

Hepatitis C

Liz Highleyman

HCV Superinfection

HCV superinfection may occur with a frequency similar to that of first-time infections, according to a study reported in the October 15, 2004 *Journal of Infectious Diseases*. "Superinfection" refers to a second or subsequent infection with another variant of the same pathogen. Belinda Herring and colleagues used polymerase chain reaction (PCR) technology to amplify HCV from 25 young (under age 30), recently infected injection drug users (IDUs) in San Francisco over an average period of 12 months. Subjects had been infected with HCV for an average of five months, and at the longest about a year. Comparing viral genetic sequences over time, the researchers identified five individuals (20%) with evidence of HCV superinfection after their initial

seroconversion. Two of these were superinfected with HCV of a different genotype, while the remaining three were superinfected with divergent strains of the same genotype. In this cohort, the incidence of new initial HCV infections was 25%, only slightly higher than the superinfection rate. Superinfection with a second strain of HCV did not seem to lead to higher HCV viral loads^{3/4} in contrast to HIV, where being infected with multiple strains is associated with more aggressive disease. The occurrence of superinfection suggests that protective immunity against HCV does not develop that could provide cross-protection against infection with divergent strains^{3/4} a roadblock to an effective HCV vaccine. "The high frequency of HCV superinfections that we detected among young IDUs indicates the ease with which a

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

© 2004
Hepatitis C Support Project

new viral strain can surmount immune responses directed at the resident strain,” the authors concluded.

Liver Steatosis

Several recent journal articles have looked at steatosis, or fatty liver. In the September 2004 *Journal of Clinical Gastroenterology*, Zobair

Younossi and colleagues reported that superimposed (co-existing) non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) contribute to fibrosis progression in people with chronic hepatitis C. The researchers studied 120 patients with HCV (70% male, 80% white, average age about 48 years) who had available liver biopsy results. This study, like others previously, showed that obese individuals are at higher risk for steatosis. Subjects with higher grades of steatosis had greater waist-to-hip ratios and higher body mass index (BMI) than those with lower grades. (BMI refers to weight divided by height; a BMI of 18.5-24.9 is considered normal weight, 25-29.9 is considered overweight, and more than 30 is considered obese.) The 22 patients with NASH were more likely to be obese, more likely to have genotype 3, and had more advanced fibrosis than the 49 patients with simple steatosis or the 49 without steatosis (BMI 30.64,

29.90, and 27.33, respectively). While patients with NASH and simple steatosis had similar rates of genotype 3 infection (14% vs 12%), no cases of genotype 3 HCV were detected among the subjects without any steatosis. No independent association was found between steatosis and race, sex, or age.

In the October 2004 issue of *Hepatology*, Eduardo Fassio and colleagues reported, like Younossi’s team, that NASH was associated with more advanced fibrosis, this time in patients without viral hepatitis. Fassio’s team analyzed repeat liver biopsies, taken at least three years apart (mean 4.3 years), from 22 patients with NASH. The median age was 45 years, 13 patients were women, 10 were obese, and eight had diabetes. Seven patients (about 30%) showed evidence of fibrosis progression between one biopsy and the next. Obesity was significantly more common among the progressors than the non-progressors (86% vs 27%), and BMI was significantly higher (median 33.2 vs 29.0). Obesity and BMI were the only variables independently associated with fibrosis progression. Four of seven progressors (57%) had diabetes compared to four of 15 non-progressors (27%), but ³/₄ in contrast to some past research ³/₄ diabetes was not

found to be an independent predictor of advancing fibrosis in this small study. These findings suggest that even among patients with steatosis or NASH, fibrosis is less likely to progress if they maintain a healthy body weight.

Finally, in the September 2004 *Journal of Viral Hepatitis*, C. Hezode and colleagues reported that steatosis associated with HCV genotype 1 is due to a different mechanism than steatosis which occurs in individuals with genotype 3. In patients with genotype 1, steatosis appears to be primarily a metabolic condition associated with obesity, insulin resistance (a precursor to diabetes), and elevated blood lipids (total cholesterol and triglycerides). In patients with genotype 3, in contrast, steatosis seems to be directly induced by the virus. As evidence of this, steatosis severity was correlated with higher HCV viral loads in people with genotype 3, but not in those with genotype 1.

New Doctors’ Knowledge about Hepatitis C

According to a study reported in the September 2004 *American Journal of Gastroenterology*, residents training to become primary care physicians have a lot to

learn about hepatitis C. Angelo Coppola and colleagues administered a one-page questionnaire to 180 primary care residents in five U.S. training programs. More than 40% of the residents had seen more than 11 patients with hepatitis C in the past year. Residents reported that they tested patients for HCV if they had increased transaminase (ALT and AST) levels (83%), a history of blood transfusions (46%), multiple tattoos (57%), evidence of antineutrophil cytoplasmic antibodies (16%), or were heavy drinkers (31%); 16% of residents tested all patients. Just 41% reported that they would vaccinate hepatitis C patients against hepatitis A and 65% would vaccinate against hepatitis B³important because coinfection with a second type of viral hepatitis can lead to more aggressive disease and fulminant liver failure. Although more than three-quarters knew the correct hepatitis B vaccine schedule, only 19% knew the hepatitis A vaccine schedule. Interestingly, about two-thirds said they would recommend vaccination against hepatitis C, even though no such vaccine exists. About one-third knew that HCV genotype 1 is the most common and the most difficult to treat. Just over half said they would recommend a biopsy before

treatment, and about the same percentage knew that interferon plus ribavirin is standard initial therapy for hepatitis C. About one-quarter recommended ribavirin alone, amantadine (a flu medication under study but not approved for HCV), or lamivudine (a drug used to treat hepatitis B and HIV). More than two-thirds said they thought there was insufficient information on HCV³although they apparently failed to avail themselves of the information that does exist. While residents specializing in hepatology or gastroenterology would likely have scored higher, it is important that primary care physicians have a basic familiarity with hepatitis as well, since they are often the first link between patients with HCV and the health-care system.

Treatment for Genotype 4

Patients with genotype 4 HCV can be successfully treated with pegylated interferon plus ribavirin, according to a study published in the September 2004 *American Journal of Gastroenterology*. Genotype 4, the predominant strain of HCV in the Middle East and North Africa, has not been studied as extensively as genotypes 1, 2, and 3. Faud Hasan from Kuwait Univer-

sity and colleagues treated 66 genotype 4 patients with pegylated interferon alfa-2b (Peg-Intron) 1.5 mcg/kg/week plus ribavirin 1,000-1,200 mg/day for 48 weeks. All patients had elevated ALT and the mean pretreatment HCV viral load was 4.2×10^6 copies/mL; 29% had severe fibrosis or cirrhosis, but none were decompensated. At the end of treatment, the virological response rate was 77%. After 72 weeks (48 weeks of therapy plus 24 weeks of follow-up), the sustained virological response (SVR) rate was 68%. SVR occurred less often in subjects who started with higher HCV viral loads than in those with lower baseline HCV RNA levels (55% vs 86%), and patients with severe fibrosis or cirrhosis responded less well than those with mild or no fibrosis (29% vs 84%). Some researchers have classified genotype 4 along with genotype 1 as a “hard to treat” type of HCV. This study suggests that genotype 4 is roughly midway between genotype 1 (SVR with pegylated interferon plus ribavirin of about 45% in various studies) and genotypes 2 or 3 (SVR of about 80%).