



FACTSHEET

Hepatitis C

What is hepatitis C?

Hepatitis C is an infection of the liver caused by the hepatitis C virus (HCV).

How do people get hepatitis C?

HCV is spread when your blood comes into contact with the blood of a person who is infected with the virus. This can happen when people share needles, pipes, straws or other implements for drug use or when unsterile or contaminated needles or ink are used for tattooing or piercing. You can also get HCV from products made from the blood of an infected person. This can happen when you receive blood (in a transfusion) that has not been tested for HCV. Sharing straws when snorting cocaine can also spread HCV. Among HIV-negative people, HCV is not commonly spread during sex or from mother-to-child during childbirth. However, HCV can be transmitted by these methods in HIV-positive people. Although some people can fight off HCV infection, most people exposed to HCV become chronically infected with the virus. That means that their bodies continue to make the virus. People with chronic HCV infection often feel completely healthy even though they carry the virus. They can, however, transmit HCV to others who come in contact with their blood.

Testing for HCV

There are several tests used to find out if you have HCV:

- **HCV antibody test.** This test detects an antibody your immune system makes to attack HCV. If the antibody is detected, it means that you have been exposed to HCV. However, some HIV-positive people whose immune systems are weakened may not produce this antibody or take months to make this antibody even though they are infected. That's why the RNA test (see below) is important.
- **HCV RNA test.** This test checks for the presence of HCV's genetic material; this can confirm HCV infection and tell how much virus is in the blood.
- **HCV genotyping test.** There are at least six types of HCV—1, 2, 3, 4 and so on—and many subtypes—1a, 1b, etc. This test will tell you which type (and possibly subtype) of HCV you have. Type 1 is the most common in North America.

Initial HCV infection

When first infected with HCV, most people do not develop symptoms of this viral infection. In some people, the following symptoms may occur:

- Tiredness;
- loss of appetite;

- nausea;
- diarrhea.

In rare cases, jaundice (yellowing of the skin and whites of the eyes) develops. These symptoms of initial HCV infection usually fade after a few weeks.

Long-term HCV infection

In a process that takes many years, the effects of HCV infection slowly spreads throughout the liver and perhaps into other parts of the body, though only the liver appears to show any damage. Healthy liver tissue is gradually replaced with scarred and damaged tissue. The spread of scar tissue throughout the liver is called cirrhosis. Once cirrhosis sets in, the risk of developing liver failure or liver cancer increases. Factors that can speed up liver damage include the following:

- use of alcohol—try to cut down or quit
- ongoing use of medications that may affect the health of the liver can include the following:
 - antidiabetic drugs called “glitazones;”
 - antibiotics such as isoniazid;
 - in rare cases, NSAIDS (non-steroidal anti-inflammatory agents) such as acetaminophen (Tylenol), ibuprofen (Advil, Motrin), indomethacin (Indocid) and naproxen (Naprosyn);
- HIV infection.

Why is the liver important?

The liver is an important organ because it performs many vital functions such as:

- detoxifying the blood by breaking down foreign substances, such as medicines, nutrients, drugs and alcohol;
- producing and storing sugar (glucose) for energy;

- making proteins involved in blood clotting;
- controlling the level of thyroid and sex hormones;
- regulating the level of certain vitamins and minerals.

Monitoring liver health

Higher-than-normal levels of liver enzymes in the blood suggest liver damage. HCV-positive people do not always have high levels of liver enzymes, nor are these levels always linked to the extent and severity of liver damage. Examples of liver enzymes include the following:

- ALT—alanine aminotransferase;
- AST—aspartate aminotransferase;
- AP—alkaline phosphatase;
- GGT—gamma-glutamyltransferase.

Liver biopsy

Although ultrasound, X-ray (CAT scans) and magnetic (MRI) scans can detect signs of liver inflammation, they do not reveal the degree of scarring that has occurred. For this reason, doctors rely on liver biopsy—the removal of a small sample of tissue from the liver. The sample can help rule out liver damage from causes other than HCV, including the following:

- alcohol abuse;
- overuse of certain medication(s);
- iron build-up;
- metabolic liver disease (fatty liver);
- autoimmune liver disease.

In general, performing a liver biopsy is a fast and safe way to find out what’s going on with the liver. However, people with liver cancer or hemophilia are at increased risk of bleeding from this procedure. After biopsy, about 25% of people can develop temporary tenderness in their upper right abdomen or pain in their right shoulder.

Newer tests

Researchers are conducting experiments to find out if certain blood tests—such as Fibrotest—can help them assess liver health. These tests are not as useful as a liver biopsy. Similarly, special ultrasound scans of the liver—called FibroScan—are being used to try and help doctors assess liver health. FibroScans are routinely used in France and other parts of Western Europe. However, FibroScan has limitations and may not always correctly assess liver damage. In North America, most liver specialists prefer to use a liver biopsy and FibroScan remains a research tool.

HCV viral load test

This test measures the amount of HCV in the blood. It is useful in order to find out if your anti-HCV treatment is working.

Treatment of HCV

Over the past decade, treatment of HCV has evolved from the use of interferon on its own to a combination of interferon and the nucleoside analogue, ribavirin. Interferon has antiviral activity and also helps mobilize the immune system to fight HCV.

Researchers have attached one or more molecules of PEG (polyethylene glycol) to interferon, creating peg-interferon. The PEG provides a protective barrier that shields the interferon from being broken down, thus prolonging the time it remains in the blood. Regular interferon needs to be injected at least three times weekly. Peg-interferon only has to be injected once a week. Peg-interferon also appears to be stronger than regular interferon. There are currently two forms of peg-interferon that have similar activity and side effects:

- Pegasys (interferon-alfa-2a)—made by Hoffman-La Roche
- Pegetron (interferon-alfa-2b)—made by Schering-Plough

Combination therapy—peg-interferon and ribavirin—may be used to try and wipe out HCV infection.

For more information about these two types of interferon, please see the CATIE Fact Sheets on Pegasys and Pegetron at www.catie.ca/facts.nsf.

Ribavirin

Ribavirin is a nucleoside analogue, or nuke. When taken on its own, it has weak anti-HCV activity. However, when used with peg-interferon, the combination is powerful.

Genotype matters

A rule of thumb is that HCV genotypes 2 and 3 respond better to therapy than genotypes 1 and 4.

HIV and HCV co-infection

Research suggests that people living with both HIV and HCV can develop cirrhosis more quickly than those who are HIV-negative. It is a good idea for people who are co-infected to consult a liver specialist and an HIV specialist as well as their primary care doctor to manage both conditions.

Because HIV weakens the immune system, rates of recovery from HCV co-infection are not as high as in HIV-negative people. For HIV-positive people, the chances of recovery from HCV co-infection will depend on a number of factors:

- the degree of damage to your liver;
- the genotype of HCV that you have;
- your ability to tolerate and take your interferon and ribavirin as directed by your doctor;
- how quickly and by how much HCV levels in your blood fall when you take hepatitis therapy;
- whether or not you have diabetes or pre-diabetes (insulin-resistance).

Your hepatitis or infectious disease specialist can tell you more about your chances of recovery from HCV.

In cases of co-infection, treatment for HCV, if it starts to work, usually lasts for 48 weeks. After this period, doctors wait another 24 weeks before conducting further tests to find out if you have cleared HCV. So altogether, it can take up to 72 weeks to know if you are cured.

Further information about HCV treatment and recovery appear in our in-depth factsheets on Pegasys and Pegatron available at: www.catie.ca/facts.nsf.

Is treatment working?

During therapy for HCV, you will need regular visits to your doctor and lab to have blood tests done to monitor your health and to find out if you are recovering from HCV infection. Terms that you might hear include the following:

- RVR (rapid virologic response)—HCV levels in your blood have become undetectable after the first four weeks of therapy.
- EVR (early virologic response)—HCV levels in your blood have significantly decreased after 12 weeks of therapy (and the virus should be undetectable).
- Partial response—the viral load at week 12 has decreased less than 2 log and is still detectable. As a result, your treatment period may be extended. Talk to your doctor.
- No response—HCV levels in the blood after 12 weeks are detectable and increasing. This means treatment is not working

Research with HIV-positive people co-infected with HCV suggests that having the following increases the chances of recovery from HCV after treatment:

- infection with genotype 2 or 3;

- a rapid HCV virologic response (RVR)—this means having HCV that becomes undetectable after the first four weeks of treatment;
- an early HCV virologic response (EVR)—having no detectable virus after the first 12 weeks of treatment;
- extending treatment, in some cases, beyond 48 weeks.

Reinfection

Although treatment can wipe out HCV in some people, this does not mean that your body is immune to HCV. You can become re-infected with HCV if you engage in unprotected sex or needle use again, whether or not you are co-infected with HIV.

Having HIV infection likely makes some people more susceptible to HCV infection. Support for this idea has arisen because studies have found the following:

- The immune system in the intestinal tract of HIV-positive people is particularly weak.
- This could result in weakened local immunity in the vagina, anus and rectum. It may also explain why HIV-positive people are susceptible to HCV infection regardless of their CD4+ count.
- Another factor could be that high levels of HCV have been found in the semen of HIV/HCV co-infected men. If these men then have unprotected intercourse, their risk for transmitting HCV would be relatively high.
- Sexually transmitted infections (STIs) are common in some men who have sex with other men (MSM). Many STIs can cause sores or lesions and could weaken local immunity in the genitals. These factors increase the risk that STIs can help facilitate the transmission of HCV.

Much of the research on the sexual transmission of HCV has been done with gay or bisexual men. In one study, researchers assessed the behaviour

of men who became infected with HCV and found that they were more likely to have engaged in the following behaviours:

- unprotected anal sex (active or passive) with or without ejaculation;
- unprotected group sex;
- fisting;
- rimming;
- use of sex toys;
- substance use.

Although this study was done with MSM, HIV-positive women are probably also at risk for HCV infection if they engage in unprotected intercourse and other risky behaviours.

Which infection should be treated first—HIV or HCV?

The answer to this question varies from person to person. Some doctors choose to treat HIV first because this will raise CD4+ cell counts. HIV-positive people who have moderate CD4+ counts (more than 500 cells) will likely have better responses to combination HCV therapy. Other factors that may play a role in the decision about HCV therapy include the following:

- the length of time you have had HCV;
- your overall state of health;
- the health of your liver;
- drug interactions.

Another issue to bear in mind is the interaction between the nucleoside analogue (nuke) ribavirin and the nukes used as part of anti-HIV therapy. In lab experiments with cells, ribavirin weakened the anti-HIV activity of the following drugs:

- AZT (zidovudine, Retrovir; also in the co-formulations Combivir and Trizivir)
- d4T (stavudine, Zerit)
- ddl (didanosine, Videx)

This interaction does not appear to be the case when HIV-positive people who use highly active antiretroviral therapy (HAART) also use ribavirin as part of combination therapy for HCV.

Ribavirin may increase the toxicity of nukes used in the treatment of HIV. Some HAART users, particularly those using nukes such as ddl or d4T, have developed higher-than-normal levels of lactic acid in their blood. This complication, called lactic acidosis, leads to fatigue and in some cases can cause damage to organs such as the pancreas and liver.

Several years ago there was a report that users of the anti-HIV drug abacavir (Ziagen and in the co-formulations Kivexa and Trizivir) may not respond to HCV therapy as well as people who are not using abacavir, possibly because this drug interacts with ribavirin. It may be that these results occurred because relatively low doses of ribavirin were used. Clinical trials are underway to explore this interaction.

Nowadays, hepatitis specialists often use higher doses of ribavirin (such as 1,000 mg/day or higher, depending on body weight) when treating HCV infection. One study has reported that when the dose of ribavirin was adjusted for the weight of the person (averaging between 1,000 and 1,200 mg/day of ribavirin), abacavir use did not have any effect on the effectiveness of hepatitis therapy.

HAART and the liver

In general, anti-HIV therapy can sometimes cause a degree of liver toxicity. This may occur because two classes of therapies used in HAART—protease inhibitors and non-nukes—are processed by the liver. Speak to your infectious disease and liver specialists about which type of HAART is best for you and your liver. Regular medical visits and blood tests will help you and your doctor be aware of your liver's health.

A journey to health

Your decision to begin therapy against hepatitis is a step on the road to better health. Additional steps, where necessary, you can take to improve your health include the following:

- getting help and support for quitting alcohol, tobacco and other substances;
- getting a referral from your doctor for mental health counselling;
- getting a balance of rest and exercise;
- eating a balanced diet.

Supplements and herbs

Although there is no evidence from well-designed randomized, controlled trials, some people with HIV believe that antioxidants may help protect the liver from some of the damage associated with the use of medications. Examples of antioxidants that may be liver-friendly include the following:

- co-enzyme Q10
- vitamin C
- vitamin E
- alpha-lipoic acid
- N-acetyl-cysteine (NAC)

The herb milk thistle and its extracts have traditionally been used in liver diseases. However, use of milk thistle or any other supplement(s) by itself cannot undo years of damage caused by HCV infection. And milk thistle has the potential to interact with many medications commonly used by people with HCV or HIV to treat the following conditions:

- anxiety;
- depression;
- diabetes;
- high lipid levels;

- high blood pressure;
- HIV infection.

Such interactions have the potential to cause new side effects, make existing side effects worse and reduce the effectiveness of therapy for HIV and these other conditions. Use herbs with caution as many can be toxic to the liver. You may wish to consult a naturopathic doctor who is knowledgeable with AIDS and hepatitis about your use of supplements.

For more information about these supplements, please refer to the following documents on the CATIE website at www.catie.ca:

- Supplement Sheets (www.catie.ca/supple-e.nsf)
- *A Practical Guide to HIV Drug Side Effects* (www.catie.ca/sideeffects_e.nsf)
- “13 Ways to Love Your Liver,” *The Positive Side*, spring/summer 2002 (www.positiveside.ca/e/V6I1/Liver_e.htm)
- *A Practical Guide to Nutrition for People living with HIV* (www.catie.ca/ng_e.nsf)

Useful websites

CATIE’s Hepatitis C web site:
<http://www.hepcinfo.ca/>

Canadian Association for the Study of the Liver:
www.hepatology.ca

Canadian Liver Foundation: www.liver.ca

HIVandHepatitis.com: www.HIVandhepatitis.com

Availability of treatments

In Canada both formulations of peg-interferon and ribavirin are approved for treating HCV. Conditions for subsidized access to these medicines are different in each province and territory—speak to your infectious disease or liver specialist to find out more.

Acknowledgement

We would like to thank the following researcher for his helpful comments and expert review of this factsheet:

- Matthias Banasch, MD, St Josef-Hospital, Bochum, Germany;

Credits

Author: Sean R. Hosein
Revised 2009

References

Sulkowski MS. Management of hepatic complications in HIV-infected persons. *Journal of Infectious Diseases* 2008 May 15;197 Suppl 3:S279-S293.

Blackard JT, Sherman KE. HCV/ HIV co-infection: time to re-evaluate the role of HIV in the liver? *Journal of Viral Hepatitis* 2008 May;15(5):323-330.

Soriano V, Puoti M, Sulkowski M, et al. Care of patients coinfecting with HIV and hepatitis C virus: 2007 updated recommendations from the HCV-HIV International Panel. *AIDS* 2007 May 31;21(9):1073-1089.

Halfon C. Insulin resistance impairs sustained response rate to Peginterferon Plus Ribavirin in HIV/HCV co-infected patients: HOMAVIC-ANRS HC-02 Study. *4th International HIV and Hepatitis Co-infection Workshop* 19-21 June 2008, Madrid, Spain. Abstract 2.

Rauch A, Rickenbach M, Weber R, et al. Unsafe sex and increased incidence of hepatitis C virus infection among HIV-infected men who have sex with men: the Swiss HIV Cohort Study. *Clinical Infectious Diseases* 2005 Aug 1;41(3):395-402.

van de Laar TJW, van der Bij AK, Prins M, et al. Increase in HCV incidence among men who have sex with men in Amsterdam most likely caused by sexual transmission. *Journal of Infectious Diseases* 2007; 196:230-238.

Danta M, Brown D, Bhagani S, et al. Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours. HIV and Acute HCV (HAAC) Group. *AIDS* 2007; 21:983-91.

Cohen DE, Russell CJ, Golub SA, Mayer KH. Prevalence of hepatitis C virus infection among men who have sex with men at a Boston community health center and its association with markers of high-risk behavior. *AIDS Patient Care & STDs* 2006; 20:557-64.

Giraudon I, Ruf M, Maguire H, et al. Increase in diagnosed newly acquired hepatitis C in HIV-positive men who have sex with men

across London and Brighton, 2002-2006: is this an outbreak? *Sexually Transmitted Infections* 2008 Apr;84(2):111-5.

Jones R, Low E, Rodgers A, et al. Hepatitis C (HC) viraemia following sustained virological response (SVR) to Pegylated Interferon (Peg-IFN) and Ribavirin (RBV) in HIV positive men who have sex with men (MSM)—Re-infection or Late Relapse? *4th International HIV and Hepatitis Co-infection Workshop*. 19-21 June 2008, Madrid, Spain. Abstract 12.

Gallotta G, Gali L, De Bona A, et al. Acute hepatitis C virus in HIV co-infected men who have sex with men: Milan 1996-2007. *4th International HIV and Hepatitis Co-infection Workshop*. 19-21 June 2008, Madrid, Spain. Abstract 47.

Fierer DS, Uriel AJ, Carriero DC, et al. Liver Fibrosis during an Outbreak of Acute Hepatitis C Virus Infection in HIV-Infected Men: A Prospective Cohort Study. *Journal of Infectious Diseases* 2008 Sep 1;198(5):683-686.

Grünhage F, Wasmuth J-C, Vidovic N, et al. No difference in liver fibrosis in a cohort of HIV/HCV-coinfecting patients on HAART as compared to HIV-negative HCV-patients assessed by transient elastography. *4th International HIV and Hepatitis Co-infection Workshop*. 19-21 June 2008, Madrid, Spain. Abstract 8.

Janke M, Luchters G, Vogel M, et al. Which factors predict early and sustained virological response under combination hepatitis C therapy in HIV/HCV co-infected patients? *4th International HIV and Hepatitis Co-infection Workshop*. 19-21 June 2008, Madrid, Spain. Abstract 14.

Scott LJ and Perry CM. Interferon alfa-2b plus ribavirin: a review of its use in the management of chronic hepatitis C. *Drugs* 2002; 62(3):507-556.

Perry CM and Jarvis B. Peginterferon alfa-2a (40kD): a review of its use in the management of chronic hepatitis C. *Drugs* 2001; 61(15):2263-2288.

Lafeuillade A, Hittinger G and Chadapaud S. Increased mitochondrial toxicity with ribavirin in HIV/HCV coinfection. *Lancet* 2001;357:280-281.

Kakuda TN and Brinkman Kees. Mitochondrial toxic effects and ribavirin. *Lancet* 2001;357;1802-1803.

Salmon-Céron D, Chauvelot-Moachon L, Abad S, et al. Mitochondrial toxic effects and ribavirin. *Lancet* 2001;357; 1803-1804.

Laskus T, Radkowski M, Piasek A, et al. Hepatitis C virus in lymphoid cells of patients coinfecting with human immunodeficiency virus type 1: evidence of active replication in monocytes/macrophages and lymphocytes. *Journal of Infectious Diseases* 2002;181(2):442-448.

Katze MG, He Y and Gale M. Viruses and interferon: A fight for supremacy. *Nature Immunology Reviews* 2002;2(9):675-687.

Haley RW, Fischer RP. Commercial tattooing as a potentially important source of hepatitis C infection. *Clinical epidemiology*

of 626 consecutive patients unaware of their hepatitis C serologic status. *Medicine* (Baltimore) 2001 Mar;80(2):134-151.

Brinkman K, Vrouenraets S, Kauffmann R, et al. Treatment of nucleoside reverse transcriptase inhibitor-induced lactic acidosis. *AIDS* 2000;14(17):2801-2802.

Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV-related illness and the treatments in question.

The Canadian AIDS Treatment Information Exchange (CATIE) in good faith provides information resources to help people living with HIV/AIDS who wish to manage their own health care in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

We do not guarantee the accuracy or completeness of any information accessed through or published or provided by CATIE. Users relying on this information do so entirely at their own risk. Neither CATIE nor the Public Health Agency of Canada nor any of their employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. The views expressed herein or in any article or publication accessed or published or provided by CATIE are solely those of the authors and do not reflect the policies or opinions of CATIE or the official policy of the Minister of Health Canada.

Permission to reproduce

This document is copyrighted. It may be reprinted and distributed in its entirety for non-commercial purposes without prior permission, but permission must be obtained to edit its content. The following credit must appear on any reprint: *This information was provided by the Canadian AIDS Treatment Information Exchange (CATIE). For more information, contact CATIE at 1.800.263.1638.*

Contact CATIE

by telephone
1.800.263.1638
416.203.7122

by fax
416.203.8284

by e-mail
info@catie.ca

on the Web
www.catie.ca

by mail
505-555 Richmond Street West
Toronto ON M5V 3B1 Canada

Funding has been provided by the Public Health Agency of Canada.

