

# GUIDE TO HEPATITIS C FOR PEOPLE LIVING WITH HIV:

testing, coinfection, treatment, and support

**First questions**

**Dealing with a new diagnosis**

**Treatment for HCV**

**Living with coinfection**



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testing, coinfection, treatment, and support



Treatment Action Group  
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**Thanks to TAG's board, staff, and generous donors.  
This work would not be possible without your support.**

Treatment Action Group is an independent AIDS research and policy think tank fighting for better treatment, a vaccine, and a cure for AIDS. TAG works to ensure that all people with HIV receive life-saving treatment, care, and information.

We are science-based treatment activists working to expand and accelerate vital research and effective community engagement with research and policy institutions.

TAG catalyzes open collective action by all affected communities, scientists, and policy makers to end AIDS.

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**Disclaimer:** *Information in this booklet is not intended to replace information from your doctor or other healthcare providers. Decisions related to your treatment should be made in consultation with your doctor.*

Guide to hepatitis C for people living with HIV:  
testing, coinfection, treatment, and support

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# introduction

Welcome to our treatment guide for HIV-positive people who also have the hepatitis C virus (called HCV, for short).

The people who wrote this guide have direct experience with HIV and hepatitis C. We have written this guide to encourage you to explore the range of care and treatment choices available to you. We hope this information helps you feel more in control of some of your HCV treatment choices, so that you can focus on other things you want to do in life.

This booklet focuses on coinfection with HIV and hepatitis C. Other hepatitis viruses (A, B, D, E, etc.) are very different from HCV and are only briefly discussed.

Because HIV and hepatitis viruses are transmitted in similar ways, having both HIV and hepatitis C (called HCV/HIV coinfection) is not unusual. In some countries, coinfection is more common than having HIV alone.

Some people have been living with HCV for over 20 years and have chosen to go without treatment. Others were infected more recently. Some of these recently infected people have had HIV for many years. Longstanding HIV infection may be a factor in deciding to treat HCV earlier rather than later. This range of experience underscores the fact that an individual approach to your own health care is essential.

We have included short personal quotations throughout this guide. You can find more detailed stories from people living with coinfection in the online United Kingdom version, and you can add your own story to this resource (<http://www.ibase.info/guides/hepc/stories/index.html>). The online United Kingdom version of this guide also includes hepatitis information not covered in the print version; see <http://www.i-base.info/guides/hepc/extras/index.html>.

An online US version will be available at <http://www.treatmentactiongroup.org>.

At the end of this booklet, we have included a list of organizations, web links, and online sources of support. We have also included a glossary that defines some of the medical terms used in this guide. Glossary terms are highlighted in the text in bold.

Our understanding of HCV/HIV coinfection is likely to change as new research findings emerge. Please check online for updates, especially if you are reading this edition after June 2008.



**first questions**

We would like to briefly address the most basic questions about HCV and HIV up front. You can read more about many of these issues in later chapters.

## What is hepatitis C?

The word *hepatitis* just means inflammation of the liver. Hepatitis C is a virus that lives mostly in the blood and in liver cells. Infection with the hepatitis C virus can cause liver inflammation and scarring. Mild scarring is known as **fibrosis** and more serious scarring is known as **cirrhosis**. Liver scarring resulting from long-term HCV infection reduces the liver's ability to perform essential functions. Liver damage from hepatitis C usually develops slowly over many years.

## How did I get HCV?

Hepatitis C is transmitted when blood from a person who has HCV—a person who is already infected with this virus—directly enters another person's bloodstream. There are a number of ways this can happen. The most common are:

- Injecting drugs using shared equipment (spoons, caps, and other cookers; cotton; water; and ties) and possibly snorting drugs using shared straws or bills;
- Tattooing or piercing with unsterilized needles or ink wells contaminated with blood;
- Needlestick injuries (to people who work in health care settings);
- Receiving a blood transfusion before 1992, or blood products such as clotting factors before 1987; and
- Having unprotected sex with someone who has HCV (see pages 8, 13, and 14).

Some people will never know for sure how they got infected, especially people who have had HCV for many years. Knowing how hepatitis C is spread can help you avoid being infected a second time with a different strain of HCV, and also can help you protect other people.

## How serious is HCV?

Unlike HIV, hepatitis C can be cured. There are two ways this can happen:

1. Your immune system responds effectively to the virus during the first few months of infection and eliminates it from your body; or
2. A combination of medical treatments (see “How is HCV treated?” page 41) taken for a limited time rids your body of HCV.

If HCV is cured either by your immune system or through treatment, then you may not experience any long-term health consequences.

More than 45% of HIV-negative people and up to 20% of HIV-positive people clear HCV *without* medical treatment during the first six months after they are infected, a period known as **acute infection**. Clearing HCV during acute infection means that the hepatitis C virus is gone from your body, and that *you are no longer infected*; this outcome is sometimes referred to as **spontaneous viral clearance** or **spontaneous clearance**.

**Chronic infection** refers to cases in which the hepatitis C virus remains in the body after the acute phase. Most people with HCV are chronically infected. Chronic HCV can have a very wide range of outcomes. Some people will never develop significant liver damage, some will have mild liver scarring, and others (between 20% and 30%) will eventually develop **cirrhosis**.

In a smaller percentage of people, chronic HCV can cause liver cancer and liver failure. Someone experiencing liver failure needs a liver transplant in order to survive. Liver failure resulting from hepatitis C occurs in only a handful of people, usually those who have been infected for many years.

Because HCV generally progresses very slowly, there is usually plenty of time to consider your treatment options.

HCV progresses more quickly in people who are also HIV-positive and HCV treatment is less successful in HIV-positive people than HIV-negative people. We’ve written this brochure to help answer questions about hepatitis C treatment for HIV-positive people.

## **Will HCV make my HIV worse or more difficult to treat?**

Generally, coinfection with HIV and HCV complicates both diseases.

HIV causes HCV to progress more quickly, although we don't know why this happens.

It is not clear what effect HCV has on HIV. Some studies suggest that coinfecting people do not respond as well to HIV medicines. Factors such as ongoing drug or alcohol use, lack of access to health care, homelessness, and poor nutrition may be involved.

There are a few drug interactions between HCV and HIV treatments that you need to be careful to avoid. These are discussed in detail in the treatment section of this booklet (see pages 61 and 62). Luckily, although response rates to treatment vary, most people living with coinfection can be treated for both HIV and hepatitis C.

People who are coinfecting have a higher risk of liver damage from HIV drugs, but the benefits of HIV treatment generally outweigh the risk of additional liver-related side effects. A stronger immune system slows down liver damage from HCV.

## **How common is HCV/HIV coinfection?**

An estimated four to five million people in the United States have been infected with hepatitis C. Some of these people cleared the hepatitis C virus and are no longer infected, so the number of people who are chronically infected is smaller, though precise figures for chronic HCV infection are difficult to obtain.

More than one million people in the United States have HIV/AIDS, and 25% to 30% of them are coinfecting with HCV.

Worldwide, about four to five million people are coinfecting with HIV and hepatitis C. Coinfection rates range from about 9% of HIV-positive people in the United Kingdom to almost 50% in Spain and Italy. Coinfection rates as high as 60% to 70% have been found in groups of injection drug users (IDUs) in various countries, including the United States, which has very high coinfection rates in some urban areas.

Globally, sexual transmission accounts for the majority of new HIV infections each year. However, injection drug use is driving the HIV epidemics in Eastern Europe and Central Asia. Coinfection with

hepatitis C and HIV is common among current and former IDUs, especially in countries where access to syringes and/or substitution treatment (methadone or buprenorphine, or heroin maintenance) is uneven, severely restricted, or nonexistent.

## **What should I do first after learning that I have HCV?**

Many people are living with HIV and HCV, and have done so for many years. If you have been HIV-positive for a while, the shock of being diagnosed with another chronic illness can be difficult to deal with.

Give yourself time to deal with your reactions. Some people need a few days or weeks to adjust to the news, and some people need significantly longer. Coming to terms with your diagnosis is important before you can make rational decisions about what to do next. As you think through the situation, you may feel angry, scared, or withdrawn. These feelings are normal, and many people with HCV have had them.

Coming to terms with an HCV diagnosis also involves learning more about hepatitis C, and seeking support.

You may be able to find information and support from many sources, including friends and family; support groups; your doctors, nurses, and other health care providers; and the Internet.

As with HIV, learning you have HCV may cause you to re-evaluate how you think about your health and well being, your personal relationships, and the role of the medical system in your life. Some people who find out they have hepatitis C have not been to a doctor for years. They may have had negative experiences with—or have negative feelings about—hospitals, emergency rooms, and clinics.

One of the best things you can do for yourself is find a doctor who is familiar with HIV and hepatitis C. Also, it's important to remember that both HIV and HCV are treatable for most people, including the majority of HIV-positive people. Even if you do not want to receive treatment for HCV, it's still important to see a doctor for at least one round of medical tests to monitor your overall health.

Many people find that being monitored or treated for HCV leads them to reflect on health-related behaviors and on the activities, patterns, and relationships in their day-to-day lives.

Many newly diagnosed people fear that they have given HCV to friends, partners, or family members. You may be worried about your sexual and drug-using partners. You can learn about HCV transmission, and how to lower the risk of passing on HIV or HCV to other people.

### **Who should I tell?**

When you first receive an HCV diagnosis, talking to a friend, partner, or relative can be helpful. But it's up to you to decide who should know. Take time to think about this issue, and about how you would like to share this information.

### **Are people around me now at risk?**

You can only pass HCV on to someone if he or she comes into direct contact with your blood. Unlike HIV, HCV can live outside of the body for days to weeks and is infectious even after blood has dried.

In practice, protecting the people around you means that you should avoid sharing anything that may contain traces of blood—even dried blood—such as syringes and other injection equipment; toothbrushes; razors; and manicuring tools.

### **Can I pass on HCV through sex?**

The risk of sexual transmission is generally much lower than through direct blood contact, but may be more common than we previously believed. Unlike HIV, which is present in blood, semen, vaginal fluids, and breast milk, *the hepatitis C virus is primarily found in blood*. However, any type of sex that may involve blood is an opportunity for HCV transmission. This includes fisting; anal or rough vaginal sex without condoms; and sex during menstruation. Being infected with a sexually transmitted disease (STD) such as herpes, gonorrhea, or syphilis increases the risk for sexually transmitted HCV.

Recently, there have been reports of new HCV diagnoses in cohorts of HIV-positive gay men. The overall number of infections has been low. However, the fact that HCV is spreading among HIV-positive gay men via sexual transmission emphasizes the need to pay attention to which types of sexual activity may be more risky than others.

## Can I be re-infected with another strain of HCV?

Having one type of HCV doesn't protect you from being infected with a different type of HCV (see the information on HCV **genotype** on pages 31, 42, and 43).

Also, people who have cleared HCV can become infected again in the future, in any of the ways discussed in this guide.

## Are there other types of hepatitis?

As noted earlier, *hepatitis* is the medical name for liver inflammation. Some causes of hepatitis include heavy alcohol consumption; exposure to chemical fumes; and certain medications.

Several different viruses also cause hepatitis. The viruses are named alphabetically (A, B, C, D, E, and G) in the order they were discovered. Before hepatitis C was discovered in 1989, the virus was referred to as "non-A non-B hepatitis."

## Hepatitis A and B

After an HCV diagnosis, it's important to find out whether you are protected against hepatitis A and B—you really don't want another hepatitis virus to complicate your health. People who have been infected with and cleared these viruses in the past have antibodies in their blood that should protect them from being infected by the same viruses in the future. If you do not have antibodies, you can be vaccinated against hepatitis A (HAV) and hepatitis B (HBV).

## **Hepatitis A and B vaccination**

Vaccines work by generating an immune response to part of a virus. The effectiveness of HAV and HBV vaccination depends on your CD4 count. The higher your count, the greater the chance that the vaccine will “take.”

Some HIV-positive people need to repeat the vaccination series or use high-dose titers in order to produce antibodies sufficient for protection. If your CD4 count is low and you are not immune to HAV or HBV, it may be better to first start HIV treatment and then be vaccinated later, when your immune system is stronger. You can increase the chance of a successful vaccination by using a higher dose of the vaccine.

After you’ve been vaccinated, be sure to have your clinic check your titer levels annually to see if you have sufficient antibody protection. You may need a vaccination booster.

Unfortunately, there is no vaccine that protects against hepatitis C. That’s why it’s so important to learn about prevention methods related to both drug use and sex.

The background features a repeating pattern of stylized human figures in a light orange color. These figures are arranged in a triangular grid that tapers from left to right, with the top row having one figure and the bottom row having ten. The figures are simple, consisting of a circular head and a trapezoidal body.

# hepatitis C transmission

HCV is mainly transmitted when infected blood from one person directly enters another person's bloodstream. HCV has been detected in semen and vaginal fluid, so genital fluids may be infectious. Saliva and tears are not.

HCV, like HIV, *cannot* be transmitted by touching, kissing, hugging, sharing eating utensils, or drinking from the same glass. However, unlike HIV, which dies in less than a minute outside the body, HCV survives and is infectious in dried blood for days or even weeks. People can become infected by sharing items that contain only tiny traces of dried blood.

HCV can be transmitted through:

- injecting drugs using shared syringes and/or spoons, caps, and other cookers; water; filters; and ties that may have been used by someone else;
- tattooing or piercing using unsterilized needles, contaminated ink, or inkwells;
- needlestick accidents (a problem for health care workers);
- medical or dental procedures with unsterilized equipment, including kidney dialysis (rare);
- sharing items that may contain blood, such as razors, toothbrushes, and manicuring equipment; and
- unprotected sex with someone who has HCV.

Hepatitis C can also be transmitted from a pregnant woman to her fetus in the womb or to an infant during labor and delivery.

Before thorough screening of the blood supply began in the early 1990s, some people received blood or blood products containing HCV. Since then, infection control procedures have virtually eliminated the risk in the United States and Western Europe.

However, up to 90% of people with hemophilia were infected with HIV and HCV after being treated with unscreened clotting factors; screening and viral inactivation procedures were introduced in the late 1980s.

In some countries, infections still occur from blood transfusions because blood is not screened. Unsafe medical procedures, such as

using unsterilized equipment to vaccinate people, continue to spread HIV and hepatitis C in many parts of the world.

## Hepatitis C and injection drug use

Worldwide, most HCV infections are attributable to injection drug use. This happens when people share injection equipment, including syringes, cookers, possibly cottons, and other injection paraphernalia.

Hepatitis C is a smaller, more durable virus than HIV. As discussed above, the hepatitis C virus can live in syringes and other objects for days or weeks. This is why it's so important to talk to people you get high with about how to make sure you're getting high safely, and in a way that protects everyone.

Cleaning syringes with bleach reduces the risk for HIV transmission but may be less effective against hepatitis C. If you're getting high, *use a new set each time you inject*. If you're injecting drugs with other people, mark your equipment and be sure that everyone has his/her own spoon or cooker. Using clean needles and your own works each time you inject stops both HIV and HCV transmission.

## What about hepatitis C in drug users who don't inject?

*“I also worry about sharing a rolled-up note when I do coke—but it doesn't stop me from doing it or my friends from being willing to share. I guess this all comes down to individuals agreeing to own and share risks that they feel to be acceptable. These risks feel okay most but not all of the time.”*

Hepatitis C is more common among non-injection drug users than among the general population. Researchers are not sure why. Since HCV is so common among IDUs, most drug users—whether they inject or not—know people who have HCV.

It may be possible to get HCV from sharing straws or rolled dollar bills for snorting drugs, and possibly from sharing crack pipes. Use your own bills and straws, and if you're smoking crack or heroin, use a stem to protect yourself.

## HIV, HCV, and sex

### Sexual transmission of HIV

Worldwide, sexual transmission accounts for the majority of new HIV infections each year. The risk of sexual transmission is greatly reduced by using condoms during sex.

The ways that HIV is transmitted are well understood. HIV is present in blood, semen, vaginal fluid, and breast milk.

We also know that different sexual acts carry different risk factors. For example, mutual masturbation and body rubbing are zero risk, and oral sex is very low risk. On the other hand, anal or vaginal sex without a condom is high risk. A high viral load in the HIV-positive partner increases the risk for infection, and a low or undetectable viral load will reduce the risk.

An HIV-positive person with untreated STDs (such as herpes, gonorrhea, and syphilis), is more likely to transmit HIV. This is because STDs increase the amount of HIV virus in genital fluids and make the HIV-positive partner more infectious. Similarly, an HIV-negative partner with untreated STDs is more vulnerable to HIV infection.

## **Sexual transmission of HCV**

The risk for sexually transmitted HCV is very low in monogamous, HIV-negative, heterosexual couples in which one partner has HCV. One study following almost 900 heterosexual monogamous couples did not report any HCV infections over ten years of follow-up. These couples did not use condoms, but also did not have anal sex or sex during menstruation. Presumably, the uninfected partner in these couples may have had less exposure to blood, and therefore less chance of catching HCV during sex.

The risk for sexually transmitted HCV is higher for HIV-positive gay men and is probably also higher for men or women who have numerous partners and/or lots of anal or vaginal sex without condoms.

HCV is usually contracted when infected blood from one person enters another person's body. Although the hepatitis C virus has been found in semen and vaginal fluid, it is unclear whether and to what extent these fluids are infectious.

Sex is riskier if it involves exposure to blood. This could include longer and more energetic sex, anal sex, fisting, sex with a woman during menstruation, and group sex. Condoms can reduce these risks. Latex gloves can reduce exposure to blood during fisting.

## HIV-positive gay men

In the United Kingdom, more than 300 cases of sexually transmitted HCV infection have been reported in HIV-positive gay men. A similar link between HCV sexual transmission and HIV-positive gay men has been reported in some other European and US cities.

So far, new cases of HCV sexual transmission in HIV-negative gay men are not being reported nearly as often. This suggests that HIV plays an important role.

Some studies have reported associations between HCV transmission and the following risk factors among gay men:

- anal intercourse without condoms;
- “heavier” sex, longer periods of sex, fisting, and sharing sex toys;
- sex with a higher number of partners;
- group sex;
- use of some recreational drugs that lower inhibitions and may make condom use less likely;
- infection with other sexually transmitted diseases, especially syphilis; and
- meeting partners online.

We can speculate about each of these points, but there is still a lack of clear information about why HIV-positive gay men seem more likely than HIV-negative gay men to acquire HCV through sexual contact.

### **Crystal meth, ecstasy, cocaine, and HCV infection**

Although sex seems to be the route of HCV infection among the HIV-positive gay men discussed above, taking drugs in this situation can increase the risk, even if the drugs are not injected. Drugs like ecstasy, coke, and crystal meth, all of which can make people less careful than usual, are frequently found at parties where there is group sex. Under these circumstances, the desire to dispense with condoms may be high.

## Mother-to-child transmission of HCV

HCV, like HIV, can pass from a pregnant woman to her fetus in the womb or to an infant during labor and delivery. The risk of transmitting HCV to an infant is three to four times higher if you have both HCV and HIV. This means that up to 20% of pregnant women who are coinfecting may pass HCV to their infants.

HIV treatment dramatically reduces the risk of mother-to-child transmission of HIV, regardless of the mother's hepatitis C status, and it may also lower the risk of HCV transmission.

It is not currently possible to take hepatitis C treatment during pregnancy to reduce the chance of HCV transmission. This is because one of the two primary HCV drugs (ribavirin) causes birth defects, and the other (interferon) can cause brain damage in infants less than two years old. Planned delivery by caesarean section (C-section) reduces the risk of mother-to-child transmission among coinfecting mothers. But this is not a standard recommendation in the United States for women who have HCV alone, due to the invasive nature of the procedure.

Generally, HCV either spontaneously clears or progresses slowly in people who were infected at birth or during early childhood. HCV may progress more rapidly in coinfecting children.

For more information about HIV and pregnancy, see the i-Base guide to HIV, pregnancy, and women's health, available online at <http://www.i-base.info/guides/pregnancy/index.html>.

*“We need a lot more information and research about transmission of mother to child—and transmission in general. A friend who is coinfecting recently had a child. Even though her HIV viral load was undetectable, and her CD4 count was high, she had to have a caesarean section because of her HCV.”*

The background features a repeating pattern of stylized human figures in a light orange color. These figures are arranged in a triangular shape, with the number of figures decreasing from left to right and top to bottom. Each figure consists of a circular head and a trapezoidal body.

# **what happens to people who have hepatitis C**

## The natural history of HCV

Although hepatitis C also affects other parts of the body, your liver is the organ most affected.

Your liver is an essential organ with hundreds of functions. On a daily basis, it:

- filters chemicals and waste from the blood;
- stores vitamins, minerals, and iron;
- converts nutrients from food into energy;
- helps to balance levels of sugar and hormones;
- produces cholesterol;
- makes bile (necessary for digestion); and
- creates the hormone that helps to produce platelets (to stop bleeding).

Hepatitis C does not directly damage your liver. Instead, after infection, the immune system reacts to hepatitis C by trying to rid the liver of infected cells. This immune response can cause liver inflammation, which in turn leads to scarring. As the immune system tries to isolate infected cells, the scarring worsens. The result is that the liver hardens and becomes less elastic. Therefore, scarring makes it increasingly difficult for blood and other necessary fluids to flow freely through the liver.

Even though a badly damaged liver can keep working, the ongoing effects of HCV and inflammation can slowly interfere with liver function. A person with chronic HCV experiences health complications when his or her liver is no longer able to carry out important tasks.

## Acute HCV

The first six months of HCV infection are referred to as the acute infection period. Eighty percent of people do not have symptoms during acute infection, so HCV is rarely diagnosed at this time. When symptoms do occur during acute infection, they include fever, fatigue, abdominal pain, nausea, vomiting, dark urine, and **jaundice**.

During acute HCV infection, a person's liver enzyme levels can be 10 to 20 times normal. People receiving HIV treatment get their liver enzyme levels checked regularly. Sometimes, in the course of this routine monitoring, doctors find abnormally high liver enzyme levels that signal HCV. This can help them to diagnose acute HCV in HIV-positive patients.

In the first few months after HCV infection, some people will eliminate the virus from their bodies without treatment. This is called spontaneous clearance. The people most likely to clear HCV during acute infection are those who are symptomatic, female, and under age 40.

HIV-positive people are only half as likely to spontaneously clear hepatitis C.

People of African descent are less likely to clear hepatitis C than those of European descent. The reasons for this difference are unclear.

If you've cleared the virus during acute infection, you may test positive for antibodies to HCV. However, the virus is not detectable in your blood, and you are no longer infected.

If HCV does not clear spontaneously within the first few months, some people choose to start treatment during acute infection because there are higher success rates at this stage. It is important to discuss the risks and benefits of treating acute hepatitis C with your doctor.

## Chronic HCV

An HCV infection that still exists after the acute infection period has ended is referred to as chronic HCV.

In HIV-negative people, HCV progresses very slowly, usually over decades, with a wide range of outcomes. The liver might not be the only part of the body affected. The i-Base guide available online at <http://www.i-base.info/guides/hepc/outside.html> provides more information about non-liver-related consequences of HCV.

Some people never seem to experience significant consequences of HCV infection. Others may develop mild to moderate **fibrosis** (liver scarring) and experience symptoms such as fatigue, depression, and confusion (often called **brain fog**). There seems to be no clear

relationship between the symptoms a person has and the degree of liver damage.

Some people may develop fat in their liver cells, a condition known as **steatosis**. Steatosis is linked with more serious liver disease.

About 20% to 30% of people with chronic, untreated HCV will progress to **cirrhosis** (serious liver scarring). A cirrhotic liver can still function; this condition is called **compensated cirrhosis**.

## End-stage liver disease

Compensated cirrhosis may progress to end-stage liver disease, which occurs when a person's liver can no longer function. This is known as **decompensated cirrhosis**. A person with decompensated cirrhosis needs a liver transplant in order to survive. The majority of liver transplants in the United States and Europe are attributed to complications of HCV.

Each year, between 1% and 5% of people with cirrhosis develop **hepatocellular carcinoma** (HCC; liver cancer).

## HIV and hepatitis C coinfection

Hepatitis C behaves differently in HIV-positive people. HIV accelerates hepatitis C disease progression. (Still, many people have lived with both HIV and hepatitis C for years, often without knowing that they are coinfecting.) The risk of serious liver damage is greatest among HIV-positive people with fewer than 200 CD4 cells.

HCV can be treated, regardless of a person's HIV status. Antiretroviral therapy has dramatically reduced the number of deaths from HIV. Now, end-stage liver disease from hepatitis C coinfection has become a leading cause of death among HIV-positive people in parts of the United States and Western Europe. This is partly because HCV may not be diagnosed until after severe liver damage has already occurred.

## The effect of hepatitis C on HIV

Hepatitis C does not worsen HIV but may complicate HIV treatment, since many HIV drugs are metabolized by the liver. Coinfected people are at greater risk for **ART**-associated hepatotoxicity than those with HIV alone. Still, the benefit of HIV treatment outweighs the risk of liver toxicity. (For more information, see “Drug interactions between HCV treatment and HIV drugs,” page 61.)

### Factors that accelerate HCV progression

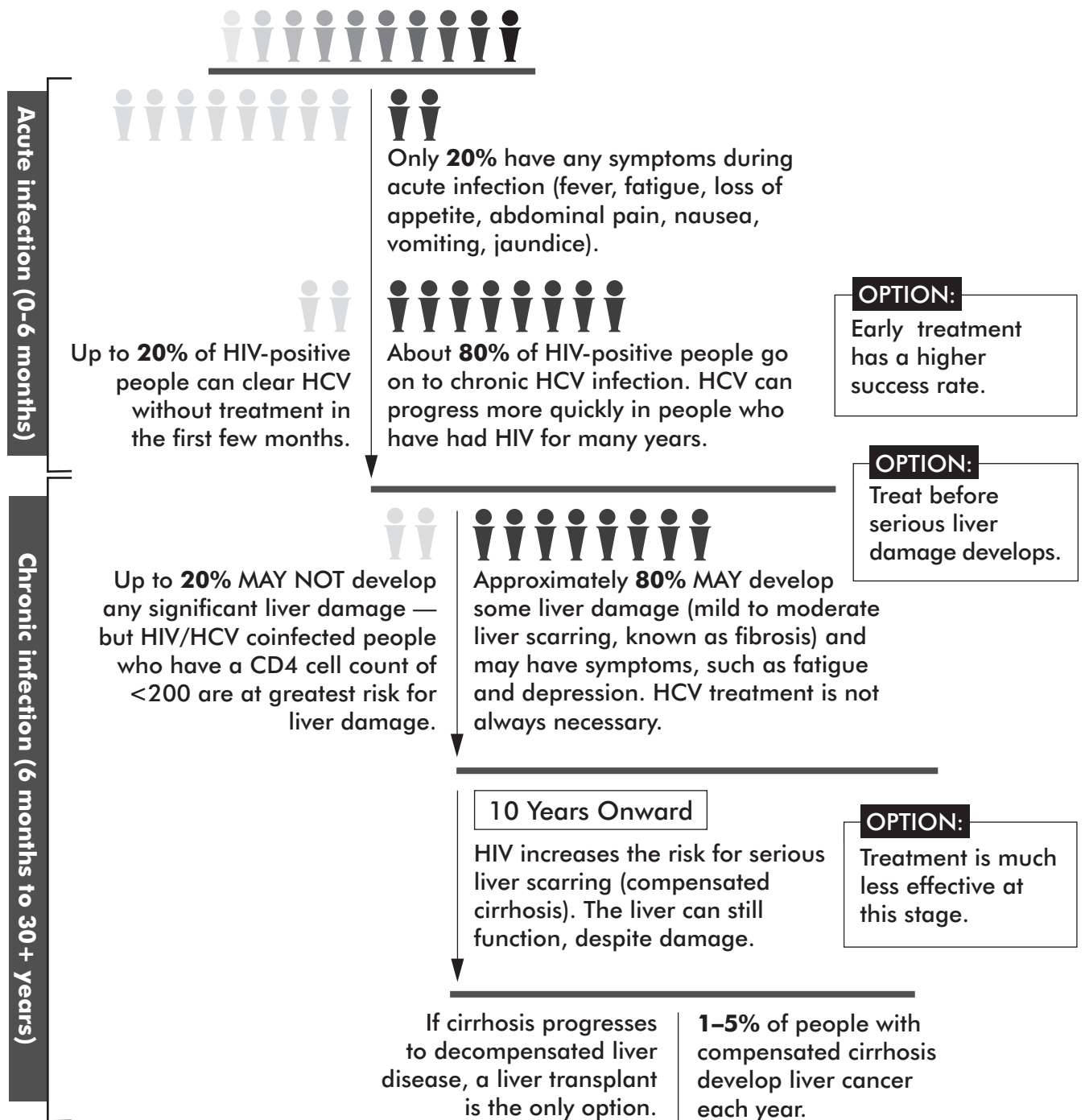
- HIV coinfection
- Alcohol intake, especially more than 50 grams/day, or the equivalent of four to five glasses of wine (see “Alcohol and HCV,” page 69, for more information)
- Aging
- Duration of infection
- Older at time of infection (over 40 years of age)
- Hepatitis B coinfection
- Male sex

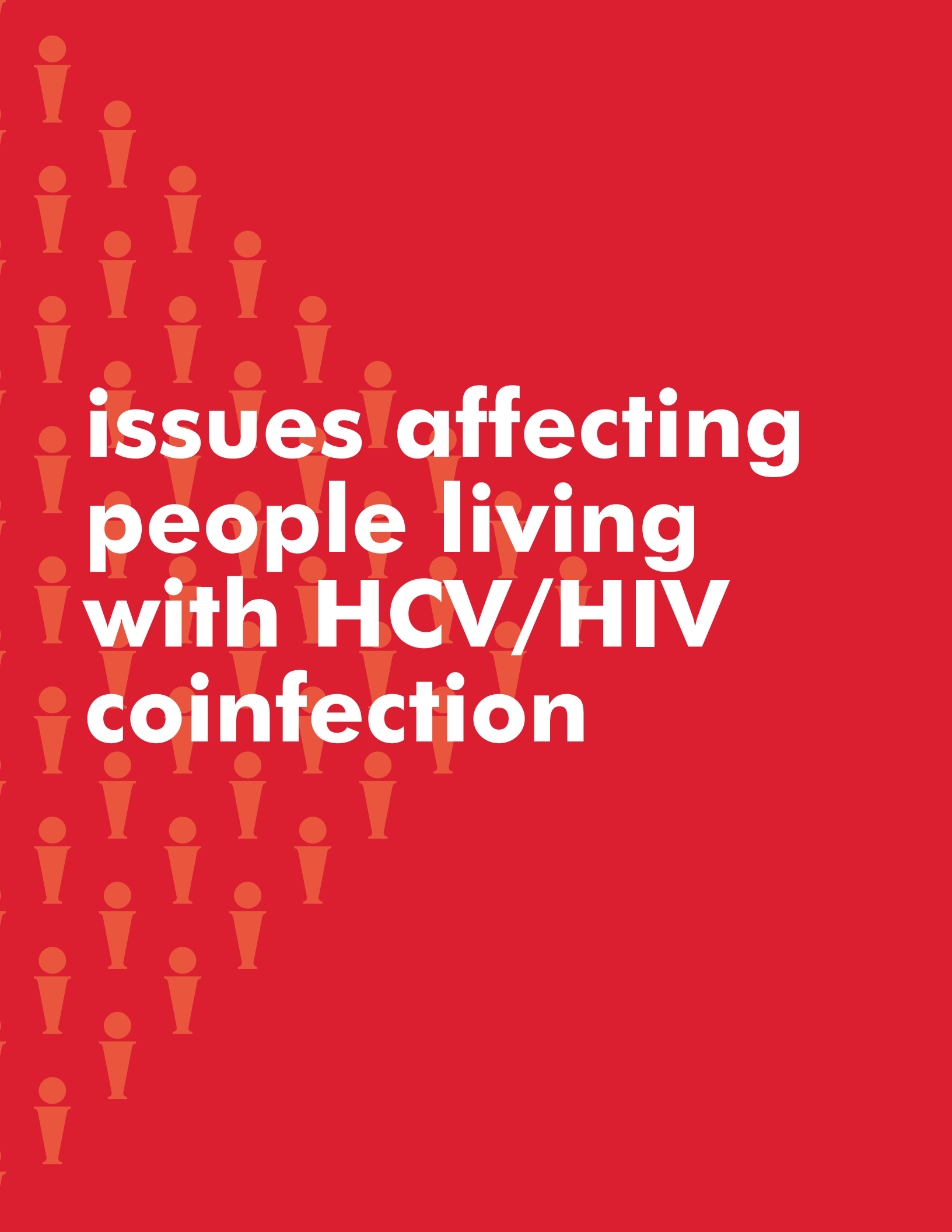
### How can you protect your liver?

There are many things that you can do to support liver health:

- Having another viral infection in your liver can worsen HCV, so get vaccinated against hepatitis A and hepatitis B.
- Drink less or stop drinking alcohol altogether—the less you drink, the better for your liver. *Sometimes drinking less, or not at all, is more important than treating HCV.*
- Maintain normal weight—being overweight increases your risk for fat deposits in the liver, which makes HCV harder to treat.
- Drink a lot of water to help your liver filter out waste and toxins.
- Eat less fatty, salty, and sugary food when possible.
- Try to eat more fresh fruit and vegetables, complex carbohydrates, low-fat, high-fiber foods, and an adequate amount of protein.
- Ask questions and get support. Talk with other people who are living with hepatitis C or HIV and HCV.

**Fig. 1: Risk of HCV progression in HIV-positive people**





**issues affecting  
people living  
with HCV/HIV  
coinfection**

# Acute HCV infection in HIV-positive gay men

## Dealing with a new diagnosis, disclosure, and treatment decisions

Outbreaks of acute HCV infection have been reported among HIV-positive gay men in the United States, the United Kingdom, France, and the Netherlands. Many of these cases were sexually transmitted. In the United Kingdom, HIV clinics identified many cases of acute HCV through routine monitoring of liver enzymes, which is required during HIV treatment.

These men were open about their HIV status and selected other HIV-positive men as sex partners, as part of their choice to responsibly deal with HIV. Unfortunately, the lack of information about sexually transmitted HCV meant that they did not know that they were at risk, or how to protect themselves and their partners.

Being diagnosed with HCV after many years of living with HIV can be very hard to deal with. Some people say it brings back feelings they experienced when they were diagnosed with HIV.

The advantage of finding hepatitis C infection during the acute phase is that treatment is more likely to clear the virus. This is especially important for people who have a harder-to-treat HCV **genotype**, such as 1 or 4. But the decision to treat early—although medically recommended—needs to be balanced against a person’s life circumstances, concerns about how they will deal with side effects of HCV treatment, the risk of developing liver damage in the future, and optimism that newer, easier-to-tolerate drugs may become available in the next five to ten years. Some people choose to treat their HCV as soon as possible, to reduce further sexual transmission.

*“It changes how you think about sexual risk.”*

*“Prior to the HCV infection, I had a reasonably active sex life, mostly with other HIV-positive men. In these circles, the issue of HIV disclosure is resolved by the simple fact that everyone is HIV-positive. However, because I do not really understand how I acquired my HCV, I am less clear about how to protect others from onward transmission. I suspect that disclosure within the group of HIV-positive men would be very similar to disclosing one’s HIV status to a prospective sexual partner who was HIV-negative, indeed maybe harder because of the lack of understanding over what steps to take to protect them. The solution of finding other men in a similar position to mine means that my sexual partners would have to come from an even smaller group than they do at present.”*

*“Living with HCV has been difficult. When I discovered my HIV infection I told almost no one. When I discovered my HCV infection I told too many people, which I now regret since it means I have less control over who knows and who does not.”*

*“At the time I was diagnosed, I had been feeling really ill for about six weeks—tired all the time, pains everywhere. My regular doctor failed to diagnose it but my HIV clinic picked it up straight away. In a way it was a relief because at last I knew what was causing it.”*

*“After diagnosis, I was determined to have the treatment immediately....”*

*“I needed not to be infectious....”*

*“... My concern turned to my partner, and I resolved to get rid of the HCV as quickly as possible. Six months after treatment I feel very lucky to have a ‘sustained virological response.’ I had all the side effects during treatment, and it truly was the worst time in my life, but it was all worth it.”*

*“I know I am not an easy patient. I don’t think I could have done the treatment if it had not been for the unflinching support of someone who was totally devoted to me.”*

*“Deciding on treatment for the HCV was a difficult process. I have an excellent relationship with my HIV doctor, but there was considerable pressure from the HCV specialist for me to start treatment immediately. Because I have lost the sight in one eye as a result of CMV in the 1990s, I also consulted my ophthalmologist. She told me that the current HCV treatment carries a risk (for a minority of people) of causing fuzzy spots in the eyes. As a result of this information I decided not to use HCV treatment at the time. I was not willing to risk any further damage to my eyesight. I do not drink, which will hopefully slow down the progression of any liver damage. In twenty years I will be in my seventies, and I suspect that it will not be the HCV that kills me. Over this time I gamble that HCV treatment will improve.”*

# Chronic HCV/HIV coinfection

## Living with HIV and hepatitis C over the long-term

It is very common for people who became HIV-positive through blood products or sharing injection drug equipment to also be infected with viral hepatitis, including HCV.

Most people in this situation were likely to have been infected with HIV and HCV around the same time, and many have been living with both infections for many years.

Many people in this situation are concerned about the higher risk of HCV-related complications and liver damage due to the fact that they've had HCV for so long. Long-term coinfection may tilt the balance in favor of hepatitis C treatment.

## HCV transmission to sex partners

Heterosexual couples are often told that they are at little or no risk of sexually transmitted HCV.

When one or both partners are coinfecting with HIV, assessing risk becomes more complicated. Although being on HIV treatment and having an undetectable viral load reduces the risk of sexual transmission of HIV, it does not provide complete protection.

## Treatment decisions

The choice about when to treat HCV is different for people who have had either infection for a very long time.

HCV treatment is difficult because most people get side effects that make them feel more tired and unwell. This can interfere with work and family commitments and with general quality of life. HCV treatment can affect mood and increase depression. Some people use alcohol to manage anxiety and depression, even though alcohol itself causes depression and liver damage. Cutting out—or cutting down on—alcohol during HCV treatment can be difficult but very beneficial. Since response rates to treatment are lower in people infected with HCV genotype 1 or 4, some of those people choose to wait for better treatment.

*“Even though I was diagnosed in the early '80s when HCV was called non-A non-B, that diagnosis was irrelevant compared to HIV. Now it has changed: while HIV is often under control, HCV has become the main cause of death for coinfecting people.”*

*“I can't remember exactly when it was that I learned I had HCV but it was within a couple of years or so of receiving my HIV diagnosis and that was in early 1987. While I had experienced my HIV diagnosis as a devastating and life-changing blow, it barely registered when I was told I had HCV. The only people I told were other ex-junkies who I knew were also being tested. Even though my family and friends knew that I was HIV-positive, I didn't consider HCV big news.”*

*“I am hoping that in a year or so, some of the drugs in the pipeline will prove to be more effective. I hope that my liver will hold that long. I am really not looking forward to starting treatment with what is available at the moment—but will do if that is what is required. But I am fearful because my quality of life is gonna drop to the floor—and for a long period....”*

*“Careful monitoring is really the key to safely being able to delay treatment, especially if your liver enzymes remain stable and scans show little fibrosis.”*

*“For years I was told that the risk of sexual transmission of HCV was very low. In fact, condom use is not recommended for heterosexual couples in which one partner is HCV-positive.”*

*“Since {our} diagnosis with HIV we have practiced safe sex—condoms—primarily because of issues of HIV reinfection (especially as we are both on different combinations). But we had unsafe sex for nearly three years and he’s not HCV-positive....”*

*“More recently, after my (HIV) viral load had been undetectable for several years, my partner and I stopped using condoms, although sometimes we worry about the potential risks of HIV and HCV infection.”*

*“I know people doing very well on HCV treatment, but at the moment, I don’t feel strong enough to try it. The fact that there are new treatments coming in a few years, even though they will probably be added to the current treatment, has helped me to take the decision to check my liver every one to two years (by FibroScan or biopsy) and wait for better treatment options.”*

*“Having the experience of sharing with other people who have the same kind of health problems—it helped me to make informed decisions, it helped me to know where the information was available. They helped me understand things that were not easily understandable—because there’s quite a bit of jargon there.... Peer support, by people who are coinfecting and the coinfection clinic are crucial.”*

If your liver has already been badly damaged by HCV, then treatment is more important. In order to find out whether this is the case, you need to have some of the diagnostic tests discussed in the following pages.

Planning for treatment is important. With appropriate support, many people can manage treatment well when they need it. Many say that peer support is essential.

Access to treatment is not always straightforward, especially for uninsured people, and people who are using drugs and alcohol (see “HCV treatment and people who use drugs,” page 51).





# tests and monitoring

## Diagnostic tests

HCV testing is recommended for all HIV-positive people. Even if you've already been diagnosed with HIV and HCV, it's important to know how HCV is diagnosed and monitored. Unlike with HIV, a positive HCV antibody test result does not always mean that someone is chronically infected.

HCV testing is a two-stage process. The first test is usually an HCV antibody test. If the result is positive, it means that you have been infected with hepatitis C in the past, and that you may still be infected. People who have spontaneously cleared hepatitis C without treatment remain antibody-positive for years afterwards. On the other hand, antibody test results are sometimes negative even when someone does have chronic hepatitis C. This may occur if:

- Your CD4 cell count is low (usually below 200), because the immune system may not be producing antibodies; or
- You are tested very soon after being infected, since antibodies take 6 to 24 weeks to develop.

An HCV RNA (viral load) test is necessary to confirm whether you have chronic infection (that you have HCV). The viral load test looks for genetic material of the HCV virus in the same way as an HIV viral load test detects HIV. If you have detectable HCV RNA in your bloodstream, it means that you are currently infected with HCV. If your hepatitis C viral load is undetectable, a second test should be done six months later. If two successive test results are undetectable, then you have cleared HCV.

**Table 1: Diagnostics: acute, cleared, or chronic HCV**

<b>Diagnosis:</b>	<b>Prior, cleared HCV infection</b>	<b>Acute HCV infection</b>	<b>Chronic HCV infection</b>
<b>Antibody Test</b>	Positive	Negative; becomes positive within 6 to 24 weeks	Positive
<b>Viral Load Test</b> (HCV RNA)	Undetectable on two tests, performed at least six months apart	Detectable within 1 to 2 weeks, usually very high	Detectable
<b>ALT Test</b> (Alanine Aminotransferase, a liver enzyme)	May be normal, fluctuate, or be persistently raised	May be up to 7 to 10 times above the normal level	May be persistently normal, fluctuate, or be persistently raised

## **Hepatitis C viral load (RNA testing)**

The hepatitis C virus is much smaller than HIV, and it reproduces at a much greater rate (trillions versus millions of copies per day).

People with hepatitis C often have very high viral loads—in the tens of millions—a very different scale than HIV.

Coinfected people usually have higher hepatitis C viral loads than people with HCV alone.

Unlike HIV, the hepatitis C viral load does not indicate or predict the degree of liver damage, nor is it used to decide when to start treatment. This is sometimes confusing, especially for people who are used to using HIV viral load as a barometer for risk of disease progression and a factor in treatment decisions.

However, the pretreatment hepatitis C viral load is one of the predictors of response to treatment. HCV treatment is less effective for people with HCV RNA greater than 400,000 IU/mL.

## **About HCV RNA testing**

There are two types of viral load tests. Both measure the amount of hepatitis C virus in a blood sample, using a standard measurement, international units per milliliter (written as IU/mL).

- i) Qualitative testing is used to diagnose HCV and to monitor response to treatment, because it can detect very low levels of HCV RNA. The most sensitive qualitative test can detect a viral load as low as 5 IU/mL. Results are reported as either detectable or undetectable.
- ii) Quantitative testing measures the amount of HCV per milliliter of blood.

Quantitative testing is usually used to obtain a pretreatment viral load count. Qualitative testing is often used during diagnosis and to monitor response to treatment during HCV therapy.

## **Routine tests**

After a confirmed HCV diagnosis, your clinic should run a series of additional blood tests.

These include HCV viral load (for people who were diagnosed with a qualitative viral load test) and HCV genotype; tests for hepatitis A and B; full blood count (FBC) and clotting studies; liver enzyme tests (including **ALT/AST**, **albumin**, and **GGT**); thyroid function test (TFT); serum iron; liver autoantibodies; and liver ultrasound.

Information about these tests is included below.

## HCV genotype

There are at least six different viral strains of hepatitis C, known as genotypes, numbered from 1 to 6 in order of their discovery. Each genotype has some variations called subtypes. Subtypes are designated by alphabetical letter, also in order of their discovery. One genotype cannot change into another, but it is possible to be infected with more than one genotype at the same time, or to become reinfected with a different genotype.

It is essential to know your HCV genotype in order to plan when to use treatment and how long to stay on treatment. If your clinic hasn't done this, be more insistent. This is clearly stated as a strong recommendation in various recognized sets of guidelines for treating HCV/HIV coinfection.

**Table 2: HCV genotype by region**

<b>Region</b>	<b>Predominant HCV genotype</b>
<b>Europe, North America, Japan</b>	Genotype 1a, 1b (genotypes 2 & 3 are less common)
<b>Southeast Asia</b>	Genotype 3
<b>Egypt, the Middle East, Central Africa</b>	Genotype 4
<b>South Africa</b>	Genotype 5
<b>Asia</b>	Genotype 6

## Liver enzyme tests: ALT and AST

Liver enzymes are proteins that have specific functions. When the liver is injured, some of these enzymes leave the liver and enter the bloodstream.

Several things can cause liver enzyme levels to increase to abnormal levels, such as liver toxicity from prescription and over-the-counter medications, herbs, vitamins, and supplements; exposure to toxic fumes; heavy alcohol consumption; acute or chronic viral hepatitis; and detoxifying from drugs and/or alcohol. Many HIV medications cause liver enzyme elevations—usually not to dangerous levels. In some cases, people may need to switch or discontinue certain drugs. Keep in mind that liver enzyme levels often fluctuate or are persistently elevated in people with chronic HCV. It's really very high levels or dramatic changes that doctors are concerned about.

It's especially important for coinfecting people who are taking antiretrovirals (ARVs)—or any other drugs known to be hard on the liver—to have liver enzyme levels measured routinely. Liver enzymes are measured through a group of blood tests, often called Liver Function Tests (LFTs).

Although they are often referred to as Liver Function Tests (LFTs), these tests do not actually measure how well the liver is working. Results from each test should be evaluated in relation to other information.

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are two important liver enzymes. ALT is produced by the liver.

Increases in ALT are usually a signal of liver inflammation or damage; however, ALT is not a reliable marker for predicting whether your HCV will progress, or for indicating the severity of liver disease, since liver enzyme levels often fluctuate in people with chronic HCV. Up to a third of all people with chronic HCV have persistently normal ALT, even though some of these people have serious liver damage. ALT should be monitored routinely, since persistently increasing levels may suggest HCV progression.

AST is made in the heart, intestines, and muscles, so it is not a sensitive marker for liver injury. AST is often used to monitor liver inflammation and damage in combination with other tests.

## **Other liver enzymes, ALP, GGT, bilirubin, albumin, and prothrombin time**

It is important for people with HCV and HCV/HIV to undergo routine monitoring of ALP, GGT, bilirubin, albumin, and prothrombin time.

Alkaline phosphatase (ALP) is present in tissues throughout the body, including the liver. Increased ALP levels in the bloodstream are a sign of disease or damage to tissues. Medical providers can test specifically for ALP from the liver. Elevated ALP from the liver is a sign of blocked bile ducts caused by liver disease.

Some medications, including the HIV protease inhibitors atazanavir and indinavir, can cause ALP elevations.

Gamma glutamyl transferase (GGT) is produced in the bile ducts. GGT may be elevated by any type of liver disease, by heavy drinking, and some medications.

Bilirubin is a by-product from the breakdown of red blood cells. The liver is involved with processing bilirubin. When the liver is damaged, it may be unable to process bilirubin, and the total bilirubin level may become elevated; jaundice, dark urine, and pale stool are common signals of elevated bilirubin. Some drugs, including the HIV protease inhibitors atazanavir and indinavir, can cause elevated bilirubin levels.

Albumin is a protein made by the liver. It carries drugs, hormones, and waste products through the bloodstream and maintains fluid levels within the body. Abnormally low levels of albumin are a sign of serious liver damage.

PT (prothrombin time; ProTime): PT testing measures the amount of time it takes for blood to clot. When the liver is damaged, its ability to make clotting factors is impaired. A prolonged PT interval indicates decreased liver function.

**Table 3: Track your lab work**

Date						<b>Normal ranges (W=women; M=men)</b>
<b>CD4 count</b>						Measured in cells/mm <sup>3</sup> ; ranges from 0 to over 1,600. Higher the better; over 200 reduces risk of OIs.
<b>HIV viral load</b>						Measured in copies/mL; ranges from undetectable to over 1 million (rare).
<b>HCV viral load (RNA)</b>						Measured in IU/mL; ranges from undetectable to over 40 million. When over 400,000 it reduces the chance of treatment success.
<b>ALT</b>						W: 7–30 units/L M: 10–55 units/L
<b>AST</b>						W: 9–25 units/L M: 10–40 units/L
<b>ALP</b>						W: 30–100 units/L M: 45–115 units/L
<b>GG</b>						W: over 45 U/L M: over 65 U/L
<b>Bilirubin (direct)</b>						0.0–0.4 mg/dl (US) 0–7 umol/L (SI units)
<b>Bilirubin (total)</b>						0.0–1.0 mg/dl (US) 0–17 umol/L (SI units)
<b>Albumin</b>						3.1–4.3 g/dL (US) 31–43 g/L (SI units)
<b>PT</b>						11–13.5 seconds (PT of 1.5 to 2 times above the range is abnormal)

### Screening for liver cancer

People with HCV-related cirrhosis are at risk for liver cancer. Regular screening can detect early-stage liver cancer in people with HCV. Usually, screening consists of liver imaging by methods such as ultrasound or computed tomography (CT), and a blood test measuring alpha-fetoprotein (AFP) levels. Screening is recommended every six months.

## Liver biopsy

A liver biopsy is a procedure where a small sample of liver tissue is taken and sent to a lab, where the sample is examined under a microscope for cell abnormalities.

A liver biopsy is considered the diagnostic gold standard for assessing liver disease because it is the most reliable way to learn both the stage (amount of scarring that has already occurred) and the grade (amount of inflammation, which drives future scarring) of liver disease. It can also identify other causes of liver disease that are not hepatitis C-related.

During liver biopsy, a needle is inserted between the ribs and into the liver to remove a small sample of liver tissue. The procedure is uncomfortable, occasionally painful, and carries a small risk of complications (1–3%), such as puncturing adjoining organs or hemorrhage, and a much, much smaller risk of death.

Biopsy is not perfect; it is subject to errors in sampling and in reviewing. Results may be inaccurate when a sample is either too small or comes from a part of the liver that is more or less damaged than the rest. Samples need to be studied by a pathologist with expertise in evaluating liver disease. In addition, biopsy is an expensive procedure, though it is covered by Medicaid.

Biopsies are not pleasant, and many people with HCV are reluctant to have one. Still, a biopsy remains the best and most reliable way to know the level of liver damage. Luckily, reliance on biopsy as a requirement for HCV treatment is an area that is changing: some experts recognize that people with a high chance of response to treatment (those with genotype 2 or 3, or lower HCV viral load) do not need a biopsy before HCV treatment. Biopsy may be most useful for informing treatment decisions in people with harder-to-treat genotypes (1 and 4) who may be able to wait for newer therapies if they do not have serious liver damage.

A biopsy should only be performed by an experienced doctor with a good record of successful biopsies. Preferably, liver biopsy should be guided by ultrasound to reduce the chance of puncturing an adjoining organ, and to pinpoint areas of damaged liver tissue for sampling. If you are concerned about the pain, ask your doctor about your options for pain management during and after the procedure. Ask around—it may be easier to find a good doctor by talking with people who have had a biopsy.

*“So, right now I am considering treatment because I see a lot of people dying from hep C and I’ve had it for a long time. My viral load is OK, my liver enzymes are OK, but we know that the only way to know the real situation is a liver biopsy. But to be honest, I am ready to start treatment tomorrow but I don’t want a doctor to put a needle in my liver.”*

Researchers are looking at less invasive alternatives to biopsy (see below and next page).

### Interpreting biopsy results

There are different systems for measuring liver inflammation and fibrosis. All go from zero to a maximum score; the higher the number, the more inflammation or fibrosis. The Ishak scale measures inflammation on a scale of 0 to 18, and fibrosis on a scale of 0 to 6. The METAVIR scale measures inflammation on a scale of A0 to A3 (“A” is for activity), and fibrosis on a scale of F0 to F4 (“F” is for fibrosis). Guidelines define mild liver damage as a modified Ishak score of 3 or less and a fibrosis score of 2 or less, and moderate liver damage has an inflammation score of 4 or more and/or a fibrosis score of 3 to 5.

	<b>Inflammation</b>	<b>Fibrosis</b>
<b>Ishak</b>	0–18	0–6
<b>Metavir</b>	A0–A3	F0–F4
<b>Knodell</b>	0–18	0–4

### When should you get a biopsy?

Having a biopsy can help you make a treatment decision by identifying how much liver damage you have. Despite the discomfort and risk of complications it involves, biopsy is still an important test for assessing the need for treatment and for monitoring HCV progression over time. It is therefore recommended periodically during chronic infection (more frequently for coinfecting people compared to HIV-negative people), and especially recommended before deciding to start treatment.

In untreated people, a follow-up biopsy is recommended every five years for persons with HCV alone, and every two to three years for coinfecting people.

### Alternatives to a biopsy: non-invasive markers of liver disease

There is new research to see whether results from lab tests can be used in place of a biopsy to predict the extent of liver damage. This area of research is important, as it could change how HCV is managed in the future.

Recent studies evaluating combinations of these blood markers suggest they are useful for identifying serious liver damage in mono- and coinfecting persons, but it remains controversial whether they are ready for “prime time” (meaning: not yet a reliable substitute for a liver biopsy).

### Measuring liver stiffness (“FibroScan”)

The FibroScan is a non-invasive approach that is already showing promising results. FibroScan measures the stiffness or elasticity of the liver using an ultrasound probe on a vibrating apparatus to create waves and measure their speed. Wave speed reflects liver stiffness;

the harder the liver tissue, the more rapidly the waves will pass through it. Although this scan is much less sensitive in detecting mild or moderate liver damage, it is very sensitive to severe damage and can identify people who may urgently need HCV treatment.

FibroScan is not painful or invasive. In the US, some clinics are using FibroScan to monitor people with HCV/HIV coinfection.

### **Non-invasive biomarkers of liver disease (blood tests)**

Combinations of blood tests are being used to assess liver damage, in both HCV-monoinfected and HCV/HIV-coinfected people. These tests are most useful for identifying or ruling out cirrhosis rather than mild-to-moderate liver damage.

Tests that have shown promising results in people with coinfection who are taking ARVs include:

- SHASTA Index
- FibroTest
- Hepascore
- Fibrometer

*“I refused to have a biopsy and for years argued with the specialists, but last month I had a FibroScan using a new machine. This tests how stiff the liver is and can give an indication of the extent of liver damage. It was easy and painless.*

*The consultant told me I should get the test re-done every six months. Given that for a long time I'd been getting worrying results from my blood tests on an on-and-off basis, getting results from the scan were very reassuring.”*

The background of the slide features a repeating pattern of stylized human figures. Each figure is composed of a small circle for a head and a larger, inverted triangle for a body, all in a light orange color. These figures are arranged in a grid that tapers from left to right, creating a sense of depth and movement. The overall color scheme is a vibrant red.

# **managing and treating HCV**

One approach is to decide first exactly what your priority is. Clearing the virus now is not the most important goal for everyone. In some cases, treatment may be more likely to improve the condition of your liver than to clear the virus. In other cases, treatment may not be necessary right away, or ever.

For some people, deciding whether to do treatment is an easy decision; for most, it isn't. There are a lot of factors to be considered.

This section focuses on conventional treatment. Lifestyle-related choices that help your liver are covered later in the section, "Living with coinfection," page 69.

## Deciding whether to treat HCV

Deciding whether or not to treat hepatitis C is an individual and complex decision. Some people really need HCV treatment now. It may be a bridge until newer, more effective, and less toxic therapies are available. Medical need is one of several other factors to be taken into account.

You may know early on whether it is necessary to use the full course of HCV treatment. If, after 12 weeks, it looks like treatment will not work for you, you may decide to stop.

## Advantages of using HCV treatment

- You can clear the virus.
- Treatment can improve liver health by reducing inflammation. It may also reverse fibrosis. This can happen even in people who do not clear the virus, although less often.
- It will stop the risk of passing HCV to sexual and drug-using partners.
- Clearing the virus removes the risk of mother-to-infant transmission.
- Treating HCV before starting HIV treatment will reduce the risk of liver toxicity from HIV drugs.
- The treatment period is likely to be only 12 to 18 months, not lifelong.
- Treatment may reduce the risk of long-term complications, including liver cancer, even in people who do not clear HCV.

*"My doctors have warned me my health may be at more risk from HCV than HIV. I've been urged to have biopsies done of my liver and to consider going on treatment for HCV. I've decided to delay embarking on therapy for two main reasons: firstly, I have a genotype that is less responsive than others to therapy; and secondly, I don't want to take time out from work, which I'd probably need to do to accommodate the side effects. I like my life at the moment and I don't want that to change on the off-chance that I can clear the HCV. My current strategy is to wait until more effective drugs come along."*

*"Treating HCV to avoid the threat of future cirrhosis is a really good thing but, at the moment, I don't feel strong enough to try it. For me, maintaining a high CD4 count is a better way of protecting my liver."*

## Advantages of delaying treatment

*“Six months after treatment I feel very lucky to have achieved a ‘sustained virological response.’ I know of other guys who have not been able to stick to the treatment, and others for whom it has failed. I had all the side effects during treatment, and it truly was the worst time in my life, but it was all worth it. All the side effects went away as soon as I finished the treatment, and I feel pretty much like my old self now.”*

*“For me it was very important to have the HIV and HCV treated together—they are related, and their progression is related. A liver specialist is not fully prepared to deal with somebody that lives with the double stigma of having these diseases...and didn’t really understand some of the social and psychological implications.”*

*“I’ve heard about what happens in families during HCV treatment, people get so depressed, in such a mental state—the husband or wife will say: I hate you...because the people on interferon are so unbearable...it’s not worth it! There’s no guarantee you’ll get rid of it, or even get better—get worse—but your life can be ruined!”*

- The major disadvantages to treatment are the side effects and the impact they may have on your life during the treatment period.
- Occasionally, the side effects can be so severe that they force you to stop treatment. In rare instances, you could be left with an illness after you stop treatment, such as thyroid disease or diabetes.
- Some people have reported that the side effects have persisted, leaving them feeling unwell long after the end of treatment.
- Treatment might not work for you.
- There are many new drugs in development for HCV that may be more effective and easier to tolerate; however, they are unlikely to be available through clinical trials for at least five years. Trials for people with HCV alone usually begin earlier. Clinical trials in people with coinfection are likely to be delayed until after results from HCV mono-infection studies.
- If your liver is healthy, you may be able to delay treatment.
- If you are thinking of conceiving a child in the next year, consider delaying treatment, since ribavirin can cause birth defects. Men and women should take precautions to avoid pregnancy during HCV treatment and for at least six months afterward. Women who become pregnant on ribavirin need to discontinue HCV treatment. More information on ribavirin and pregnancy is available from the ribavirin pregnancy registry: <http://www.ribavirinpregnancyregistry.com/>.

## Who needs HCV treatment?

Treatment guidelines generally agree about when to treat, and who to treat, regardless of HIV status. Sometimes treatment is recommended more aggressively, such as for all coinfecting people when “the benefits of therapy outweigh the risks.”

- HCV treatment is more effective when given during acute infection.
- People with mild liver disease do not require treatment right away.

- Treatment should be offered to people with moderate liver damage, since they are at risk of progression to cirrhosis.
- People with compensated cirrhosis can be treated, but treatment is less likely to be effective, and side effects may be worse; careful monitoring is required.
- People with decompensated cirrhosis cannot be safely treated for hepatitis C; a liver transplant is the best option.

## How is HCV treated?

Hepatitis C treatment is a combination of two drugs, pegylated interferon and ribavirin. Pegylated interferon is a man-made version of a chemical messenger made by the human body. Interferon stimulates the immune system to fight viruses, so it has antiviral and immunologic activity. Pegylation means that a small molecule has been attached to interferon to keep it in the body longer, to make dosing more convenient, and to render treatment more effective.

There are two types of pegylated interferon (PegIFN):

- alpha-2a (manufactured by Roche, trade name Pegasys), and
- alpha-2b (manufactured by Schering Plough, trade name PEG-Intron)

Pegasys is a liquid that comes in one vial and is stored in the refrigerator. Everyone uses the same dose of Pegasys, regardless of their weight. PEG-Intron is a powder that has to be reconstituted with purified water, both of which come in separate vials. PEG-Intron is dosed by weight.

Both types of pegylated interferon—Pegasys and PEG-Intron—have been studied in patients with varying severity of disease. They have not been compared directly, and so it is difficult to know whether one may be better than another in different circumstances.

Ribavirin is a nucleoside analog from the same family as many HIV drugs, but it does not work against HIV. On its own, ribavirin is not an effective treatment for hepatitis C; it needs to be used with pegylated interferon. It is given as a pill or capsule, twice daily. Ribavirin is usually dosed differently depending on body weight and genotype in HCV monoinfection, and often in HCV/HIV coinfection as well.

## How long is a course of HCV treatment?

In coinfection, treatment is currently recommended for at least 48 weeks for all genotypes. Some doctors are extending treatment for people with genotypes 1 and 4.

Recent research has looked at tailoring treatment according to individual response. In particular, people who are HCV/HIV-coinfected may require a longer course of HCV treatment than those who are HCV-monoinfected, especially persons with HCV genotype 1.

## Goals of HCV treatment

### *Curing HCV*

The primary goal is to get rid of HCV— treating to cure.

In hepatitis C, a sustained virological response, or **SVR**, means that a person does not have detectable virus in his/her bloodstream six months after completing hepatitis C treatment.

Most people who have had an SVR remain virus-free, although there have been fewer long-term studies of coinfecting people than those with HCV alone.

Although some recent research has found very low levels of hepatitis C in the blood and liver tissue of some sustained virological responders, this small quantity of virus may not have any significant effect on liver health.

### *Improving liver health*

A secondary goal of HCV treatment is to improve liver health by reducing inflammation, and sometimes, reversing fibrosis. This even happens in patients who do not have an SVR, although only in about half the number of cases.

In some cases, the condition of the liver may worsen after HCV treatment, particularly among people who did not clear the virus; the reasons for this are unclear.

### *Maintenance therapy*

Maintenance therapy (with full- or reduced-dose pegylated interferon, either continuously or intermittently) may provide people

with serious liver scarring who do not respond, or who relapsed after HCV treatment, with a holding strategy until better treatments become available.

Long-term studies of people with HCV alone have reported that treatment reduces the risk of cirrhosis, liver cancer, and liver-related death, even in people who did not have an SVR.

For HCV/HIV-coinfected people, there may be an additional benefit from HCV treatment: less risk of liver-related side effects from HIV drugs.

### ***Predicting the response to treatment***

Several factors can help you predict the likelihood of HCV treatment response, but the only way to know how you will respond is to treat. The most significant factors are:

- HCV genotype (2 and 3 are more sensitive to treatment than 1 or 4);
- HCV viral load (treatment is more effective with an HCV viral load below 400,000 IU/mL);
- Race (treatment is less effective for African Americans; ongoing research is looking at this question);
- Amount of liver damage and steatosis (treatment is less effective for cirrhotics and people with steatosis);
- HIV status (treatment is less effective for HIV-positive people than for HIV-negative people);
- Body weight (treatment is less effective for people who weigh more than 75 kg [165 lbs]);
- Adherence to treatment, including maintaining the full dose of ribavirin and interferon at least 80% of the time; and
- Effective management of side effects.

## **Evaluating the response to treatment**

The response to HCV treatment is measured by HCV viral load tests at different times.

### ***SVR (sustained virological response)***

An SVR means that HCV is not detectable in blood six months after completing treatment. Many experts think of SVR as a cure, and it is an indication of long-term remission.

SVR rates are usually the most important results to look for from a clinical trial.

### ***EVR (early virological response)***

An EVR means that the hepatitis C viral load has dropped by 99% (2 logs), or is undetectable after 12 weeks of treatment.

Someone who does not have an EVR has only a very low chance of getting an SVR (only 1% to 4% chance). Usually, people choose to discontinue hepatitis C treatment if they do not have an EVR.

Some people may switch to a lower dose of pegylated interferon to prevent HCV progression at this point (maintenance therapy).

### ***ETR (end-of-treatment response)***

An end-of-treatment response means that no hepatitis C virus is detectable by an HCV viral load test at completion of therapy. Some people with an ETR will see HCV viral load return, usually within 12 to 24 weeks after they have stopped treatment.

### ***Relapser***

The term relapser refers to someone who has an EVR or ETR, but whose virus has rebounded and who didn't achieve an SVR.

### ***Non-responder***

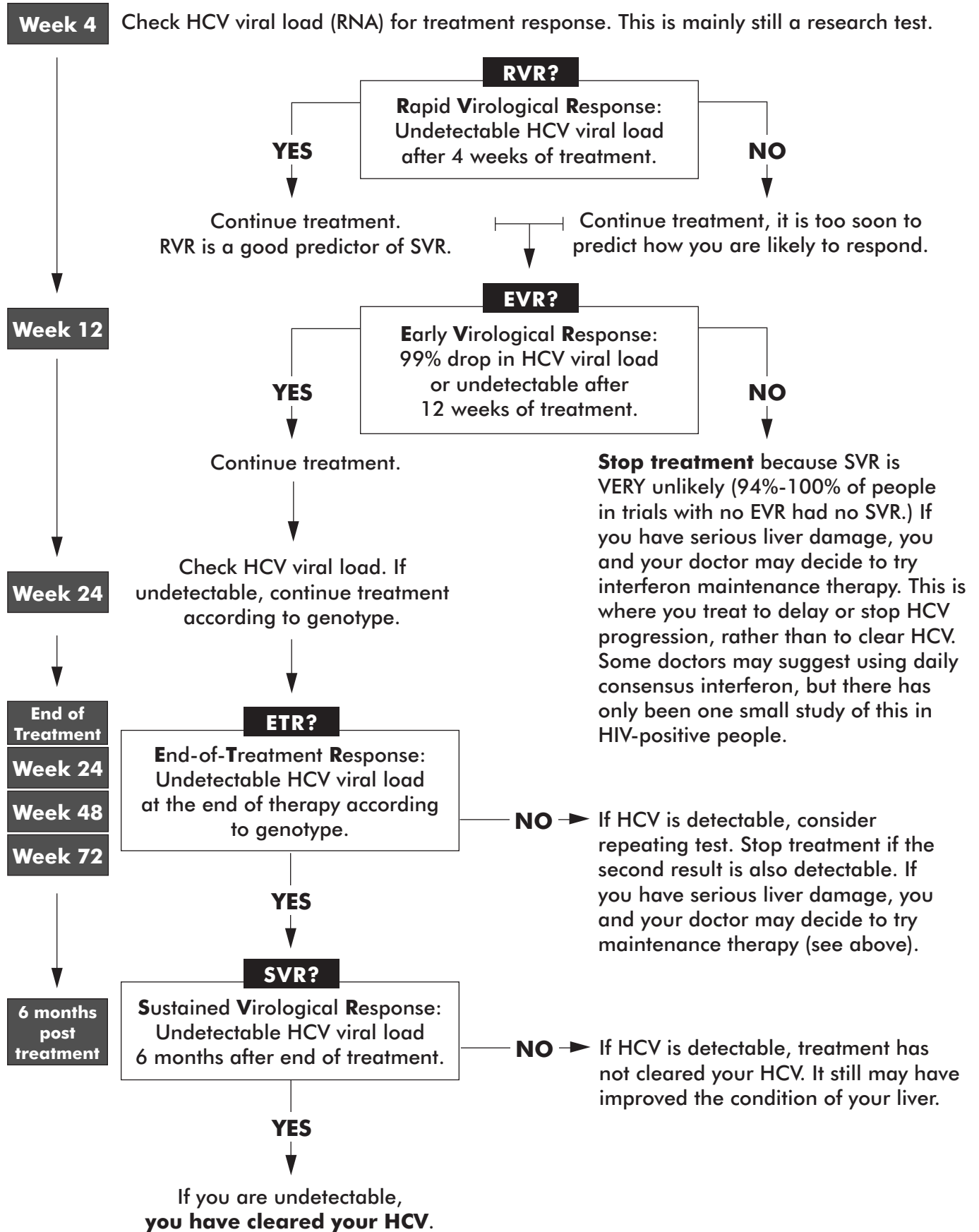
Non-responder is a general term for someone who does not have an EVR, or if they stay on treatment for 24 weeks, does not ever have a 99% drop in viral load or undetectable HCV RNA while on treatment.

### ***RVR (rapid virological response)***

Response to treatment after four weeks is called a rapid virological response (RVR). If HCV viral load is undetectable at this point, it is a good predictor of an SVR later. However, RVR is not good at predicting who is unlikely to respond, so treatment should not be stopped if there is no RVR.

RVR is currently only used in research.

**Fig. 2: Timeline for HIV-positive people on HCV treatment**

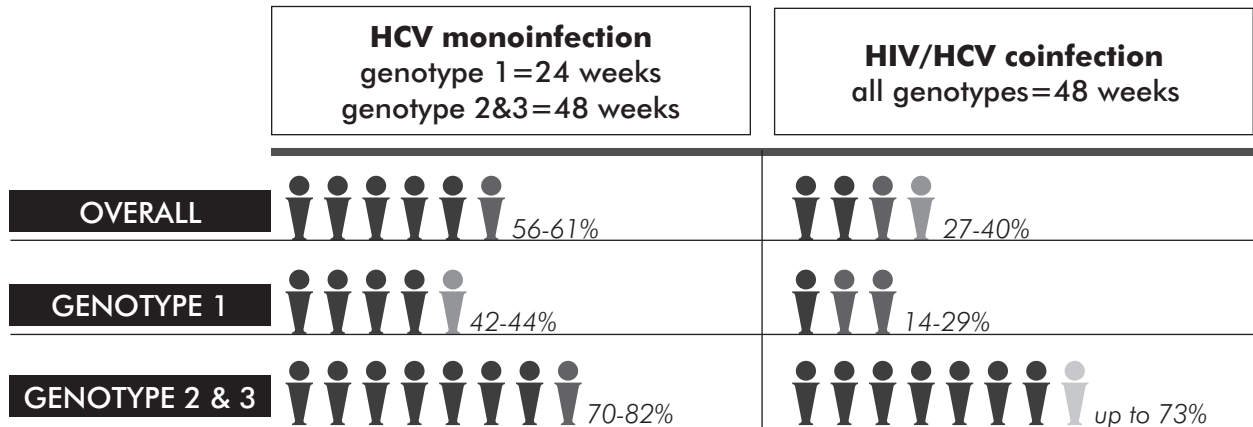


## How well does treatment work?

Clearly, many factors are involved with response to treatment.

The information in Table 4 is an overall snapshot of response rates from clinical trials of HCV treatment with pegylated interferon plus ribavirin.

**Table 4: Sustained Virological Response (SVR) to treatment per HCV genotype**



## Re-treating HCV

The number of monoinfected and HCV/HIV-coinfected people who did not clear the virus during treatment is increasing. Strategies for re-treating HCV, such as using different types of interferon, higher doses of pegylated interferon and/or ribavirin, and a longer course of treatment, are currently being researched.

## Should HIV be treated first?

Generally, HIV treatment should be started first if the CD4 count is under 200 cells/mm<sup>3</sup>, and probably started first if it is between 200 and 350 cells/mm<sup>3</sup>.

There might be some circumstances—perhaps when HCV treatment is likely to be used soon in someone whose CD4 count is already falling—where HIV treatment may be started earlier. So long as HCV infection is stable, many people—especially if they have been infected with HCV for a long time—will treat their HIV first. Treating HIV may delay HCV disease progression by maintaining immune health.

In someone whose CD4 count is already strong (above 500 cells/mm<sup>3</sup>) there is no need to use HIV treatment before HCV treatment.

Using HCV treatment depends on:

- Your willingness and readiness to start HCV treatment, and
- The need for treatment—if liver disease is mild, HCV treatment can be delayed; if moderate to serious, HCV treatment is recommended.

Detailed information about HIV treatment is available from many different sources. For example, the i-Base “Introduction to Combination Therapy” deals with many questions (see “Resources and further information,” page 79).

The most important aspects of HIV treatment are just as relevant in coinfection as in HIV mono-infection, including choice of treatment, adherence, side effects, and resistance. The main differences in considering HIV treatment for someone coinfecting with HCV relate to timing (since some studies have found that coinfecting people have a blunted CD4 cell response to HIV treatment), and concern about liver toxicity and damage as a side effect of HIV drugs.

Some HIV drugs are less liver-friendly than others, although it is not clear whether small increases in liver enzymes increase the risk of clinical disease. Caution is clearly important; ARVs should be selected carefully and liver enzyme levels monitored regularly.

(For more information, see “HIV drugs and HCV infection,” page 61).

### **When should HCV be treated first?**

If HCV treatment is necessary, it is possible to treat people on a stable ARV regimen even if their CD4 count is less than 200 cells/mm<sup>3</sup>. Studies using an older form of interferon suggested that HCV treatment is less effective for people with low CD4 counts, but in more recent studies of pegylated interferon plus ribavirin, CD4 cell count does not seem to be a factor in the success of treatment, although the overall number of people with less than 200 cells/mm<sup>3</sup> was small.

The advantage to treating HCV first if you have a strong immune system is that you can do this without worrying about drug interactions or increased risk of side effects from two sets of treatment.

If you clear HCV, it may also reduce the risk of side effects from HIV drugs when you use them in the future.

It is better not to start treatment for both HIV and HCV at the same time, because side effects can make each other worse.



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# **HCV treatment and people who use drugs**

Hepatitis C treatment has traditionally been withheld from injection drug users, even though current treatment guidelines recommend that treatment decisions be made on a case-by-case basis. Fortunately, this has begun to change. Experience with HIV treatment confirms that it is possible for drug users to adhere to ARVs; moreover, response rates from clinical trials of HCV treatment in IDUs are similar to those reported in non-users.

Don't avoid medical care just because you are using. Many drug users with HCV are being monitored regularly for disease progression and some have begun and completed HCV treatment with Pegasys or PEG-Intron.

It is important to find a doctor who is willing and able to work with drug users and who will treat your HCV. Ask other drug users to recommend a doctor—or to warn you about which ones to avoid.

Try hard not to miss medical appointments, since some doctors will use missed appointments as part of the criteria for deciding whether or not they will treat your HCV. Even if you think your HCV treatment side effects are insignificant, discuss them with your doctor and ask up front how he or she plans to help you manage these side effects so you can get through treatment. If you need pain medication, anti-anxiety drugs, or other medications sometimes associated with “drug use/abuse,” discuss this openly with your doctor before you begin treatment. Be assertive and make an agreement on how the two of you will handle this should the issue arise.

Depression and other mental health diagnoses are much more common among people with HCV, people with HIV, and drug users than in the general population. Many of these conditions can be treated successfully.

### **Working with your clinicians**

- Make sure to work with health care providers that take the time to answer your questions about HCV treatment and side effects.
- Make a list of questions before going to the doctor and bring someone with you if possible.
- Keeping medical appointments is especially important after you start your HCV treatment; your doctor needs to be able to regularly monitor your health and help you with side effects.
- If you need pain medication or other medications with abuse potential, discuss this with your doctor; make an agreement on how the two of you will handle this.
- Identify people in your life who are, or will be, a good source of support for you.
- Consider joining a support group.

People with a history of depression are more likely to develop depression during HCV treatment, although it can happen to people who have not been depressed in the past. If you are concerned about the psychiatric side effects of HCV treatment but want to treat your hepatitis C, consider professional mental health care.

Some people can manage HCV treatment while they are using drugs; others have found that stopping or cutting down on drug use help them prepare for, and stay on, HCV treatment because they feel more stable. Some therapy choices may include a self-help program; counseling; drug treatment; heroin substitution; methadone maintenance; naltrexone implants; and buprenorphine.

If you are still injecting drugs, ask your doctor or local syringe exchange program for information on safer injection practices to lower your risk of HCV re-infection (and other infections).

### **Concerns for people in recovery**

Because the side effects of interferon are very similar to opioid withdrawal, many people in recovery fear that they will relapse to active drug use. The risk of relapse is lower when side effects are promptly treated and counseling and support from peers and medical and mental health providers is available.

Some people are concerned about self-injecting pegylated interferon. If possible, the once-weekly injections can be given at a doctor's office or clinic to avoid triggering a relapse to injection drug use.



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# **side effects and management strategies**

The side effects from hepatitis C treatment can be uncomfortable, sometimes debilitating, and, rarely, even life-threatening. People who are coinfecting with HIV and hepatitis C may have more severe side effects. There are ways to manage these side effects.

It can be very helpful to talk with people who have been on hepatitis C treatment, and to ask your doctor how he/she will treat your side effects.

With the right planning and support, many side effects can be managed. Support from other people with HCV, friends, and family before and during HCV treatment plays a key role in coping with side effects.

### **Depression, anxiety, and other psychiatric side effects**

Depression and anxiety are commonly reported side effects of interferon treatment. In rare cases, people have reported that they have felt like taking their own lives, and a few people have committed suicide during their HCV treatment. People with a history of depression are at greater risk for developing these side effects during HCV treatment, although depression and anxiety have also been reported in people who never experienced them before. Interferon can also cause irritability, insomnia, mania, mood swings, and psychosis.

It's important to have access to mental health care before and during HCV treatment, so that psychiatric side effects can be treated promptly and appropriately, if it becomes necessary.

Starting an antidepressant before going on HCV treatment can help to prevent depression from interferon.

Antidepressants and other psychiatric medications have their own side effects, so other experts think it is better to provide these drugs only if and when people need them.

It is important to correctly diagnose and properly treat psychiatric symptoms of HCV treatment.

*“I stayed at work during the whole of the treatment, and while this was difficult mentally and physically, I think it was the best thing. Too much time on your hands is a bad thing when you are taking a treatment that fucks with your head. I was able to have quite a few sick days and an easier work schedule by telling the occupational health doctor at work what I was going through.”*

*“I think that to be informed is the best support. Having a real picture of what is going on can help to avoid fear and anxiety. Support and counseling are essential in deciding to go into treatment. The treatment can have very disturbing side effects and to be informed about them and how to manage them is crucial for having a greater chance of success, especially physiological disorders. I also think that peer support could be very useful in these situations.”*

*“It is difficult to consider taking a treatment that, in the long term, maybe it's going to help me—but it's going to make me very sick in the present.”*

## **Flulike symptoms**

Flulike symptoms (fever, aches and pains, headache, chills, and nausea) are common side effects of interferon.

Taking the pegylated interferon shot in the evening helps, as does a low dose of acetaminophen and anti-nausea medication and/or dronabinol (also called Marinol, a derivative of marijuana).

Drinking plenty of water helps to lessen flulike symptoms.

## **Weight loss**

Weight loss often occurs during HCV treatment, because people may lose their appetite, have diarrhea, and/or feel nauseated. If possible, eat many small, light meals to keep energy up. Dronabinol may help to stimulate appetite.

D4T (stavudine) should not be used as it can increase fat loss when used with ribavirin.

## **Fatigue**

Fatigue is also common; napping and regular but light exercise, when possible, can help. Some doctors are treating fatigue with methylphenidate (Ritalin).

## **Anemia, neutropenia, and thrombocytopenia**

HIV-positive people may have low white and/or red blood cell counts; neutropenia, anemia, and thrombocytopenia sometimes develop in persons with advanced HIV disease. Regular monitoring of white and red blood cell counts during HCV treatment is especially important for coinfecting people, since they are at greater risk for anemia, neutropenia, and thrombocytopenia.

Anemia (an abnormally low red blood cell count) is a side effect of ribavirin, and pegylated interferon can also cause anemia because it suppresses the growth of bone marrow, where blood cells develop. The most common symptom of anemia is fatigue. Anemia is a common problem for HIV-positive people, and can be caused by AZT. If possible, coinfecting people should avoid taking AZT, especially during HCV treatment. Both AZT and ribavirin can cause anemia, and combining them increases the risk. Combivir and Trizivir both contain AZT.

There are two ways to treat anemia due to ribavirin. One strategy is to lower the dose of ribavirin, but HCV treatment may not work as well. The other is to treat anemia with injections of a red cell growth factor called Epogen, which improves fatigue and helps people to stay on ribavirin. Severe anemia is treated by blood transfusions, but this can be avoided by reducing the ribavirin dose or starting red cell growth factor if anemia develops during HCV treatment.

Neutropenia is an abnormally low amount of neutrophils, the white blood cells that fight bacterial infections. Pegylated interferon can cause neutropenia. The risk of developing bacterial infections is increased in people with neutropenia. If the neutrophil count drops during HCV treatment, the dose of pegylated interferon is reduced, or neutropenia is treated with injections of white cell growth factor called Neupogen.

Thrombocytes are platelets that help stop bleeding by clotting blood. Thrombocytopenia (low platelet count) can be caused by serious liver damage (because platelets are made in the liver). It can also be caused by other medical conditions, including HIV itself, and by pegylated interferon. Severe thrombocytopenia can have life-threatening consequences, such as intracranial hemorrhage. If severe thrombocytopenia develops during HCV treatment, it is usually discontinued.

## **HCV treatment and CD4 cell count**

Although interferon can cause a temporary drop in your CD4 count, (but not your CD4 percentage), the three major HCV treatment trials for coinfecting people did not find more opportunistic infections (OIs) in people with low (under 200/mm<sup>3</sup>) CD4 cell counts.

There have been some reports of *Candida* esophagitis (a fungal infection of the esophagus), and tuberculosis among coinfecting people during HCV therapy. In some cases, prophylaxis (drugs that protect against certain OIs) may be recommended.

CD4 cell counts usually return to the pretreatment levels within a few months after HCV treatment has ended.

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# **research into new drugs to treat HCV**

Interferon-based treatment does not work for everyone and is limited by side effects that are severe enough that many people postpone treatment. However, new therapies are not likely to be approved by the FDA for several years. Waiting for better treatments may be a good option for people who don't need HCV treatment now. This includes people with mild liver damage.

For a long time, research into HCV was difficult because the virus couldn't be grown in laboratories. This changed recently when researchers successfully developed new models to study the viral life cycle, which makes it easier to develop drugs that stop viral replication.

Many new treatments for hepatitis C are being researched. Some are oral drugs with similarities to HIV medications (protease and polymerase inhibitors), though they will not be active against HIV. These new drugs are likely to be studied first in people with HCV monoinfection, although treatment activists are advocating that studies include coinfecting people much earlier in drug development.

As with HIV drugs, combination therapy may be essential in order not to develop resistance. A high level of adherence (better than 95%) is also likely to be important. In order to avoid resistance, people will probably need to use the new drugs in combination with interferon (and perhaps ribavirin) until there are enough new agents to construct interferon-free regimens. Pegylated interferon will continue to be part of HCV treatment for years to come.

To make an informed decision about starting or deferring HCV treatment, it may be helpful to learn about new drugs that may come along in the future. Only brief details are included here of some of the compounds in development, but the resources listed can keep you up-to-date with this research.

Drugs that specifically target parts of the hepatitis C virus (protease and polymerase inhibitors) are currently in development. Some have made it into clinical trials; others will follow. New formulations of interferon that can be taken less frequently are also being tested, as are immune-based therapies, and therapeutic and preventive vaccines.

### **Where to find information on new HCV drugs**

An update on HCV drugs in clinical development is included in the *TAG Pipeline Report*, available to download as a pdf file from the TAG website:  
<http://www.treatmentactiongroup.org>

Reports relating to new HCV treatment are also regularly on the NATAP website:  
[www.natap.org](http://www.natap.org)

An ongoing, detailed list of HCV drugs in development is also posted to the HCV Advocate website:  
[www.hcvadvocate.org/hepatitis/hepC/HCVDrugs.html](http://www.hcvadvocate.org/hepatitis/hepC/HCVDrugs.html)

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# **HIV drugs and HCV infection**

Although coinfecting people are at risk for liver toxicity from ARVs, the benefit of HIV treatment outweighs the risk for liver toxicity.

Some side effects are more common in people with HCV coinfection, including lipodystrophy (fat accumulation or fat loss) and abnormal levels of fat and insulin in the blood. People with HCV monoinfection are far more likely to develop diabetes than the general population, and diabetes is more common among coinfecting people than those with HIV alone. Use of HIV protease inhibitors and nucleoside analogs, especially stavudine (Zerit; d4T), has been linked with an increased risk for high blood sugar and diabetes.

However this risk should never be used as a reason to withhold HIV treatment.

### **Liver toxicity and HIV drugs**

Many HIV drugs are cleared from the body by the liver and have the potential to cause liver toxicity; HCV coinfection increases the risk by two to three times. This could be through the direct action of the drugs themselves—largely a concern with nevirapine (a non-nucleoside reverse transcriptase inhibitor, or **NNRTI**), tipranavir, and higher doses of ritonavir (both protease inhibitors, or **PIs**)—which can be managed by choosing other HIV drugs. The use of low-dose ritonavir to boost other PIs does not seem to increase this risk. Increased liver toxicity could also be the result of higher drug concentrations of NNRTIs and PIs, especially in people with more serious liver damage. Because a damaged liver is working less efficiently, the amount of drug in the blood could increase to dangerous levels and should (ideally) be checked using therapeutic drug monitoring (TDM) so that the dose can be modified if necessary.

### **Drug interactions between HCV treatment and HIV drugs**

Ddl (didanosine, Videx) should not be used during HCV treatment, because of serious interactions with ribavirin that can cause **lactic acidosis**, **pancreatitis**, and the risk of liver failure in people with advanced cirrhosis. AZT is not recommended because of the increased risk of anemia.

When possible, d4T (stavudine) should be avoided during HCV treatment. Some studies have found that people who used d4T while treating their HCV were more likely to have significant weight loss and lipoatrophy (fat loss).

Other issues relating to HIV drugs are discussed below.

### **Therapeutic drug monitoring (TDM)**

TDM is a blood test that checks whether you are getting adequate blood levels of a protease inhibitor, an NNRTI, and possibly T-20.

Doses for HIV drugs are worked out for an average person as a one-size-fits-all; however, individual differences in absorption can vary considerably in real life—especially in people with reduced liver function related to HCV coinfection.

TDM is currently available only in research settings and certain clinics in the US, but it may be an important option if you're coinfecting and having problems with your ARV regimen.





# managing cirrhosis

A damaged liver can still function, but people who have developed cirrhosis are at risk for liver failure and other serious, life-threatening complications. People with compensated cirrhosis should be screened for liver cancer and monitored regularly for decreasing liver function and **varices** (stretched and bursting veins). Beta blockers can help prevent varices. **Variceal hemorrhaging** is managed with medication and surgery.

Changing your diet may help to manage some of the complications of cirrhosis. Cutting down on salt and eating many small light meals per day, with protein from vegetables and dairy products rather than meat, can help redress nutritional imbalances. A nutritionist and your doctor can help you plan a healthy diet.

When liver function has deteriorated and hepatic decompensation occurs, a liver transplant is necessary.

### **Liver transplant in people with HCV/HIV coinfection**

In people with severe decompensated liver disease, a liver transplant is the final option.

This is a major operation, and success rates vary. It is also complicated by a scarcity of donor organs that are available for transplant.

For many years, transplant services actively avoided transplanting organs into HIV-positive people. This was due to several factors: discrimination from some surgeons, who did not want to operate on HIV-positive people; the poor long-term prognosis for HIV-positive people before effective HIV treatment was available, which meant that a donor organ would provide fewer years of additional life than it might to a person without HIV or other medical conditions, and concerns about using immunosuppressive drugs in HIV-positive people.

The effectiveness of HIV drugs has changed this. HIV is no longer an exclusion criteria for transplantation. Centers in the US, Spain, France, and the UK have transplanted livers into HIV-positive candidates. Results have been mixed; some centers have reported no significant difference in survival according to HIV status, but medical management remains complex due to drug interactions between immunosuppressants and protease inhibitors, graft rejection, recurrent HCV, and difficulty in tolerating HIV and HCV treatment after transplantation.

Since HCV infection progresses more rapidly in people with HIV coinfection, some specialists suggest that people with coinfection should be referred to transplant lists at a slightly earlier stage of disease than people with HCV mono-infection.

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# living with HCV/HIV coinfection

Probably the most important aspect of dealing with any medical condition is having time and support to become better informed about choices that affect your health.

Many people who are diagnosed with a chronic disease take the opportunity to examine their lives in order to reduce stress and improve both their quality of life and their general health.

Some of the lifestyle changes discussed below can reduce the risk for HCV progression—especially cutting down on or avoiding alcohol. Stopping smoking; eating better; resting properly; exercising; and other forms of stress reduction are important for everyone’s health.

## Alcohol and HCV

Heavy drinking is known to be harmful to the liver. Alcohol intake in amounts of more than 50 grams per day (four or five glasses of wine, beer, or mixed drinks) for men and more than 30 grams per day (two or three glasses of wine, beer, or mixed drinks) for women accelerates HCV progression.

Alcohol harms the liver by increasing both inflammation and scarring. Generally, the less you drink, the better for your liver, since no one has determined what amount of alcohol is *not* harmful to people with chronic HCV. *In some cases, drinking less—or not at all—may be more important than treating HCV.*

### Tips for reducing or avoiding alcohol intake

The following suggestions may help, whether you decide to drink less or quit drinking altogether.

If you decide to stop completely:

- Don’t keep any alcohol at home.
- Avoid people, places, or circumstances that trigger alcohol use, or develop a plan so that you are prepared and able to deal with the situation without alcohol.
- Remind yourself regularly about why you are giving up alcohol and the benefits it will bring.
- Try to keep your mind off alcohol by involving yourself in other things, particularly at times when you usually have a drink.

If you decide to cut down:

- Monitor how much alcohol you drink. Be honest, even if the total seems unreasonable. Once you know where you are starting from it will be easier to measure or monitor improvements.
- If you are drinking alcohol, drink slowly and drink plenty of water or juice as well.
- Drink alcohol with or after food as this slows down the absorption rate.
- It is better to spread your alcohol intake over the whole week, rather than drinking heavily in one session.

## Support organizations

### Alcohol and drugs

Organizations that provide information and support for people who want to reduce or stop their use of alcohol and/or drugs include:

#### Alcoholics Anonymous

[www.alcoholicsanonymous.org/en\\_information\\_aa.cfm](http://www.alcoholicsanonymous.org/en_information_aa.cfm)

#### Buprenorphine FAQs

[buprenorphine.samhsa.gov/faq.html](http://buprenorphine.samhsa.gov/faq.html)

#### Buprenorphine Physician and Treatment Locator

[buprenorphine.samhsa.gov/bwns\\_locator/index.html](http://buprenorphine.samhsa.gov/bwns_locator/index.html)

#### FAQs: A Quick Guide to Finding Effective Drug and Alcohol Treatment (from SAMHSA)

[csat.samhsa.gov/faqs.aspx](http://csat.samhsa.gov/faqs.aspx)

### Harm reduction resources

#### Directory of syringe exchange programs and other resources by State

[www.harmreduction.org/userdata\\_display?sortby=&modin=50&state=MN&search=Search](http://www.harmreduction.org/userdata_display?sortby=&modin=50&state=MN&search=Search)

#### Harm Reduction Psychotherapy and Training Associates

[www.harmreductioncounseling.com/index.html](http://www.harmreductioncounseling.com/index.html)

#### Referral to a therapist

1-888-227-7542

#### Moderation Management

[www.moderation.org/](http://www.moderation.org/)

#### Narcotics Anonymous

[www.na.org/](http://www.na.org/)

#### Opioid Treatment Program Directory

[dpt2.samhsa.gov/treatment](http://dpt2.samhsa.gov/treatment)

#### Substance Abuse Treatment Facility Locator

[findtreatment.samhsa.gov](http://findtreatment.samhsa.gov)

Alcohol increases hepatitis C viral load, which makes HCV treatment less effective. This may be why studies of treatment with an older form of interferon reported that HCV treatment was not very effective for people who drink alcohol. A few newer studies have not reported a significant difference in HCV treatment outcomes among drinkers versus non-drinkers. Nonetheless, some doctors refuse to provide HCV treatment to people who consume alcohol.

### Alcohol and liver damage

Alcohol is mainly broken down by the liver, and this process creates byproducts that damage the liver more than the alcohol itself does. Prolonged inflammation from long-term alcohol use causes an overproduction of molecules called **free radicals** that can destroy healthy liver tissue, subsequently impairing liver function.

Alcohol can also disrupt the production of antioxidants, which defend the body against free radical damage. The combination of overproduction of free radicals and loss of antioxidants can contribute to liver damage.

Women may be more prone than men to the damaging effects of alcohol.

Drinking less—or not at all—can be very difficult. Some people cut down or quit on their own, while others find that support groups, counselling, or pharmacotherapy work best for them. A list of resources is provided in this guide.

## Recreational drug use

The liver is the organ that processes most recreational drugs. These are likely to contain impurities and unspecified ingredients. If you are injecting drugs, use new, sterile equipment— syringe, cooker, filter, water, tie, and measuring syringe—each time to protect yourself from reinfection with hepatitis C and from other infections.

If you want to stop using recreational drugs, there are places where you can get help.

## Smoking

Smoking has a negative impact on everyone’s health. For people with hepatitis C, there is some weak evidence suggesting that smoking may accelerate hepatitis C progression, but most people in the studies also drank alcohol, making it hard to tell how much smoking mattered.

Stopping smoking is not easy. Quitting during hepatitis C treatment may not be the best time for some people. Giving up cigarettes may be a long-term goal for many people; it may not always be a person’s most important short-term priority.

If you feel ready to stop smoking, talk with your doctor about ways to make quitting easier.

## Diet

A healthy and balanced diet is important for general good health.

Liver abnormalities are more common in people who are overweight. These may include liver steatosis and inflammation. Liver problems are also more common among people with diabetes, and being overweight is a risk factor for developing diabetes.

Being overweight decreases the chance of being cured by HCV treatment.

When overweight people lose weight, their liver condition is likely to improve.

All foods and fluids pass through the liver to be broken down. Avoiding things that are hard for the liver to break down supports liver health.

The most appropriate diet for you depends on a number of factors including age, weight, extent of liver damage, and current symptoms. With advanced liver disease, avoiding or reducing the amount of certain foods may be important. These may include:

- Fried foods;
- Foods with a high fat content, especially if they contain saturated or hydrogenated fats;
- Very high-protein diets;
- Foods with high iron content, and iron supplements, unless your liver specialist recommends these;
- Processed food and “junk” food;
- Caffeine in coffee, tea, and some carbonated drinks;
- Salt, especially with advanced liver disease;
- Foods containing additives and pesticides;
- Sugar, since diabetes is more common among people with chronic hepatitis C; eat less food containing processed sugar and switch from white bread and pasta to whole wheat bread and pasta.

If you find it hard to lose weight or want more information on a healthier diet, ask your doctor about seeing a nutritionist.

## **Herbal medicine**

Herbal remedies have been used for centuries to treat liver disease, but they cannot cure hepatitis C. So far, no clinical trials have demonstrated that herbal remedies are safe and effective against hepatitis C. Many people use these nonetheless: some because conventional treatment has not worked for them, others because of concerns about the side effects of HCV therapy. Keep in mind that even natural or herbal products may cause stress to the liver.

Milk thistle (silymarin) is often used to treat hepatitis C, although clinical trials have not found any benefit in people with hepatitis C. Research on milk thistle and HCV is ongoing.

Licorice root (glycyrrhizin) has been used to treat HCV, although it has no effect on hepatitis C viral load. Some studies have shown that it can lower liver enzyme levels and may decrease the risk of liver cancer; however, long-term use can cause side effects such as high blood pressure and fluid retention, which are especially serious for people with cirrhosis.

Many other combinations of herbs are being sold to treat HCV or benefit the liver. Unfortunately, these products are unregulated, and they differ in purity and strength. Some may actually be harmful to the liver, and others may interact with HIV drugs and other medications. It is important to discuss the use of any herbs or supplements with your doctor.

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# **other viral hepatitis infections**

## **Hepatitis A (HAV)**

HAV is found in feces (stool). People become infected when feces from a person who is infected with HAV enters their mouth. This may occur when food (including raw or undercooked shellfish) or water is contaminated with sewage; when an infected person handles food without washing his/her hands after using the bathroom; through oral-anal sex with an infected person (also known as rimming); and, rarely, from blood transfusions.

A vaccine is available to prevent HAV infection, and every person with HIV or HCV should be vaccinated. (It may be less effective in people with low CD4 cell counts.)

Some people with HAV—especially children—don't feel sick at all; others have symptoms including nausea, vomiting, diarrhea, fever, fatigue, rash, jaundice, liver pain, and dark brown urine. There is no treatment for HAV itself, but the symptoms can be treated.

HAV is not a chronic infection—it goes away by itself, usually within two months. A person can be infected with HAV only once.

## **Hepatitis B (HBV)**

HBV can be found in blood, semen, and vaginal fluid of infected persons. Very small amounts of HBV have been found in breast milk and saliva. A person can get hepatitis B from sharing injection or tattooing equipment; from unprotected anal, vaginal, or oral sex; and from sharing personal care implements (such as toothbrushes and razors). HBV can be passed from mother to infant during childbirth.

A vaccine is available that protects against HBV infection. Every person with HIV or HCV should be vaccinated.

HBV can be treated with interferon and oral antiviral drugs, such as adefovir, entecavir, and telbivudine. Some HIV drugs are also active against HBV, such as lamivudine (3TC; Epivir), emtricitibine (FTC; Emtriva), and tenofovir (Viread).

As when treating HIV, antiviral HBV treatment should not be given as monotherapy to people with coinfection. Guidelines provide detailed information on drug choices for treating HBV and HIV. It is currently recommended that HIV treatment be started earlier, and include tenofovir plus either 3TC or FTC, plus at least one extra drug, so that there are at least three active drugs against HIV.

Another very important caution is that once HBV treatment is started, it should not be stopped unless the infection is completely cleared. This is because HBV treatment can cause a serious, sometimes fatal, flare of liver enzymes.

If HIV treatment needs to be changed, then the HIV drugs that are active against HBV should be maintained in the next regimen.

There is less research on HIV coinfection with these viral hepatitis infections:

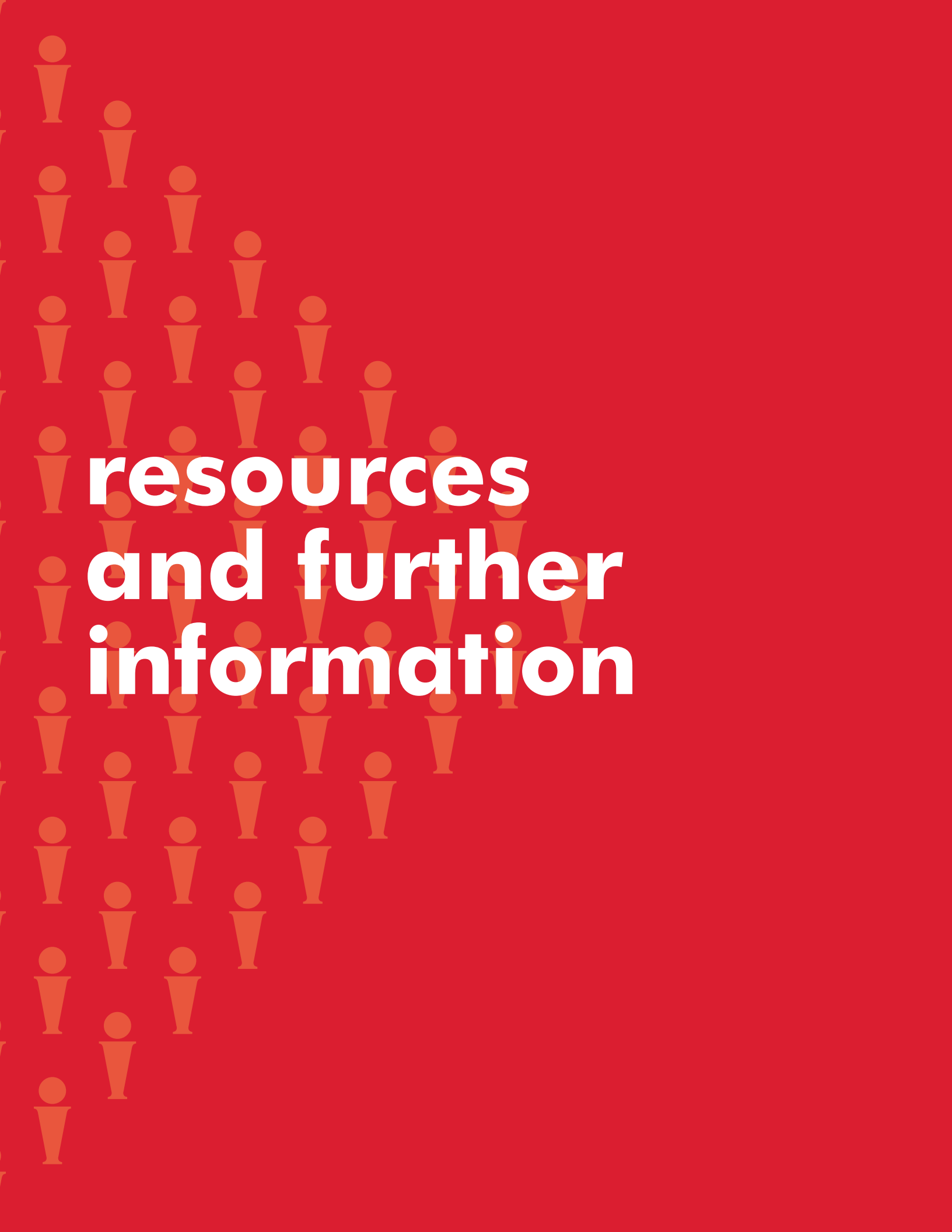
Hepatitis D (HDV) – a virus that only infects some people with hepatitis B. HDV increases the risk of cirrhosis and the rate of liver disease progression for people with HBV. A vaccination protecting against HBV also protects against HDV infection.

Hepatitis E (HEV) – an infectious virus with characteristics similar to hepatitis A. HEV will clear without treatment over several weeks to months. There is no vaccine for HEV. You can be infected with this virus only once. It is not usually serious, except during pregnancy.

Hepatitis F (HFV) – a virus thought to be similar to hepatitis B, but recent research has not confirmed this.

Hepatitis G (HGBV-C) – a virus with structural similarities to hepatitis C. The role and importance of hepatitis G is unclear, especially in people with HIV. Some research suggests that hepatitis G may slow HIV progression. Other research suggests that clearing hepatitis G can make HIV more serious.



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# **resources and further information**

The following web links include excellent resources for further information.

### **HCV Advocate**

[www.hcvadvocate.org](http://www.hcvadvocate.org)

A nonprofit organization founded in 1997 by people living with hepatitis C, it provides a wide range of HCV and HCV/HIV information online.

### **HIV i-Base**

[www.i-base.info](http://www.i-base.info)

HIV i-Base is an advocacy organization set up in April 2000 by HIV-positive advocates. I-Base produces a monthly publication for doctors and four non-technical treatment guides, all of which are available free, both in print and online.

### **Treatment Action Group (TAG)**

[www.treatmentactiongroup.org](http://www.treatmentactiongroup.org)

TAG is an HCV/HIV/TB activist group based in New York that reports new data on the epidemiology and natural history of HCV/HIV coinfection and the development of new treatments. TAG works with drug companies, government agencies, researchers, and other treatment activists. TAG also educates members of the HIV community about coinfection with HIV and hepatitis C.

TAG produces *The Pipeline Report*, which includes a review of new research. TAG also provides a listing of state ADAP programs that cover HCV treatment on its website.

### **National AIDS Treatment Advocacy Program (NATAP)**

[www.natap.org](http://www.natap.org)

NATAP is a treatment information and advocacy project that provides wide coverage of news about HIV, HCV, HBV, and other related issues. The website and e-mail lists include postings of conference presentations and full journal articles that are otherwise inaccessible due to journal subscription requirements.

NATAP publishes a 40-page HCV/HIV coinfection handbook (last edition, Summer 2005) and other publications that use non-technical language to share detailed information on most important aspects of coinfection. See [www.natap.org/2005/publications/ver5final.pdf](http://www.natap.org/2005/publications/ver5final.pdf).

### **HIV and Hepatitis.com**

*www.HIVandHepatitis.com*

Medical website that includes research reports on viral hepatitis, particularly as it relates to HIV coinfection. The site is easy to search for articles by subject (e.g., “basics,” “new HCV drugs,” “biopsy”).

### **Medical conferences**

Most of the major HIV conferences also include presentations and research relating to HCV/HIV coinfection. Hepatitis conferences tend to be less focused on coinfection.

Many HIV organizations and websites cover reports from these meetings, including NAM (*www.aidsmap.com*), HIVandHepatitis.com (*www.hivandhepatitis.com*), HIV i-Base (*www.i-base.info*), and NATAP (*www.natap.org*).



The image features a solid red background. Overlaid on this background is a pattern of stylized human figures, each consisting of a small circle for a head and a larger, inverted triangle for a body. These figures are arranged in a large, triangular shape that tapers from left to right, with the top row having one figure and the bottom row having ten. The word "glossary" is written in a bold, white, sans-serif font, centered horizontally and vertically over the pattern of figures.

# **glossary**

**Acute infection** – with hepatitis C, this refers to the first six months after infection.

**Albumin** – a protein made by the liver that carries drugs, hormones, and waste through the bloodstream, and helps maintain fluid levels within the body. Abnormally low levels of albumin can signal serious liver damage.

**ALP** – alkaline phosphatase; a liver enzyme also found in tissues throughout the body. ALP should be monitored regularly during HIV treatment and in persons with hepatitis C.

**ALT** – alanine transaminase, also called serum glutamate pyruvate transaminase, or SGPT; a key liver enzyme produced in liver cells. ALT should be monitored regularly during HIV treatment and in persons with hepatitis C.

**Antioxidant** – a substance that reduces oxidative damage (damage due to oxygen), such as that caused by free radicals (see definition below).

**ART** – antiretroviral therapy; a combination of drugs from different families used to treat HIV.

**Ascites** – an abnormal accumulation of fluid in the abdomen; a sign of serious liver damage in people with hepatitis C.

**AST** – aspartate aminotransferase, also called serum glutamic oxaloacetic transaminase, or SGOT; an enzyme made in many places throughout the body (heart, intestines, muscle). AST should be monitored regularly during HIV treatment and in persons with hepatitis C.

**Bilirubin** – a yellowish byproduct from the breakdown of old red blood cells; jaundice occurs if certain drugs or liver or bile duct damage cause bilirubin to build up in the bloodstream.

**Biopsy** – taking a small sample of body tissue for examination and testing in the laboratory.

**Brain fog** – a term used to describe confusion and forgetfulness associated with chronic hepatitis C.

**Chronic infection** – a persistent condition; with hepatitis C, this means any time following the acute phase.

**Cirrhosis** – severe scarring of the liver that makes it difficult for the liver to carry out its functions (see *fibrosis*).

**Coinfection** – infection with more than one virus.

**Compensated cirrhosis** – a scarred liver that is still able to function.

**Cryoglobulinemia** – increased blood levels of a protein that can cause inflamed blood vessels and thicken blood.

**Decompensated cirrhosis** – when liver scarring prevents the liver from functioning.

**Diabetes** – an illness related to not being able to regulate sugar in the blood.

**Encephalopathy** – degenerative brain function or disease.

**Enzyme** – a protein in the body that speeds up other chemical reactions.

**ETR** – end-of-treatment response; having an undetectable HCV viral load at the end of HCV treatment (see *SVR*).

**EVR** – early virological response; the drop in HCV viral load after 12 weeks of HCV treatment.

**Fibrosis** – mild-to-moderate scarring of the liver (see *cirrhosis*).

**FibroTest** – a test that uses results from blood tests to predict liver damage; this test may become an alternative option to liver biopsy for some patients.

**FibroScan** – a non-invasive ultrasound scan that measures the elasticity or stiffness of the liver.

**Free radical** – a chemical produced after a molecular reaction, often containing oxygen, that has one “free” (unpaired) electron on its outer surface. This makes it able to react to and damage other cells. Free radicals may perhaps increase progression of cardiovascular disease, cancers, and aging.

**Fulminant liver disease** – sudden, rapid disease progression related to liver failure.

**Genotype** – a category for different types of hepatitis C viruses; there are at least six HCV genotypes. Some are easier to treat than others.

**GGT** – gamma glutamyl transferase; a liver enzyme made in the bile ducts. GGT levels may be abnormally high from any type of liver disease, heavy drinking, or some medications.

**Grade/Grading** – The grade of hepatitis infection refers to the amount of liver inflammation found by a biopsy. It is usually measured on the Ishak scale from 1 to 18, where 0 is none and 18 is the maximum.

**Hepatocellular carcinoma** – liver cancer (HCC).

**Interferon** – a chemical messenger produced by the human body; it can also be man-made. Interferon stimulates the immune system to fight viruses.

**Jaundice** – a common symptom of hepatitis where increased levels of bilirubin lead to a yellowing of the skin or eyes.

**Lactic acidosis** – abnormal build-up of lactate in the blood, caused by cellular damage associated with the use of nucleoside reverse transcriptase inhibitors; if untreated, can be fatal.

**Lipoatrophy** – fat loss, especially in the arms, legs, cheeks, and buttocks.

**Lipodystrophy** – abnormal fat accumulation or fat loss.

**Monoinfection** – infection with one virus.

**NRTI** – Nucleoside reverse transcriptase inhibitor (a type of HIV drug); also called “nucleoside.”

**NNRTI** – Non-nucleoside reverse transcriptase inhibitor (a type of HIV drug).

**Pancreatitis** – inflammation of the pancreas; can be painful and life-threatening if not treated.

**PI** – Protease inhibitor (a type of HIV drug).

**Portal hypertension** – increased blood pressure (hypertension) in the vein carrying blood to the liver.

**Ribavirin** – a nucleoside analog taken in pill or capsule form as part of combination therapy for hepatitis C.

**SGOT** – see *AST*.

**SGPT** – see *ALT*.

**Spontaneous viral clearance/spontaneous clearance** – when the immune system is able to rid the body of the hepatitis C virus; if this occurs, it will be shortly after infection (usually within six months).

**Stage/Staging** – the stage of hepatitis infection refers to the amount of liver scarring (fibrosis) detected by biopsy. It is usually measured by either the METAVIR scale of 0 to 4, where 0 represents no scarring and 4 cirrhosis, or by the Knodell scale of 0 to 6, where 0 represents no scarring and 6 cirrhosis.

**Steatosis** – abnormal fat deposits in the liver.

**SVR** – sustained virological response; having a negative HCV viral load test six months after stopping HCV treatment. The response six months after treatment determines whether treatment has been effective in terms of clearing HCV. SVR is the most important result from an HCV treatment trial.

**Titer** – a measure of the concentration of antibodies to a specific antigen in a person's blood.

**Variceal hemorrhaging** – bleeding caused by bursting veins (see *Varices*, below).

**Varices** – extended or swollen veins that can burst; a complication of cirrhosis.



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