

# Hepatitis C

## ***Hepatitis A Vaccination is Important, but Underutilized***

In the wake of Hurricane Katrina, numerous news accounts have noted that people exposed to contaminated floodwaters are at increased risk for hepatitis A virus (HAV) infection. Hepatitis A usually resolves spontaneously without treatment, but in people with pre-existing liver disease – including chronic hepatitis C – HAV can cause life-threatening fulminant hepatitis. A safe, effective vaccine can prevent hepatitis A, but it is not widely used, even among at-risk HCV-positive individuals. As reported in the September issue of *Hepatology*, Michael Shim and colleagues

retrospectively studied 1,193 chronic HCV patients. During 1,646 person-years of follow-up, 640 patients were tested for HAV antibodies. Of these, 50% remained susceptible to HAV, meaning they did not have antibodies indicating past infection. In the group as a whole, only 8% had been vaccinated against HAV (27% of those known to be susceptible and 1% of those never tested for HAV antibodies). Among the 94 vaccinated individuals, half received only one dose of the two-dose series. Three of the unvaccinated patients experienced acute HAV infection during follow-up, one of whom died of fulminant liver failure. The authors recommended that public health programs are needed to raise awareness and encourage

### **Hepatitis Journal Review**

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HAV vaccination of people with chronic liver disease.

## **HIV/HCV Coinfection News**

Several recent journal articles have looked at the natural history of HIV/HCV coinfection. While having HIV clearly appears to worsen liver disease progression associated with hepatitis C, data are conflicting as to whether having HCV worsens HIV disease progression. Adding to the debate, Jürgen Rockstroh and colleagues analyzed data from 5,957 HIV-positive individuals in the large EuroSIDA cohort, 1,960 (33%) of whom were HCV coinfecting; results were reported in the September 15 *Journal of Infectious Diseases*. *Coinfected patients responded to combination anti-HIV therapy (HAART) about as well as those with HIV alone, with 91% vs 89%, respectively, achieving undetectable HIV viral load, and 80% and 83%, respectively, experiencing CD4 cell increases of at least 50 cells. After adjusting for demographic characteristics, initiation of HAART, and CD4 cell*

changes, the researchers concluded that HCV coinfection did not increase the risk of HIV disease progression, development of AIDS-defining illnesses, or death due to AIDS. However, the risk of liver-related death was significantly higher among the coinfecting patients.

In contrast, researchers from London's Chelsea and Westminster Hospital found that HIV/HCV coinfecting patients were significantly more likely to develop AIDS-defining illnesses or advanced immune suppression (CD4 counts below 200 cells) than those with HIV alone. Justin Stebbing and colleagues analyzed data from about 1,500 HIV-positive patients tested for HCV since HAART became widely available (January 1996); 85 subjects (about 6%) were coinfecting with HCV. In a multivariate analysis, coinfecting patients were 52% more likely to develop an AIDS-defining illness or progress to a CD4 cell count below 200 cells, although the rate of CD4 cell decline was similar in both groups. The researchers, who published their findings in the September 15 *Clinical Infectious Dis-*

*eases, said their data suggest that, "HCV infection is having an effect on HIV-1 disease progression that is not reflected in CD4 cell count."*

Further, Lisa Backus and colleagues reported in the August 15 *Journal of Acquired Immune Deficiency Syndromes* that HCV coinfection may increase the risk of death among HIV positive individuals by 30-80%. This research team analyzed data from a cohort of 12,200 HIV-positive U.S. veterans, 4,668 (38%) of them coinfecting with HCV, who first received HAART between 1997 and 2003. Coinfecting patients and those with HIV alone had a similar virological response to HAART (80% in both groups achieved undetectable viral load), but CD4 cell increases were less in the coinfecting patients (median 199 vs 239 cells). The overall mortality rate was 22% in the coinfecting group, compared with 14% among those with HIV alone.

Melissa Farmer Miller and colleagues also added to the evidence that HCV impairs response to HAART. As reported in the September 1 *Clinical Infectious Diseases*, the researchers conducted a

meta-analysis of data from eight trials involving 6,216 HIV-positive participants with and without HCV. They found that HIV/HCV coinfecting patients had an average CD4 cell increase that was 33.4 cells less than the increase seen in patients with HIV alone. They concluded that patients with HIV/HCV coinfection “do, in fact, have less immune reconstitution” than those with HIV alone. Likewise, Giorgio Antonucci and colleagues reported in the online edition of *Clinical Infectious Diseases* that coinfecting patients with detectable HCV - and especially those with genotype 3 HCV - took longer to reach a CD4 count of at least 300 cells after starting HAART. And in the online edition of *Journal of Hepatology*, A. Moreno and colleagues reported that coinfection may impair response to HCV treatment as well. In a study of 40 coinfecting subjects and 61 with HCV alone, sustained virological response to pegylated interferon plus ribavirin was significantly lower in the coinfecting group (18% vs. 39%). HCV viral load reductions were smaller in the coinfecting group after 4, 12, and 24

weeks of therapy. The researchers concluded that HIV coinfection was independently associated with HCV treatment failure and led to significantly slower HCV clearance.

### ***Treatment of Advanced Hepatitis C***

Hepatitis C treatment dramatically reduces the risk of developing advanced liver disease progression. Even patients who do not achieve sustained virological response may still experience slowed - or even reversed - fibrosis progression. Patients who already have advanced liver disease do not respond as well to anti-HCV therapy, but much research is ongoing in this area. As reported in the August issue of *Hepatology*, Gregory Everson and colleagues evaluated the effectiveness and tolerability of a low accelerating dose regimen (LADR) of antiviral therapy in treating 124 patients with advanced hepatitis C (age 37-71 years; 70% genotype 1). Nearly two-thirds had clinical complications of cirrhosis such as as-

cites, varices, and/or encephalopathy; the mean Child-Turcotte-Pugh score was 7.4 and the mean MELD score was 11.0. Despite the advanced status of this population, 13% of genotype 1 and 50% of non-1 patients achieved SVR. Pre-transplant treatment is important, since it may reduce the high rate of HCV reinfection of the new liver. In this study, 12 out of 15 patients who achieved undetectable pre-transplant HCV viral load remained undetectable six months or more after transplantation. The researchers concluded that for a “sizeable proportion” of patients with advanced hepatitis C, LADR may clear HCV, stabilize the clinical course, and prevent post-transplant HCV recurrence.

