

Tip of the iceberg



We've only just begun to see the grave impact of hepatitis C co-infection

by Paula Braitstein

We've known for several years now that the hepatitis C virus (HCV) was going to be bad news for people living with HIV/AIDS. However, until recently, we didn't quite fully comprehend just how bad the situation is. Hepatitis C co-infection is a huge problem, and it is only going to get bigger.

Have you noticed all those people who look like they are probably living on and/or off the streets, but they have big bellies? You think they're well fed so you decide not to give them spare change. In fact, most of them have ascites, a condition that develops when cirrhosis or scarring of the liver occurs. Because the liver isn't processing anything properly, all the fluid that is consumed through eating and drinking doesn't get processed either. This

fluid accumulates in the belly—and later in the legs, genitals, face, and other areas of the body—until the person looks like he or she is nine months pregnant. It's painful and extremely uncomfortable.

A trip to the HIV ward on the 10th floor of St. Paul's Hospital in downtown Vancouver underscores the problem. In nearly every bed, there are people whose bodies are wasted everywhere but their abdomens. Lactulose, a syrup that induces frequent bowel movements in the hopes of excreting ammonia and other toxins which will otherwise accumulate in the brain and cause brain dysfunction, is doled out to patients like candy. At nearly every door, trays stand full of equipment for paracenteses, a procedure to drain fluid from the abdomen using a large needle.

The leading cause of death

Last year, the BC Centre for Excellence in HIV/AIDS (BCCfE) checked their data to see if hepatitis C was a leading cause of death among people on antiretrovirals. It was not. This year, they had another look at the same question and discovered otherwise—and that's after taking into account viral loads and CD4 counts when people start therapy. Of the 1516 individuals who started naïve (that is, for the first time) on triple-combination antiretroviral therapy, 235 of them—16 percent—had antibodies to hepatitis C. However, only 552 of the total group of 1516 had ever been tested for hepatitis C. Thus, when you examine the prevalence of hepatitis C from this perspective, 43% of the 552 people tested were HCV-positive.

Considering how important and dangerous hepatitis C is, it is surprising that more people aren't getting tested, especially since two years ago, the BCCfE wrote a strongly worded letter to BC physicians recommending that all HIV-positive patients, regardless of their risk factors, be tested. If they test antibody-negative but are having liver problems, they should get a PCR test to see if there is actual HCV present, even if the immune system isn't working well enough to create antibodies to the virus. The BCCfE found (in unpublished data) that women and people who had physicians with limited HIV experience were more likely to not be tested.

The reason that the BCCfE didn't discover that HCV was a leading cause of death in HIV-positive people until recently is probably because of the timing of when most people actually became infected. Although a large proportion of people with hepatitis C are not injection drug users (in this instance meaning anyone who has used injection drugs even once in their lifetime), an equally large proportion of people are. The epidemic of HIV and hepatitis C among IDUs in Vancouver spiraled out of control in 1996 or 1997. While HCV can take twenty to thirty years to develop in people who have HCV only, people with both HIV and hepatitis C can expect their hepatitis C disease to progress in seven to ten years. Thus, for people infected in 1996, the brunt of the disease is only beginning to be felt now.

A devastating effect on HIV

It is still not clearly understood why hepatitis C has such a devastating effect on HIV. However, scientists believe that having an altered immune status has an effect on the body's ability to cope with HCV. It may be that with fewer CD4 cells, a greater number of HCV quasi-species or strains can develop, and that the more types of HCV you have, the worse your disease will be. It may be that HIV can somehow kill

liver cells directly, or perhaps it interrupts the immune system's way of preventing liver disease.

Does HCV viral load play a role? Although no relationship appears to exist between HCV viral load and disease progression in people who are mono-infected with HCV (in sharp contrast to HIV disease, where there is a direct and causal relationship between HIV viral load and disease progression), people who are co-infected tend to have higher HCV viral loads than people who are mono-infected.

The other major problem in terms of the interaction between HIV and hepatitis C is related to CD4 counts. People with higher CD4 counts are more likely to respond to HCV treatment and less likely to have rapidly progressing liver disease. Unfortunately, people with low CD4 counts almost uniformly respond poorly to HCV treatment and tend to progress quickly in their liver disease. Immune restoration can also sometimes be a double-edged sword in HCV. People with lower CD4 counts who start antiretroviral therapy may also be kick-starting HCV disease when they do. This scenario is similar to when people with low CD4 counts start antiretrovirals and suddenly develop mycobacterium avium complex (MAC, an opportunistic infection), since it is the immune system's reaction to the disease that causes the symptoms rather than the disease itself. All of this is debated in the literature, and there are no firm answers.

Go to a doctor for testing

Should you be worried? Well, that depends. Have you ever had a tattoo? Have you ever snorted cocaine? Ever shot drugs? Had sex? Had acupuncture? Shared a toothbrush? If the answer to any one of these questions is yes, then you should be concerned. Here's what you should do:

- Get tested. And don't take "no" for an answer. Many doctors still fallaciously believe that only drug addicts are at risk. However, hepatitis C is spread by blood, and it is hundreds of times more infectious than HIV. All it takes is a minute amount of blood to spread. A little rough sex, an old tattoo, a line or two of coke could all easily allow HCV to spread.
- Don't assume you're healthy, even if your lab work suggests you are. There are more questions than answers with hepatitis C. For example, your liver function tests (LFTs), and particularly your AST/ALT, may be normal. If they're elevated, then you know there's something going on—it could be HCV, it could be antiretroviral toxicity, or any number of other things.
- Even if your LFTs are not elevated, that doesn't mean there isn't a problem. Many people have very advanced liver disease, yet their LFTs are normal or close to normal. You

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may have elevated bilirubin. Your doctor might tell you that it's not a clinically relevant reading because all it causes is a little jaundice, or yellowing of skin and eyes. However, jaundice isn't normal, and you need to find out what's going on. If your antibody test was negative, demand a PCR test which tests for the virus itself.

- Pay attention to your body. Feeling excessively tired, losing your appetite, or experiencing changes in your taste or sleeping patterns are all symptoms of liver disease. If you have any of these symptoms, get a referral to a hepatologist—a liver specialist.

Do what you can to support your liver. Avoid alcohol as much as possible. Reduce your salt intake. Consult an HIV-specialist dietitian and/or pharmacist to discuss changes to your diet or supplementing. Don't start supplementing with too many herbs or minerals—you can do more harm than good.

- Get vaccinated for hepatitis A and hepatitis B. Some evidence suggests that hepatitis A combined with hepatitis C can be deadly, quickly. And you don't want hepatitis B. It, too, can cause long-term liver damage, and it is preventable. If you do have hepatitis C, consider treating it early.

To treat or not to treat

One of the biggest questions in the management of HCV disease is whether and when to treat it. Treatments for HCV include combining alfa-interferon and ribavirin, usually taken together in a combination called Rebetron. Both of these drugs are very toxic, especially the ribavirin, and cause quite debilitating and sometimes irreversible side effects such as anemia, loss of salivary production, taste perversion, and depression. They are difficult drugs to take, and they are expensive. The government is usually only willing to pay for a six-month course, even though we know that people with HIV in particular need to take them for at least one year to have any substantial impact.

Perhaps most importantly, Rebetron only “works”—meaning a sustained virologic response where the HCV becomes undetectable and stays that way for at least six months—in about 40% of people who are HCV mono-infected and in only about 20% of people who have both HIV and HCV. This difference may be related to HIV, but it may also be related to the HCV genotype.

Contributing factors to successful treatment

HCV has four major genotypes: 1 (including 1a and 1b), 2, 3, and 4. Genotypes 1 and 4 are the worst—they cause faster disease and lead to poorer treatment responses. Unfortunately, they are also the most common genotypes in people living with HIV. Even the new pegylated interferon

doesn't work as well in people with genotypes 1 and 4. Response rates for people with genotypes 2 or 3 taking pegylated interferon are close to 70%. In people with genotypes 1 or 4, they are closer to 50%.

Successful treatment depends on many factors, including genotype. Other success factors include being under 50, premenopausal female (men and post-menopausal women tend to do more poorly), and HCV viral load. Oddly, although HCV viral load doesn't appear to be related to disease progression, it is related to treatment outcomes.

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Unfortunately, the treatment of HCV in people living with HIV/AIDS has not been adequately studied. However, it is known that the higher the CD4 count, the more likely you are to have a sustained viral response. In other words, treating early is better. Treating your HCV before treating your HIV is probably a good idea, although very little data exist to prove this.

This brief overview touched on some of the major challenges of the rapidly emerging problem of co-infection. The issues are complex and multi-factorial. Hepatitis C is quite different in people who have only have hepatitis C versus people who have both hepatitis C and HIV. So much so, that the definition of HCV as a co-infection rather than as an opportunistic infection will need to be re-evaluated in the near future. ⊕

For more information, contact the BCPWA Society Treatment Information Program at 604-893-2243 or email tip@bcpwa.org. In addition, the US-based National AIDS Treatment Advocacy Project (NATAP) has an excellent website for co-infection resources: < www.natap.org>.



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