

# Hepatitis C

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## Spontaneous HCV Clearance

It has traditionally been assumed that about 75-90% of individuals infected with HCV go on to develop chronic hepatitis C (lasting longer than six months). However, more recent research indicates that the rate of spontaneous HCV clearance (eradication by the immune system without treatment) may be considerably higher. In the October 2004 *Journal of Infectious Diseases*, Marianna Jauncey and colleagues reported that as many as 42% of injection drug users (IDUs) may spontaneously clear HCV within two years of infection, based on a retrospective analysis of stored blood samples from 99 IDUs seen at a Sydney clinic.

The average time to clearance was about six months (range 1.4-11.2 months). When the researchers restricted their analysis to individuals who previously had a documented detectable HCV viral load, the rate of spontaneous clearance was lower (24%), suggesting that some of the original 42% had a false-positive HCV antibody diagnosis. Using a model, the researchers predicted that HCV clearance should occur in 23% of newly infected individuals by six months and in 38% by 12 months, leveling off to 40% by 24 months.

Previous studies have shown that women and whites are more likely to spontaneously eradicate HCV than men and blacks, but in the Sydney cohort (mostly white and about half female), spontaneous

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clearance was not associated with any specific demographic, behavioral, or clinical factors (although there was a non-significant association between normalized ALT and HCV clearance). Past research also suggested that people with symptomatic acute hepatitis C are more likely to clear the virus (perhaps due to a more vigorous immune response), but symptoms were rare in this cohort. In another recent study, reported in the October 2004 issue of *Hepatology*, Barbara Piasecki and colleagues found that among a group of nearly 500 U.S. veterans (203 with spontaneous clearance; 293 with chronic infection), spontaneous HCV eradication was less likely to occur in individuals who were heavy alcohol drinkers or were coinfecting with HIV, while coinfection with hepatitis B virus increased the probability of HCV clearance. Black race was associated with lower rates of clearance in a univariate analysis, but not after adjusting for various other factors. Finally, E. Spada and colleagues reported in the November 2004 issue of *Gut* that in a study of 34 patients, 10 (29%) of whom spontaneously cleared HCV, self-

limiting hepatitis C was associated with fast viral clearance (within the first month) and with broader T cell responses, suggesting that differences in cell-mediated immunity play an important role in spontaneous HCV clearance.

### **HIV/HCV Coinfection**

Several recent journal articles have looked at the impact of hepatitis C on HIV disease progression, and vice versa, in coinfecting individuals. In the November 15, 2004 *Clinical Infectious Diseases*, K. Anderson and colleagues reported that based on a retrospective review of data from 970 subjects in the HIV Atlanta Cohort Study, coinfecting patients (32% of the total) had shorter survival times after HIV diagnosis and after AIDS diagnosis than those with HIV alone. While some research has shown that coinfecting individuals experience slower immune recovery after starting highly active antiretroviral therapy for HIV (HAART), in this study coinfecting subjects and those with HIV alone showed comparable short- and long-term CD4 cell recovery. Interestingly, researchers studying this

same cohort previously reported that HCV did not appear to affect HIV disease progression, based on data mostly collected before the advent of HAART.

On a similar note, Maria Dorrucchi and colleagues reported in the November 19, 2004 issue of *AIDS* that before the HAART era, HCV coinfection did not seem to have a deleterious effect on HIV progression, but that since HAART became widely available, HCV has been associated with accelerated HIV disease progression. The authors noted that it is not yet known whether this change is due to a direct effect of HCV, or whether it instead reflects differences in the use of antiretroviral therapy, such as length of time on treatment. In the same issue, Massimo Puoti and colleagues reported that coinfecting individuals in Northern Italy were more likely to develop hepatocellular carcinoma (HCC) compared to those with hepatitis C alone. HIV coinfection was also associated with a more aggressive clinical course of HCC and shorter survival times.

Looking at the impact of HIV on hepatitis C,

Eugenia Mariné-Barjoan and colleagues reported in the November 5, 2004 issue of *AIDS* that HIV infection seemed to worsen HCV-related liver disease progression, but suggested that early use of HAART could slow this progression. In a case-control study of 116 HIV/HCV coinfecting subjects and 235 with HCV alone (all untreated for hepatitis C) matched by sex, presumed age at infection, and duration of infection, the coinfecting subjects were significantly more likely to have severe (stage F3 or F4) fibrosis (26% of coinfecting vs 7% with HCV alone) and a faster rate of fibrosis progression (0.106 vs 0.071 “fibrosis units” per year, respectively). Among coinfecting patients, higher fibrosis scores were associated with lower CD4 cell counts. However, individuals who started HAART sooner after HCV infection had more moderate fibrosis scores, and those using HAART had significantly slower fibrosis progression.

Finally, in an overview of special considerations when treating coinfecting people for HIV published in the November 19 *AIDS*, Paula Braitstein and col-

leagues suggested that individuals with HCV/HIV should perhaps initiate HAART at a higher CD4 cell threshold than those with HIV alone, since immune suppression appears to affect liver disease progression. They also noted that extra caution is warranted when treating coinfecting people for HIV, since some of the side effects of HAART—including insulin resistance, diabetes, and mitochondrial dysfunction—overlap with comorbid conditions more commonly seen in people with hepatitis C.

### ***Estrogen and Fibrosis Progression***

It is well known that female sex is associated with less aggressive HCV-related liver disease progression, and many experts believe estrogen may have an antifibrotic effect. In the December 2004 issue of *Hepatology*, P. Lebray and colleagues reported on a study looking at the influence of pregnancy history, use of oral contraceptives, menopause, and hormone replacement therapy (HRT)<sup>3</sup>all of which affect estrogen levels<sup>3</sup>on liver fibrosis in women with hepatitis C. Analyz-

ing self-reported survey data from 201 women, the researchers found that fibrosis progression was greater in postmenopausal women (whose ovaries have stopped producing estrogen) and those who had never borne children, while use of oral contraceptives did not have an effect. Among the postmenopausal women, the rate of fibrosis progression was lower in those using HRT (which replaces estrogen and/or progesterone), and in fact was similar to the rate in premenopausal women. The authors concluded that menopause was associated with accelerated liver disease progression, which might be prevented by using HRT. However, the large Women’s Health Initiative study showed that the risks of HRT (including increased rates of breast cancer, heart attack, and strokes) outweigh its benefits for many women.

