

close up



HIV + Hepatitis C

The challenge of staying healthy
with co-infection

by Dr. Curtis L. Cooper

Hepatitis C is a blood-borne infection caused by the hepatitis C virus (HCV). This virus causes damage to the liver that may result in chronic infection and disease. About a quarter to a third of all people living with HIV are co-infected with HCV. This rises to between 50% and 90% among IV drug users. Exposure to HCV can also occur through tattooing, cocaine snorting and sex .

Chronic viral hepatitis in HIV infection

HCV infection is identified by the detection of antibodies to the virus in the blood. It's not related to any of the other known hepatitis viruses (A, B, D and E). In acute HCV the inflammation develops quickly, lasts only a short period of time, and you recover completely in a few months. More commonly, however, HCV sticks around at a low level and becomes chronic. HIV changes the way your body reacts to the hepatitis C virus. Less than 10% of people living with HIV are able to clear acute HCV infection on their own after they've been exposed and HCV virus levels in the blood tend to be higher.

The effects of HCV are worse and come on more quickly when HIV is also present. The risks of liver cirrhosis, liver failure and liver-related deaths are also higher.

Effect of chronic viral hepatitis on HIV progression

While the presence of HIV worsens hepatitis C infection, the inverse relationship doesn't hold true. HCV has minimal effect on the progression of HIV. Chronic HCV infection may weaken immune function somewhat but produces no devastating effects. However, the presence of HCV can make HIV treatment with highly active antiretroviral therapy (HAART) more difficult, as will be discussed later.

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It's important for people with both HCV and HIV to receive hepatitis A and hepatitis B vaccinations (if they have not previously been exposed to these viruses) to prevent further liver damage from these infections. Though antibody concentrations following vaccination tend to be lower in people with HCV, the vaccinations offer people living with HIV adequate protection and are especially important for those who participate in risky sexual activities.

Antiretroviral therapy

Despite the odd case of flare-ups of HCV infection following the initiation of HAART, most evidence suggests that antiretroviral therapy also slows HCV disease progression. In people who achieve HIV suppression and remain on therapy for more than six months, HCV levels often fall below baseline and liver enzyme levels (i.e. AST, ALT — indicators of liver cell inflammation) generally remain similar to baseline levels. In fact, AST and ALT may fall below baseline in people who had high pretreatment levels. Compared to those receiving no therapy, people with both HIV and HCV infections who are on HAART have less severe and less frequent liver fibrosis and less severe inflammation.

The incidence of liver toxicity with HAART is generally higher among people with HBV and/or HCV co-infection. There's ongoing debate as to whether certain antiretroviral classes and specific drugs within these classes should be preferred in this patient group to avoid liver toxicity.

The majority of patients (90%+) taking protease inhibitor-containing therapy do not develop liver complications. Ritonavir, a protease inhibitor (PI), used at high

dose (6 pills twice a day) may cause liver problems in co-infected patients. With low-dose ritonavir-boosted HAART regimens (100-200 mg daily or twice daily), which is the current standard of care for HIV infection, the incidence of increases in liver enzymes is between 5 and 10%, similar to that of other protease inhibitor-based HAART regimens.

Nucleoside treatment can produce liver complications such as fatty liver inflammation and lactic acidosis, a life-threatening condition caused by too much lactate in the blood and low blood pH. Efavirenz and nevirapine-containing HAART, given to treatment-naïve patients, was shown to have a 2 to 4% incidence of liver enzyme flares. A nevirapine hypersensitivity syndrome consisting of fever, rash, and liver enzyme elevation, which indicates liver inflammation, occurs very rarely but warrants

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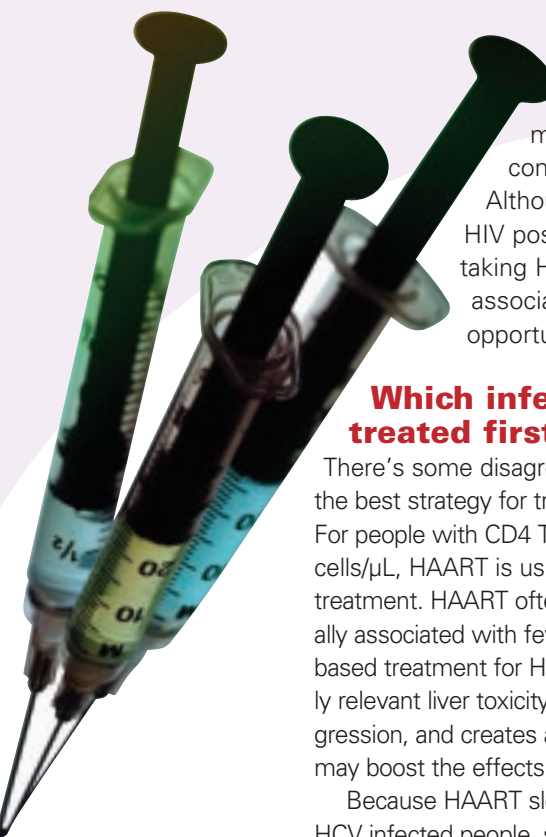
immediate discontinuation of the drug. The fusion inhibitor enfuvirtide (T20 or Fuzeon®) only rarely is associated with liver toxicity, and additional research will determine whether other fusion inhibitors and entry inhibitors will become "liver friendly" treatment options in HIV-viral hepatitis co-infected individuals. Clinical trials of several fusion inhibitors are underway, some of which have had to be stopped due to liver toxicities.

No matter what HIV regimen you're on, careful monitoring of enzymes and liver function through blood tests is essential for anyone also infected with HCV. However, the majority of people with both infections who take HAART don't experience treatment-limiting liver toxicity, and can achieve virologic suppression and see their immune system improved.

Viral hepatitis therapy

The objective of HCV therapy is to achieve a sustained virologic response (SVR), which is defined as persistently undetectable HCV virus in the blood six months after completion of treatment. The overall success rate with pegylated interferon-ribavirin regimens in HIV-HCV co-infection is 30-40% — well below the rates for people infected only with HCV. The duration of therapy and the percentage of people who achieve sustained response depends on the subtype of HCV you have.

The side effects with HCV treatment are not inconsequential but are no worse in HIV-infected patients than in others. Severe adverse interactions between highly-active antiretroviral therapy (HAART) and HCV antiviral therapy are rare and can usually be



avoided by careful laboratory monitoring and avoiding certain combinations of medications. Although CD4 counts fall in half of HIV positive people while they're taking HCV treatment, this fall isn't associated with an increase in opportunistic infections.

Which infection should be treated first?

There's some disagreement among experts about the best strategy for treating HIV-HCV co-infection. For people with CD4 T lymphocyte counts below 350 cells/ μ L, HAART is usually the most beneficial initial treatment. HAART often controls HIV disease, is usually associated with fewer side effects than interferon-based treatment for HCV, infrequently causes clinically relevant liver toxicity, likely slows HCV disease progression, and creates an immune environment which may boost the effects of HCV drug therapy.

Because HAART slows the rate of liver damage in HCV infected people, some believe that HAART should be started sooner than usual in people who also have HCV (i.e. CD4 count 350-500 cells/ μ L). In cases in which the CD4 count has never fallen below 350 cells/ μ L, a reasonable strategy is to first treat HCV and then HIV in order to avoid the combined toxicities of these medications.

The decision to treat HCV at all should, at least in part, be based on liver fibrosis scores determined by liver biopsy. In those with little or no scarring after many years of infection, the chances are minimal that liver dysfunction will ever occur. Avoiding difficult to take HCV therapy under these circumstances seems justified.

Liver transplantation

Despite therapies for HIV, hepatitis B (HBV) and HCV, viral liver disease remains a significant cause of death among people living with HIV. Liver transplantation remains almost impossible to obtain if you're HIV positive. Accumulating data suggest that carefully selected HIV-HBV and HIV-HCV transplanted patients can achieve 1, 2, and 3-year survival rates that are similar to patients without HIV infection. Antiretroviral therapy remains effective and opportunistic infections are rare despite the need to use powerful immune suppressants to prevent organ rejection. A limited supply of organs, inexperience and reluctance among transplant teams, and the difficulties of living with a transplanted organ will hopefully improve with time. For the moment, these factors shouldn't be used to justify a blanket policy denying this procedure to those living with HIV. **R**

The hepatitis alphabet

Several different viruses can cause hepatitis, and each has its own letter of the alphabet. Here's what distinguishes one from the other and what you can do to reduce the risk of getting them.

Hepatitis A

- Transmitted through oral-fecal contact (usually via food or water).
- Acute phase lasts from 4-6 weeks with or without jaundice, fatigue and enlarged liver. The virus usually clears up after 6 weeks but recovery can take months.
- T-cell counts may drop sharply but rebound in 6-12 weeks after acute infection. HAART should be discontinued in the acute phase.
- Plenty of water, bed rest and good nutrition are all essential for a complete recovery.
- Vaccination now available; can be considered as preventive therapy for HIV positive people.

Hepatitis B

- Transmitted via blood and body fluids, for example through needle sharing, blood transfusion, unprotected sex and from mother to child at birth.
- Long incubation period followed by vague symptoms that can include joint pain, rash, nausea, vomiting and less commonly jaundice.
- Chronic hepatitis B occurs after an acute infection in about 20% of patients. The infection may develop into an enlarged liver, liver failure and/or primary liver cancer.
- Acute hepatitis B usually clears on its own but can be treated with lamivudine if severe. Chronic hepatitis B is treated with alpha interferon, peginterferon, lamivudine or adefovir dipivoxil.
- Vaccine available.

Hepatitis C

- Transmitted primarily through contact with infected blood and, less commonly, through sex and childbirth.
- Hepatitis C can resolve on its own but often becomes chronic. Drug treatment includes peginterferon alone or with ribavirin.
- No vaccine available.

Hepatitis D

- Transmitted through contact with infected blood. Only occurs in people already infected with hepatitis B.
- Chronic infection is treated with alpha interferon.
- Vaccination against hepatitis B.

Hepatitis E

- Transmitted by oral-fecal contact, like hepatitis A, in some parts of the world.
- Usually resolves on its own after a few weeks.
- No vaccine available.