

Frequently Asked Questions and Answers About Coinfection with HIV and Hepatitis C Virus

Why should HIV-infected persons be concerned about coinfection with HCV?

About one quarter of HIV-infected persons in the United States are also infected with hepatitis C virus (HCV). HCV is one of the most important causes of chronic liver disease in the United States and HCV infection progresses more rapidly to liver damage in HIV-infected persons. HCV infection may also impact the course and management of HIV infection.

The latest US Public Health Service/Infectious Diseases Society of America (USPHS/IDSA) guidelines recommend that all HIV-infected persons should be screened for HCV infection. Prevention of HCV infection for those not already infected and reducing chronic liver disease in those who are infected are important concerns for HIV-infected individuals and their health care providers.

Who is likely to have HIV-HCV coinfection?

The hepatitis C virus (HCV) is transmitted primarily by large or repeated direct percutaneous (i.e., passage through the skin by puncture) exposures to contaminated blood. Therefore, coinfection with HIV and HCV is common (50%-90%) among HIV-infected injection drug users (IDUs). Coinfection is also common among persons with hemophilia who received clotting factor concentrates before concentrates were effectively treated to inactivate both viruses (i.e., products made before 1987). The risk for acquiring infection through perinatal or sexual exposures is much lower for HCV than for HIV. For persons infected with HIV through sexual exposure (e.g., male-to-male sexual activity), coinfection with HCV is no more common than among similarly aged adults in the general population (3%-5%).

What are the effects of coinfection on disease progression of HCV and HIV?

Chronic HCV infection develops in 75%-85% of infected persons and leads to chronic liver disease in 70% of these chronically infected persons. HIV-HCV coinfection has been associated with higher titers of HCV, more rapid progression to HCV-related liver disease, and an increased risk for HCV-related cirrhosis (scarring) of the liver. Because of this, HCV infection has been viewed as an opportunistic infection in HIV-infected persons and was included in the 1999 USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with Human Immunodeficiency Virus. It is not, however, considered an AIDS-defining illness. As highly active antiretroviral therapy (HAART) and prophylaxis of opportunistic infections increase the life span of persons living with HIV, HCV-related liver disease has become a major cause of hospital admissions and deaths among HIV-infected persons.

The effects of HCV coinfection on HIV disease progression are less certain. Some studies have suggested that infection with certain HCV genotypes is associated with more rapid progression to AIDS or death. However, the subject remains controversial. Since coinfecting patients are living longer on HAART, more data are needed to determine if HCV infection influences the long-term natural history of HIV infection.

How can coinfection with HCV be prevented?

Persons living with HIV who are not already coinfecting with HCV can adopt measures to prevent acquiring HCV. Such measures will also reduce the chance of transmitting their HIV infection to others.

Not injecting or stopping injection drug use would eliminate the chief route of HCV transmission; substance-abuse treatment and relapse-prevention programs should be recommended. If patients continue to inject, they should be counseled about safer injection practices; that is, to use new, sterile syringes every time they inject drugs and never reuse or share syringes, needles, water, or drug preparation equipment.

Toothbrushes, razors, and other personal care items that might be contaminated with blood should not be shared. Although there are no data from the United States indicating that tattooing and body piercing place persons at increased risk for HCV infection, these procedures may be a source for infection with any bloodborne pathogen if proper infection control practices are not followed.

Although consistent data are lacking regarding the extent to which sexual activity contributes to HCV transmission, persons having multiple sex partners are at risk for other sexually transmitted diseases (STDs) as well as for transmitting HIV to others. They should be counseled accordingly.

How should patients coinfectd with HIV and HCV be managed?

General guidelines

Patients coinfectd with HIV and HCV should be encouraged to adopt safe behaviors (as described in the previous section) to prevent transmission of HIV and HCV to others.

Individuals with evidence of HCV infection should be given information about prevention of liver damage, undergo evaluation for chronic liver disease and, if indicated, be considered for treatment. Persons coinfectd with HIV and HCV should be advised not to drink excessive amounts of alcohol. Avoiding alcohol altogether might be wise because the effects of even moderate or low amounts of alcohol (e.g., 12 oz. of beer, 5 oz. of wine or 1.5 oz. hard liquor per day) on disease progression are unknown. When appropriate, referral should be made to alcohol treatment and relapse-prevention programs. Because of possible effects on the liver, HCV-infected patients should consult with their health care professional before taking any new medicines, including over-the-counter, alternative or herbal medicines.

Susceptible coinfectd patients should receive hepatitis A vaccine because the risk for fulminant hepatitis associated with hepatitis A is increased in persons with chronic liver disease. Susceptible patients should receive hepatitis B vaccine because most HIV-infected persons are at risk for HBV infection. The vaccines appear safe for these patients and more than two-thirds of those vaccinated develop antibody responses. Prevacination screening for antibodies against hepatitis A and hepatitis B in this high-prevalence population is generally cost-effective. Postvaccination testing for hepatitis A is not recommended, but testing for antibody to hepatitis B surface antigen (anti-HBs) should be performed 1-2 months after completion of the primary series of hepatitis B vaccine. Persons who fail to respond should be revaccinated with up to three additional doses.

HAART has no significant effect on HCV. However, coinfectd persons may be at increased risk for HAART-associated liver toxicity and should be closely monitored during antiretroviral therapy. Data suggest that the majority of these persons do not appear to develop significant and/or symptomatic hepatitis after initiation of antiretroviral therapy.

Treatment for HCV Infection

A Consensus Development Conference Panel convened by the National Institutes of Health in 1997 recommended antiviral therapy for patients with chronic hepatitis C who are at the greatest

risk for progression to cirrhosis. These persons include anti-HCV positive patients with persistently elevated liver enzymes, detectable HCV RNA, and a liver biopsy that indicates either portal or bridging fibrosis or at least moderate degrees of inflammation and necrosis. Patients with less severe histological disease should be managed on an individual basis.

In the United States, two different regimens have been approved as therapy for chronic hepatitis C: monotherapy with alpha interferon and combination therapy with alpha interferon and ribavirin. Among HIV-negative persons with chronic hepatitis C, combination therapy consistently yields higher rates (30%-40%) of sustained response than monotherapy (10%-20%). Combination therapy is more effective against viral genotypes 2 and 3, and requires a shorter course of treatment; however, viral genotype 1 is the most common among US patients. Combination therapy is associated with more side effects than monotherapy, but, in most situations, it is preferable. At present, interferon monotherapy is reserved for patients who have contraindications to the use of ribavirin.

Studies thus far, although not extensive, have indicated that response rates in HIV-infected patients to alpha interferon monotherapy for HCV were lower than in non-HIV-infected patients, but the differences were not statistically significant. Monotherapy appears to be reasonably well tolerated in coinfecting patients. There are no published articles on the long-term effect of combination therapy in coinfecting patients, but studies currently underway suggest it is superior to monotherapy. However, the side effects of combination therapy are greater in coinfecting patients. Thus, combination therapy should be used with caution until more data are available.

The decision to treat people coinfecting with HIV and HCV must also take into consideration their concurrent medications and medical conditions. If CD4 counts are normal or minimally abnormal (> 400/uL), there is little difference in treatment success rates between those who are coinfecting and those who are infected with HCV alone.

Other Treatment Considerations

Persons with chronic hepatitis C who continue to abuse alcohol are at risk for ongoing liver injury, and antiviral therapy may be ineffective. Therefore, strict abstinence from alcohol is recommended during antiviral therapy, and interferon should be given with caution to a patient who has only recently stopped alcohol abuse. Typically, a six-month abstinence is recommended for alcohol abusers before starting therapy; such patients should be treated with the support and collaboration of alcohol abuse treatment programs.

Although there is limited experience with antiviral treatment for chronic hepatitis C of persons who are recovering from long-term injection drug use, there are concerns that interferon therapy could be associated with relapse into drug use, both because of its side effects and because it is administered by injection. There is even less experience with treatment of persons who are active injection drug users, and an additional concern for this group is the risk for reinfection with HCV. Although a six-month abstinence before starting therapy also has been recommended for injection drug users, additional research is needed on the benefits and drawbacks of treating these patients. Regardless, when patients with past or continuing problems of substance abuse are being considered for treatment, such patients should be treated only in collaboration with substance abuse specialists or counselors. Patients can be successfully treated while on methadone maintenance treatment of addiction.

Because many coinfecting patients have conditions or factors (such as major depression or active illicit drug or alcohol use) that may prevent or complicate antiviral therapy, treatment for chronic hepatitis C in HIV-infected patients should be coordinated by health care providers with experience in treating coinfecting patients or in clinical trials. It is not known if maintenance therapy is needed after successful therapy, but patients should be counseled to avoid injection

drug use and other behaviors that could lead to reinfection with HCV and should continue to abstain from alcohol.

Infections in Infants and Children

The average rate of HCV infection among infants born to women coinfecting with HCV and HIV is 14% to 17%, higher than among infants born to women infected with HCV alone. Data are limited on the natural history of HCV infection in children, and antiviral drugs for chronic hepatitis C are not FDA-approved for use in children under aged 18 years. Therefore, children should be referred to a pediatric hepatologist or similar specialist for management and for determination for eligibility in clinical trials.

What research is needed on HIV-HCV coinfection?

Many important questions remain about HIV-HCV coinfection:

- By what mechanism does HIV infection affect the natural history of hepatitis C?
- Does HAART affect the impact of HIV on the natural history of HCV infection?
- Does HCV affect the natural history of HIV and, if so, by what mechanism?
- How can we effectively and safely treat chronic hepatitis C in HIV-infected patients?
- How can we distinguish between liver toxicity caused by antiretrovirals and that caused by HCV infection?
- What is the best protocol for treating both HIV and chronic hepatitis C in the coinfecting patient?