

Guide to hepatitis C for people living with HIV

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First questions
HCV and sexual transmission
New drugs to treat HCV
Living with coinfection

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Disclaimer: information in this booklet is not intended to replace information from your doctor. Treatment decisions should always be taken in consultation with your doctor.

HIV and HCV information dates quickly, please call to see if an up-date is available.

Thanks to the Monument Trust for funding this guide.

Welcome the i-Base guide to HIV and hepatitis C coinfection.

This booklet will help you:

- Have accurate, up-to-date information about HIV and hepatitis C.
- Get the most out of your relationship with your doctor and other health professionals.
- Feel more in control of your health and your treatment options.
- Get better medical care and improved health, and
- Achieve a better **quality-of-life**.

“I have lived with HCV for almost 20 years now, all the time waiting for a newer treatment to become available so I wouldn’t have to take Interferon.

Because a FibroScan showed my liver to be in relatively good condition, I felt I had time on my side. Though tiredness and fatigue had just become a part of life.

I am currently on a trial of a new drug (still taken with Ribavirin). So far things have been ok though I still get days where I’m so tired I can hardly move. But compared to the side effects of interferon I think I’ve got off lightly.

Waiting for this new treatment has been a good idea for me. Though if I had to use treatment earlier I would have done interferon.

The thought that I might be cured of HCV is amazing and makes me very emotional.

Introduction

This is an exciting time for hepatitis C (HCV) because so many new drugs are in development.

Since the last edition of this guide, two new HCV drugs have been approved that improved cure rates for some types of HCV. But, their difficult side effects means that much better treatment is still needed - and this is on the way.

Monitoring HCV has also become easier and safer by the increased use of FibroScan instead of liver biopsy.

Other new HCV drugs are called direct acting antivirals (DAAs). Several DAAs will be approved over the next two years and this will change treatment even more dramatically. This will include shorter treatment, fewer side effects and oral-only combinations that don't need interferon injections and/or ribavirin.

So at the moment a major focus is deciding whether to treat with current HCV drugs or wait until better treatment becomes available.

The information in this guide should help you feel more in control of this and other treatment decisions.

People living with HIV, HCV or coinfection, have contributed to this guide. Some have been living with HIV and HCV for over 20 years and have not yet chosen to treat HCV.

Other people – many of whom have been HIV positive for years – were only recently infected with HCV and decided on early treatment.

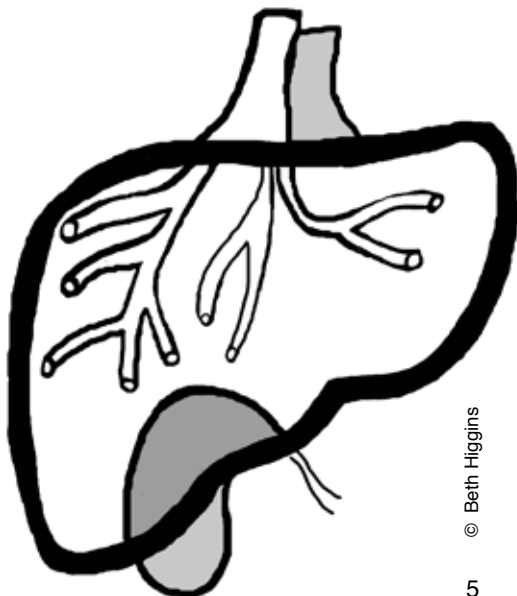
This shows something of the range of experience and choices.

This guide has links to other resources and support organisations and references for the medical information are online.

A glossary is included to help with medical words.

Finally, the sections on HCV research and on controversial aspects of treatment highlight areas where options are most likely to change in the near future.

With this in mind, always check that information is up-to-date. By the next update of this guide a lot is likely to change.



First questions

If you are just finding out about HCV these first questions may help.

Most of these subjects are also discussed in more detail later in this guide.

What is hepatitis C?

Hepatitis C is liver disease caused by the hepatitis C virus (HCV).

HCV is mainly in blood but it also infects liver cells where it can result in inflammation and scarring.

This scarring is called fibrosis when it is mild and cirrhosis when it is more serious. Liver scarring reduces how well the liver works.

It usually takes many years before HCV causes liver damage, but sometimes this can happen more quickly.

How did I get HCV?

HCV can be transmitted if blood from a person with HCV gets into another person's blood.

Common risk factors for this are:

- Sharing unsterilised syringes and other equipment used to take drugs.
- Tattooing or piercing with unsterilised needles, ink or inkwells.
- Receiving a blood transfusion before 1992 or blood products before 1985.
- Needlestick injuries among health workers.
- Medical or dental treatment with unsterilised equipment or in facilities that do not practice adequate infection control procedures, such as kidney dialysis centres.
- Through sexual contact.

HCV transmission is discussed in more detail on pages 14-16.

Sexual HCV transmission is discussed on pages 17-23.

Knowing how you caught HCV can help prevent the risk of passing HCV to other people. It can also protect you from catching another strain of HCV.

However, as with HIV, many people never know how they caught HCV, especially if this is likely to have been many years ago.

How serious is HCV?

HCV is a serious infection. However, if you clear HCV, either with or without treatment, then it may not have any serious effect on your long-term health.

About 25% of HIV negative people clear HCV without treatment but rates are lower in HIV positive people.

This only usually happens within the first six months of infection but it does not provide protection against catching HCV again in the future.

Chronic HCV refers to infection that has not cleared in the first few months.

There is a wide range of outcomes among people with chronic HCV.

Some people will never develop significant liver damage, some will have mild liver scarring, and 20-30% will develop more serious damage called cirrhosis.

In people with cirrhosis, HCV can cause liver cancer and liver failure (when a transplant is needed). This is usually only after many years. Because HCV generally progresses slowly, there is usually plenty of time to decide on treatment.

Luckily, HCV can usually be treated. Drugs in development will also make treatment more effective and easier over the next few years.

See pages 26-27 for more information about HCV and the risk of liver damage.

See pages 78-82 for information on the latest research.

Does coinfection make HIV or HCV more difficult to treat?

Having both HIV and HCV complicates each infection.

HIV increases the chance that HCV will progress and it causes HCV to progress more quickly. Serious liver damage is also more likely to develop with coinfection than with HCV alone. We don't know why this happens.

Keeping your immune system strong by using antiretroviral therapy (ART) to treat your HIV may delay HCV progression.

The benefits of ART generally outweigh the risk from side effects, even though people with coinfection have a higher risk of liver damage with some HIV drugs.

It is not clear whether HCV makes HIV worse but it complicates HIV treatment. This mainly involves the choice of ART, monitoring liver function and being aware of drug interactions.

See pages 38-48 for information on monitoring and pages 60-61 for information on drug interactions.

Glossary

cirrhosis Severe scarring of the liver that makes it difficult for it to keep working.

ART AntiRetroviral Treatment - HIV meds.

How common is HIV/HCV coinfection?

In the UK, approximately 100,000 people are HIV positive and 216,000 have HCV.

Around 5,000 of these people are likely to have HIV and HCV coinfection.

At least 10% of people with coinfection in the UK are HIV positive gay men who caught HCV due to sexual transmission.

Worldwide, about 4 to 5 million people have both HIV and HCV.

Rates of HIV positive people with coinfection range from about 9% in the UK to almost 50% in Spain and Italy. In the United States more than a million people have HIV with 25-30% also having HCV.

In countries where access to syringes and/or substitution treatment (methadone, buprenorphine or heroin) is limited or nonexistent, coinfection is common among people who inject drugs (PWID).

What should I do after an HCV diagnosis?

The first thing is to give yourself time to let the news sink in. This can take a few days or weeks, or much longer.

Accepting a new diagnosis is important before you can make rational decisions about what to do next. This will usually involve getting more information.

You can get information from your doctor, from friends and support groups and from other sources including the Internet.

As with HIV, learning about HCV can affect:

- Your health. This will involve getting information about monitoring, treatment and things you can change in your day-to-day life.
- The health of sexual and drug using partners. This will include information about how to minimise the risk of transmitting HIV or HCV.

“After six years of being HIV positive I mistakenly believed I’d already been hit by the bus and survived so nothing else could hurt me.

I only discovered my HCV status by accident after I volunteered for a trial at my hospital for people who had run out of ARV options for their HIV. It wasn’t a surprise (because of my previous drug use) but I had assumed I would be dead by the time HCV kicked in.

For me it was very important to have the HIV and HCV treated together – they are related ... 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 doesn’t really understand some of the social and psychological implications.”

Newly diagnosed with HCV?

If you have been HIV positive for a while and were recently diagnosed with HCV, the shock of a second serious infection can be difficult.

Some of the strengths you brought to your HIV diagnosis will help you now.

It is important to have a doctor who knows about and takes responsibility for both HIV and HCV.

Pages 32-34 are focused on recent HCV infection, especially if this was related to sexual transmission.

Newly diagnosed with both HCV and HIV?

If you have been diagnosed with both HIV and HCV at the same time, this can feel like a double blow.

If you are more worried about HIV than HCV, you may find HIV support groups and organisations more useful. Because HIV has been around for longer there are probably more community organisations that can help.

i-Base is just one of many groups that provides information about HIV treatment in non-technical language.

Treatment for both HIV and HCV is very effective and will continue to improve.

Who knows and who should I tell?

When you find out that you have HCV, only you and your health workers will know. Your doctor can only inform other health workers who are directly involved in your care.

You can take as much time as you need before deciding who else you want to tell.

It helps to be able to talk to a friend, partner or relative that you trust, so that you don't deal with this on your own. But who you tell is up to you.

In the UK, your HIV clinic should discuss the advantages of telling your GP.

Are people around me at risk?

People around you are not at risk of catching HCV from most daily activities.

The only risk comes from contact with your blood, which means taking care not to share anything that may contain traces of blood. This includes toothbrushes, razors, hair clippers, nail scissors, tweezers and nail files.

HCV remains infectious outside of the body for much longer than HIV. This can be for days or perhaps weeks, even after blood has dried.

Are my sexual partners at risk?

The risk of sexual transmission is complicated.

The risk to partners who are HIV negative is generally very low but it can occur.

The risk of sexual transmission is higher if your partner is HIV positive - with highest rates of sexual transmission among HIV positive gay men.

HIV seems to be a risk factor, but the reasons for this are not yet understood.

HCV and sexual transmission is discussed in more detail on pages 17-23.

Can you be infected with more than one type of HCV or HIV?

There are at least seven main types of HCV, called genotypes.

Unfortunately, having one doesn't protect you from being infected with another.

If you clear HCV you can still become infected again, with the same or a different genotype.

Reinfection with a different strain of HIV is more controversial. It certainly happens, but it seems uncommon.

HIV reinfection usually only has serious implications when the new virus is resistant to HIV treatment.

See page 39 for more information about HCV genotype and subtype.

Glossary

genotype A category for different types of similar viruses.

subtype A sub category for differences between viruses with the same genotype..

What about other types of hepatitis?

The word hepatitis just means inflammation of the liver.

Hepatitis can be caused by viral or bacterial infections, autoimmunity, heavy alcohol use, chemical fumes, and some medicines.

There are several different types of viral hepatitis. These were named alphabetically, in the order that they were discovered.

Before it was discovered in 1989, hepatitis C was called “non-A non-B hepatitis”.

Other types of viral hepatitis are included on pages 86-87.

Hepatitis A and B

If you have HCV, it is important to be protected against hepatitis A and B (HAV and HBV).

You really don't want another hepatitis virus to complicate your health.

Your clinic should check whether you are already protected against hepatitis A and hepatitis B and if not you should be offered vaccinations.

In the UK, these are free and available from your HIV or HCV clinic, from a sexual health clinic, or from your general doctor (GP).

Vaccinations for hepatitis A and B

HIV positive people should be vaccinated against hepatitis A (HAV) and hepatitis B (HBV) if they are not already protected.

How well vaccinations work is related to your CD4 cell count. The higher your count, the more likely that they work.

A low CD4 count (less than 200) reduces the chance that your immune system will respond to the vaccine, so an additional vaccine dose is often needed.

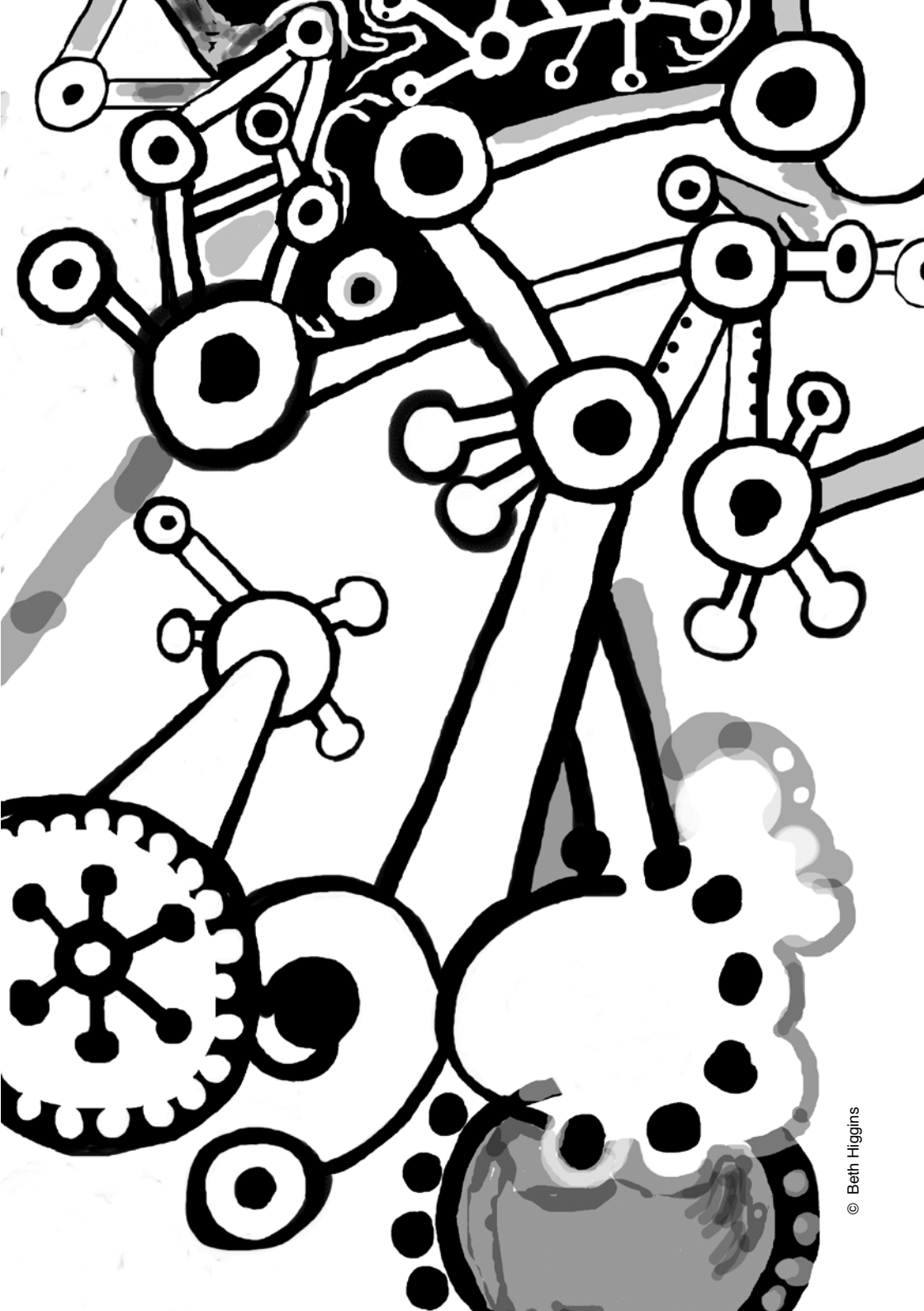
If your CD4 cell count is low, and you are at low risk for HAV or HBV, it may be better to start HIV treatment first.

Then you can be vaccinated when your CD4 count is stronger. Some guidelines recommend a higher dose of the vaccine for HIV positive people.

For example, UK guidelines recommend a double dose (40 µg) HBV vaccine for HIV positive people, given on months 0, 1, 2, and 6. A rapid course of HBV vaccine is available but is less effective in people with HIV and only used in specific circumstances.

Every year, your clinic should check that the vaccines are still working. If the protection has dropped, the clinic should give you a booster vaccination.

There is no vaccine against HCV.



HCV transmission

How HCV is caught and passed on

Most HCV infections come from blood to blood transmission.

This is when HCV infected blood directly enters another person's bloodstream. Saliva and tears are not infectious.

Semen and genital fluids may be infectious but there is less research on this.

As with HIV, you cannot transmit or catch HCV by touching, kissing, hugging, or from sharing cutlery, cups or dishes.

Unlike HIV, which dies in a few minutes outside the body, HCV remains infectious for at least a day even after blood has dried, and in some circumstances, perhaps for a week or longer. This is why you should not share items that may contain even tiny traces of blood.

Ways that HCV can be transmitted:

- Injecting, smoking or snorting drugs with shared, unsterilised equipment.
- Tattooing or piercing when needles, ink, inkwells and other equipment are shared.
- Medical or dental procedures with unsterilised equipment, including kidney dialysis.
- Needlestick accidents to health workers.
- Sharing items that may contain blood, such as razors, toothbrushes, nail scissors and nail files.
- Sex with someone who has HCV but see pages 17-23 as this is a complex subject.
- To a baby during pregnancy, labour or at birth (see pages 24-25).
- From a blood transfusion or blood products before blood screening. This risk is now virtually zero in the UK, Western Europe and the US. However, up to 90% of people with haemophilia who were treated with clotting factors before 1985 were infected with both HIV and HCV.

In some countries, infections still occur from reused, unsterilised equipment or blood transfusions if blood is not screened thoroughly.

“In terms of injection drug use, transmission of HIV and HCV differ ... because HCV is not just transmitted by sharing a needle, and HCV is much more infectious than HIV. So, I know many people who are taking exactly the same measures to prevent transmission of both, but we know that’s not enough to prevent HCV.

Sometimes people make decisions based on insufficient information, both in terms of HCV prevention and treatment.

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 ok most, but not all of the time.”

Injecting drug use and HCV

Worldwide, most HCV infections are related to injection drug use. This includes medical and non-medical settings, through sharing needles and other equipment.

HCV is a tougher and smaller virus than HIV. It can remain infectious for days to weeks in syringes, cookers, cotton, water, measuring syringes and ties.

Cleaning syringes with bleach reduces the risk of HIV transmission, but it is less effective against HCV.

Using clean needles and your own works each time you inject stops both HIV and HCV transmission (and reinfection).

It also reduces the risk of other infections.

If you caught HIV from drug use, you were probably infected with HCV first, before HIV. This is because HCV is a smaller virus that is not easily killed by bleach, making it more infectious than HIV.

Please see pages 35-37 for more information on long-term coinfection and pages 62-63 for information about HCV treatment for people who use drugs.

Sharing injecting recreational drugs including mephedrone and crystal meth in UK gay clubs and/or sex parties has a high risk of HCV transmission, see also page 19.

HCV and non-injecting drug use

HCV is more common among non-injecting drug users than the general population. It is not clear why.

It may be possible to catch HCV from snorting drugs through shared straws or rolled bank notes, or from sharing pipes to smoke crack or methamphetamine.

Sharing these items is therefore not recommended.

Recreational drug use is one of the main risk factors associated with sexual HCV transmission in gay men, see pages 17-23. This is because these drugs can affect biological, physical and behavioural risk factors.

HIV, HCV and sexual transmission

Sexual transmission of HIV

The majority of new HIV infections globally each year are because of sexual transmission.

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

Different types of sex carry different risks; for example, body rubbing and mutual masturbation are zero risk, oral sex is usually low risk, and anal or vaginal sex without a condom is usually high risk. Condoms are very effective at reducing HIV transmission.

Viral load in the HIV positive partner is related to each of these risks. Risks are dramatically lower when HIV viral load is undetectable.

Some other sexually transmitted infections (STIs), including herpes, gonorrhoea and syphilis, increase the risk of transmitting HIV. This is because they increase the amount of HIV in genital fluids and make the HIV positive partner more infectious.

STIs also increase the risk of catching HIV in several ways. An open sore is an easy route of infection but also immune responses to an STI make it easier for HIV to take hold.

All this information is important when talking about HCV.

Sexual transmission of HCV

The risk for sexually transmitted HCV is more complicated.

HCV is still primarily a blood borne infection so sex that includes contact with blood has the highest risk.

Although HCV has been found in semen, and vaginal fluid it is unclear whether these fluids are infectious, because HCV is generally at very low levels.

However, some studies have also reported that HCV levels can be high in semen and that this doesn't always match HCV levels in blood.

The risk of HCV sexual transmission is low from vaginal sex, in monogamous, HIV negative heterosexual couples in which one partner has HCV. However, much higher rates of sexual transmission have been reported in HIV positive gay men, for reasons that are not clear.

The importance of two aspects of this increased risk still have to be explained.

- The role of HIV, perhaps because of reduced immune protection or higher HCV viral load in HIV positive people with coinfection.
- The type of sex some HIV positive men have - behavioural differences - and how this may be different to HIV negative gay men as a group. This may be because of a higher risk of blood-to-blood contact.

Because cases of HCV have been reported where sexual transmission is the most likely route – both from heterosexual and gay sex – UK guidelines currently recommend that people with coinfection use condoms for penetrative sex.

Heterosexual transmission of HCV

The risk of heterosexual sexual transmission of HCV in people who are HIV negative is so low that condoms are not routinely recommended.

The risk is generally reported as less than 1% per year.

In these studies, couples did not use condoms, but also did not have anal sex or have sex during menstruation. The reason for this protection is likely to be through reduced exposure to blood-to-blood contact.

Although contact with menstrual blood has not been reported as a common factor in heterosexual partners, this has not been well studied.

In HIV positive people, the risk for sexually acquiring HCV is higher than that reported for monogamous, HIV negative heterosexual couples.

One study reported that sexual exposure is a risk factor for HIV positive women who do not inject drugs but have male partners with HCV.

There is very little information about whether these women were using HIV treatment and whether their HIV viral load was undetectable, or about the HIV status of their partners.

HCV is still primarily a blood borne infection so sex that includes contact with blood has the highest risk for sexual transmission.

Sexual transmission of HCV in gay men

HCV sexual transmission among HIV positive gay men has been reported in cities in the UK, Europe, Asia, Australia and the US.

Limited research has associated sexual HCV transmission with several risks which may or may not be directly related:

- Being HIV positive.
- Recreational drug use.
- Group sex and sex parties.
- Sharing sex toys.
- Rougher sex (longer fucking or fisting).
- Barebacking (insertive or receptive anal sex without condoms),
- Other STIs (especially syphilis).
- Meeting partners online.
- Number of partners.
- Rectal bleeding from surgical procedures and/or rough sex.

As many of these experiences overlap, it is difficult to identify the exact cause.

Some HIV positive gay men have caught HCV sexually without these risks, for example, without fisting, using recreational drugs or taking part in group sex.

HIV as a factor

HIV seems to be an important factor in catching HCV because sexual transmission in HIV negative gay men has been much less reported.

Even with a high CD4 count and low viral load, immune responses to HCV are lower than in HIV negative people.

This is shown by a lower rate of spontaneous clearance and a longer time to develop antibodies.

HIV positive people may also be more infectious as HCV viral load is higher (by about 1 log copies/mL) compared to HIV negative men.

The role of blood vs genital fluids?

When HCV is detected in genital fluids, levels are generally low – levels in blood are much higher. Blood is therefore likely to be much more infectious compared to semen during acute HCV infection.

In the few studies measuring HCV in semen one found higher levels in HIV positive compared to HIV negative men and one found no difference.

This second study found that acute HCV was linked to higher HCV levels in semen which might be the important difference given most HCV infections in gay men have been recent.

Although higher HCV viral load increases the chance of HCV in semen, some men have very high HCV in blood and undetectable levels in semen.

Recreational drug and HCV infection

Although HCV is transmitted during sex seems among HIV positive gay men, recreational drug use is a factor that increases this risk in several ways.

This includes non-injection use of “party drugs” such as crystal meth, cocaine and ecstasy.

Recreational drugs can lower your immune responses so you may be more vulnerable to HCV infection.

Drugs that dilate blood vessels make the lining of the anus more vulnerable to tears and bleeding.

Drugs that act as muscle relaxants allow longer and more energetic sex.

Recreational drugs also reduce inhibitions and are commonly a key factor for group sex.

Injecting recreational drugs including mephedrone and crystal meth has a high risk of HCV transmission if this involves sharing needles or other equipment.

Antidote is a drug and alcohol service for lesbian, gay, transgender and bisexual people, based in London with a national phoneline.

020 7833 1674 (10am-6pm,
Monday to Friday)

“There is so little information on the exact mechanism for HCV sexual transmission, and so little awareness amongst gay men or knowledge about what is safer HCV sex for an HIV positive man that many people stop having sex until their HCV is cleared.

I immediately told my partner and two fuck buddies who I was concerned I had put at risk. All were tested but none were infected. As my partner and fuck buddies had not become infected, I decided that bareback sex alone was not enough to transmit it.”

Type of sex, group sex and sex parties

Any activity with a risk for contact with traces of blood (rather than semen which is the route for most STIs) is likely to be important for HCV transmission rather than sexual fluids in someone who has been HCV positive for more than six months.

In group sex, someone who fists more than one partner can transfer HCV without having become infected himself.

Semen may be infectious if a partner is in acute HCV infection.

This includes use of some recreational drugs, sharing toys and lube, rougher anal sex, fisting, and group sex.

Because HCV is so much more infectious than HIV, it is more easily transmitted during group sex. If the sex is rougher this increases the chance of bleeding.

Recreational drugs are strongly associated with this risk: tissue is more vulnerable to damage, sexual inhibition can change behaviour, sex may be rougher and go on for longer.

At least one study found that sex after recent surgery or treatment for anal warts was a high risk for catching HCV, because this would be an easy route for infection to enter the bloodstream.

HIV positive gay men may be at higher risk when serosorting by HIV status. This is because the percentage of HIV positive men with HCV is currently higher than the percentage in HIV negative men.

Other STIs, especially syphilis, are linked to acute HCV infection. Routine health checks are important to protect yourself and your partners.

Safer HCV sex for gay men

Although similar safer sex information is often given for HCV as for HIV, the risk from HCV is more likely to come from contact with blood than semen.

- Blood is likely to be much infectious compared to semen during chronic HCV. Semen may be more infectious during acute HCV infection. UK guidelines recommend condoms for penetrative sex.
- **Use a new condom with each partner.**
- Use latex gloves for fisting and a new glove with each partner.
- **Any cause of anal bleeding, including recent surgery, increases the chance of HCV sexual transmission.**
- Condoms and gloves need to be discarded more carefully than when just considering HIV. Unlike with HIV, the outside of the condom (or glove) may be more infectious than the inside.
- **Don't use shared lube from a pot. Traces of blood will not be visible and HCV remains infectious out of the body for at least 16 hours.**
- Recreational drugs can increase the risk of bleeding because blood flow is increased, sex can be rougher for longer and they change behaviour.
- **Use condoms on sex toys. Do not share sex toys without using a new condom each time you share them.**
- Be aware that in group sex HCV could be transmitted by a partner who is not HCV positive. For example, if someone has traces of blood on their hands or cock from a previous partner.
- **Other STIs are linked to acute HCV infection. Routine health checks are easy and important.**

Transmission of HCV to a baby during pregnancy

HCV can be transmitted to a baby during pregnancy or at birth. This risk is 3-4 times higher if the mother has both HIV and HCV.

HIV treatment dramatically reduces the risk of vertical transmission of HIV, regardless of the mother's HCV status. It also lowers the risk of HCV transmission.

HCV cannot be treated during pregnancy with pegylated interferon or ribavirin. This is because ribavirin causes birth defects, and interferon can cause brain and nerve damage in infants.

Women who discover they are pregnant while on these treatments should discontinue both drugs immediately.

Hopefully, some of the new HCV drugs, called direct-acting antivirals (DAAs), will be safe for use during pregnancy or in children with HCV.

UK guidelines recommend normal vaginal delivery if the mother is receiving ART, unless there are obstetric complications which require a C-section.

Guidelines for HIV positive pregnant women also recommend:

- Screening for HCV during each pregnancy.
- Screening for hepatitis A (HAV) and hepatitis B (HBV). This is because of an increased risk of complications during pregnancy from these infections. Vaccination against HAV and HBV is recommended in all non-immune HCV coinfecting women after the first trimester. An additional dose may be needed if the CD4 cell count is below 300.



- ART is recommended during pregnancy (as for HIV positive women without HCV).
- Counselling women with HIV and HCV coinfection who are receiving ART about signs and symptoms of liver toxicity. Liver enzyme tests are recommended one month after starting ART, and then every three months.
- The mode of delivery in coinfection should be based on standard obstetric and HIV-related indications.

For more information:

i-Base Guide to HIV, Pregnancy and Women's Health (2013).

<http://i-base.info/guides/pregnancy>

BHIVA guidelines for the management of HIV infection in pregnant women (2012).

<http://www.bhiva.org>

“We need more information and research about HCV transmission from mother to child – and HCV transmission in general.

A friend who is co-infected recently had to have a Caesarean section because of the HCV. Her viral load was undetectable and CD4 count was high – so she could have delivered vaginally but she was not able to because of HCV.

It bothers me that even in the HIV community there is discrimination against drug users... Assumptions are often made by other HIV positive women regarding drug users, especially if they want to have children ... It is the same with some doctors ... and sometimes they don't pass on the information that we need...”

Natural history of HCV

What does your liver do?

Although HCV also get into other parts of the body, it is the liver that is most affected.

Your liver is an essential organ that has hundreds of jobs, including:

- Filtering chemicals and waste from the blood.
- Storing vitamins, minerals and iron and converting nutrients from food into energy.
- Helping to balance levels of sugar and hormones.
- Producing cholesterol.
- Making bile (necessary for digestion), and creating the hormone that helps to produce platelets (to stop bleeding).

How does HCV damage your liver?

HCV does not directly damage your liver. It is the way that the immune system reacts to the virus that causes liver inflammation.

As the immune system attempts to surround and isolate infected cells to protect the liver, scarring develops and worsens.

As the liver becomes more scarred it hardens and becomes less elastic. This makes it increasingly difficult for blood and other fluids to flow through it.

Even though the liver can operate when badly damaged, the continuous effect of HCV can slowly interfere with liver function. Complications develop when the liver is unable to carry out important tasks.

These complications include:

- Fat build up in the liver (steatosis) – more common with HCV genotype 3.
- Jaundice (yellowed skin and eyes).
- Oesophageal varices (when veins in the esophagus – the tube that connects the throat to the stomach – become swollen due to high blood pressure from the liver).
- Ascites (fluid build-up in the abdomen) – symptoms include swollen ankles.
- Encephalopathy (when toxins that the liver usually removes from the bloodstream build up in brain, causing dysfunction).
- Portal hypertension (high blood pressure in the vein that carries blood to the liver).
- Kidney damage, thyroid disease, and malnutrition from appetite loss.

Natural history of HCV

The natural history of an infection is the term for describing what happens if the infection is not treated.

The natural history of HCV infection includes three possible stages:

- Acute infection.
- Chronic infection.
- End stage liver disease (ESLD).

Acute infection

Acute infection refers to the first six months after HCV infection.

Unless it causes symptoms – and about 80% of people do not have any symptoms—acute HCV is rarely diagnosed. Symptoms, when they do occur, include fever, fatigue, abdominal pain, nausea, vomiting, dark urine, pale faeces and jaundice.

Acute HCV infection in HIV positive people has generally been detected because of routine monitoring if they are on treatment. Unexplained abnormal liver enzymes should prompt checking for acute HCV.

HIV positive gay men should have an annual screen for HCV and this should be offered by your HIV clinic.

In the first few months after infection, up some people clear the virus without HCV treatment.

This is called spontaneous viral clearance and is more common if:

- You had symptoms during acute HCV.
- You are a female.

- You are under 40 years old.
- You have the IL28B CC gene (it is not recommended to test for this in the UK - see page 50).
- Your CD4 cell count is high.

HIV positive people are only half as likely to spontaneously clear HCV as HIV negative people. People of African descent are less likely to clear HCV than Caucasians.

Genetics are part of the reason for these differences, but other factors that we don't know are also involved.

People who clear HCV without treatment are no longer infectious. They may still test positive to an HCV antibody test because they were previously infected, but HCV will not be detectable in blood.

If HCV does not clear spontaneously, UK guidelines recommend considering treatment within the next 12 weeks because of higher cure rates when HCV is treated in the acute stage.

If you are diagnosed with acute HCV, it is important to discuss with your doctor the risks and benefits of treatment.

Glossary

acites An abnormal accumulation of fluid in the abdomen, a sign of serious liver damage in people with HCV.

varices Extended or swollen veins that can burst, a complication of cirrhosis.

Chronic infection

Chronic infection refers to any time after acute infection (the first six months after infection).

In HIV negative people, HCV usually progresses very slowly, often over decades and there is a wide range of possible outcomes.

If HCV affects other areas of the body than the liver these conditions are called extrahepatic.

Whatever the timescale, some people will never have significant liver damage or symptoms. However, others will develop mild-to moderate liver scarring (fibrosis) which can cause symptoms such as fatigue, depression and confusion.

There seems to be no clear relationship between the degree of liver damage and the experience of symptoms.

HCV can contribute to a build-up of fat in liver cells called steatosis (or fatty liver). This can worsen liver damage and makes HCV harder to treat. Fatty liver is most common in people with HCV genotype 3.

In people with HCV genotype 1, fatty liver is more likely in those who are overweight, have insulin resistance or type 2 diabetes, high blood pressure, heavy alcohol use and liver inflammation.

Fatty liver can lead to more serious liver scarring. In people with coinfection, it is linked with several factors. These include use of some older HIV drugs (especially d4T and ddI), low levels of HDL (good cholesterol), being overweight and having lipodystrophy (fat accumulation or fat loss).

About 20-30% of HIV negative people with chronic, untreated HCV will progress to cirrhosis (serious liver scarring).

Even with cirrhosis, the liver can still function.

When a cirrhotic liver can compensate for the damage this is called compensated cirrhosis.

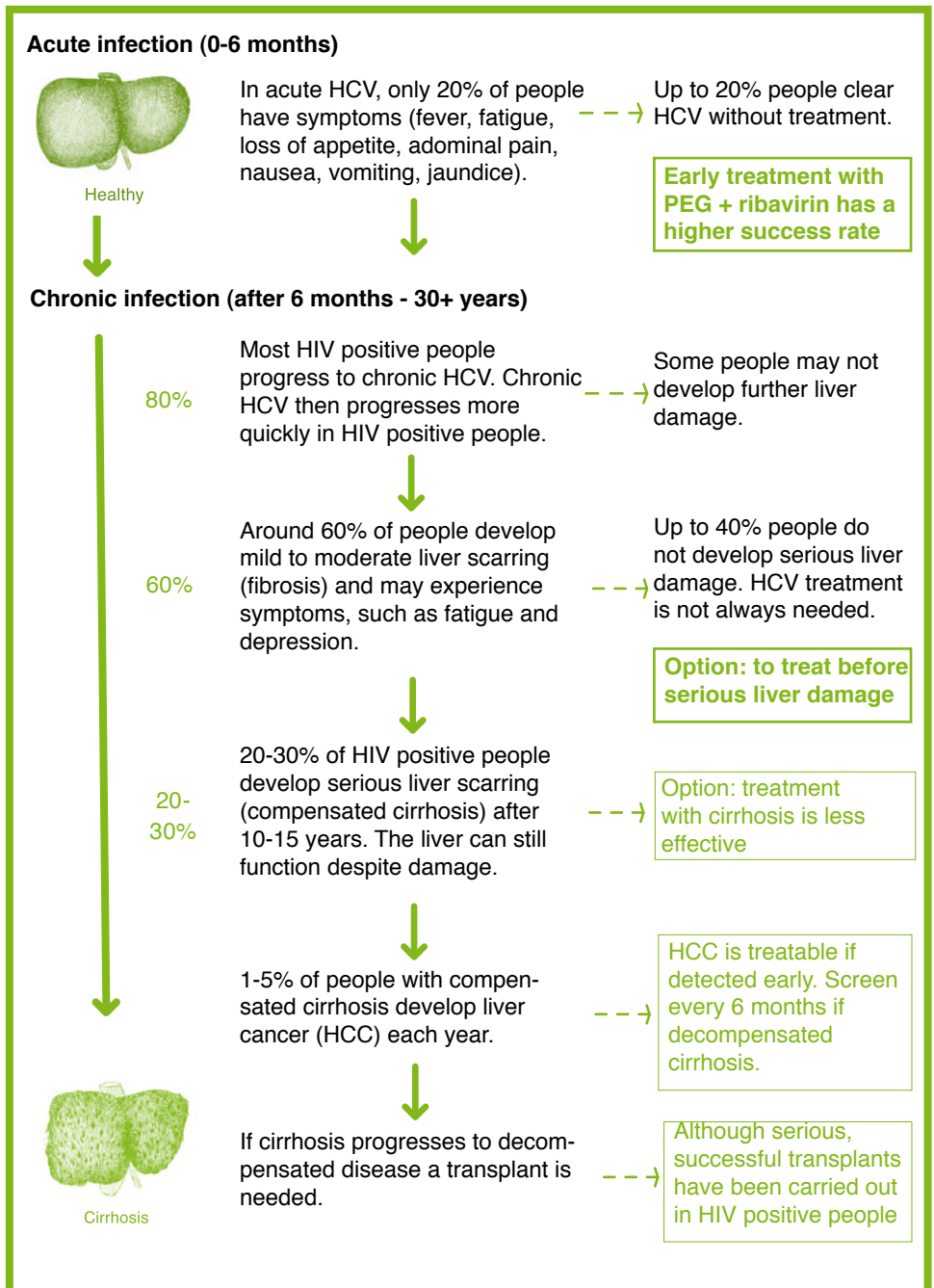
When the liver becomes too damaged to function properly, this is referred to as decompensated cirrhosis or end stage liver disease (ESLD).

End stage liver disease

Decompensated cirrhosis requires a liver transplant. Although it is a serious operation, successful liver transplants have been carried out in people with coinfection.

Each year, 1-5% of people with cirrhosis develop liver cancer. This is also called hepatocellular carcinoma (HCC). This can be successfully treated, especially if it is diagnosed early.

UK guidelines recommend that people with HIV/HCV coinfection and cirrhosis should be routinely screened for HCC every six months.

Fig 1: HCV progression in coinfection

HIV and HCV coinfection

Although many people have lived with HIV and HCV for many years, HIV makes HCV progress more quickly. The risk of serious liver damage is greatest if your CD4 count is less than 200.

HIV drugs have enabled many people to lead much longer lives. This means that people with coinfection are now living long enough for the HCV to become a concern. End stage liver disease is now a leading cause of death among HIV positive people.

However, HCV can be treated and cured, regardless of a person's HIV status. Some coinfection-related deaths are due to late HCV diagnosis, or late HCV treatment after severe liver damage has already occurred.

New drugs that are more effective, safe and tolerable will soon become available for HIV positive people.

Effect of HCV on HIV

HCV is not thought to worsen HIV, but it can make HIV treatment more complicated. This is mainly because the liver processes most HIV drugs.

HCV increases the risk for liver-related side effects from HIV drugs. But the benefit of HIV treatment still outweighs this risk.

Some HIV drugs require lower doses for people with advanced liver disease. Dosing can be individualised by measuring HIV drug levels in a sample of blood.

Factors that speed up HCV progression include:

- HIV coinfection.
- Alcohol intake, especially more than 50 grams/day. This is about 6 units per day: 2-3 pints of beer or 4-5 glasses of wine.
- Ageing (over 40 years old).
- Duration of HCV infection.
- Older age when infected with HCV (over 40 years old).
- HBV coinfection.
- HCV may progress faster in men than women.

How can I protect my liver?

There are many things that can help your liver stay healthy. These include:

- Things that are good for your general health like a balanced diet, keeping active and not smoking, are also good for your liver.
- Get vaccinated against hepatitis A and B. Other viral infections in your liver can worsen HCV.
- Drink less, or stop drinking alcohol. The less you drink, the better for your liver. Sometimes drinking less – or not at all – is more important than treating HCV.
- Cure HCV with treatment.
- Maintain a normal weight; being overweight increases your risk for fatty liver.
- Drink plenty of water to help your liver filter waste and toxins.
- Diet changes (see page 85) include eating fewer foods that are high in fat, salt or sugar especially in advanced HCV. A good diet includes eating more fresh fruit and vegetables, complex carbohydrates (whole grains, breads, rice, pasta), food that is low in fat and high in fibre and an adequate amount but not excess protein.
- Three cups of coffee (with or without caffeine) a day can delay fibrosis progression and lower the risk of liver cancer.
- Eating dark chocolate (85% cocoa) every day has been linked to better liver health and reduced risk of heart problems.
- Ask questions and get support. Talk with other people who are living with HCV or coinfection.

See pages 82-86 for more information about life style changes.

New HCV coinfection

New HCV infections in HIV positive gay men

Over the last ten years, most cases of acute HCV in HIV positive people have been gay men.

The majority of these cases occurred from sexual exposure, which is new. Previously, based on heterosexual studies, HCV was not thought of as a sexually transmitted infection.

In the UK, many hundreds of cases of acute HCV have been reported. And HCV has generally only been detected because routine monitoring of people on HIV treatment picked up increases in their liver enzyme levels.

“At the time I was diagnosed, I had been feeling really ill for about six weeks – tired all the time, pains everywhere. My GP 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.”

Even though the UK has had public health campaigns about sexually transmitted HCV for gay men, awareness of HCV is still low.

For some people, the impact of HCV may be lessened because they see HIV as more serious. But for many, being diagnosed with HCV after many years of living with HIV is traumatic.

“It was like getting an HIV diagnosis all over again. It changes how you think about sexual risk.”

Many positive gay men are open about their HIV status and chose positive partners so that HIV is not a problem.

HIV-related discrimination from negative or untested men may also have lessened. This is due to the growing awareness that an undetectable HIV viral load dramatically reduces the risk of sexual transmission.

An HCV diagnosis changes this.

The lack of information about risk and protection makes HCV disclosure complicated in ways that have been overcome for HIV. An HCV diagnosis can dramatically change someone's social and sexual network.

“... 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 sexual transmission. Consequently, my sex life has declined dramatically and I see no sign of it improving.

I suspect that disclosure within the group of HIV positive men would be very similar to disclosing ones 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.”

Responses to an HCV diagnosis are individual. The stigma and lack of information about hepatitis C can make an HCV diagnosis more difficult than HIV.

“I told my immediate family but that was all ... I decided not to tell my casual sexual partners - many men “don’t ask, don’t tell” and it was never an issue.

I didn’t tell any of my friends because of possible stigma and I hoped the treatment would cure me and could put the whole experience behind me.”

Peginterferon and ribavirin are more likely to cure people with HCV genotypes 1 or 4 during acute infection, even though these drugs are less effective for people with chronic HCV.

Some studies have reported that acute HCV can progress rapidly in people who are already HIV positive, but this is controversial. HCV progression depends on many factors and some people may already have liver damage from other causes before they become infected with HCV.

The chance to clear HCV and protect sexual partners can be an important reason to use treatment.

“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.”

The decision to treat early, although recommended because of higher clearance rates, also needs to be balanced against the side effects. Some people do not treat early because they are waiting for better treatment that will be easier to tolerate.

“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 my first HCV specialist for me to start treatment immediately after first diagnosis six years ago. I was uncomfortable with this and so moved to another clinic.

Because I have lost the sight in one eye due to CMV in the 1990s, I also consulted my ophthalmologist. She told me that the then usual HCV treatment with Interferon carried a risk for a minority of people of causing fuzzy spots in the eyes.

Because of this I decided not to use HCV treatment at that time. I was not willing to risk any further damage to my eyesight. I now monitor new treatments for HCV with my current HCV specialist and would start treatment once one is available which does not include Interferon or ribavirin.

I do not drink, which will hopefully slow down the progression of any liver damage. In twenty years, I will be in my late 70s and I suspect that it will not be the HCV that kills me. I am banking on a new and effective treatment for HCV becoming available before my liver begins to seriously deteriorate.”

It was like getting an HIV diagnosis all over again. It changes how you think about sexual risk.

There is a lack of information about HCV in the gay community, even among HIV positive men. This makes a new diagnosis difficult at a time when you need most support. Some people say it felt like getting their original HIV diagnosis again.

“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.”

But again there are many approaches to dealing with a new HCV diagnosis:

“I regret not relying on my friends for support, because I know it put an enormous burden on my partner who had to juggle being both partner and sole carer for me. 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.”

It is easier to talk about HCV once you feel stronger and have more information, or after a successful response to treatment. As with HIV, knowing other people in the same situation may be the most positive support.

“There was no co-infection support group when I first went. I was the only HIV positive man at a group run by the Hepatitis C Trust... but it was tremendously useful. I got just as much from helping other people as I did from their support.

They also run a fantastic helpline and everyone there has or has had HCV and they really understand what support means.”

The Hepatitis C Trust Helpline and Support Groups

0845 223 4424

Monday to Friday, 10.30 to 4.30pm

Calls are charged at the national rate.

The Hepatitis C Trust run support groups that are women-only, men-only and mixed.

They also run a Gay Men’s support group and a group for gay men co-infected with HIV and HCV.

For information on support groups:
<http://www.hepctrust.org.uk>

* [www](#) – More detailed stories about new HCV infections are linked to the the web-based version of this guide

Long-term coinfection

Generally people who are HCV positive from blood products or through injecting drug use

It is very common for people who became HIV positive through blood products or sharing injection drug equipment, to also have HCV.

Most people in this situation have been living with both infections for many years.

One activist said:

“Even though I was diagnosed in the early 80’s 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 co-infected people.”

And others explained:

“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. As an event, it pretty much went unnoticed as far as I was concerned. 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 as big news.”

Dealing with HCV has now become the most important health concern.

Many people with coinfection have lived with HCV for years, without treating it.

Some people decided against HCV treatment because they did not have serious liver damage, because they were worried about side effects or because the success rate with older treatment was low. Many people chose to wait for newer treatments.

“I am hoping that in a year or so some of the drugs on 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 I will do if that it is required. But I am fearful because my quality of life is gonna drop to the floor – and for at least a year...”

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.”

HCV treatment decisions

Deciding when to treat HCV is often different for people who have had HCV or coinfection for a long time.

Getting the right balance between delaying treatment and not waiting too long is difficult. Treatment is less effective if the liver becomes seriously scarred.

Although many drugs are in development, peginterferon and ribavirin are still used in most combinations. Adding boceprevir or telaprevir for people with genotype 1 increases success rates but difficult side effects are likely to interfere with work and affect your general quality of life.

HCV treatment can affect mood and increase depression. Alcohol, sometimes used as a way to cope, is likely to increase anxiety and depression and cause liver damage. Alcohol can make adherence to treatment more difficult. Cutting out alcohol or cutting down is more likely to help.

There are many drugs in development with good results in HCV mono-infection so continuing to wait may be safer for some people. Others may need to treat HCV sooner to prevent liver damage from worsening.

“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 1-2 years (by FibroScan or biopsy) and wait for a better treatment options.”

If your liver has already been badly damaged by HCV, then treatment is more important.

Planning for treatment can make a big difference. With support, many people can manage treatment well when they need it.

Access to treatment is not always easy, especially for those people who are heavy drinkers or who are using heroin and other drugs (see pages 60-61).

“Having the experience of sharing with other people who have the same kind of health problems 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 co-infected and the co-infection clinic is crucial.”

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“For years, I was told that the risk of sexual transmission of HCV was very low, in fact recommendations for heterosexual couples in which one of them is HCV positive is not to use condoms.

Since diagnosis with HIV, we have practised safe sex by using condoms – primarily because of issues of re-infection (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.”

Testing and monitoring

Tests to diagnose HCV

Annual HCV testing is routinely recommended in the UK as part of HIV monitoring. This is especially important for anyone who has had another STI and/or is sexually active or injecting drugs.

HCV testing is also recommended if liver enzymes become raised.

HCV testing is a two-stage process.

1) The first test is usually an **HCV antibody test**.

A positive result means that you either have had HCV and cleared it or that you still have HCV.

A negative result can also mean that you have HCV. This test will not detect acute HCV because it can take 6-24 weeks after infection for HCV antibodies to

develop. Also, if your CD4 count is less than 200 you may not make antibodies to HCV.

2) An **HCV viral load test (RNA)** will confirm or rule out chronic infection.

The viral load test looks for genetic material of HCV in the same way as an HIV viral load test detects HIV.

If you have detectable HCV viral load, it means that you are currently infected with HCV.

If your HCV viral load is undetectable, a second test should be done six months later. If two successive test results are undetectable, you have spontaneously cleared HCV.

See Table 1 for information about HCV tests.

Table 1: HCV tests and what the results mean for HCV infection

Type of test			
Diagnosis	Antibody test result	HCV RNA (Viral load test)	ALT: liver enzyme
Prior, cleared HCV Infection	Positive	Undetectable on two tests, performed at least 6 months apart	May be up to 7 times above normal, fluctuate, or be persistently raised
Acute HCV Infection	Negative; and becomes positive within 6-24 weeks	Detectable within 1-2 weeks, usually very high	May be up to 7-10 times above normal level
Chronic HCV Infection	Positive	Detectable	May be persistently normal, fluctuate, or persistently raised

Routine blood tests

After an HCV diagnosis, your doctor should run other blood tests.

These include HCV genotype, testing for hepatitis A and B, complete blood count (CBC) and blood clotting time, liver enzyme tests (including ALT/AST, albumin and GGT), thyroid function test (TFT), serum iron, liver autoantibodies, and liver ultrasound.

These are described in more detail below and in Table 3 which includes space to record your own results.

Hepatitis C viral load (RNA testing)

HCV viral load tests, similar to HIV, measure levels of virus in a sample of blood.

But HCV replicates at a much greater rate than HIV, producing trillions vs. millions of copies per day. It is therefore common for HCV viral load to be much higher – sometimes in the tens of millions of copies/mL.

People with HIV also have higher hepatitis C viral loads than people with HCV alone.

In the UK, HCV viral load testing is routinely recommended for everyone with coinfection.

Unlike HIV, hepatitis C viral load is not related to the risk of the disease getting worse. Nor is it used to decide when to start treatment.

HCV viral load that is less than 400,000 IU/mL is called low and has a better treatment response to peginterferon and ribavirin. Viral load level is likely to be less important with DAAs.

Glossary

Antibody A protein that is part of the immune system and which recognises an infection

DAAs Direct Acting Antivirals - this refers to the new HCV drugs in development.

About HCV viral load testing

There are two types of HCV viral load tests.

Qualitative testing

Qualitative testing is usually 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 ('International Units per millilitre of blood').

Results are reported as either detectable or undetectable depending on whether the virus is either found or not.

Quantitative testing

Quantitative testing measures the amount of HCV in a blood sample. Results are reported as international units per millilitre, or IU/mL.

Quantitative testing is usually used to obtain a baseline (pre-treatment) viral load. Qualitative testing is often used to monitor response to treatment during HCV therapy.

Understanding HCV RNA test results

Results from HCV RNA testing are reported in one of three ways:

- Detectable (Quantifiable) – viral load given in IU/L.
- Detectable but below lower limit of quantification (LLOQ). The LLOQ is the smallest amount of HCV RNA that a test can measure. This threshold differs according to the type of test that is used.
- Undetectable – ie below the lower limit of detection (LLOD). The LLOD varies by test.

HCV genotype

There are at least seven different types of HCV, known as genotypes that are more commonly reported in different regions see Table 2.

Genotypes are numbered from 1-7, in the order that they were discovered.

These genotypes also have variations, called subtypes which are named by lower-case letter (i.e. a, b, c, etc), also in the order that they were discovered.

Each genotype and subtype is a distinct virus. You can be infected - and reinfected - by more than one genotype or subtype. You can also be reinfected with the same or a different genotype after successfully clearing HCV.

You need to know your genotype to plan your treatment and, in some cases, to know how long treatment should be used.

Many of the DAAs in development are only active against genotype 1 (and some are more active against 1b than 1a).

In the UK, everyone with coinfection should have an HCV genotype test. This is a test to insist on.

Liver enzyme tests: ALT and AST

Liver enzymes are proteins with specific functions (and inconveniently long names).

If the liver becomes damaged, some of these enzymes leave the liver and enter the blood.

Many things can cause liver enzyme levels to increase.

These include:

- Prescription and over-the-counter medicines.
- Herbs, vitamins and supplements.
- Toxic fumes
- High alcohol intake or coming off drugs and/or alcohol.
- New or existing hepatitis infection.

HIV drugs can cause liver enzymes to increase – though usually not to dangerous levels. In some cases, these drugs need to be stopped or switched.

HCV drugs increase liver enzymes and frequent monitoring during HCV treatment is important.

Table 2: Most common HCV genotypes by region

Region	Main HCV genotype
UK	1 and 3
Asia	1, 2 and 3
Egypt, the Middle East, Central and West Africa	1, 2 and 4
Mainland Europe, North America, Japan	1a and 1b. G2 and 3 are less common, G4 is increasing.
South Africa	2 and 5
South East Asia	1, 3, 6 and 7

People taking HIV drugs (or any other drugs processed by the liver) need to have liver enzymes routinely measured with other blood tests. This is especially important with HCV coinfection.

The results from these tests should be looked at in relation to other information.

Although they are often called liver function tests (LFTs), enzyme levels are not really a measure of liver function.

Two important enzymes are ALT (alanine aminotransferase) and AST (aspartate aminotransferase).

ALT is produced in the liver and increases are usually a sign of liver inflammation or damage. However, ALT is not a good marker of either liver damage or changes in liver health. This is because HCV itself causes levels to go up and down.

Up to a third of people with chronic HCV always have a normal ALT, even with serious liver damage.

If an increase in ALT continues to rise, or is getting worse, it may mean continued HCV related inflammation which may eventually lead to scarring (fibrosis).

AST is an enzyme that is made in the heart, intestines, and muscles. AST is only used to monitor liver inflammation and damage in combination with other tests.

Normal liver enzymes, even over time, do not mean there is no liver damage.

Raised liver enzymes do not always mean there is liver damage, but if they are persistently high this can be a sign of ongoing damage, and that treatment may be a good idea.

Other liver enzymes:

ALP, GGT, bilirubin, albumin and prothrombin time

Routine monitoring in coinfection also includes ALP, GGT, bilirubin, albumin and prothrombin time (PT).

ALP (alkaline phosphatase) is an enzyme that is present throughout the body, including the liver. If blood levels of ALP increase, this can be a sign of tissue disease or damage. Your doctor can also test specifically for ALP from the liver. Some medications, including the HIV protease inhibitor atazanavir, can increase ALP. Elevated ALP from the liver is a sign of blocked bile ducts caused by liver disease.

GGT (gamma glutamyl transferase) is an enzyme involved in metabolism that is produced in the bile ducts. Any liver disease, heavy drinking, and some medications can all increase GGT.

Bilirubin is a waste product from the breakdown of red blood cells. Before it passes through the liver, where it is mixed with sugars to become water-soluble, it is called indirect or unconjugated bilirubin. Once it has been processed through the liver it is called direct or conjugated bilirubin.

A damaged liver may be unable to process bilirubin, causing an increase in the total bilirubin levels. Usually, a laboratory will subtract the amount of direct bilirubin from the total amount of bilirubin in the bloodstream; the leftover is indirect bilirubin.

Table 3: Track your lab results

Note: These ranges are included as a guide. Different laboratories may use different ranges, and it is important to refer to the reference range that your laboratory is using.

	Date and Lab results					Normal Ranges (W= Women M= Men)
CD4 Count						Measured in cells/mm ³ . Range 0 to over 1600 - higher is better. Over 200 reduces risk of infections.
HIV Viral load						Measured in copies/mL. Range from undetectable to over 1 million (rare)
HCV Viral load (RNA)						Measured in IU/mL. Range from undetectable to over 40 million. Over 400,00 reduces the chance of treatment success with peginterferon and ribavirin.
ALT						W: 7 - 30 units/L M: 10 - 55 units/L
AST						W: 9 - 25 units/L M: 10 - 40 units/L
ALP						W: 30 - 100 units/L M: 45 - 115 units/L
GG						W: Over 45 U/L M: Over 65 U/L
Bilirubin (Direct)						0.0 - 0.4 mg/dL (US) 0 - 7 umol/L (SI units)
Bilirubin (Total)						0.0 - 1.0 mg/dL (US) 0 - 17 umol/L (SI units)
Albumin						3.1 - 4.3 g/dL (US) 31 - 43 g/L (SI units)
PT						11 - 13.5 seconds PT 1.5 - 2 times control is abnormal

Jaundice is an increased level of bilirubin and common signs include a yellowing of the skin and eyes, dark urine or pale stools. Some drugs, including the HIV protease inhibitor atazanavir, and HCV protease inhibitors, can increase bilirubin.

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

PT (prothrombin time; pro-time) testing measures the amount of time it takes for blood to clot. A damaged liver is less able to make clotting factors. When this time increases – referred to as a “prolonged PT” – the liver is not working normally.

Screening for liver cancer in people with cirrhosis

People with HCV cirrhosis are at risk for liver cancer, even if they have been cured by HCV treatment. Regular screening can detect early-stage liver cancer.

Usually, screening consists of a liver scan by ultrasound, computed tomography (CT) or Magnetic Resonant Imaging (MRI), and a blood test measuring alpha-fetoprotein (AFP; a protein made in foetal liver tissue). Screening is recommended every six months.

Measuring liver damage

The amount of liver damage is defined in two ways:

- 1) The **stage** measures the amount of fibrosis (scarring).
- 2) The **grade** measures the amount of inflammation, which relates to rate of future scarring.

In the UK, non-invasive tests like a FibroScan or blood tests are generally preferred to a liver biopsy which involves taking a sample of your liver with a needle to test in the laboratory.

Liver stiffness (FibroScan)

The stage of liver disease can be estimated by measuring liver stiffness using a FibroScan.

This scan is painless, takes less than ten minutes and produces immediate results. FibroScan has dramatically reduced the need for having a liver biopsy (see below).

FibroScan measures how quickly vibration waves pass through the liver. The more damaged or stiff the liver, the more rapidly the waves will pass through it. Results are presented as a number in kilopascals (kPa). A higher number indicates more liver damage.

Results from FibroScan need to be interpreted based on other factors.

However, a score of over 7.2 kPa indicates higher likelihood of significant fibrosis (F2 or greater on Metavir scale). A score over 14.5 kPa in someone with HCV/HIV coinfection indicates cirrhosis (F4 on the Metavir scale).

The Metavir scale is used to score results from a biopsy, see Tables 4 and 5.

In the UK, scans such as FibroScan are recommended for monitoring liver health in people with coinfection.

FibroScan is not a perfect test and does not work for everyone.

Disadvantages include:

- It may be too difficult to perform and results may be unreliable in people who are obese or who have ascites. Ascites are a build up of fluids in the abdomen and are a symptom of serious liver damage.
- It may overestimate damage in acute HCV.
- It is less sensitive at detecting small differences between mild or moderate liver damage.

However, FibroScan it is very sensitive at picking up severe damage.

It can therefore identify people who need HCV treatment more urgently.

If FibroScan results indicate serious liver damage, the test should be repeated.

Table 4: Interpreting FibroScan results with HCV (UK guidelines)

Result (kPa)	Interpretation
Above 7.2	Fibrosis (Metavir* F2)
Above 14.5	Cirrhosis (Metavir* F4)

* Metavir: see page 45 and Table 5.

YouTube videos



www.youtube.com/watch?v=I_E4ZGmKooA

Dr Sanjay Baghani from the Royal Free Hospital in London shows how a Fibroscan works.



www.youtube.com/watch?v=PXTdt_ZtlgM

Dr Douglas Dieterich from the Mount Sinai Hospital in New York performs a biopsy.

Alternatives to a biopsy: non-invasive biomarkers of liver disease

If FibroScan is not available, results from a panel of blood tests can sometimes be used to assess liver damage.

Studies using combinations of these lab results suggest they are useful for identifying serious liver damage. Results are pretty good but they are not quite as useful as a FibroScan or biopsy.

In the UK, if a FibroScan is not available, or if FibroScan results are not clear, then monitoring using non-invasive blood panel tests is recommended before deciding on a biopsy.

These tests include APR, FIB-4, ELF, FibroMeter and FibroTest.

Liver biopsy

A liver biopsy measures liver damage by taking a small sample of your liver to look at under a microscope.

This is still considered a good way to assess liver disease. However, it only used in the UK when other tests are not appropriate because it is an invasive test. A biopsy provides information about both the stage and the grade. It can also identify other causes of liver disease.

A liver biopsy involves having a needle inserted between the ribs, and into the liver. The needle then clips and removes several tiny samples of liver.

The procedure can be painful, and carries a small risk of complications (1-3%). These include a risk of puncturing other organs or bleeding, and a much smaller risk of complication that is fatal (0.1% to 0.01% - one in 1000 to 1 in 10,000).

Some clinics in the UK use a transjugular (TJ) liver biopsy. This is where the liver is reached via the large vein in your neck which reduces the risk of some complications from needle biopsies.

However, even a biopsy is not perfect. This is because there can be errors in taking the sample and in reviewing it. The results may not be accurate if the sample is too small, or if it came from an area in the liver that is either more or less damaged than the rest.

Because a biopsy is not pleasant, many people are reluctant to have this test. Although some doctors still think that biopsy offers the best way to measure liver damage, it is becoming more common to use other tests, such as FibroScan.

When is a biopsy important?

A biopsy is sometimes recommended if the results from a FibroScan and blood tests are not clear or to diagnose other causes of hepatitis.

If a biopsy shows less liver damage it makes it easier to wait for new drugs. Moderate to serious liver scarring shows the importance of treatment to prevent liver damage from getting worse.

Only an experienced doctor with a good record of successful biopsies should perform these tests.

The doctor should also use an ultrasound scan to guide the needle and reduce the chance of puncturing another organ. The ultrasound also helps pick which area of damaged liver to sample.

Ask your doctor about options for pain management during and after the procedure. Ask other people about their experiences. It may be easier to find a good doctor by talking with people who have had a biopsy.

Interpreting biopsy results

There are different systems for measuring liver inflammation and fibrosis from a biopsy. All range from zero to a maximum score with a higher number indicating more inflammation or fibrosis.

Two scoring systems, Metavir and Ishak, are commonly used to grade and stage liver biopsy results.

The Metavir system scores inflammation from A0-A3 and fibrosis from F0-F4. The Ishak system scores inflammation from 0 to 18 and fibrosis from 0 to 6, see Table 5.

UK (BHIVA) guidelines define mild liver damage as a modified Ishak fibrosis score of 3 or less and a Metavir fibrosis score of 2 or less. Moderate liver damage is an Ishak inflammatory score of 4 or more and/or a fibrosis score of 3 to 5.

However, these scoring systems are not used in every hospital and some clinics prefer to just stage biopsies as mild, moderate or cirrhosis.

Table 5: Interpreting biopsy scores

	Inflammation	Fibrosis
Metavir	A0 - A3	F0-F4
Ishak	0 - 18	0 - 6

HCV treatment and management

Introduction

This section is focused on conventional medical treatments for HCV.

It includes the goals of treatment, choice of drugs, duration of treatment, who should use treatment, how effectiveness is measured and whether HIV or HCV should be treated first.

Deciding whether to use treatment is discussed afterwards on pages 74-76.

Managing HCV with lifestyle changes is discussed on pages 83-86.

What are the goals of treatment?

There are two goals of HCV treatment.

One is to cure HCV and the other is to improve liver health.

Curing HCV

The first goal of treatment is to clear HCV. This is called a cure.

A cure is defined as an undetectable HCV viral load during treatment and at 24 weeks after treatment has ended. Recent research suggests that 12 weeks after treatment is usually enough time for most people to know if they have been cured.

The technical terms for these outcomes are SVR-24 and SVR-12 respectively. SVR stands for sustained virologic (ie viral) response.

Up to 99% of people who have an SVR-24 remain free from HCV many years later. This is regardless of HIV status.

Although HCV can sometimes return after an SVR-24 (known as relapse), this is very unusual, except in the case of HCV reinfection.

Improving liver health

A second goal of HCV treatment is to improve liver health.

This occurs from reducing liver inflammation. As well as preventing further damage, sometimes fibrosis can even be reversed.

These improvements in liver health usually happen in people who are cured, and rarely in people who do not have an SVR.

SVR reduces the risk of liver cirrhosis, liver cancer and liver failure in both HIV negative and HIV positive people. In HIV positive people, SVR lowers the risk of death from liver-related and HIV-related causes, even if you have cirrhosis.

For HIV positive people, there may be an additional benefit from HCV treatment in reducing the risk of liver-related side effects from HIV drugs.

However, for some people the condition of the liver may worsen after HCV treatment, particularly if the treatment was not successful at clearing the virus. It is not clear why this happens.

Even after an SVR, continued monitoring is important. For example, people who have cirrhosis still need to be monitored regularly for liver cancer.

Who needs HCV treatment?

Most HIV positive people with HCV coinfection should be offered HCV treatment.

However, several factors need to be considered to make sure that “the benefits of therapy outweigh the risks”.

This will depend on:

- HIV status. HCV treatment is used earlier for people with coinfection than for HIV negative people with HCV.
- Whether HCV is acute (early) or chronic. Treatment is more effective during if started within six months of infection.
- HCV genotype can be a factor in deciding when to treat and when to wait.
- How you feel about treatment.
- The amount of liver damage.

Mild liver disease does not need treating and this makes it is easier to decide to wait for better drugs. Regular monitoring to assess fibrosis is important.

Moderate liver damage has a risk of progression to cirrhosis and a greater need for treatment.

Compensated cirrhosis can be treated, but treatment is less likely to be effective, and side effects may be worse. Careful monitoring is needed.

Decompensated cirrhosis cannot be safely treated with PEG-IFN and RBV. Hopefully, future treatments will be safe and effective for people with decompensated cirrhosis. Currently, referral for liver transplantation and management of portal hypertension (high blood pressure in the portal vein) and hepatic insufficiency (partial or total failure of liver function) are recommended for people with decompensated cirrhosis.

How is HCV treated?

Currently, HCV treatment involves using interferon plus ribavirin for most patients.

In addition, people with genotype 1 also use an HCV protease inhibitor – either boceprevir or telaprevir.

Treatment generally lasts for 48 weeks but may be 24 weeks for some people.

Combinations that do not use peginterferon and ribavirin and that use even shorter treatment are being studied in clinical trials.

However, with the indicated approval of sofosbuvir in the EU (in November 2013), to treat genotype 2 and 3, the first all oral combination will soon be available for some people.

The results from these trials are expected to change the way HCV is treated within the next few years. See pages 78-82.

Peginterferon

Interferon is a man-made version of a chemical that your body already produces. It works directly against HCV but also stimulates the immune system to fight viruses.

Peginterferon (pegylated interferon) is a long-lasting formulation that only needs to be given once a week.

Non-pegylated interferon is not recommended, since it is less effective.

There are two types of peginterferon, both given by injection.

1. Alpha-2a (trade name Pegasys and manufactured by Roche). This comes as a liquid and is stored in the refrigerator. All adults use the same dose.
2. Alpha-2b (trade names PegIntron or ViraferonPeg and manufactured by Merck). This comes as a powder that has to be reconstituted with purified water, both of which come in separate vials. The dose of PegIntron depends on your body weight.

Different formulations have been studied differently in patients with different 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.

One study comparing 14 other trials suggested that alpha-2a might be better than alpha-2b, but these differences were modest.

Ribavirin

Ribavirin is a nucleoside analogue similar to some HIV drugs (“nukes”).

On its own, ribavirin does not directly work against HCV or HIV. When it is used with peginterferon it improves the response to HCV treatment.

Ribavirin is an oral drug, given as pills or capsules, twice daily. It is usually dosed by body weight. Brand names for ribavirin include Copegus, Rebetrol and Ribasphere.

HCV protease inhibitors: boceprevir, telaprevir (and simeprevir)

Boceprevir and telaprevir were the first direct-acting antivirals (DAAs) to be approved. Simeprevir approval is expected in 2014. These drugs are used in combination with peginterferon and ribavirin.

They are HCV protease inhibitors (PIs) and similar to HIV PIs, but boceprevir and telaprevir are only used to treat HCV genotype 1. Simeprevir is also used to treat HCV genotype 4.

Boceprevir, telaprevir and simeprevir have different side effects and drug interactions. Simeprevir and telaprevir are used for 12 weeks boceprevir is used from 24 to 44 weeks. Peginterferon and ribavirin are used from 24 to 48 weeks with these drugs.

Simeprevir is taken once daily, with food. Boceprevir and telaprevir are oral drugs that need to be taken three times a day with a meal or snack. Telaprevir can be taken twice daily, although this dosing schedule is not recommended for HIV positive patients on HIV treatment because of drug-drug interactions.

These drugs significantly improve the chance of curing HCV but they are still linked to difficult side effects.

These include:

- Low white and red blood cell counts.
- Low platelet counts.
- Rash that ranges from mild to very serious, even life-threatening (although this is rare).
- Fatigue, nausea, vomiting and diarrhoea.
- Photosensitivity.
- Taste changes (dysgeusia), and
- Anal itching, burning and haemorrhoids.

How long is HCV treatment?

Current treatments are usually 48 weeks in someone who is HIV positive.

Some studies are looking at whether 24 weeks will be okay for some people. This depends on HCV genotype and on having an early response to treatment.

Sometimes, if it is not working, treatment may be stopped after the first 4-8 weeks.

Some of new drugs will reduce treatment to only 12 weeks, but this is early research.

Fact sheets: boceprevir and telaprevir

<http://www.treatmentactiongroup.org/hcv/factsheets/victrelis-boceprevir>

<http://www.treatmentactiongroup.org/hcv/factsheets/incivek-telaprevir>

Predicting the response to treatment

Several factors predict how well HCV treatment will work. Many of these are more important with peginterferon and ribavirin and less important with DAAs.

These include:

- Having an undetectable HCV viral load after four weeks of treatment.
- HCV genotype and subtype. Highest cure rates are in genotype 2, either with peginterferon and ribavirin or DAAs. Genotype 1 has become easy to cure with DAAs, but curing genotype 3 without peginterferon is a bit tricky; ongoing research is looking at the best length and type of treatment. Genotype 1b is easier to cure with most DAAs than 1a.
- HCV treatment is less effective for people with cirrhosis
- Genetics and race, although these are less important when DAAs are used with or instead of peginterferon (see box).
- Adherence. Not missing doses is especially important with HCV protease inhibitors and other DAAs.
- Body weight and age. Peginterferon plus ribavirin are less effective for people who weigh more than 165 lbs (75 kg) or who are older than 40. Weight or age are not important with DAAs.
- HIV status. Although HCV treatment used to be less effective for HIV positive people, cure rates are similar when DAAs are used with or instead of peginterferon.

- Effectively managing side effects.
- HCV viral load under 400,000 IU/mL, although this is much less important with DAAs.

As with HIV, starting treatment is the only way to know how well you will respond.

HCV, genetics and race

The interleukin-28B (IL28B) gene affects how well pegylated interferon plus ribavirin works.

Of the three possible IL28B genotypes (CC, CT or TT), people with CC have a stronger immune response.

Having the CC genotype has also been linked to a higher chance of clearing HCV without treatment.

African Americans and people of African ancestry are more likely to have non-CC genotypes. This explains – in part – why peginterferon-based treatment is less effective for African Americans. Asian people and people with Asian ancestry are most likely to have the IL28B CC genotype.

IL28B genotype is less important with some of the new DAAs, especially when they are used without peginterferon.

UK guidelines do not recommend routinely testing for IL28B.

How well does treatment work?

Cure rates in clinical studies vary depending on which HCV drugs are being used and which genotype is being treated.

They also vary based on the people in the study. For example, people with advanced liver damage may be less likely to respond. This is especially if previous treatment has been unsuccessful.

The response rates in Table 6 are only approximate because they do not include these details, but they do show how treatment is getting better.

These studies are generally in people with less advanced liver damage, but some DAA studies include people with cirrhosis.

The next HCV drugs (expected in early 2014) will be simeprevir (an HCV protease inhibitor for genotypes 1 and 4), and sofosbuvir (an HCV nucleotide polymerase inhibitor for all HCV genotypes).

Simeprevir was developed with peginterferon and ribavirin, and is being studied with other oral drugs (including sofosbuvir).

Sofosbuvir has been studied with peginterferon and ribavirin, ribavirin alone, and with other oral drugs.

Both drugs are being studied in coinfecting people: simeprevir with peginterferon and ribavirin; sofosbuvir with peginterferon and ribavirin, ribavirin alone, and with ledipasvir (an HCV NS5A inhibitor).

Cure rates in coinfecting people from the simeprevir trial, were 79% for people treated for the first time.

Cure rates in coinfecting people treated with sofosbuvir plus peginterferon and ribavirin for 12 weeks were 85-90%. In HIV negative people who got the same treatment, cure rates were higher than 90%. After 12 or 24 weeks of sofosbuvir plus ribavirin cure rates in coinfecting people were 76% in G1, 88% in G2 and 67% in G3.

Another coinfection study with sofosbuvir and ribavirin is ongoing. Cure rates in HIV negative studies were 95% for genotype 2 and 56% with genotype 3 after 12 weeks, an 48-68% with genotype 1 after 24 weeks, all in people who had not been treated before. In genotype 3, 24 weeks of treatment is more effective than 12 weeks.

See pages 78-82 for more information about DAAs in development.

Glossary

DAAs Direct Acting Antivirals - the new HCV drugs in development.

Table 6: Response rates to HCV treatment in HIV positive and negative people

Treatment	Geno-type	% cure (SVR)		Comment
		HIV pos	HIV neg	
PEG + RBV: 48 weeks	1 and 4	25%	42-44%	Rates are much lower for HIV positive people.
PEG + RBV: 24 wks in HCV mono. 48 wks in HIV/HCV.	2 and 3	up to 73%	70-82%	Result unclear for G2 vs G3. Also RBV was not weight-based.
boceprevir plus PEG + RBV: 48 weeks	1	61%	63-66% (naive)	7% stop due to severe side effects. HIV neg data in naive.
telaprevir plus PEG + RBV: 48 weeks		74%	69% (naive)	9% stop due to severe side effects. HIV neg data in naive.
faldaprevir plus PEG + RBV: 24 or 48 weeks	1	ongoing	up to 80%	Ongoing in coinfection. May be used without PEG+RBV.
simeprevir plus PEG + RBV: 24 or 48 weeks	1	79%	~ 80%	5% stop treatment due to side effects.
simeprevir + sofosbuvir +/- RBV: 12 or 24 weeks	1	no data	>90%	Good results in hard to treat patients but combination no longer studied.
sofosbuvir + ledipasvir +/- RBV or GS9669: 12 weeks	1	no data; trial is ongoing.	70-100%	Results in treatment-experienced patients with cirrhosis.
sofosbuvir + IFN + RBV: 12 weeks	1-6 (HCV) 1,2,3,4 (HIV/HCV)	90%	~90% in G 1, 4, 5 & 6; 96% in G2; 83% in G3.	80% in HIV negative people with cirrhosis.
sofosbuvir + RBV 12 wks G2; 24 wks G1 & G3.	1, 2 & 3	76% G1 88% G2 67% G3	68% G1 93% G2 85% G3	In HCV, cure rates lower in experienced patients with cirrhosis, especially G3.
ABT450/r + ABT 267 + ABT-333 + RBV: 12 weeks	1, 2	91%	over 90%	Results from 12 weeks of treatment. Different responses by genotype.

Key: PEG = pegylated interferon; RBV = ribavirin; ABT = Abbott; G = genotype; wks = weeks.

When should HIV be treated before HCV?

Using HCV treatment depends on:

- Wanting and being ready to start HCV treatment.
- The need for treatment based on liver damage.

As with HIV treatment the choice of drugs, adherence, side effects and resistance are important with HCV treatment.

UK (BHIVA) guidelines recommend that HIV treatment should be started first in the following circumstances.

- When the CD4 count is less than 350.
- When the CD4 count is less than 500 as long as there is no urgent need for treating HCV. This is because HIV treatment is recommended for anyone with coinfection with a CD4 count less than 500.
- HIV treatment is also suggested at CD4 counts above 500 in someone with coinfection.

When should HCV be treated before HIV?

Unless HCV treatment is needed urgently HCV treatment is usually started first when the CD4 count is above 500.

It is best not to start treatment for both HIV and HCV at the same time. This is because side effects from both treatments make this too difficult.

If HCV treatment is needed, people on a stable HIV regimen should be treated, even if their CD4 cell count is less than 200.

HCV treatment and CD4 cell count

Peginterferon can cause your CD4 count to drop, even if you are taking HIV treatment and your viral load is undetectable.

However, your CD4 percentage usually remains the same, or may even increase and CD4 cell count returns to the pre-treatment level after stopping peginterferon. This shows that there is unlikely to be a real change in your immune system.

Three large studies did not find more opportunistic infections (OIs) among people with CD4 cell counts less than 200 cells/mm³ when using HCV treatment.

There have been some reports of oesophageal candida (thrush) and tuberculosis in HIV positive people using HCV therapy. Prophylaxis treatment to prevent some OIs may be recommended.

This will become less important in the future because new DAAs use peginterferon for a shorter time, or not at all (see pages 78-82).

HIV treatment concerns in people with coinfection

The main concerns when choosing HIV treatment for someone with HCV are:

- Avoiding liver toxicity and damage from HIV drugs, and
- Awareness of drug interactions with HCV treatment.

Only a few HIV drugs are not recommended because of liver toxicity. Liver-related side effects are more common in people with HCV coinfection though, but the benefits of HIV treatment still outweigh these generally low risks.

HIV drugs that are not recommended are d4T (stavudine), ddI, AZT and tipranavir – none of which are widely used in the UK. Caution is needed with nevirapine, other NNRTIs, darunavir and fosamprenavir because of the risk of a hypersensitivity reaction. These risks are higher if liver disease is also advanced.

It is not clear whether small increases in liver enzymes increase the risk of clinical disease. Caution is clearly important and liver enzyme levels monitored regularly.

Side effects that occur more frequently in people with HCV coinfection, include lipodystrophy and abnormal blood fat and insulin levels.

HCV increases the risk of developing type 2 diabetes and this risk is higher in HIV positive people. Use of HIV protease inhibitors and nucleoside analogues, especially d4T, has been linked with an increased risk for high blood sugar and type 2 diabetes.

But, even these risks are outweighed by the benefits of HIV treatment.

How is the response to HCV treatment measured?

A wide range of medical terms and abbreviations are used to describe responses to HCV treatment (see Table 7).

Most relate to HCV viral load results at different times during and after treatment.

Some of these terms were used to describe the response to peginterferon and ribavirin. New terms are being used for latest HCV drugs (DAAs).

Knowing your treatment history will be important for choosing your HCV combination.

Table 7: Terms used to describe responses to HCV treatment

Term	Meaning	Comment
RVR	Rapid viral response: an undetectable viral load after 4 weeks treatment (RVR-4)	People who have an RVR are more likely to be cured than those who don't.
eRVR	Extended RVR: an undetectable after 4 weeks treatment that stays this low at week 12.	People who have an eRVR are more likely to be cured than those who don't.
EVR	Early viral response: undetectable viral load or drop by 99% after 12 weeks of treatment.	People who do not get an EVR usually stop treatment after week 12 as the chance of getting an SVR is only 1-4%.
ETR	End of treatment response: undetectable viral load at the end of treatment.	Some people who get an ETR will have viral load rebound so this is not helpful for predicting long-term response.
SVR	Sustained viral response: undetectable viral load 24 weeks (SVR-24) and 12 weeks (SVR-12) after treatment ended. SVR-4 is used in research but is a less reliable predictor.	SVR-24 is considered a cure. SVR rates are usually the most important results to look for from a clinical trial. Most people with SVR-12 also have SVR-24.
Viral break-through	When viral load was undetectable but then increases during treatment.	
Relapser	When viral load becomes undetectable on treatment but rebounds after stopping it.	
Partial responder	Someone who gets an EVR but does not become undetectable by week 24.	
Null responder	Someone who doesn't get an EVR at week 12.	
Non responder	Someone whose viral load doesn't respond to peginterferon and ribavirin.	This is a wide encompassing term that covers failure with treatment.
treatment-experienced	Someone who has used treatment - i.e. protease inhibitor experienced.	This may become used more than relapser, non responder and null responder.

Retreating HCV

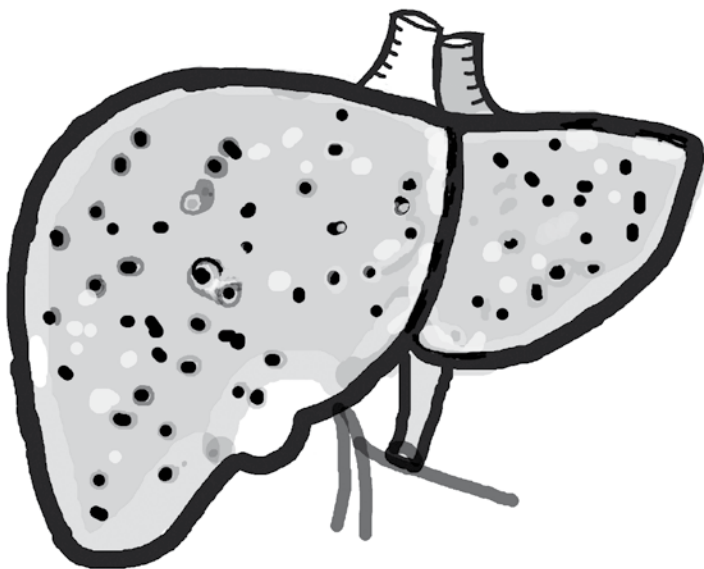
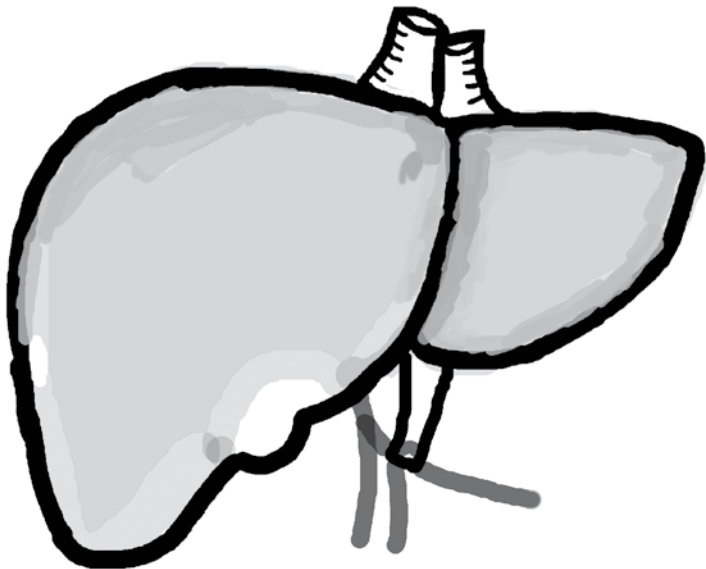
Greater access to treatment also means that the number of people who do not clear the virus during treatment is also increasing.

If you did not respond to earlier treatment which was less effective, retreatment with newer drugs may be more successful.

Triple therapy with peginterferon, ribavirin and an HCV protease inhibitor is more effective for people who were treated before, especially relapsers; less so for prior null responders.

Some DAAs are being studied in people who were unsuccessfully treated for HCV with peginterferon and ribavirin.

Some of the all-oral DAA regimens in development have been very effective for prior null responders with HCV mono-infection; they have not been studied in coinfecting, treatment-experienced people yet.



Drug interactions between HCV and HIV meds

HCV drugs have the potential to interact with a wide range of other medicines including those used to treat HIV.

Your doctor therefore needs to check for these interactions. This will continue to be a complex area as the new DAAs are also likely to interact with HIV meds.

The best online resource on interactions with HCV meds is from Liverpool University as it is regularly updated as new information becomes available.

<http://www.hep-druginteractions.org>

This site includes interaction charts that use a traffic light summary:

- Red when drugs should not be used together because of an interaction.
- Amber for a caution or when additional monitoring is needed.
- Green when no interaction is likely.

Details on each interaction and reports can be printed for any combination.

Sometimes the recommendation is based on a theoretical risk.

Your doctor needs to know about all drugs you take, whether these are prescribed or over-the-counter, together with any supplements, herbal remedies and recreational or street drugs.

Table 8 summarises the main known interactions. As only a few combinations have been studied, not being listed does not guarantee there is no interaction.

Drug interactions with recreational drugs

It is also important to be aware that recreational drugs have the potential to interact with HCV drugs, just as with HIV meds.

Although there is currently little information on interactions between HCV treatment and recreational drugs such as cocaine, methamphetamine and ecstasy, this will be important in a real world setting.

Your doctor needs to be aware of all potential interactions when you are using HCV meds.

Table 8: Current data on drug interactions between HCV and HIV drugs

	ARV interaction details	Comments
ribavirin	Do NOT use with ddl, AZT and d4T.	Side effects can be life threatening.
boceprevir	Do NOT use with EFV (or Atripla), DRV/r, FOS/r or LPV/r. Use 150 mg MVC twice-daily.	Caution with TDF, ETV and ATV/r.
telaprevir	Increase dose of telaprevir with EFV or Atripla. Do not use with DRV/r, FOS/r or LPV/r. Use 150 mg MVC twice-daily.	Can be used with TDF and ATV/r.
faldaprevir	Increase dose to 240 mg with EFV and reduce to 120 mg with ATV/r or DRV/r.	No data on ETV, RPV, FOS/r or LPV/r.
simeprevir	Do NOT use with EFV, ATV/r, DRV/r, FOS/r or LPV/r.	No interaction with FTC, RPV or TDF.
daclatasvir	Increase dose to 90 mg with EFV and reduce to 30 mg with ATV/r.	No data on other NNRTIs or PIs. Use standard dose with rilpivirine.
sofosbuvir	No interaction with TDF, EFV, RPV and DRV/r.	No data on other NNRTIs and PIs.

Key: ATV/r = atazanavir/ritonavir; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETV = etravirine; FOS/r = fosamprenavir/ritonavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; RPV = rilpivirine; TDF = tenofovir.

HCV treatment and People who Inject Drugs (PWIDs)

People who use drugs often have the most difficulty getting HCV treatment - even when there is a clear medical need.

This continues, even though current guidelines recommend that decisions about HCV treatment should be made on a case-by-case basis.

Fortunately, this has begun to change.

Both injection-and non-injection drug users have successfully used HIV and HCV treatment. This shows that concerns about adherence should not be a barrier to treatment.

Some HCV studies report response rates can be similar for users compared to non-users.

The following suggestions may make it easier to access treatment.

- Try not to miss medical appointments. Some doctors will use this as part of the criteria for not treating your HCV.

- Do not avoid medical care just because you are using drugs.

This is especially important while you are on HCV treatment, because your doctor will need to monitor and treat your side effects.

- If you are on methadone, wait until after treating HCV before stopping or tapering off. Some people find that methadone helps them through HCV treatment.
- 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 steer you away from one. This can be a good place to start.
- Discuss with your doctor how side effects of HCV treatment will be managed. If you need pain medication or other meds that are seen as having a potential to abuse, discuss this with your doctor. Make an agreement on how the two of you will handle this.

Depression and other mental health diagnoses are much more common among people with HCV, people with HIV, and PWID than the general population. Many of these conditions are treatable.

Depression is a common side effect of peginterferon. This may be more likely if you had depression in the past but it can also happen in people without this history. If you are concerned about the psychiatric side effects but want to treat your HCV, support from mental health care services may help.

Some people can manage HCV treatment while they are using drugs. Others have found that stopping or cutting down on drug use has helped them to prepare for, and stay on HCV treatment.

This could be from a self-help programme or with counselling. It can also be from a drug treatment, or medication-assisted treatment with methadone, or buprenorphine. Increasing the dose of methadone has helped some people manage side effects of HCV treatment.

If you are still injecting drugs, ask your doctor or local syringe exchange programme for information on safer injection. This will lower your risk of HCV reinfection (and other infections).

Concerns for people in recovery

Many people fear that they will relapse to active drug use, because side effects from peginterferon are very similar to opioid withdrawal.

The risk of relapse is lower when side effects are promptly and effectively treated, and when counselling and support from peers and medical and mental health providers is available.

Some people are concerned about self-injecting peginterferon. If this is needed, injections can be given once weekly by a nurse to avoid triggering a relapse to injection drug use.

Advanced liver disease

Management of cirrhosis

A damaged liver can still function, but cirrhosis increases the risk for liver failure and other serious and life-threatening complications.

If you develop compensated cirrhosis, you should be screened for liver cancer every six months and monitored regularly for decreasing liver function and varices.

Varices are veins in the stomach or oesophagus (gullet) that have become stretched and are at risk of bursting. They come about as a result of high pressure around the blood flow to the liver from liver scarring.

Drugs called beta-blockers can help to prevent varices. Bleeding varices need medication and surgery.

Changing your diet can help to manage some of the complications of cirrhosis.

This includes cutting down on salt, eating many small light meals per day and getting protein from vegetables (broccoli, sprouts, kale, peas) and dairy products (milk and cheese) rather than meat. A nutritionist and your doctor can help you plan a healthy diet.

Child-Pugh score

The Child-Pugh score is used to grade the severity of cirrhosis and end stage liver disease (ESLD).

It is calculated based on results from several tests including bilirubin, albumin and PT and the presence of ascites and encephalopathy.

Class A and B categorise compensated cirrhosis with Class C indicating decompensated disease, see Table 9.

Table 9: Child-Pugh scores

Grade	Score (points)	Cirrhosis
Class A	5-6	Compensated
Class B	7-9	Compensated
Class C	10-15	Decompensated

Liver transplant in people with HIV/HCV coinfection

When the liver can no longer adjust (or compensate) for damage, and liver function has become worse this is called hepatic decompensation (or decompensated cirrhosis).

In people with decompensated liver disease, HCV treatment can no longer be used and a liver transplant is needed.

A transplant is a major operation, and success rates vary. It is also complicated by a lack of donor organs.

For many years, transplant services actively avoided liver transplants in HIV positive people. HIV was an exclusion criteria for a liver transplant.

Effective HIV treatment changed this and centres in the UK, Spain, France, Italy and the US have reported successful transplants in HIV positive people. Some centres have reported similar survival rates as HIV negative people.

Medical management remains complex and success is largely related to the risk of HCV reinfection of the new liver. There is also the risk of graft rejection.

Drug interactions between drugs used to suppress the immune system after the transplant and HIV/HCV protease inhibitors need to be carefully managed and it can also be difficult to tolerate HIV and HCV treatment after the transplant.

New HCV drugs may be more effective, safe and tolerable both before and after a liver transplant, although information is so far very limited.

HCV progresses more quickly in people with HIV positive people, and survival after decompensation is shorter than HIV negative people.

This makes it important for people with coinfection to be referred for transplantation at an earlier stage of disease than people with HCV monoinfection.

Only a few transplant centres perform liver transplants in people with coinfection, and referral to one of these centres is essential.

How to manage side effects from HCV drugs *

Side effects from HCV treatment can occur more often in people who are HIV positive.

Although side effects can be difficult, they are rarely life-threatening.

The information below includes ways to manage them.

Ask your doctor how he/she will treat your side effects. With the right planning and support, their impact can be reduced.

Support from other people with HCV, friends, and family before and during HCV treatment plays a key role in coping with this.

* The i-Base booklet *HIV and Your Quality of Life* is about avoiding and managing side effects and other complications of HIV drugs.

It is just as relevant for HCV treatment.

This guide provides more detail about ways to manage most of the side effects listed below including depression, mood changes, diarrhoea, fatigue, nausea, weight loss, skin problems and insomnia.

It is also available online:

<http://i-base.info/guides/sides>

and in PDF format:

<http://i-base.info/guides/files/2012/06/Side-effect-2012e-FINAL2.pdf>

Depression, anxiety, and other psychiatric side effects

Depression and anxiety are commonly reported with peginterferon and ribavirin.

In rare cases, this includes feeling suicidal, and a few people have committed suicide during their HCV treatment.

A history of depression may increase this risk, although these side effects are also common in people without this history. Peginterferon can also cause mood swings, irritability, difficulty sleeping and psychosis.

Access to mental health care before, during and sometimes after HCV treatment is important. This will help treat psychiatric side effects promptly and appropriately.

Some people start an antidepressant before going on peginterferon. You may need to try more than one antidepressant to find one that is effective. Because antidepressants and other psychiatric drugs have their own side effects, other people only use these drugs only if and when they get symptoms.

An antidepressant can make a big difference. Depression causes some people to stop HCV treatment too early, when it was otherwise working well.

Your own history and how you feel about this are also important.

If you have not had depression or mental illness you will need to know about the symptoms. This makes it important to talk to your doctor about this before starting 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. Fortunately, he was not obliged to go into the details of my illness with my line manager, so my confidentiality was maintained.”

Flu-like symptoms

Flu-like symptoms (fever, aches and pains, headache, chills, nausea) are common side effects of peginterferon. They usually appear 2 to 24 hours after an injection, and tend to lessen in the days after.

Taking the peginterferon injection in the evening helps, as does a low dose of paracetamol.

Ibuprofen and aspirin are NOT recommended for people with cirrhosis.

Anti-nausea medication may be helpful.

Warm baths can help with muscle pain.

Drinking plenty of water is important to help symptoms and to stay hydrated. (Grapefruit juice is not recommended because of potential drug interactions, and citrus juices are not good if you have stomach acid problems).



Fatigue (feeling tired)

Fatigue is also common.

It can be a symptom of anaemia another side effect of HCV treatment (see below).

It can also be related to not eating enough (see “weight loss” below).

Napping and regular light exercise, when possible, can help.

Getting proper rest at night is important and this is more likely if your bedroom is comfortable.

Some doctors treat fatigue with the antidepressant methylphenidate (Ritalin).



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Anaemia, neutropenia and thrombocytopenia

A low CD4 cell count sometimes causes low white and/or red blood cell counts (neutropenia or anaemia) or a low platelet count (thrombocytopenia).

Regular blood tests during HCV treatment are especially important for people with coinfection.

Anaemia is a side effect of ribavirin, peginterferon and HCV protease inhibitors.

The most common symptom of anaemia is fatigue. Anaemia can also be caused by AZT although this is rarely used in the UK, especially during HCV treatment.

Frequent monitoring is important when using any HCV treatment because anaemia can develop quickly. With both telaprevir and boceprevir, monitoring is recommended with any symptoms and at weeks 2, 4, 8 and 12.

People with coinfection may need more aggressive management of anaemia, especially if they have cirrhosis.

Three main ways to treat anaemia are:

- 1) With boceprevir- and telaprevir-based treatment, it is best to lower the dose of ribavirin. This will not make treatment less effective. When just using peginterferon and ribavirin, the impact of dose reduction is less clear.
- 2) Another strategy is to use epoetin-alpha (EPO). This is a red blood cell growth factor, given by injection, which reduces fatigue and helps people to stay on ribavirin.
- 3) Severe anaemia is treated by blood transfusions.

Neutropenia is an abnormally low amount of neutrophils. These are white blood cells that fight bacterial infections. Peginterferon, boceprevir and telaprevir can cause neutropenia and this increases the risk of bacterial infections. A low neutrophil count can be managed by reducing the dose of peginterferon or by using injections of white cell growth factor called filgrastim (Neupogen).

Thrombocytopenia (low platelets) can be caused by serious liver damage.

This is because the hormone that stimulates platelet production is made in the liver.

It can also be caused by other medical conditions including HIV and is a side effect of peginterferon, boceprevir and telaprevir.

Platelets prevent bleeding by causing blood to clot. If platelets are very low, this increases the risk of internal bleeding which can be life-threatening.

Options include lowering the dose of peginterferon, using an oral medicine called eltrombopag to increase platelet counts or stopping treatment.

HCV treatment is usually stopped if it is severe.

Weight loss

Weight loss often occurs during HCV treatment. This can be because of appetite loss, diarrhoea, and/or nausea. Eating smaller lighter meals more frequently will help avoid weight loss and keep energy levels up.

Dronabinol (a derivative from marijuana), available as a pill, may help to stimulate appetite, but this is not available in the UK.

If you lose more than 2 pounds (1 kg) a week, your weight loss should be treated more aggressively.

Certain foods (including bananas, apples, rice, cereals and toast) can help with diarrhoea but loperamide (Imodium) is safe and more effective. Your doctor should check for other causes of diarrhoea.

Rash

HCV treatment can cause many skin problems including injection site reactions, dry skin, itching and rash. Ribavirin can cause a rash that is usually mild and non-itchy.

Boceprevir, telaprevir, faldaprevir and simeprevir can all cause rash. This can range from mild to serious, and even life threatening.

It is important to let your doctor know as soon as a rash develops or if it gets worse when taking HCV treatment.

Use a moisturising cream every day to avoid dry skin. Hydrocortisone cream or oral antihistamines can help with a mild rash. If these do not work, ask to be referred to a skin specialist.

Photosensitivity

Simeprevir and faldaprevir cause photosensitivity, which starts as soon as you begin taking them. Avoid being in the sun and wear sunscreen, hats and protective clothing throughout treatment.

If you have a serious skin reaction from sun exposure it is important to call your doctor.

Taste changes

Boceprevir and telaprevir can cause changes in taste (called dysgeusia). This can include an unpleasant or metallic taste in the mouth.

Things that may help include:

- Not using metal cutlery
- Reduce or avoid coffee, red meat and chocolate.
- Drink more water with meals.
- Add sugar to salty or bitter tasting food.
- Eat blander foods like chicken, turkey, tofu, dairy products or eggs.

Dry mouth

Peginterferon can make your mouth dry.

This can cause dental and gum problems.

Visit the dentist before, during, and after HCV treatment.

A soft toothbrush reduces risk of bleeding gums, and brushing after each meal may help.



Being short of breath, coughing

If you feel breathless or develop a cough, tell your doctor.

Breathlessness can be a symptom of anaemia.

Common treatments for cough are appropriate: to drink more water, avoid smoky places and try over-the-counter cough syrups.

Insomnia

Not sleeping well adds to the impact of other side effects, especially those related to your mood and how you feel.

The i-Base guide has tips on how to improve sleep.

Your doctor needs to know if this is a problem, so that sleeping pills can be an option.

Irritability

Irritability can be a common side effect.

It is not surprising that you feel bad if you have other side effects. This is why it is important that these are treated, especially if they affect your sleep.

Your friends, family and support network can help - especially if they are prepared for mood changes beforehand. Avoiding stress and using relaxation techniques including exercise, meditation and deep breathing can sometimes help.

Anal burning and itching; haemorrhoids

Telaprevir can cause anal burning and itching and (with no disrespect to Johnny Cash) this is sometimes referred to as the “ring of fire”.

Things that may help include:

- Wearing loose clothing and underwear made from natural fibres.
- Wash and dry the anus after going to the toilet.
- Keep the anal area dry. Baby powder can help. Try not to scrub or scratch.
- Over-the-counter creams and ointments, including preparation H, calamine lotion, and products that contain hydrocortisone or zinc oxide.
- Avoiding caffeine, alcohol and citrus fruits.

If these do not help, talk to your medical provider.

Other complications

HCV treatment can also cause other complications including thyroid (hormone regulating) or visual problems (blurred vision).

Tell your doctor about any symptoms and be sure that she or he takes these seriously.

Liver toxicity and HIV drugs

Many HIV drugs are cleared from the body by the liver. This has the potential to cause liver toxicity which is increased with HCV coinfection. This could be through the direct action of these drugs.

This mainly concerns nevirapine (an NNRTI) and the HIV protease inhibitors (PIs) tipranavir and high dose ritonavir. As these are rarely used it should be easy to use alternative HIV drugs. The use of low-dose ritonavir to boost other HIV protease inhibitors does not seem to increase liver problems.

Other NNRTIs and PIs can also cause problems as these drugs may reach higher levels if your liver is already working less well. Because a damaged liver works less efficiently, some drugs can take longer to clear from your body.

A blood test (called Therapeutic drug monitoring or TDM), can check drug levels of some HIV drugs, to see if a different dose is needed.

Therapeutic drug monitoring (TDM)

Therapeutic drug monitoring (TDM) can check blood levels of HIV protease inhibitors, NNRTIs, raltegravir, maraviroc and T-20.

Doses for HIV drugs are worked out for an average person. However, individual differences in absorption can vary considerably in real life.

In people whose liver is seriously damaged, drug levels can be much higher.

This can increase the risk of side effects.

TDM is easy to access in the UK and some other European countries. In the US and some other countries the test may be more difficult to get but it is worth asking about.

“The flu-like side effects were strong for the first three weeks. After this they became more like a tense headache that I could manage with painkillers and an early night. I developed anaemia which has been difficult and made me very weak and dizzy.

All through this time I fixed my mind on getting to the end of the year and knowing that I could beat this infection even if I can’t beat the HIV. I’m currently in month four of treatment. The anaemia is better and I’m still HCV negative.

I can’t wait to get to the end of treatment and use the C word - CURE.”

Deciding whether and when to treat HCV

For some people, deciding whether to treat is easy, but for most, it is more difficult.

The most important reason to treat is to cure HCV but there are a lot of factors involved in the decision.

- Although HCV is more likely to become serious in people who are HIV positive, not everyone will need treatment.
- Some people may choose lifestyle changes first, see pages 83-86.
- Others may want to wait for new drugs, see pages 78-82.

Whether or not to treat HCV also depends on the condition of your liver.

- People who have mild liver damage may choose to monitor their liver and wait for new HCV treatment.
- People with advanced fibrosis or cirrhosis need to be treated for HCV sooner.
- HCV treatment is less effective for people with serious liver scarring (cirrhosis), so it may be important to treat before it reaches this stage.

“After diagnosis, I was determined to have the treatment immediately... but I had to leave the country for family reasons soon after starting the treatment and was unable to continue the treatment beyond the first month.

A few years later when things had calmed down, my concern turned to my partner and I resolved to get rid of the HCV as quickly as possible.”

If you are unlucky and treatment doesn't work, you can find out within 4 to 12 weeks if it is possible to stop early.

One doctor said, “people don't have to sign a binding contract to stay on HCV treatment for 48 weeks. If they start, and it is much worse than they were prepared for, they can stop. They can try again in the future when they feel better, or when new treatments are available.”

Some people weigh up the risks and benefits for their situation and decide to monitor rather than treat.

“Over the last seven or so years, as my general health has vastly improved, my doctors have warned me my health may be at more risk from HCV than HIV.

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. 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.”

Another advocate who has been diagnosed with HCV for over 10 years said:

“For me, keeping my CD4 high is a way of protecting my liver from histological damage. Side effects are the most important reason for delaying treatment as I have seen a lot of people on HCV treatment and in some cases it is really hard.

I also know people that are doing very well on treatment and avoiding the threat of cirrhosis is a really good thing. For me though, at the moment, I don’t feel strong enough to try it.”

Some people choose earlier treatment, to reduce the risk of sexual transmission to partners.

“Six months after treatment I feel very lucky to have achieved a “sustained virological response”. I know of other people have not been able to stick to the treatment and others for whom it has failed.

The doctors tell you that even if you don’t succeed in eliminating it from your body, eleven months on treatment will put you in the clear of liver disease for years to come, but for me that would not have been enough.

I didn’t care about the liver disease, but I needed to be not infectious. 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.”

Advantages of using HCV treatment

- You can be cured of HCV. This can reduce the risk of liver-related and HIV-related illness and death.
- Being cured can improve liver health by reducing inflammation.
- Effective treatment may reverse fibrosis.
- You will no longer be infectious to sexual and drug-using partners.
- Clearing the virus removes the risk of mother to infant transmission.
- Treating HCV before HIV treatment reduces the risk of liver-related side effects from HIV drugs later.
- Treatment is 12 months or less, not lifelong.
- If treatment is not working you can find out after 4 -12 weeks.

Treatment tips

- Find people in your life who will be a good source of support.
- Be prepared before seeing your doctor; make a list of questions in advance.
- Take someone with you to appointments. This is important if you want to discuss psychological side effects.
- Consider joining a support group.

Advantages for delaying treatment

- The major disadvantages of treatment are side effects and the impact they could have on your life during treatment.
- Occasionally side effects (especially from peginterferon) mean you need to stop treatment. In rare instances, they can be long-term including as thyroid disease or type 1 diabetes.
- Some people report that the side effects continue long after the end of treatment.
- Treatment might not work.
- New HCV drugs in development are more effective and be easier to tolerate. Some of these will be approved in the near future and others will be available through clinical trials in the next few years.
- If your liver is healthy you may be able to delay treatment.
- If you are thinking of getting pregnant in the next year, consider delaying treatment, since ribavirin causes birth defects.
- Men and women should not conceive during treatment and for at least 6 months afterwards. Women who become pregnant on ribavirin must consider terminating the pregnancy.

“Talking to peers worked for me.... we have long exchanges as most of my friends are co-infected.

But I also think that as co-infected people we might need to have some specific support group, especially as regards treatment issues – and coping with treatment!”

“I am squeamish and I thought I would never manage to self-inject. I asked to see the needles and when I saw how tiny they are I was reassured but still frightened. I asked the nurse do the first three and when it came to doing it myself I was thrilled to find that I could.

It was painless and over in a flash. This made me so proud that I almost wanted to do it twice!”

Research into new HCV drugs (DAAs)

Current HCV drugs do not work for everyone.

They also have side effects that are daunting enough for some people to stop or defer treatment until newer HCV drugs are available.

Waiting for better treatments may be a good option if you don't need HCV treatment now. This will be an easier decision if you only have mild liver damage, are being monitored regularly, and if your HCV is not progressing quickly.

To make an informed decision about starting or deferring HCV treatment, you also need to know about drugs in development. How soon they may become available is just as important, although this is usually difficult to predict.

We only include brief details of some of these treatments because this information will change quickly. The resources listed at the end of this section can keep you up-to-date with this research.

New drugs in development - there are many!

Over 60 new oral HCV drugs are in development. At least 25 of these are already in advanced stage research (in phase 2 and 3 studies), see Table 10.

These are called DAAs (direct-acting antivirals) because they target the virus rather than your immune response.

Most of the studies are in HIV negative people but a few are already reporting promising results in HIV positive people.

As with HIV drugs, each class of DAA works at a different stage of the HCV life cycle.

These classes are:

- Protease inhibitors.
- Non-nucleoside, nucleoside and nucleotide polymerase inhibitors.
- NS5A inhibitors.

Adherence is very important with DAAs. This is defined as taking more than 95% of doses on time.

DAAs are used either in combination with each other, or with peginterferon and/or ribavirin.

Since many companies are developing DAA combinations with their own drugs, only a few of many potential combinations are being studied.

This research is very competitive and it is not yet clear which of these many potential drugs will be most effective.

Current studies

For at least the next year, the only way to access most new DAAs will be by joining a clinical trial.

The advantage of joining a study includes the chance to use promising drugs several years before they are approved. As these drugs will have been studied in HIV negative people, there should already be promising results about how well they work and how safely.

Disadvantages include that the study drug may not turn out to be most effective. There is likely to be little or no data on a drug on coinfection and potential drug interactions may not yet be known. If you develop resistance to either your HIV or HCV medications, this may limit the benefit or other similar drugs in the future.

Joining a study may limit the chance to join others studies in the future – though if the treatment works this will not be something to worry about.

Although the first studies are in HIV negative people, some coinfection studies are already running and others are expected to start soon.

These include studies using:

- Sofosbuvir (Sovaldi, GS-7977).
- Ledipasvir (GS-5885).
- Daclatasvir (BMS-790052).
- Simeprevir (Olysio, TMC-435).
- Faldaprevir (BI 201335).
- ABT-450/r/ABT-267/ABT-333 (three DAAs from one company being used together).

Results from studies in HIV negative people will provide information to decide on which of these compounds may be more appropriate for your situation.

Clinical trials with DAAs also use different strategies:

- Using early responses to decide length of treatment (response-guided therapy).
- Using shorter treatment but with a fixed-duration – ie 12 or 24 weeks.
- Using DAAs without peginterferon and/or ribavirin.
- Rescue therapy – where, after unsuccessful DAA treatment, DAAs are used with peginterferon and ribavirin.

Some oral DAA combinations report SVR rates close to 100% in HIV negative studies, sometimes after only 12 weeks.

Several trials have proven that HCV can be cured without peginterferon or ribavirin in HIV negative people.

In people with coinfection, trials of peginterferon and ribavirin plus an HCV protease inhibitor have reported SVR rates similar to those from trials in HIV negative people. However, there is little information yet on how well DAA combinations will work in people with coinfection.

Other peginterferon-free HCV treatment trials in coinfecting people are expected in the near future, due to pressure from treatment advocates and regulatory agencies.

Table 10: DAAs in phase 2 and 3 studies *

Protease inhibitors (PIs)	
<p>Phase 3</p> <p>ABT-450/r (RTV boosted; once-daily)</p> <p>asunaprevir (twice-daily)</p> <p>faldaprevir (once-daily)</p> <p>simeprevir (Olysio), (once-daily)</p> <p>Phase 2</p> <p>danoprevir/r (RTV boosted, twice-daily)</p> <p>GS-9451 (once-daily)</p> <p>MK-5172 (once-daily)</p> <p>sofaprevir (once-daily; current study on hold due to a drug-drug interaction).</p>	<p>PIs are mainly active against genotype 1 but some also work for genotype 4.</p> <p>Some need to be boosted by ritonavir (ABT-450 and danoprevir).</p> <p>They have the potential to interactions with some HIV meds.</p> <p>Studies use response-guided treatment with peginterferon and ribavirin or in combination with other DAAs (plus ribavirin).</p> <p>Faldaprevir and simeprevir (with peginterferon and ribavirin) are already being studied in HIV positive people.</p>
Non-nucleoside polymerase inhibitors	
<p>Phase 3</p> <p>ABT-333 (twice-daily)</p> <p>deleobuvir (twice-daily)</p> <p>Phase 2</p> <p>GS-9669 (once-daily)</p> <p>setrobuvir (twice-daily)</p> <p>VX-222 (twice-daily)</p> <p>TMC 647055 (RTV-boost, twice-daily)</p>	<p>These drugs are only active against genotype 1.</p> <p>Some need to be boosted by ritonavir (TMC 647055).</p> <p>Used with peginterferon and ribavirin, or other DAAs (plus ribavirin).</p> <p>No studies yet in coinfection.</p> <p>No data on drug-drug interactions with ARVs.</p>
Nucleoside/nucleotide polymerase inhibitors	
<p>Phase 3</p> <p>sofosbuvir (Sovaldi), (once-daily)</p> <p>Phase 2</p> <p>mericitabine (twice-daily)</p> <p>VX-135 (study on hold at doses above 100 mg/day; twice-daily).</p>	<p>These drugs are active against genotypes 1, 2, 3, 4, 5 and 6; mainly used in genotypes 1, 2, 3 and 4.</p> <p>Used with peginterferon and ribavirin.</p> <p>Used with other DAAs (with and without ribavirin).</p> <p>Sofosbuvir is currently being studied with ribavirin and with another DAA, ledipasvir, in coinfection.</p>

NS5A inhibitors	
<p>Phase 3</p> <p>ABT-267 (once-daily)</p> <p>daclatasvir (once-daily)</p> <p>ledipasvir (once-daily)</p> <p>Phase 2</p> <p>ACH-3102 (once-daily)</p> <p>GS-5816 (once-daily)</p> <p>GSK2336805 (once-daily)</p> <p>IDX-719 (once-daily)</p> <p>MK-8472 (once-daily)</p>	<p>These drugs are active against genotypes 1,2, 3, 4, 5, 6; used in genotypes 1, 2 and 3.</p> <p>Interactions with some ARVs.</p> <p>Being studied with peginterferon and ribavirin or other DAAs (with and without ribavirin).</p> <p>Daclatasvir is currently being studied with peginterferon and ribavirin in coinfection.</p> <p>Ledipasvir is being studied with sofosbuvir in a fixed-dose combination.</p>

* Phase 2 studies look at different doses and usually include several hundred people. Phase 3 studies are used to decide whether a drug should be approved and can include several thousand people.

Keeping up-to-date on research

The following websites provide a range of information and news on the latest developments.

The annual i-Base/TAG Pipeline Report reviews the latest information about HIV and HCV drugs in development.

<http://www.pipelinerreport.org>

A wealth of reports from journals, meetings and conferences are posted on the National AIDS Treatment Advocacy Project (NATAP) website.

<http://www.natap.org>

An updated list of HCV drugs in development is available on the HCV Advocate Website.

<http://hcvadvocate.blogspot.ca>

HIVandHepatitis.com covers medical conferences and HCV-related news.

<http://www.hivandhepatitis.com>

Updates are also available on the Hepatitis C New Drug Research and Liver Health website.

<http://www.hepatitisnewdrugresearch.com>

Hepatitis news and information (for patient advocates and people working in Europe) is available at: www.infohep.org

Clinical Care Options is a medical site that reports from most conferences.

<http://www.clinicaloptions.com/Hepatitis/Topics/HCV.aspx>

Living with co-infection: reducing stress and lifestyle changes

Any medical condition can be stressful.

This makes it important to have the time and support to learn about choices that affect your health.

Another common experience is for people to want to reduce stress by looking at other aspects of their life.

This can also improve both your quality of life and general health. Some lifestyle changes can also reduce the risk for HCV progression, especially cutting down or avoiding alcohol.

General things like stopping smoking, eating and resting properly, reducing stress, and taking exercise are important for everyone.

Alcohol and HCV

Heavy drinking is known to be harmful to the liver, whether or not a person has HCV.

Alcohol intake in amounts over 50 grams per day for men and over 30 grams per day for women accelerates HCV progression.

Fifty grams is equivalent to 4-5 glasses of wine or 2-3 pints of beer. Binge drinking is more harmful for your liver than moderate daily drinking.

Alcohol harms the liver by increasing both inflammation and scarring. The less you drink, the better for your liver, but no one has determined a safe amount for chronic HCV. Drinking less – or not at all – may be more important than treating HCV.

Alcohol increases hepatitis C viral load, which makes with peginterferon and ribavirin less effective.

This may be why studies using interferon (since replaced by a combination of peginterferon and ribavirin) reported that HCV treatment was not very effective for people who drink alcohol.

A few more recent studies have not reported much difference in HCV treatment outcomes among drinkers vs. non-drinkers with similar adherence. Nonetheless, many doctors will not treat people who consume alcohol.

Alcohol and liver damage

Alcohol is mainly broken down by the liver, but during this process by-products are produced that damage the liver more than the alcohol itself.

Prolonged inflammation from long-term alcohol use results in the over production of molecules called free radicals. These can destroy healthy liver tissue and subsequently impair liver function.

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

Women may be more vulnerable to the damaging effect of alcohol than men.

Drinking less – or not at all – can be very difficult. Some people cut down or quit on their own, others find that support groups, counselling, and/or pharmacotherapy works best for them.

A list of resources to help with reducing alcohol is on page 91.

Tips for reducing alcohol

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. Grapefruit juice is not recommended because of potential drug interactions, and citrus juices are not good if you have stomach acid problems.
- Drink with or after food as this slows down the absorption rate.
- Spread your alcohol intake over the whole week, rather than drinking heavily in one session.

Recreational drugs

The liver is the organ that processes most recreational drugs.

Some are more toxic than others, but all will stress your liver to some extent.

Street drugs are also likely to contain impurities and other ingredients that can be toxic. In general, injecting drugs is more dangerous than snorting or swallowing them, because injecting goes directly into the bloodstream, bypasses the filtering system of the stomach.

If you are injecting drugs, using sterile equipment (syringe, cooker, filter, water, tie and measuring syringe) will protect you from HCV and other infections.

If you want to reduce or stop your use of recreational drugs, see pages 91-92 for some organisations that can help.

Smoking

Smoking is not good for your health.

There is some weak data to suggest that smoking may encourage the progression of HCV, but most people in the studies also drank alcohol.

Stopping smoking is not easy.

It is probably not a good idea to decide to quit during HCV treatment, especially if you feel it gives you support. While this may be an important long-term goal, you will have plenty of time to do this afterwards.

Body fat and body weight

Liver abnormalities are more common in people who are overweight. This is usually defined as having a Body Mass Index (BMI) higher than 25 kg/m².

These include fatty deposits found in the liver and fatty inflammation or fatty liver; this is more common in people who have type 2 diabetes. Fat in the liver can cause it to become enlarged and can lead to raised liver enzymes.

People who are overweight and who have a fatty liver, and who subsequently reduce their weight, are likely to have an improvement in fat-related liver abnormalities. Losing weight increases the chance of a better response to peginterferon and ribavirin.

If you find it hard to maintain lower weight, ask to see a dietician for specialist advice.

Diet

A healthy and balanced diet is important for general good health, but avoiding certain foods with advanced liver disease may be more important. These include:

- Fried foods and fatty foods especially saturated and hydrogenated fats.
- Foods high in iron and iron supplements (unless advised by your doctor).
- Processed food and fast food.
- Salt, especially with advanced liver disease. Less than 500 mg/day is recommended for people with ascites.
- Foods containing additives and pesticides.
- Protein. Guidelines recommend 1 to 1.5 grams of protein per kilogram of body weight.
- Eat less processed sugars and keep sugar levels more constant to reduce the risk of type-2 diabetes. Switch from white bread and pasta to whole wheat bread and pasta that releases sugar more slowly.



Foods that may help include:

- Drinking plenty of water to help your liver filter waste and toxins.
- Eating more fresh fruit and vegetables, complex carbohydrates (whole grains, breads, rice, pasta, cereals, vegetables, fruits, beans, nuts and seeds), low-fat foods, high-fibre foods and an adequate amount of protein.
- Three cups of coffee a day (with or without caffeine) can delay fibrosis progression and lower the risk of liver cancer.
- Eating dark chocolate (85% cocoa) every day can be good for your liver and heart.



Herbal remedies

Herbal remedies have been used for centuries to treat liver disease, but they cannot cure HCV. So far, no clinical trials have demonstrated that herbal remedies are effective against HCV, but many people use them anyway.

Sometimes this is because conventional treatment has not worked, or because of concerns about side effects of HCV therapy.

People with HCV often use oral milk thistle (silymarin) but clinical trials have not found any benefit. A different, more effective form of silymarin, given by infusion, is under study.

Liquorice root (glycyrrhizin) has been used, although it has no effect on HCV 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, that 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 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.

Other viral hepatitis infections

Hepatitis A (HAV)

HAV is found in faeces and can be transmitted when food (including raw or undercooked shellfish) or water are contaminated with sewage.

Or when an infected person handles food without washing his/her hands after going to the toilet.

Other ways of transmitting HAV include by oral-anal sex (rimming) and from blood transfusions, though this is rare.

Getting vaccinated against HAV is recommended for all HIV positive people, see page 12.

Symptoms include: nausea, vomiting, diarrhoea, fever, fatigue, rash, jaundice (yellow skin and eyes), liver pain, and dark brown urine - but some people, especially children, don't get sick at all.

There is no treatment for HAV, but the symptoms can be treated. It is not a chronic infection.

A person can only be infected with HAV once. HAV goes away by itself, usually within two months.

Hepatitis B (HBV)

HBV is mainly found in blood, semen, and vaginal fluid of infected persons with very small amounts in breast milk and saliva.

HBV can be transmitted by sharing injection or tattooing equipment, from anal or vaginal sex without a condom, from oral sex, and by sharing personal care implements (such as toothbrushes and razors).

HBV can be passed from mother to child during birth and within families.

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

As with HIV, antiviral HBV treatment should not be given as monotherapy to people with coinfection. Coinfection guidelines provide detailed information on drug choices. For example, they currently recommend starting HIV treatment earlier, and including tenofovir plus either 3TC or FTC, plus at least one extra HIV drug so that there are at least three active drugs against HIV.

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

If HIV treatment needs to be changed, then the HIV drugs that are active against HBV need to be continued.

Other viral hepatitis infections

There is less research on coinfection with other viral hepatitis infections.

These include:

Hepatitis D

Hepatitis D only occurs in some people with hepatitis B. HDV increases the risk of cirrhosis and the rate of liver disease progression for people with HBV. Vaccination protection against HBV also protects against HDV.

Hepatitis E

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

Hepatitis G

Hepatitis G (HGBV-C) is similar to HCV. The importance of hepatitis G is unclear, especially in someone with HIV, but it may not be harmful.

Controversial aspects of HCV treatment

Drugs in development

Given how many new drugs are in development it will take a few years until we know which are best and in different situations.

- Some drugs may be approved in one combination and then used in another.
- Some drugs may be approved based on results in HIV negative people but need to be used by HIV positive people before coinfection studies are approved. This means that there will be more limited information about people with HIV and HCV.
- Some DAA studies still use peginterferon and/or ribavirin when this may no longer be necessary.
- Others may not use them and find out later that they are needed.

With so many studies it is difficult to know which may have advantages for people with coinfection.

The controversial aspect of drug development is that there will be a lot of research in the next few years but the data on coinfection will be limited.

Earlier access to research drugs

Even though HCV drugs are first studied in people with less complicated liver disease, the most urgent need is people who are the most sick.

This includes HIV positive people who cannot wait for approval in HIV negative people.

To be able to get early access to drugs before they are approved, HIV positive people need to know about potential drug interactions with HIV meds.

Drug interactions studies need to be performed on any promising HCV drug. Then early access should be made available to new HCV drugs, similar to programmes developed for HIV meds.

This is currently taking time to arrange.

How long to treat genotype 2 and 3

HIV positive people with HCV genotype 2 or 3 are usually treated for a year with peginterferon plus ribavirin.

However, even though relapse rates are higher in some studies, six months may be okay for people who have a rapid viral response (RVR), have low levels of liver damage and who use a weight-based ribavirin dose.

There have been high cure rates in genotype 2 after 12 weeks with DAAs.

Retreatment

There is currently little data on retreatment with DAAs in HIV/HCV coinfection.

Although the numbers were small (53 treatment-experienced people) were included in the simeprevir coinfection trial. SVR rates were 87% for prior relapsers, 70% for prior partial responders, and 57% for prior null responders.

But, using these drugs (with or without peginterferon and ribavirin) has been effective in HCV mono-infection, especially in HCV genotype 1.

There will be more HCV retreatment trials, especially in coinfection.

Liver biopsy

Some doctors in some countries still require a biopsy before treating HCV. This is likely to become less common as FibroScan becomes more widely available. Each country is likely to develop guidelines based on access to non-invasive ways to measure liver damage.

Access to HCV treatment for drinkers

Many doctors will not treat people who have not stopped drinking. This is because alcohol can reduce adherence and therefore the chance of successful treatment.

On the other hand, because alcohol makes HCV progress more rapidly, drinkers are at greater risk for serious liver damage.

As guidelines also recommend treating people at risk for progression to cirrhosis, this is a contradiction that is difficult to resolve, perhaps requiring more intensive support.

Access to HCV treatment for PWID

HCV treatment is often withheld from people who inject drugs (PWID). This is despite guidelines that already recommend looking at each case individually based on medical need and being ready for treatment.

PWID can be, and have been, treated for HCV, despite ongoing drug use.

Successful programmes recommend including peer support and education groups, demonstration of safer injection techniques, access to syringes and/or a syringe exchange programme and mental health care.

Light-to-moderate alcohol intake

Heavy alcohol use causes liver damage even without HCV.

In people with HCV, drinking >50 g/day accelerates liver damage – equivalent to six or more glasses of wine, bottles of beer, or mixed drinks (8g = 1 unit).

As a safe amount of alcohol intake has not been determined for people with HCV, most doctors advise to stop drinking, or to limit this to occasionally having one drink. Until future research is able to find a safe level to drink, this is good advice.

Sexual transmission

The mechanisms for why some HIV positive people have a higher risk of sexual HCV transmission will hopefully become more clear.

This is essential for providing accurate information on how to reduce the risk of sexual transmission and for people with coinfection to know how to protect their partners.

DAA's may reduce sexual transmissions because more people will hopefully respond to treatment, reducing the number of people who are still infectious.

In this context, the issue of avoiding reinfection is likely to continue to be important.

Further information

HIV i-Base

HIV i-Base is an treatment activist, advocacy and education organisation based in London, set up in April 2000.

i-Base runs a treatment information phoneline on 0808 800 6013 on Monday, Tuesday, Wednesday from 12-4pm.

i-Base publishes non-technical treatment guides, and a monthly bulletin for doctors, all of which are available free in print, and online:

www.i-Base.info

Treatment Action Group (TAG)

TAG is an HIV/HCV/TB activist-run research and policy think tank based in New York. TAG follows epidemiology and natural history of HCV and HIV/HCV coinfection and the development of and access to new treatments.

TAG works with drug companies, government agencies, researchers and other treatment activists. It also educates members of the HIV community about coinfection with HIV and HCV.

www.treatmentactiongroup.org

TAG's Hepatitis/HIV Project draws from the core values and history of HIV activism, while incorporating hepatitis C-specific information and strategies.

i-Base/TAG annual pipeline report

HIV i-Base and TAG produce a pipeline report each year that includes a review of new HCV research:

www.PipelineReport.org

Keeping up to date with research

See page 81 for organisations and links to keep up to date on latest research into new HCV treatment.

Support organisations

The Hepatitis C Trust (UK)

0845 223 4424

<http://www.hepctrust.org.uk>

Antidote is a drug and alcohol service for lesbian/gay/transsexual/bisexual people, based in London with a national phoneline. 020 7833 1674 (10am-6pm, Monday to Friday).

This service includes counselling and other 1-2-1 support based at several London HIV clinics.

<http://londonfriend.org.uk>

<https://www.facebook.com/antidotelgbt>

Alcoholics Anonymous

<http://www.aa.org>

Narcotics Anonymous

<http://www.na.org>

Moderation management

<http://www.moderation.org>

Addiction Treatment Watchdog Forum

A forum for people on methadone and buprenorphine for opioid addiction.

<http://atwatchdog.lefora.com>

Buprenorphine FAQ's

<http://buprenorphine.samhsa.gov/faq.html>

National Alliance of Advocates for Buprenorphine Treatment (US)

<http://www.naabt.org>

Methamphetamine

Crystal Meth Anonymous

www.crystalmeth.org

Meth.org.au

<http://www.meth.org.au>

Harm reduction resources and forums

Harm Reduction Coalition (US)

Information and news about HCV best practices, tools and advocacy and harm reduction resources (US)

<http://harmreduction.org>

North American Syringe Exchange Network (NASEN)

US Syringe Exchange Programs

<http://www.nasen.org/programs/>

Harm Reduction Psychotherapy and Training Associates

<http://www.harmreductioncounseling.com>

EROWID: Information about psychoactive substances

<http://www.erowid.org/general/about/about.shtml>

Drugs Forum: An information hub and platform to discuss recreational drugs

<http://www.drugs-forum.com/index.php>

The Fix: addiction and recovery news

<http://www.thefix.com>

Glossary

ALT

(alanine transaminase, also called serum glutamate pyruvate transaminase; SGPT). A key liver enzyme produced in liver cells. ALT is routinely monitored in HIV positive people on ART to detect liver toxicity from HIV drugs (or other medications). Elevated ALT signals liver injury, but does not indicate how serious liver damage is.

antioxidant

A substance that reduces oxidative damage (damage due to oxygen) such as that caused by free radicals.

ascites

An abnormal accumulation of fluid in the abdomen, a sign of serious liver damage in people with HCV.

ART

Antiretroviral treatment - i.e. HIV meds.

AST

(aspartate aminotransferase; serum glutamic-oxaloacetic transaminase; SGOT). An enzyme that is made in many places throughout the body (heart, intestines, muscle). AST is routinely monitored in HIV positive people on ART to detect liver toxicity from HIV drugs (or other medications). Elevated AST that is specifically made in the liver signals liver injury, but does not indicate how serious liver damage is.

bile duct

A tube that carries bile from the liver to the gallbladder and then to the small intestine.

biopsy

Taking a small sample of body tissue for examination and testing in the laboratory.

BMI

(Body Mass Index) A calculation from your height and weight that is used to determine if someone is over or under weight. See:

<http://www.nhlbisupport.com/bmi>

cirrhosis

Severe scarring of the liver (see fibrosis) that makes it difficult for the liver to work well.

coinfection

Infection with more than one virus

cryoglobulinaemia

Increased blood levels of abnormal proteins called cryoglobulins that can inflame blood vessels and thicken blood.

DAA

Direct Acting Antivirals - the new HCV drugs in development.

encephalopathy

Degenerative brain function or disease.

enzyme

A protein produced 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 - a 99% (2-log) 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 combines results from other different blood tests to predict liver damage. This test, or other similar combinations of blood tests, especially when used in combination with FibroScan, may be an alternative option to liver biopsy in some patients.

FibroScan

Non-invasive ultrasound scan that measures the elasticity or stiffness of the liver.

www.youtube.com/watch?v=_E4ZGmKooA

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 and damage other cells, and 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 similar viruses. The HCV genotype is a strong predictor of response to peginterferon and ribavirin, and can determine both type and length of treatment used.

grade/grading

The grade of hepatitis infection refers to the amount of inflammation in liver tissue, found by a biopsy. It is usually measured on the Metavir scale (from 0 to 4) or the Ishak scale (from 1-18) where 0 is none and 18 is the maximum.

hepatic encephalopathy

Brain disease that occurs when serious liver damage prevents toxic substances from being filtered out of the blood, and they enter the brain.

hepatotoxicity

The medical term for liver related side effects.

IDU

Injecting drug user.

jaundice

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

mono-infection

Infection with one virus.

NNRTI

Non-Nucleoside Reverse Transcriptase Inhibitor (a type of HIV drug).

pegylated interferon (PEG-IFN)

The main current treatment for HCV when used in combination with ribavirin. Given as a once-weekly injection.

PI (Protease Inhibitor)

A type of HIV or HCV drug.

Notes

portal hypertension

Increased blood pressure (hypertension) in the vein carrying blood to the liver.

PWID

People who inject drugs.

ribavirin

A drug that makes interferon more effective. Given as twice-daily capsules.

RTI (Reverse Transcriptase Inhibitor)

A type of HIV drug - also called nucleoside or nuke.

RVR

Rapid Virological Response - undetectable HCV viral load after 4 weeks of treatment.

stage/staging

The stage of hepatitis infection refers to the amount of scarring (fibrosis), from results from a biopsy. It is usually measured on the Metavir scale of 0 to 4, where 0 represents no scarring and 4 cirrhosis, or on the Knodell scale of 0 to 6, where 0 is no scarring and 6 cirrhosis.

SVR

Sustained Virological Response - having a negative HCV viral load test 12 or 24 weeks after stopping HCV treatment. SVR is the most important result as it shows that HCV is cured.

toxicity

The harm related to a side effect of treatment.

varices

Extended or swollen veins that can burst, a complication of cirrhosis.

[illegible]

[illegible]



i-Base publications

All i-Base publications are available free
Treatment guides are written in everyday language
HTB is written in more technical medical language

Please photocopy or cut out this form and post to

HIV i-Base

4th Floor, 57 Great Suffolk Street, London, SE1 0BB

or fax to **020 7407 8489**

or order online **www.i-Base.info**

Please send me

- | | |
|--|--------------------------|
| Guide to hepatitis C for people living with HIV | <input type="checkbox"/> |
| Changing treatment: guide to second-line therapy | <input type="checkbox"/> |
| Pregnancy and womens health | <input type="checkbox"/> |
| HIV & your quality of life: side effects and other complications | <input type="checkbox"/> |
| HIV testing and risks of sexual transmission | <input type="checkbox"/> |
| HIV Treatment Bulletin (HTB) | <input type="checkbox"/> |

Name

Address

Postcode Tel

Email



Call us on
0808 800 6013

**i-Base Treatment
information Phonenumber**

**Monday to Wednesday
12 noon to 4pm**

i-Base can also answer your
questions by email or online

**questions@i-Base.org.uk
www.i-Base.info/questions**

