

HEPATITIS C VIRUS (HCV) INFECTION: WHY IT IS SUCH A GROWING PROBLEM

By

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HCV Infection-History

Infection by Hepatitis C Virus (HCV) is similar to infection by the Human Immunodeficiency Virus (HIV), in that most infections resulting from both of these viruses become persistent over many years before any symptoms arise. Moreover, the origins of the symptoms of chronic HCV infection resemble those of HIV infection, in that they result from **failure** of the infected tissues and cells. In the case of HIV, which infects the immune system itself, the failure of the immune system becomes noticeable as AIDS, and infected individuals become susceptible to microbes that normally would be combated by a healthy immune system. In the case of HCV, which infects the liver, the failure of normal liver function becomes noticeable as the lack of normal liver products, such as blood clotting factors and other blood proteins. As well, liver failure results in a deficiency of waste removal, a vital bodily function normally performed by the liver. Left untreated, liver failure is fatal.

There are now an estimated 4 million Americans infected chronically with HCV. This is 4 times the incidence of HIV infection in this country. Consequently, liver failure as a result of HCV infection is the major

indication leading to liver transplantation today. This prevalence is a consequence of the fact that HCV infection has only been diagnosable within the past decade, subsequent to the identification of the virus in 1989. When tests became available to detect HCV in blood samples, it was realized that 10% of the blood donors in the U.S. were infected. Consequently, if you received a blood transfusion in the U.S. before 1992, you had a 10% chance of becoming infected with HCV. The other major source of HCV infection is via contaminated needles, which are often shared by intravenous drug abusers. By comparison with Hepatitis B Virus (HBV) and HIV infection, transmission of HCV through sexual intercourse is much less of a risk. Accordingly, HCV infection requires intimate contact with virus-infected blood, and cannot be transmitted via routine social contact with infected individuals, and is not carried by insects such as mosquitoes, as is West Nile Virus, another member of the Flavivirus family.

Standard Therapy for HCV Infection

Over the past decade, treatments for HCV infection have been tested and made available that impair the capacity of the virus to reproduce. At

present, the standard therapy of HCV infection is comprised of a drug called pegylated interferon-alpha (PEG-IFN- α), combined with a drug termed Ribavirin (RBV) administered for one year. Clinical trials have shown that this treatment results in cures of ~ 50% of those who complete a full course of therapy for 1 year. However, HCV comes in slightly different strains, classified by types I-IV. Type I HCV accounts for ~ 75% of the infections in this country. In addition, individuals who have a very high amount of HCV in the blood, > 2 million particles/mL, account for ~ 75% of all those infected with genotype I, thereby accounting for more than half of all those infected in the U.S. Unfortunately, only ~ 1/3 of these individuals can expect to be cured by standard therapy.

Immunity to HCV

The strength of the immune reaction to most virus infections is responsible for a successful outcome, in that protective immune responses kill virus-infected cells, impair the virus reproduction, and ultimately eliminate replicating virus from the body. Most individuals infected with HCV cannot eliminate the virus, so that ~ 85% go on to a persistent infection. However, ~ 15% of those infected can clear the virus, so that they go on to a state of life-long immunity to HCV. Detailed studies of individuals who have cleared HCV reveal that they have strong immune reactivity to the virus, while those individuals with persistent infection do not have readily detectable immune

responses. Moreover, those chronically infected individuals who respond well to standard antiviral therapy are those who have readily detectable immune responses to HCV, while those who do not respond to antiviral therapy do not have easily detectable immune responses to HCV.

New Approaches to HCV Therapy: Immunotherapy

Because of the known role of the immune system in combating viral infections, we have explored ways to boost immunity to HCV. We have extensive experience in the administration of a natural hormone of the immune system that was originally called T Cell Growth Factor, and is now known as interleukin 2 (IL2). Our earliest experiments led to the discovery of the IL2 molecule, and the IL2 receptor. Subsequently, over the course of more than 10 years, we studied and characterized how IL2 promotes the survival, reproduction and function of T cells, the primary cells responsible for combating viral infections. Since 1994, at Weill Cornell-New York Presbyterian Medical Center in New York City, we have conducted clinical trials, testing how to give IL2 safely and without toxicity to individuals infected with HIV. Now in 2002, after 5 trials of the use of IL2 in HIV infection, we are poised to begin IL2 therapy in HCV infection to determine whether we can improve upon the results obtained with standard therapy of PEG-IFN- α and RBV.

In conjunction with Dr. Ira Jacobson, Chief of the Division of Hepatology and Gastroenterology at Weill Cornell, we have initiated a study for individuals who are infected with HCV type 1, and who have high concentrations of virus in the blood, > 2 million virus particles/mL or > 800,000 IU/mL of blood. The study is directed toward individuals who are not co-infected with HIV, and who have never received treatment with IL2 or with PEG-IFN- α and RBV.

If you are interested in learning more about this research study, please contact us @ 1-800-HIV-0200. More information about us can be obtained via the web @ www.hivhcvtrials.net