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Hepatitis C and HIV

Those who carry both viruses await answers as to their reciprocal effects and the impact of HIV drugs on liver disease

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by Bob Roehr

Does infection with both HIV and hepatitis C virus (known as HCV) result in a synergy that causes one or both diseases to progress more rapidly? Is there a possibility that anti-HIV medications metabolized in the liver might cause HCV disease to progress more rapidly?

A National Institutes of Health Consensus Development Conference on the management of hepatitis C answered neither of those questions. The three-day meeting at the NIH campus, which concluded March 23, called for research on the first question but did not even raise the second. That troubles AIDS researchers and treatment activists.

Hepatitis C virus, which can cause chronic liver infection, was isolated and identified only in 1989. An estimated 4 million people in the United States are infected with HCV, four times as many as have HIV. It has become the leading reason for liver transplants in the country. Screening of the blood supply since 1990 has greatly reduced the annual number of new infections. Still, about 8,000 people each year die from HCV-related illness, and the number may well triple within 20 years.

HCV shares many similarities with HIV. Both can have long periods between infection and the onset of clinical symptoms, so people may not know they carry the virus. The viruses are spread similarly—through blood products, sharing needles, sexual contact and failure of universal medical precautions—though HCV appears to be more difficult to transmit sexually.

Hepatitis C virus is found in 80 percent of people with HIV who have ever injected drugs, 10 to 15 percent of HIV-positive heterosexuals who have not injected drugs, and only 2 percent of HIV-positive homosexuals who have not injected drugs. David L. Thomas, a hepatitis researcher at Johns Hopkins University, finds an explanation in two factors. One is that HCV is not as efficiently transmitted through sex as is HIV, the other is that "the reservoir of infection is lower" among gay men, so that they are less likely to meet someone with HCV. However that is no reason to be complacent, as there are likely pockets or clusters of gay men among whom the rate of HCV infection is high.

HCV infection is underdiagnosed because of physician ignorance, the limited accuracy of tests for HCV, and the slow progression of the disease.

Both viruses are highly unstable, that is they mutate easily, so it is difficult to fashion vaccines and therapy. The most successful treatment to date for HCV has been interferon alpha, administered, sometimes with the antiviral drug ribavirin, for a 12-month period. But the rate of success, as measured by clearance of the virus and nonrecurrence when therapy is stopped, has never climbed above 20 percent.

Miriam J. Alter is chief of the epidemiology section of the hepatitis branch of the Centers for Disease Control. She says that it is not unusual for individuals to become infected with a combination of hepatitis B virus (HBV), HCV and HIV, because they are transmitted or acquired in much the same way. The rates of infection are highest for HCV, she says, and it "appears to be acquired first, before either HBV or HIV."

Thomas cited data indicating that people infected with both HIV and HCV have a more rapid progression to liver disease. He called the reverse—the suggestion that HCV infection promotes HIV progression—a "murky area" with little supporting evidence.

Howard Grossman, a physician in Manhattan with a large HIV practice of gay men, tests "everybody who comes through the door" for hepatitis A, B and C. He hasn't found many cases of HCV and notes that the rate of HBV infection has declined from earlier in the epidemic. "If they haven't been exposed," he says, "we vaccinate [for A and B]." But he does not believe that practice is standard care for most physicians, in part because "we have to fight the managed care companies to do that."

"Clearly any active infection causes HIV to replicate faster," says Grossman. He notes that people with an underlying liver infection "tend to be somewhat harder to treat," but he says he has seen no clear evidence that they progress more quickly with their HIV disease.

Brenda Lein, of Project Inform in San Francisco, encourages people with dual infection "to pay more attention to their liver enzymes." She calls it "a cautionary note" and "not a reason to not treat, one way or the other."

Grossman points to "some indication that there may be some benefit from 3TC" for patients who are co-infected with hepatitis B virus. He has also used interferon to treat hepatitis and seen residual positive effect on the HIV as well.

Conference chairman D.W. Powell, of the University of Texas Medical Branch at Galveston, called for "develop[ing] protease inhibitors for hepatitis C."

The conference draft report also stated: "While alcohol ingestion clearly worsens the course of hepatitis C, the reasons for this interaction are unknown." One hypothesis is that alcohol reduces liver functions which hold HCV in check, allowing the infection to progress more rapidly.

Which raises the question of whether pharmaceuticals that depress certain liver functions may also promote a more rapid progression of HCV. Many anti-HIV drugs are metabolized in the liver and can depress that organ's capacity to function, sometimes to the point of its failure. So it is logical to speculate as to whether certain anti-HIV therapies may promote HCV-related liver disease in people who are infected with both viruses.

The answer is, we don't know.

Spencer Cox, of the Treatment Action Group in New York, says that anti-HIV medications have been tested in "people with decreased liver functions. And predictably there has been a slightly higher risk of liver enzyme elevations requiring discontinuation of therapy." He voices concern that the trials have been very small and aimed at demonstrating immediate, highly toxic reactions. They have not measured long-term effects such as a chronic hepatitis.

As protease inhibitors and other therapies extend the life expectancy of people infected with HIV, medical problems such as hepatitis C that develop more slowly are likely to emerge as significant health problems.