

EASL: 2007



Liz Highleyman

The 42nd Annual Meeting of the European Association for the Study of the Liver (EASL) took place April 11-15 in Barcelona, Spain. One of the key annual meetings devoted to viral hepatitis and other types of liver disease, this year's EASL conference featured numerous presentations on topics including refinements to standard hepatitis C treatment, noninvasive assessment of liver fibrosis, and HIV/HCV coinfection.

NOVEL ANTI-HCV DRUGS

Many presentations concerned new antiviral agents with direct activity against HCV. Notable at this meeting was the number of very early studies looking at combinations of these agents in the preclinical stage of development. It is already clear that directly targeted agents are prone to resistance, which can be delayed or prevented by using combination therapy, especially regimens that combine drugs with different mechanisms of action. Studying these agents in combination early on should help prevent unexpected drawbacks once they reach the clinical stage, such as detrimental interactions or additive toxicities.

Telaprevir

The most eagerly awaited data came in a late-breaker presentation

by J.G. McHutchison and colleagues on the Vertex/Tibotec oral HCV protease inhibitor telaprevir (VX-950). The Phase IIb PROVE 1 trial included 250 patients with genotype 1 chronic hepatitis C who were randomly assigned to receive 750 mg telaprevir every 8 hours or placebo plus 180 mcg/week pegylated interferon alfa-2a (Pegasys) and 1,000-1,200 mg/day ribavirin for 12 weeks. Thereafter, participants received Pegasys/ribavirin without telaprevir for 0, 12, or 36 weeks. In the three telaprevir arms combined, 79% of subjects achieved rapid virological response (RVR) at Week 4 (HCV RNA < 10 IU/mL), compared with 11% in the placebo arm. At Week 12, 70% of patients taking telaprevir still had undetectable HCV RNA. Skin rash was more common in the telaprevir arms; 11% of patients in these arms discontinued therapy due to adverse events, compared with 3% in the placebo arm.

In a planned interim analysis, 6 out of 9 patients (67%) who achieved RVR and finished all therapy at 12 weeks continued to have undetectable viral load at Week 20 of follow-up. While the usual measure of successful treatment is sustained virological response (SVR) 24 weeks after completion of therapy, these promising results suggest that using telaprevir in a



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combination regimen may allow for a shorter duration of therapy for some genotype 1 patients. Vertex and Tibotec plan to initiate Phase III clinical trials of telaprevir combination therapy by the fourth quarter of 2007.

Valopicitabine

Valopicitabine (NM 283) is an oral HCV NS5B polymerase inhibitor being developed by Idenix. N. Afdhal reported data from a Phase IIb trial that included 178 genotype 1 nonresponders to prior therapy. Participants were initially assigned to receive oral doses of valopicitabine ranging from 400 to 800 mg/day, with or without Pegasys; the dose was later reduced to 400 mg for all patients due to gastrointestinal side effects. A control group received standard therapy with Pegasys plus 1,000-1,200 mg/day

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ribavirin. Treatment continued for nine months after subjects achieved undetectable HCV viral loads, up to a maximum of 72 weeks; the valopicitabine monotherapy arm was discontinued early due to lack of efficacy. At Week 48, similar proportions of patients receiving valopicitabine/Pegasys/ribavirin and those retreated with standard therapy achieved undetectable HCV RNA (15%-20% vs 24%), demonstrating the difficulty of fully suppressing HCV replication in prior nonresponders.

However, in another Phase IIb study by E. Lawitz and colleagues, valopicitabine performed better in genotype 1 patients being treated for the first time. This trial included 173 participants randomly assigned to receive valopicitabine at doses ranging from 200 to 800 mg/day in various combination regimens with Pegasys (none received ribavirin); here too, the maximum dose was reduced to 400 mg due to side effects. The initial rate of HCV RNA decline was dependent on valopicitabine dose. At Week 24, 50%-70% of participants had undetectable HCV RNA, and most had an end of treatment response at Week 48. These data suggest that for some treatment-naive patients, valopicitabine may be used with pegylated interferon instead of ribavirin, but SVR data will be needed to confirm this hypothesis.

HCV-796

HCV-796 is a non-nucleoside HCV NS5B polymerase inhibitor that demonstrated antiviral activity against all HCV genotypes when administered as monotherapy. S.A. Villano and colleagues presented data from a study of 65 treatment-

naive patients (about 65% with genotype 1) randomly assigned to receive oral HCV-796 (100, 250, 500, or 1000 mg) every 12 hours, or placebo, in combination with pegylated interferon alfa-2b (PegIntron); none received ribavirin. At all doses tested, HCV-796 plus PegIntron reduced plasma HCV viral loads more than PegIntron alone, with mean HCV RNA reductions of 3.3-3.5 logs in the combination arms (vs 1.6 logs in the PegIntron monotherapy arm). No dose-limiting side effects related to HCV-796 were noted.

Boceprevir

Many observers wondered about the fate of Schering-Plough's HCV NS3 protease inhibitor SCH 503034 – now named boceprevir – when no new information was presented at the AASLD meeting last October. At EASL, researchers presented data from several studies of the drug, but these did not include results from Schering's ongoing Phase II study of boceprevir plus pegylated interferon/ribavirin in genotype 1 non-responders, which is expected to be available later this year.

R. Ralston and colleagues presented data from an *in vitro* study of boceprevir in combination with NM 107, the active prodrug of valopicitabine. In a genotype 1b HCV replicon model, combining the two drugs led to enhanced inhibition of viral replication, compared with the effects of each agent alone. Combining the drugs also reduced the emergence of drug resistance, which is a known drawback of directly targeted anti-HCV drugs. Shifting to clinical trials, R.A. Preston and colleagues reported that in an open-label, single-dose (400 mg) pharmacokinetic study, boceprevir was well tolerated and safe in patients with mild, moderate, and

severe liver impairment.

Celgosivir

The active metabolite of celgosivir (MX-3253), castanospermine, is a potent inhibitor of alpha-glucosidase, a host enzyme required for HCV assembly and release. K. Kaita and colleagues reported on a Phase II double-blind study of celgosivir in 57 genotype 1 patients classified as prior nonresponders (36) or partial responders (21). Subjects were randomly assigned to receive 400 mg once daily celgosivir plus PegIntron, with or without ribavirin, or standard PegIntron/ribavirin therapy. Data were analyzed twice, since half the viral load samples required re-testing after the initial analysis. In the second analysis, 42% of patients in the celgosivir/PegIntron/ribavirin arm achieved early virological response (at least a 2 log reduction in HCV RNA by Week 12), compared with 10% in the PegIntron/ribavirin arm. Treatment was well-tolerated, with the most common celgosivir-related side effect being mostly mild gastrointestinal symptoms.

OTHER NOVEL AGENTS

Researchers also presented earlier stage data from new agents further back in the drug development pipeline. F. Gray and colleagues reported on GSK625433, an HCV NS5B polymerase inhibitor candidate from GlaxoSmithKline. Using a genotype 1a/1b replicon system, they found that GSK625433 potently and selectively inhibited HCV polymerase, exhibited synergistic activity when combined with interferon, and retained activity against HCV that was resistant to other types of polymerase inhibitors.

Abbott also has an HCV NS5B

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HealthWise:

Hepatitis Awareness



Lucinda K. Porter, RN

May is designated as worldwide Hepatitis Awareness Month. This is an opportunity to brush up on the basics of hepatitis. The word *hepatitis* means inflammation of the liver. The *hepat* part of the word comes from the Greek for liver. The *itis* part simply refers to inflammation. If you think about other common words with *itis*, you will see a pattern. *Tonsillitis* means inflammation of the tonsils, *appendicitis* indicates inflammation of the appendix, *arthritis* signifies inflammation of the joints and so on.

Hepatitis is a general term and does not tell us about the cause of the inflammation. Alcohol, drugs, toxins, microorganisms, autoimmune and genetic factors can all cause hepatitis. Another type of hepatitis is related to a high fat diet or to being overweight. These controllable factors can lead to excess accumulation of fat around the liver, causing it to become inflamed.

Viruses cause the contagious forms of hepatitis. These viral diseases are labeled by letters of the alphabet. The most common are hepatitis A (HAV), hepatitis B (HBV), and hepatitis C (HCV). There are also hepatitis D, E, and G. (*Hepatitis* is also an acceptable plural.) For a while, there was a hepatitis F, but it was removed from the list. Hepatitis F may be non-existent or a mutation of one of the other viruses. Some experts believe that hepatitis F is still existent, but until more is known, F is left out of the alphabet soup.

Although A, B, C, D, E, and G are all liver diseases caused by viruses, the differences between them are significant. Hepatitis A is no more like hepatitis C than a monkey is to a human. One can see the obvious similarities, but the differences are clear.

SIMILARITIES

Regardless of the cause, there are not necessarily symptoms for all the hepatitises. The liver is a non-

complaining organ and might not let you know when there is a problem. However, when the liver does complain, the symptoms are similar. Fatigue is the most common. There may be nausea, loss of appetite, *malaise* (plain old not feeling well). Vomiting, diarrhea, stomach pain, and fever may occur. The skin and eyes may turn yellow, which is known as *jaundice*. Urine may be a dark tea-color while the stools may turn the color of pale clay. Your medical provider may feel an enlarged liver. Lab tests to measure liver enzymes may be abnormal.

DIFFERENCES

Hepatitis A and E are transmitted by fecal-oral routes. Hepatitis E is found outside the United States and rarely seen in this country. Hepatitis A outbreaks commonly occur in families, day care centers, and from food. HAV prevention strategies include hand washing before eating and preparing food, after using the bathroom, and after changing diapers. Avoid raw or undercooked shellfish such as oysters and clams. When traveling in areas with a high risk of hepatitis E, do not drink any water that has not been properly treated. Avoid ice, raw or undercooked shellfish, and all uncooked fruits and vegetables that have not been peeled.

Hepatitis A and E are not chronic diseases. This means that if you get them, eventually you will recover and you will not be infected again. Complications and death are uncommon in these two viruses except that about 20% of women in their third trimester of pregnancy die of complications from HEV. There is no specific treatment for HAV and HEV. There is a vaccine against hepatitis A. Everyone with chronic hepatitis B and C, who has never had HAV, should be immunized.

Hepatitis B, C, D and G are transmitted via blood and body fluids. Prevention practices include avoid-

“Of the more than 2 billion people who have contracted HBV, 350 million have become chronic carriers, with over a half million deaths annually.”

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Extrahepatic Manifestations: *Peripheral Neuropathy (PN)*



Alan Franciscus, Editor-in-Chief

Neuropathy is a medical term for any disease of the nerves. There are four major forms of neuropathy – polyneuropathy, autonomic neuropathy, mononeuropathy and the most common form, peripheral polyneuropathy – more commonly called peripheral neuropathy (PN). Peripheral neuropathy damages the nerves in the legs and arms. Usually the first area that PN affects are the feet and legs before the hands and arms.

This article will discuss the HCV-related form of peripheral neuropathy including the cause, symptoms, and treatments. (*See page 9 for a related article on PN.*)

CAUSE

The exact cause of HCV-related PN is not completely understood, but there is some speculation that it could be caused by HCV RNA deposits in blood vessels that supply oxygen to the nerves, HCV infection of the nerves, an inflammation process in the nerves, and/or an HCV-related immune disorder. In the past it was believed that only people with cryoglobulinemia developed HCV-related PN but it has been proven that HCV-related PN can occur even in the absence of cryoglobulinemia. Studies have found that up to 15.3% of the HCV population has PN. The most common cause of PN is diabetes – in fact it is estimated that 34% of the diabetic population has PN. This compares to the prevalence of 2.4-8% in the general population.

SYMPTOMS

The most common symptoms of PN are numbness, tingling, sharp pain or cramps, loss of balance and coordination, and pain. The pain is usually perceived as a steady burning, ‘pins and needles’, and/or like an electric shock. The symptoms of PN are usually worse at night. PN can also cause muscle weakness, loss of reflexes (especially in the ankles), and foot problems including sores and blisters that could potentially lead to infections of the skin and bone. PN doesn’t always progress or become worse; so just because a person develops symptoms of PN it doesn’t mean that it is going to become worse.

PN is usually diagnosed on the basis of physical symptoms and direct examination. It is important to know that many people with PN have no symptoms so it may be difficult to diagnose. An extensive examination of the foot is the most common way PN is diagnosed. A doctor will look for specific signs of PN including skin lesions, circulation problems, and test the degree of sensation by touching a filament to different areas of the foot or leg. There are other tests that can be done to determine the type and extent of nerve damage such as nerve conduction studies, electromyography, quantitative sensory testing, heart rate variability, ultrasound, and nerve or skin biopsy.

TREATMENT

The most common treatment of PN consists of managing the symptoms. A medical provider may rec-

ommend aspirin, acetaminophen, or a non-steroidal anti-inflammatory drug (NSAID). There are other measures to control more severe symptoms including topical creams, opioid analgesics, tricyclic antidepressants, anticonvulsants, and another class of antidepressants called serotonin norepinephrine reuptake inhibitors (SSNRI). Other measures include transcutaneous electrical nerve stimulation (TENS), which uses electricity to block pain signals, hypnosis, biofeedback and acupuncture. In general, antidepressants seem to work better to manage constant burning pain.

Treatment for most HCV-related extrahepatic manifestations is by treating the underlying cause (hepatitis C) with interferon. However, treatment of PN with interferon has produced mixed results and there is a chance that interferon could actually exacerbate existing PN. Generally, treatment of PN in someone with hepatitis C is done on a case by case basis evaluating the person with PN based on the severity of the PN and chances of responding to various treatments including interferon.

FOOT CARE

As discussed earlier PN usually affects the feet and legs first. Because NP can cause loss of sensation to the lower extremities it is of utmost importance that people with PN pay special attention to their feet. The loss of sensation caused by PN can lead to unrecognized cuts, blisters and other damage to the feet. If a condition or injury goes unchecked it could lead to infections and ulcerations that may spread to the bone. Severe bone infection can lead to amputation of the infected bone. There are many ways to take care of and protect

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Fatigue



Alan Franciscus, Editor-in-Chief

Fatigue is the most common symptom reported by people living with hepatitis C and many other liver conditions. Fatigue can range from mild to severe and can be so debilitating that it can affect every area of a person's life. What causes liver-related fatigue? Unfortunately, we don't have the answer to this important question, but there are some interesting theories that have emerged in the last few years as more studies are focusing on the reason for and management of liver-related fatigue. In this article, I will focus on the information in a paper titled "Fatigue in liver disease: Pathophysiology and clinical management, *Canadian Journal of Gastroenterology* 2006 Mar;20(3):181-188," by Mark, G. Swain MD, MSc, PRCPC.

In this review, Dr. Swain discusses the various types or classification of fatigue. There are two separate types – peripheral fatigue and central fatigue. **Peripheral fatigue** is characterized as neuromuscular dysfunction. This type of fatigue is related to muscle overuse, underuse and weakness. The author points out that this type of fatigue is generally not the type of fatigue that is associated with liver disease except for people with severe liver disease progression such as the type that people experience from decompensated cirrhosis. **Central fatigue** is the result of altered neurotransmission within the brain and is the type of fatigue most commonly associated with a liver disease. It was also noted that the degree of fatigue does not necessarily correlate with

the degree or severity of liver disease, making the measurement of liver-related fatigue more difficult. The difficulty of zeroing in on the cause of the liver-related fatigue of liver disease is compounded by other factors, such as depression and anxiety over having a chronic illness, stigma associated with a disease, side effects of prescribed and over-the-counter medications, sleep problems, lack of exercise and many other factors.

As mentioned above, the exact cause of liver-related fatigue is unknown. It is theorized that the liver-related fatigue is caused by malfunction of the neurotransmitter systems of the central nervous system, which includes the brain. The chemicals that are believed to cause liver-related fatigue include corticotrophin-releasing hormone (CRH), serotonin, noradrenaline and other neurotransmitter chemicals.

- **CRH's** have been identified as being widely distributed throughout the central nervous system and are involved in arousal (alertness or the state of being prepared to act) and behavioral activation (the way that someone behaves or reacts). It is theorized that defective CRH release may be a cause of liver-related fatigue.

- Abnormal levels of a brain chemical called serotonin are known to cause depression, anxiety and general fatigue. Selective serotonin reuptake inhibitors (SSRI) have been used to treat depression as well as chronic fatigue syndrome; however, the use of SSRI's is not always successful in

treating fatigue.

- Norepinephrine or noradrenaline is a stress hormone and neurotransmitter released by the brain and is most commonly associated with the 'fight-or-flight response.' Low functioning of norepinephrine has been associated with fatigue and depression although the role of norepinephrine on fatigue has not been well studied. Norepinephrine reuptake inhibitors (NRIs) are used to treat depression, smoking cessation (bupropion) and fatigue (off-label).

- Other neurotransmitters include the chemicals dopaminergic and cannabinoid in the brain, but no research has been conducted on the role of these neurotransmitters in relation to liver-related fatigue.

- Communication between the liver and the brain has also been theorized as the cause of liver-related fatigue due to cytokines (chemical messengers released by the immune system to fight disease) that find their way into the brain. Up until recently it was believed that cytokine molecules were too large to enter the brain, but it has been found that there are certain pathways or access points for larger molecules to enter the brain. This theory has been tested in rats and the results suggest that cytokines can enter and/or are synthesized within the brain and "in the setting of liver disease can induce fatigue when present at levels that are without effect in

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FATIGUE

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healthy patients.”

The paper goes on to discuss the approaches to managing fatigue:

- Rule out other causes of fatigue such as sleep patterns, caffeine and alcohol consumption
- Examination and lab tests to rule out other conditions such as hypothyroidism
- Psychological work-up to make sure that a person is not depressed or anxious, which can cause fatigue
- A review of a person’s prescription medication, over-the-counter drug, and health supplement use to rule out possible drug interactions or side effects
- Set up a plan with a patient to increase healthy choices that includes cognitive behavioral therapy as well as diet and exercise programs and support for the psychosocial aspect of living with a liver-related condition

Unfortunately, there are no drugs approved to treat liver-related fatigue. Modafinil (brand name Provigil) has been shown to help with central fatigue, but more studies are needed in people with liver disease.

One of the best strategies for people living with liver-related fatigue is to learn as much as they can about which triggers increase their fatigue and to take the necessary steps to help manage their fatigue. For practical tips on managing fatigue see HCSP’s *A Guide to Understanding and Managing Fatigue*.



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polymerase inhibitor candidate in development, A-848837. As reported by A. Molla and colleagues, the drug was active in a replicon model and had a favorable pharmacokinetic profile in chimpanzees. However, resistance emerged via a variety of mutation pathways.

Data were also presented on the HCV polymerase inhibitors R1479 and BILB1941; PSI-6130, the “parent” molecule of the nucleoside analog polymerase inhibitor R7128; the HCV protease inhibitor ACH-806 (GS9132); the toll-like receptor 9 (TLR9) agonist CPG 10101 (Actilon); and the cyclophilin inhibitors DEBIO-025 and NIM811.

REFINING STANDARD THERAPY

Beyond novel anti-HCV agents, researchers at EASL also presented numerous studies looking at refinements to standard hepatitis C treatment using pegylated interferon plus ribavirin.

- In separate presentations, S. Zeuzem, A.U. Neumann, and V.G. Bain reported data showing that albumin interferon, or Albuferon, may be as or more effective than pegylated interferon, but with fewer side effects.
- E. Zehnter and colleagues found that nearly 90% of genotype 2/3 patients and about 70% of genotype 1/4 patients with RVR at Week 4 went on to achieve SVR. They suggested that the standard 24- or 48-week course of therapy may be “too much” for many rapid responders, but urged caution – including ensuring optimal adherence and evaluating other

predictive factors – when attempting to shorten the duration of therapy.

- O. Dalgard and colleagues reported that among 428 patients with genotype 2 or 3 chronic hepatitis C who achieve RVR by Week 4 of treatment with PegIntron plus ribavirin, those treated for a total of 14 weeks were as likely to achieve sustained response as those treated for the standard 24 weeks (91% vs 95%).
- Looking at genotype 2/3 patients who did not achieve RVR in the ACCELERATE study, B. Willems and colleagues found that intensified treatment for 48 weeks with Pegasys plus 1000-1200 mg ribavirin reduced the risk of relapse and produced an SVR rate of about 75%, compared with about 65% for patients treated for the standard 24-week duration and/or using a lower 800 mg dose of ribavirin.
- Finally, in a long-term follow-up study of nearly 1000 patients, M.G. Swain and colleagues found that more than 99% of patients who achieved sustained response with pegylated interferon alone or in combination with ribavirin still had undetectable HCV RNA as long as five years after completing therapy, suggesting that SVR can be regarded as a “cure.”

For EASL 2007 abstracts, see

<http://www.easl.ch/liver-meeting/Program/SessionIndex.asp>



AWARENESS

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ance of everything where there is even a remote chance of contact with blood or body fluid: Practice safer sex, do not share drugs or drug preparation tools, and make sure tattooing, piercing, and manicuring are performed safely.

HBV is very contagious. It is more contagious than HCV or HIV. HBV is passed sexually, via contaminated drug utensils, and from mother to fetus. In the United States, many adults who contract HBV usually get over it without it turning into a chronic disease. They develop natural protection against re-infection. However, HBV may become chronic, leading to serious liver problems including cirrhosis, cancer, and death. Worldwide, HBV is a huge problem. Of the more than 2 billion people who have contracted HBV, 350 million have become chronic carriers, with over a half million deaths annually. There is treatment for HBV, although it is not always effective. The best way to avoid acquiring HBV is by immunization. Everyone with chronic hepatitis C who has not had HBV should be vaccinated.

HDV is unusual in that it does not appear on its own. It is found in the presence of HBV. HDV can be very serious and lead to death. There is no HDV vaccine, but in a sense, the HBV vaccine provides protection, since without HBV there can be no HDV.

Regular *HCV Advocate* readers are virtual authorities on HCV, so I will only mention it briefly. HCV is chronic in about 80% of those who are infected. Treatment is effective about half of the time. Treatment that is initiated in the first 6 months of onset is almost 100%

effective. Unlike HBV, HCV is not officially categorized as a sexually transmitted disease. Although the rate of sexual transmission is low, safer sexual practices is always a good idea. There is no vaccine against HCV.

Not much is known about HGV. Blood transfusions are the common route for this virus. It has not been determined if HGV is anything to be concerned about. In certain cases, HGV may even provide beneficial effects. There is no HGV vaccine.

Hepatitis is often a preventable disease regardless if the cause is viral, toxic, substance, or lifestyle. It is easy to take the liver for granted since it doesn't complain much. If we abuse our stomachs or our backs, usually we change our habits. However, since the liver is quiet, we don't get immediate feedback if we are harming it. Don't wait until it's too late. Take care of your liver starting now.

Resources

- American Liver Foundation
www.liverfoundation.org
- Center for Disease Control
www.cdc.gov
- HCV Advocate
www.hcvadvocate.org
- Hepatitis Foundation International
www.hepfi.org
- World Health Organization
www.who.int/en



EXTRAHEPATIC: PN

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your feet. The recommendations from The American Diabetes Association can be easily adapted to foot care for everyone with PN.

- Check all the areas of the feet every single day. Look for red spots, cuts, swelling and blisters. If you can not see the bottom of your feet, use a mirror or ask someone to inspect it for you.
- Be more active.
- Wash your feet everyday. Dry them carefully, especially between the toes.
- Moisturize your feet daily (but not between the toes).
- Never go barefoot – always wear comfortable shoes and socks. This is because people with PN can cut or damage their feet and may not even notice or feel the pain.
- Keep toe nails trimmed so that the nails don't rub or cut nearby toes.
- Be careful not to expose your feet to hot and cold temperatures.
- Keep the blood circulating throughout the feet. The ADA recommends wiggling your ankles up and down for 5 minutes – two or three times a day. Don't cross your legs for long periods of time.
- Stop smoking cigarettes.
- Check with your medical provider about the need for special shoes (orthotics).

For more information about peripheral neuropathy visit:

- American Diabetes Association:
www.diabetes.org
- The Neuropathy Association:
www.neuropathy.org



CONNECTICUT ORGAN DONOR REGISTRY

May is Hepatitis Awareness month. Did you know that the majority of patients who are on the liver transplant waiting list are there because of some type of hepatitis? Hepatitis is often preventable. You can help with disease prevention and reduce the need for organs by raising awareness. Educate yourself and others about the different forms of hepatitis. Talk to friends, family, and other associates about the critical need for donated organs.

It is easy to register to be a potential organ donor in the state of Connecticut. The best way is to sign up at the state’s Department of Motor Vehicles website. Although Connecticut does not require family notification, even with documentation it is best to notify your family and close ones about your wishes.

www.ssl01.state.ct.us/dmv/coa.htm

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Peripheral Neuropathy: A Study on Prevalence & Characteristics



Alan Franciscus, Editor-in-Chief

Peripheral neuropathy (PN) is an established extrahepatic manifestation of hepatitis C. In the past it was thought that only people who have HCV-related cryoglobulinemia would develop PN, but more studies are finding that this isn't the case. One large study from Italy found that the prevalence of PN in the HCV population is higher than previously believed, and that PN is present in people with hepatitis C even without HCV-related cryoglobulinemia.

In this study, L. Santoro and colleagues consecutively enrolled 234 patients (120 women and 114 men) with HCV infection in seven Italian centers from January 2001 to December 2003. Mean average age was 52.3 (range 18-89 yo), duration of HCV infection was 36 months (range 1-156). All patients were untreated for HCV infection. Other causes of PN (diabetes, alcohol abuse, renal failure, vitamin deficiency, thyroid disorders, neoplasm, toxic agents) were ruled out. All patients were evaluated by an expert neurologist. A diagnosis of clinical neuropathy was based on symptoms and electrophysiological examination.

A total of 36 out of 234 patients (15.3%) were diagnosed with PN by electrophysiological examinations – 10.6% were diagnosed with clinical PN based on symptoms and an additional 4.7% were diagnosed with subclinical PN. Cryoglobulinemia was found in 29.3% of the patients – PN was found in 21% of

the patients with cryoglobulinemia compared to 13% of the patients without cryoglobulinemia. The occurrence of cryoglobulinemia and PN was significantly increased with age. No correlation was found between HCV-RNA (viral load) levels and the presence of PN.

The authors concluded that the prevalence of HCV-related PN was lower than that observed in the diabetic population (34%), but higher than reported in neoplastic patients (2-5%), or in the general population (2.4-8%). The authors also concluded that “cryoglobulinemia is not a risk factor for neuropathy” and that “an electrophysiological examination should always be done to avoid underestimating PN, particularly in older HCV patients.”

Reference:

Santoro, L. Prevalence and characteristics of peripheral neuropathy in hepatitis C population. *J Neurosurg Psychiatry* 2006;77:626-629

What Is Peripheral Neuropathy?

Peripheral Neuropathy is an injury to the nerves that supply sensation to the arms and legs.

Subclinical: a disease without clear symptoms. The stage before signs and symptoms become detectable.

Neoplastic: formation of abnormal tissue growth (both cancerous and non-cancerous).



HEPATITIS C
SUPPORT PROJECT

Executive Director Editor-in-Chief, HCSP Publications

Alan Franciscus
alanfranciscus@hcvadvocate.org

Managing Editor, Webmaster

C.D. Mazoff, PhD
cdmazoff@hcvadvocate.org

Contributing Authors

Liz Highleyman
Lucinda K. Porter, RN

Design

Paula Fener
Blue Kangaroo Design
blueroodesign@aol.com

Contact information:

Hepatitis C Support Project
PO Box 427037
San Francisco, CA 94142-7037

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P.O. Box 427037
San Francisco, CA
94142-7037