

Hepatitis C

Retreatment of Nonresponders and Relapsers

With the sustained virological response (SVR) rate for hepatitis C therapy hovering around 50%, increasing research has been devoted to retreatment of patients who did not achieve sustained HCV clearance with their first attempt. In the November 2005 *American Journal of Gastroenterology*, Ira Jacobson and colleagues reported that among 321 patients previously treated with conventional interferon plus ribavirin, relapsers (in whom HCV viral load decreased substantially but later increased) were more likely than nonresponders (who never experienced substantial HCV viral load decline) to achieve SVR when subsequently treated with pegylated interferon (Peg-Intron) plus ribavirin (42% vs 8%, respectively). Further, nonre-

sponders who previously received interferon monotherapy had a higher retreatment SVR rate than nonresponders previously treated with combination therapy (21% vs 8%, respectively.) However, increasing the dosage of ribavirin from 800 to 1,000-1,200 mg daily did not improve the response rate. At the November 2005 AASLD meeting, Dr. Jacobson presented data from a larger study which also showed that increased ribavirin dosing did not improve treatment response, but several other researchers reported that higher doses of ribavirin or pegylated interferon increased the likelihood of successful treatment.

Spleen Embolization May Enable Treatment During Cirrhosis

One of the ironies of hepatitis C is that the patients who most need treatment – those with advanced cirrhosis – are

Hepatitis Journal Review

A publication of the Hepatitis C Support Project

Executive Director
Editor-in-Chief,
HCSP Publications
Alan Franciscus

Contributor:
Liz Highleyman

Managing Editor, Webmaster
C.D. Mazoff, PhD

Design/Production
Alan Franciscus

Contact Information:
The Hepatitis C Support Project
PO Box 427037
San Francisco, CA 94142

www.hcvadvocate.org

© 2005
Hepatitis C Support Project

often unable to tolerate therapy. Many people with cirrhosis develop hypersplenism, a condition in which the spleen filters and destroys blood cells. The resulting blood cell deficiencies (anemia, neutropenia, and/or thrombocytopenia) may preclude treatment with interferon (which can reduce white blood cell count) and ribavirin (which can cause hemolytic anemia). But as reported in the November 2005 *European Journal of Gastroenterology and Hepatology*, a technique called partial splenic embolization (PSE) – injecting compounds to block part of the spleen’s blood supply – may enable patients with cirrhosis to tolerate HCV therapy. Jose Foruny and colleagues treated eight cirrhotic patients with severe hypersplenism who underwent PSE. The procedure led to significant increases in red cell, white cell, and platelet counts. After an average 20 weeks post-PSE, the patients started on full standard doses of pegylated interferon plus ribavirin. Three patients (38%) achieved SVR. The authors concluded that, “PSE allowed the safe use of [pegylated interferon] plus ribavirin in HCV cirrhotic patients with severe cytopenias who otherwise would never have been treated.” In an accompanying editorial, Birger Palsson and Hans Verbaan wrote that, “[t]he use of

PSE as a ‘pretreatment’ in order to make more patients with HCV-induced cirrhosis and pancytopenia suitable for antiviral therapy... is a new, promising concept,” and recommended further research to determine which patients could benefit most.

Insulin Resistance and Fatty Liver

As the Western population grows ever more obese, more people are developing a metabolic syndrome characterized by abdominal fat accumulation, high blood fat levels, and blood glucose abnormalities – all of which increase the risk of cardiovascular disease. Several recent journal articles have examined the links between the metabolic syndrome, insulin resistance (a condition in which the body does not respond normally to insulin, ultimately leading to type 2 diabetes), and fatty liver (steatosis).

In the November 2005 issue of *Hepatology*, Elisabetta Bugianesi and colleagues presented an overview of insulin resistance as a “metabolic pathway to chronic liver disease.” Nonalcoholic fatty liver disease (NAFLD) – and its more severe form, nonalcoholic steatohepatitis (NASH) – is increasingly acknowledged as a component of the metabolic syndrome. In patients with NAFLD, glucose

homeostasis is impaired; abnormal fat metabolism can lead to accumulation of triglycerides in the liver, which in turn contributes to impaired glucose metabolism and reduced insulin sensitivity. NAFLD can lead to liver fibrosis, cirrhosis, and hepatocellular carcinoma in HCV negative individuals. In people with chronic hepatitis C, obesity and steatosis accelerate the progression of fibrosis and are associated with reduced response to interferon-based therapy. Environmental factors such as diet and individual genetic variations likely interact to cause fatty liver.

The November 2005 issue of *Alimentary Pharmacology and Therapeutics* was entirely devoted to the metabolic syndrome, with several articles on the link with steatosis. In her concluding remarks, Helen Cortez-Pinto noted that NAFLD “has a significant risk of progressing to end-stage liver disease and death”; in one comparison, people with type 2 diabetes were more likely to die from liver disease than cardiovascular disease. (Dr. Cortez-Pinto and colleagues also presented an overview of NAFLD in the January 2006 *Journal of Hepatology*.) But fortunately, as reported by Ayako Suzuki and colleagues in the December 2005 *Journal of Hepatology*, lifestyle changes, includ-

ing weight loss and regular exercise, can improve liver inflammation and steatosis – which may in turn ameliorate other problems associated with fatty liver.

Mother-to-Child HCV Transmission More Common in Girls than Boys

Infant girls are more than twice as likely as boys to contract HCV from their mothers during pregnancy or birth, according to a study reported in the December 1, 2005 *Journal of Infectious Diseases*. Researchers with the European Pediatric Hepatitis C Virus Network studied 1,787 pregnant HCV positive women and their infants at 33 medical centers. The overall mother-to-child HCV transmission rate was 6.2%; the rate was slightly higher – though the difference was not statistically significant – among women coinfecting with HIV compared to those with HCV alone (8.7% vs 5.5%, respectively). Female infants were twice as likely to contract HCV (odds ratio 2.07). Transmission was more likely from mothers with detectable HCV RNA during pregnancy or delivery, but a few nonviremic women also transmitted the virus. Elective cesarean section did not protect infants against contracting the virus, and breast-feeding

did not increase the transmission risk. But the duration between rupture of membranes (“water breaking”) and birth was significantly longer among the HCV-infected infants. The authors recommended that “women should neither be offered an elective [cesarean section] nor be discouraged from breast-feeding on the basis of HCV infection alone.” They suggested that the higher rate of hepatitis C transmission to girls “likely reflects hormonal or genetic differences in susceptibility or response to infection.” In an accompanying editorial entitled “Nature Usually Favors Females,” R. Palmer Beasley suggested that the higher infection rate among girls may be due to an “excess male mortality in utero.” Interestingly, some past studies indicate that HIV may also be more readily transmitted to female infants.

In the same issue, Eric Mast and colleagues reported on a smaller American study of risk factors for perinatal HCV transmission. The researchers studied 244 infants born to HCV positive mothers. Here, the perinatal transmission rate was 4.7% from mothers with detectable HCV RNA, but no infants of mothers with undetectable HCV viral load were infected. In this study, the HCV transmission rate was significantly higher from the eight coinfecting mothers com-

pared to mothers with HCV alone (25.0% vs 3.8%, respectively). Here, too, girls were twice as likely as boys to be infected, though the difference was not significant since the total number of infected infants was so small (nine). Membrane rupture longer than six hours and use of invasive fetal monitoring were also associated with higher HCV transmission rates. Again, breast-feeding was not linked to greater transmission risk. Three of the HCV-infected infants spontaneously cleared the virus. The authors recommended that HCV RNA testing of infants should be done after 18 months to reduce the likelihood of false-positive results; before two months, detectable HCV RNA may reflect contamination from maternal blood rather than true infection of the infant. Even though women with undetectable HCV did not transmit the virus in this study, the researchers acknowledged that transmission from women with very low viral load has been observed, and thus, “HCV RNA level cannot be used to counsel HCV RNA positive women about their risk for perinatal HCV transmission.”

