find, and extended my love and support to those who may need it. It is located at <http://members.home.com/casia>.

Before school ended during my junior year of high school, I made the most difficult decision of my life based on the results of the liver biopsy: to start a yearlong combination therapy of Interferon and Ribavirin at the end of June. With all the changes in my life over the past year, this experience has often seemed surreal, and yet it is all too real.

While undergoing the treatment, there were many times when I was ready to give up. However, maintaining my web site has helped me from going insane at the climax of my frustration and the painful side effects. I

must remain focused on my vision, even after learning at six months that the treatment was unsuccessful. Although this news was incredibly difficult to hear, I realize how valuable this whole experience has been to me. I have been fortunate to learn more about life and myself than most people ever learn. It is certainly not easy to accept that you have hepatitis C.

However, as with all things, the sooner we learn acceptance, the sooner we can move on with our lives and find joy in them. Some of the most meaningful words of encouragement came from my dad when he asked me, "Well, would you rather be dead as you would have been without that transfusion, or live with this virus?" I am grateful for my life, because even these circumstances can and will pave the way to new opportunities in which to fulfill my destiny.

Casia is 18 years old and lives in Northern California. Next fall she will be attending Lewis & Clark College in Portland, Oregon where she will probably major in international affairs. Her passions include writing poetry, playing the piano, community service and more recently, web site design.

# **Treatment Advocate: Preliminary Report from Digestive Diseases Week 2000: Pegasys, Pegasys, Pegasys**

By Joe Shaw

By now, all of the doctors, patients and others attending the Digestive Diseases Week in San Diego must be feeling a little like Jan Brady. But instead of "Marcia, Marcia, Marcia," they're probably saying "Pegasys, Pegasys, Pegasys."

From a patient perspective, the big news this week had to be Hoffmann-LaRoche's release of studies and other important developments about Pegasys, a pegylated interferon being developed by that pharmaceutical company.

First it was announced that the company has submitted a Biologics License Application to the U.S. Food and Drug Administration (FDA) for approval to market Pegasys (peginterferon alfa-2a) for the treatment of chronic hepatitis C.

In clinical studies, Pegasys showed response rates similar to those reported with the current combination interferon/ribavirin treatment, according to Hoffmann-LaRoche. Clinical studies have demonstrated favorable results compared to interferon monotherapy, even in cirrhotic patients. Pegasys is a ready-to-use solution which would be injected subcutaneously once a week for a year, in comparison to standard treatment, which must be taken three times per week. Schering-Plough has also developed a pegylated interferon called Peg-Intron. Pegylated interferon is a longer-lasting form of interferon for the treatment of hepatitis C.

Here are highlights of some of the studies presented by Hoffmann-LaRoche at the conference, you may view full length articles about these studies and others online at [www.hcvadvocate.org](http://www.hcvadvocate.org):

## Histological Improvement with Pegasys in Non-Cirrhotic Patients

Data released today from a study of patients with chronic hepatitis C without cirrhosis showed that 63 percent of patients who received Pegasys experienced histologic improvement. Researchers believe that patients with histologic improvement may have a slower progression of liver disease.

## Pegasys/Ribavirin Combination Study

Data also released this week indicate that Pegasys and ribavirin combination therapy produces favorable antiviral activity in the treatment of chronic hepatitis C.

## Pegasys May Offer Improved Liver Histology in Hepatitis C Patients With Cirrhosis

Pegasys (peginterferon alfa-2a), an investigational, longer-lasting form of interferon, may provide significant histologic improvement over standard interferon therapy in chronic hepatitis C patients with cirrhosis. Many researchers believe that patients with histological improvement may have a slower progression of liver disease. Histological response is measured by objective criteria obtained from liver biopsies before and after treatment.

## Pegasys Selected for Major New National Institutes of Health Study of Chronic Hepatitis C Patients

Pegasys has been selected by the National Institutes of Health for use in a study examining the role of long-term pegylated interferon therapy for the treatment of chronic hepatitis C in patients who failed to respond to previous interferon therapy. The Hepatitis C Antiviral Long-term Treatment to prevent Cirrhosis (HALT-C)

Trial will examine approximately 900 patients treated with interferon over three-and-a-half years. The study is designed to determine if long-term interferon therapy with Pegasys can reduce the risk of histologic progression to cirrhosis, decompensated liver disease and/or hepatocellular carcinoma in patients with chronic hepatitis C and advanced fibrosis or cirrhosis who failed to respond to previous interferon therapy. Screening for the HALT-C Trial will begin in June. Trial centers will be located in California, Colorado, Maryland, Massachusetts, Michigan, Missouri, Texas and Virginia.

Joe Shaw was diagnosed with HCV in January 1998 and lives with his partner and his two pugs, Willie and Sammie in Long Beach, CA.