

TABLE OF CONTENTS

Section 1: About Hepatitis, Prevention & Transmission [How You Get It, How You Prevent It?]

Section 2: About the liver; What Happens to People with Hepatitis C & B infection?

Section 3: HCV & B diagnostics

Section 4: HCV & B diagnostics for making treatment decisions

Section 5: Treatment Issues for HIV/HCV-Co-infected People & Treatment for People Who Use Drugs or Alcohol Users

The purpose of this manual is to provide information for you and your community. This information can be used to advocate for access to prevention and diagnosis of, and care and treatment for hepatitis C virus (HCV) and B virus.

This manual is to help you understand basic information about hepatitis C and co infection with HIV: how it is transmitted, how to prevent hepatitis C, how a person can find out if he or she has hepatitis C, what happens to both HIV - Negative and HIV-positive people who have hepatitis C, information used for making treatment decisions, and treatment options.

SECTION 1: HEPATITIS, PREVENTION & TRANSMISSION: HOW YOU GET IT, HOW YOU PREVENT IT

Hepatitis Means “Swollen Liver” *Hepatitis* is a general term for swelling (inflammation) of the liver (*hepa* comes from the Greek word for liver, and *Itis* means swelling). Many things can cause your liver to become swollen, including

- drinking a lot of alcohol;
- taking certain medications or herbs;
- inhaling toxic fumes;
- auto immune diseases that cause the immune system to attack healthy tissue in the body; or
- infections, including viral hepatitis.

Viral Hepatitis:

There are six different hepatitis viruses: Hepatitis A, B, C, D, E, and G. These viruses were named alphabetically, in the order that they were discovered. Each of these viruses acts differently. Most people who have viral hepatitis don't know it, because they don't have any symptoms, but some people do have jaundice (yellow skin and eyes), appetite loss, nausea, vomiting, dark urine and pale stool, fever, aches, fatigue, and liver or abdominal swelling.

Viral Hepatitis Can Cause Serious Liver Disease Chronic HBV and HCV are “silent” illnesses; usually, people do not have symptoms until they have serious liver damage, which takes many years to develop. Many deaths from serious liver disease can be prevented with earlier diagnosis and treatment. Learning more about viral hepatitis and sharing the information with your community can help save lives.

Vaccines Can Prevent HAV and HBV:

Hepatitis A and hepatitis B can be prevented with vaccines. There is no HCV vaccine, although researchers are working to develop one. People can become infected with more than one hepatitis virus at the same time, and they can also be co infected with HIV. Co infection with more than one virus can make you sicker, which is why people who have chronic HCV or HIV should be vaccinated against HBV and HAV.

TRANSMISSION: HOW YOU GET IT, HOW YOU PREVENT IT

Hepatitis C (HCV) is spread by direct blood-to-blood contact. HCV is a bloodborne virus, spread when infected blood directly enters a person's

bloodstream. HCV is a very small virus, much smaller than HIV, so there is a lot of it even in a tiny amount of blood, but—unlike HIV—the hepatitis C virus can stay alive on surfaces outside of the body for days. HCV is 10 times more infectious than HIV. Bleaching syringes can prevent HIV, but it does not work as well to stop HCV; Sterilization of injection equipment, with heat, is the most effective way to kill HCV. Since most PWIDs don't have consistent and easy access to clean injection equipment, and HCV is not easy to kill, hepatitis C is common among people who inject drugs (PWID).

The most common ways to catch HCV are:

- Sharing *anything* that another person has used to inject drugs with, including needles, cookers, ties, cotton, straws, water, or measuring syringes;
- Getting a tattoo with any shared, unsterilized equipment: needles, ink, or inkwells;
- Getting a contaminated blood transfusion or blood product
- Undergoing surgery or other invasive medical procedures (vaccination, blood draws or donations, endoscopy) with unsterilized, shared equipment, or kidney dialysis in a facility that does not practice infection control;
- From mother to infant; the risk is about four percent, but if the mother is also HIV-positive, the risk is higher—up to 20 percent;
- Having unprotected sex with a person who has HCV; and
- Needle stick injury (for health care providers) or other occupational hazard.

When possible, avoid sharing toothbrushes, razors, manicuring equipment, or any other personal care items that may have come in contact with another person's blood.

A person who already has HCV can get infected again—this is called **reinfection**—even after being successfully treated. *You can also be infected with more than one type of hepatitis C virus at the same time.* Not sharing your injection equipment or using clean/new equipment protects you and the people that you are getting high with.

HCV can be spread during unprotected anal and vaginal sex with a person who has HCV. Although the hepatitis C virus has been found in semen and vaginal fluid, it is mainly found in blood. No one is sure whether there's enough HCV in semen and vaginal fluid to pass the virus to other people, but we do know that people have become infected from unprotected sex. HCV is more common among sex workers, men who have sex with men (MSM), and people who have had more than one sex partner. The risk for sexually transmitted HCV is greater when blood is involved, even when the amount is too small to see.

So all of the following can put a person at risk for HCV:

rough, unprotected anal and vaginal sex; fisting (also called *fist-fucking*; when a person puts his/her hand and forearm into another person's asshole [also called *anus*] or vagina); group sex; and sex with a woman during her period.

Using a condom with water-based lubricant for anal and vaginal sex, and latex gloves with plenty of water-based lubrication for fisting, can reduce the risk of sexually transmitted HCV.

HCV can be passed from mother to infant, in the womb, or during labor and delivery. If the mother has HCV—but not HIV—there is about a four percent risk that her baby will have HCV. The risk of mother-to-infant transmission (MTIT) of HCV is higher—up to 20 percent—if the mother is also HIV-positive. Pregnant women coinfecting with HIV and HCV can reduce the risk of passing HIV and HCV to their infants by taking antiretroviral therapy. HIV treatment takes care of the mother's health, and greatly lowers the risk of passing HIV and HCV to the infant. Unfortunately, it is not possible to use HCV treatment during pregnancy because one of the drugs—ribavirin—causes birth defects, and the other—interferon—is dangerous for infants and children under two years old. Because ribavirin and interferon should not be used by pregnant women, the two newer hepatitis C drugs—boceprevir (Victrelis) and telaprevir (Incivek), which must be combined with interferon and ribavirin—also cannot be used. Fortunately, researchers are studying new drugs and drug regimens that do not involve ribavirin or interferon. If these drugs are shown to be safe for pregnant women and their babies, they will likely be studied in combination to see if they can reduce the risk of mother-to-child transmission of HCV. Unlike HIV, the hepatitis C virus has not been found in breast milk. HIV-negative mothers who have HCV can safely breastfeed their infants as long as their nipples do not have any cuts or cracks.

HCV cannot be passed by sharing eating utensils or by eating food made by a person with HCV. It cannot be passed by drinking from the same glass as someone with HCV. HCV is not spread by casual contact (kissing, hugging, holding hands, etc.). Sharing non injection drug equipment (straws and pipes) It may be possible to get HCV from sharing straws and pipes (used for cocaine, heroin, crystal methamphetamine, etc.). Straws may contain tiny amounts of blood from the inside of someone's nose, and people may have burns on their lips from a hot pipe. Although it is not always possible, it is important to use clean injection equipment (needles, measuring syringes, cookers, cotton, water, and ties) every time you get high.

SECTION 2: ABOUT THE LIVER

The liver is an organ in the body that has many critical functions. When the liver becomes very damaged (such as by chronic viral hepatitis), it cannot work properly. Liver damage can lead to life threatening complications, such as cirrhosis, liver cancer, and liver failure. The Liver Performs Many Important Functions. The liver is the biggest organ inside the human body, found on the right side, underneath the rib cage. Your liver works as a filter and processing plant for your body. Anything you eat, drink, and inhale passes through the liver. Your liver also breaks down herbal remedies, vitamins, and drugs—whether or not they are legal.

Each day, your liver

- filters waste from the blood;
- stores vitamins, minerals, and iron;
- changes food into energy;
- makes bile (a liquid that your body uses to digest fat);
- helps balance sugar and hormone levels;
- makes cholesterol; and
- creates the hormone that helps to produce platelets, which stop bleeding by clotting blood.

Immune Response to Viral Hepatitis Infection Causes Liver Damage. HCV does not directly cause liver damage—the way a person’s immune system responds to the virus is what can cause liver damage. The immune system tries to get rid of infected liver cells by surrounding them and walling them off; over time, this creates scarring in the liver. Although the liver grows new cells, cells that are already scarred cannot become unscarred. As the scarring worsens, the liver hardens, making it more difficult for blood and other important fluids to pass through it. These fluids, which are usually filtered by the liver, can build up to toxic levels in the bloodstream when the liver is too damaged to function. Liver damage from HCV happens slowly, usually over decades. It can take from 15 to 50 years for an HIV-negative person who has chronic hepatitis C to develop cirrhosis.

Some things cause faster liver damage from viral hepatitis:

- Being HIV-positive—especially if you got HCV after getting HIV;
- Being coinfectd with HBV and HCV;
- Drinking alcohol, especially heavily;
- Age over 40;

- Having fat in your liver (a condition called *steatosis*), usually in overweight people, heavy drinkers, or people with metabolic disorders; and
- The amount of time you have had hepatitis C—the longer you've been infected, the more likely you are to develop liver damage.

Having chronic HCV does not always mean that you will have serious liver damage, or that you need treatment. Some people live with hepatitis C for many years and will never have liver damage.

Some people develop mild liver scarring, called *fibrosis*. Having HCV and being overweight can cause fat to build up in the liver, a condition called *steatosis*. People with steatosis are at higher risk for liver damage. *Compensated cirrhosis* means the liver is still able to function even though it is scarred. People with compensated cirrhosis are at risk for liver failure, liver cancer, and other serious complications. Liver failure, also called *decompensated cirrhosis*, or *end-stage liver disease* (ESLD), means that the liver can no longer do its job, and that a liver transplant is necessary. Liver cancer (also called *hepatocellular carcinoma*, or HCC) is very serious. It is very difficult to treat, especially if it is not caught early. Although there is not a standard test for liver cancer, doctors use a combination of tests to screen for liver cancer, and researchers are working to develop better methods for early detection of liver cancer. Preventing development or progression of liver disease by getting rid of HCV is the primary goal of HCV treatment. It is important for people to find out if they have HCV, because treatment doesn't work as well in people who already have cirrhosis. People with cirrhosis remain at risk for liver cancer even after they have been cured of HCV, and should be screened regularly.

Alcohol: Harmful to the Liver

Alcohol is hard for the liver to break down, even in people who don't have hepatitis C. In people with HCV, alcohol hurts the liver by increasing inflammation and scarring, which leads to cirrhosis. Heavy drinking increases the risk for cirrhosis in people with all types of viral hepatitis, including HCV. Even though experts have not agreed on a safe amount of alcohol, many recommend complete abstinence from alcohol, or limiting it to a small amount on special occasions. Doctors do agree that the less that a person with hepatitis drinks, the better. Some studies found that men who drink 50 grams of alcohol (4 to 5 servings of mixed drinks, shots, glasses of wine, or small bottles of beer) a day or more, and women who drink 30 grams of alcohol (2 to 3 servings) a day or more, are at higher risk for liver damage than people who drink less or not at all. Quitting or cutting down on drinking can be very difficult, but drinking less—or not at all—may be the most important thing a person with hepatitis C can do to prevent liver damage.

Street Drugs and Liver:

People who regularly use heroin, cocaine, and crystal methamphetamine may not be getting enough sleep or eating well, and may be under a great deal of stress. People who don't have access to clean injection equipment are at risk for infections such as HIV, HBV, and HCV (including reinfection after being cured of the virus). For these reasons, using street drugs—especially on a daily basis—can have a negative overall impact on a person's health. Since heroin, cocaine, and crystal methamphetamine are illegal, there is very little research or information on whether or not these drugs cause liver damage in people with chronic hepatitis. Most research on street drugs has been done *in vitro* (in a test tube), not *in vivo* (in the human body). What happens inside the human body is often very different from what happens in a test tube, so it is hard to know how the results from an *in vitro* study relate to what actually happens in a person's body.

The purity of “street drugs” (illicit drugs) varies. The other substances that are added to street drugs may be harmful to the liver, although the drug itself may not be. This makes it more difficult to know the impact of street drug use on chronic hepatitis.

Some researchers have found that daily marijuana use (one joint or more per day over several years) can cause fibrosis faster in people with chronic HCV, but other studies have not reported a link between liver scarring and marijuana use. Occasional use of marijuana has not been found to be harmful. In fact, one study found that smoking marijuana during HCV treatment helped people to deal with side effects and complete their treatment.

Prescription Drug Use:

Some people use prescription drugs to get high. This can be risky because they may interact with other medications, causing lowered or increased drug levels in a person's body. If drug levels are too low, medications may stop working, and in some cases—such as with HIV medications and antibiotics—drug resistance can develop because there is not enough drug in a person's system to stop viruses and bacteria from reproducing. Drug levels that are too high can also be dangerous,

since they can increase drug toxicity and side effects, or cause an overdose.

For example, benzodiazepines such as midazolam interact with alcohol; caffeine; sleeping pills; some antidepressants and anti-anxiety drugs; some antibiotics; hormonal contraception (birth control pills); some of the drugs used to treat TB, fungal infections, high blood pressure, and heart problems; and even cold medications (among others).

SECTION 3. HCV DIAGNOSTICS

The first step in dealing with HCV is to find out as much as you can. One way to do this is by getting some laboratory tests from the medical provider. These tests can tell

- if a person has been infected with HCV;
- which strain (genotype) of HCV the person has;
- the amount of virus (viral load) in the bloodstream;
- if the liver has been very damaged; and
- how well HCV treatment is working.

HCV Screening Tests and What the Results Mean:

POSITIVE RESULT

There are three potential meanings:

1. The person may have acute HCV; or
2. may have chronic HCV; or
3. was infected in the past, but has cleared HCV and is no longer infected.

The person needs a viral-load test to confirm.

NEGATIVE RESULT

There are three potential meanings:

1. The person has never been infected; or
2. may have been recently infected (within the last two weeks); or
3. may have chronic HCV (if the person is HIV-positive, especially with a CD4 count <200 cells/mm³).

The person needs a viral-load test to confirm.

DETECTABLE RESULT

There are two potential meanings:

1. The person may be recently infected, and has acute HCV; or
2. may have chronic HCV.

The person needs a second confirmatory viral-load test.

UNDETECTABLE RESULT

There are three potential meanings:

1. The person has never been infected; or
2. was once infected in the past, but has now cleared HCV; or
3. was recently infected but is still in the process of clearing the infection.

The person needs a second confirmatory viral-load test.

DETECTABLE RESULT

The person has chronic HCV.

UNDETECTABLE RESULT

1. The person has never been infected;
2. was infected in the past but has now cleared HCV.

The person does not have HCV.

Two different blood tests are used to diagnose HCV: antibody test and viral-load test. Diagnosing HCV is different from diagnosing HIV, although both viruses can be diagnosed with blood tests. A positive HCV-antibody test result does not always mean that someone has chronic HCV—it simply means that a person was infected with HCV in the past, and may still be infected—because people who get rid of HCV without treatment (called *spontaneous viral clearance*) usually stay HCV antibody–positive for years.

A viral-load, or HCV RNA, test looks for the actual virus—not antibodies—in a blood sample. This is the only way to determine if someone has chronic HCV. If there is hepatitis C virus in a person’s blood, that person is currently infected with HCV. If the test does not find the hepatitis C virus in a person’s blood (called *undetectable*), that person should get tested again, six months later. If the second test result is also undetectable, it means that HCV has been cleared. HCV viral loads are usually much, much higher than HIV viral loads, but a high viral load does not mean that HCV is more serious, or that liver damage will happen faster. For people with chronic HCV, viral load is a very important test if treatment is prescribed. The test helps determine if treatment is working, if it should be stopped, and if it succeeds in curing the infection. So, for a person on HCV treatment, viral-load testing is done just before starting treatment, during treatment at specific intervals, and after treatment ends.

A negative HCV-antibody test result usually means a person doesn’t have HCV—but not always. Sometimes an HCV-antibody test result is negative, even when someone does have chronic HCV. This happens for two reasons. If a person just got infected with HCV, he or she may not have antibodies yet. After hepatitis C virus has entered a person’s bloodstream, the immune system responds by making antibodies. These are sticky, Y-shaped proteins that wrap themselves around invaders, either disabling them or marking them so that the immune system can destroy them.

It takes six to 24 weeks for a person to make antibodies to HCV (often called the *window period*). HCV-antibody test results may also be negative in HIV-

positive people who have HCV. This can happen when a person has less than 200 CD4 cells, because their immune system is not able to make antibodies. *So anyone with a CD4 count of less than 200 cells/mm³, who has signs or symptoms of hepatitis, such as elevated liver enzymes, yellow skin or eyes, or fatigue, or who has been at risk for HCV, should have an HCV viral-load test, even when an HCV-antibody test is negative.*

Viral-Load Tests:

There are two different types of HCV viral-load tests: *qualitative* (measures whether or not there is HCV virus in a person's blood; results are either detectable or undetectable), and *quantitative* (measures how much hepatitis C virus there is in a person's blood).

- Qualitative testing can pick up very small amounts of HCV in a person's bloodstream. It is usually used to diagnose HCV, and sometimes used to measure response during HCV treatment.
- Quantitative testing is usually used to see how much virus a person has in his or her bloodstream before starting HCV treatment, and sometimes used to measure response during HCV treatment.

HCV treatment is more likely to work for people with a low HCV viral load. New treatments may cure HCV regardless of the viral load. The HCV viral load is one of the things that predict whether or not HCV treatment is likely to work. The lower the HCV viral load is, the more likely that HCV treatment will work. Viral-load testing is also used during and after HCV treatment, to see if treatment is working (for more information, see section 7, HCV Treatment and Side Effects).

Getting More Information about the Health of Your Liver Liver Enzyme Tests (ALT and AST) Liver enzymes are proteins that do different jobs in the body. When a person's liver is injured, increased numbers of these enzymes leave the liver cells and enter the bloodstream. Health care providers check liver enzyme levels using a group of blood tests, sometimes called *liver function tests* (LFTs). These tests do not actually measure liver function, and the results cannot predict or tell someone how much liver disease they have. Many things can cause abnormally high liver enzyme levels, such as: liver toxicity from prescription and over-the-counter medications, herbs, vitamins, and supplements; exposure to toxic fumes; heavy alcohol consumption; acute or chronic viral hepatitis and certain other infections; and while a person is detoxing from drugs or alcohol. Some HIV medications are broken down by the liver, and can cause abnormally high liver enzyme levels. All HIV-positive people who are taking ART or TB drugs—whether or not they are coinfecting with hepatitis B or C—should have their liver enzyme levels checked regularly as some HIV medications, TB

treatment and other drugs can be hard for the liver to break down. When liver enzyme levels are higher than normal for several months, it can be a signal that the liver is inflamed or damaged. Normal liver enzyme levels do not mean that a person's liver is healthy—some people may have normal liver enzyme levels for years although they have serious liver damage. It is a good idea to keep a record of your liver enzyme levels over time. If the level goes up and stays up over several tests, it may be a good time to discuss HCV treatment with your doctor, as other causes for abnormal enzyme elevations are ruled out.

SECTION 4. HCV DIAGNOSTICS FOR MAKING TREATMENT DECISIONS

There are different viral strains of HCV, called *genotypes*. There are at least six different HCV genotypes, each given a number (1, 2, 3, etc.) in the order of discovery. Within each HCV genotype there are slight differences, called *subtypes*; these are given a letter of the alphabet (a, b, c, d, etc.), so for example someone may be diagnosed with HCV genotype “3a.” A person can be infected with more than one HCV genotype, and people who already have HCV can get infected again (*reinfected*) with a different genotype. It is very important to have an HCV genotype test before starting HCV treatment, because some genotypes respond differently to treatment than others. Health care providers can order a blood test to see which HCV genotype—or genotypes—a person has. It is very important to have an HCV genotype test before starting HCV treatment, because some genotypes don't need to be treated for as long as others.

[Source: Gravitz L. Introduction: a smouldering public-health crisis. *Nature*. 2011 Jun 8;474(7350):S2–4. doi: 10.1038/474S2a.]

Genotype 3 is most common in Thailand. People who have genotype 3 are more likely to have steatosis (fat in the liver); this can make treatment less effective. Genotype 1 is most common in the United States. People with genotype 1 are more likely to have high hepatitis C viral loads. HCV treatment is less likely to work for people with a high viral load. However, new treatments are in development, many specifically made to work against genotype

1. Some of these may be more effective for people with genotype 1b (vs. genotype 1a), so it is important to ask your doctor about your subtype. New treatments are also in development for other genotypes. Since some HCV genotypes are harder to treat than others, it is important to avoid getting reinfected with HCV when possible.

Genotype Testing:

IL28B is a gene in our body that plays a role in the immune system's defense against certain viruses. Everyone gets one IL28B gene from each parent—either

“C” or “T.” In turn, a person can either have the IL28B “CC,” “CT,” or “TT” genotype. You can find out your IL28B genotype through a blood test (called the *IL28B genotype test*). People with the IL28B CC genotype are more likely to be cured by HCV treatment with peginterferon than people with the TT genotype. Cure rates among people with the CT genotype fall somewhere in between. New treatments that are not influenced by IL28B genotype are being developed. Because IL28B is inherited, your ancestry can help determine which genotype you have.

African 23–55%

European 53–86%

South Asian 65–98%

East Asian 90–100%

A person’s IL28B genotype never changes, so this test needs to be taken only once. Knowing your IL28B genotype can be helpful to you and your doctor when discussing treatment options. Your IL28B genotype may determine what medications you take and how long you need to take them.

Liver Biopsy:

A liver biopsy is the best way to find out what condition a person’s liver is in, because health care providers can see how much inflammation (*grade*) and scarring (*stage*) there is in a sample of liver tissue. During a liver biopsy, a very small piece of liver tissue is removed with a needle. The tissue is then examined to see how much damage there is, and what is causing the damage. Usually, a person will stay in the hospital for a few hours afterward to make sure that there are no complications. There are drawbacks to liver biopsy. If the tissue sample is not large enough, or is taken from a less damaged part of the liver, the results will not be accurate. Biopsy is expensive, and many people are not able to have a biopsy done for this reason. Liver biopsy can also be painful. There is a small risk of complications—such as internal bleeding, or missing the liver and piercing a nearby organ—and a much, much smaller risk of death. It is always important to ask how much experience a doctor has had in performing biopsies, what kind of pain medication will be offered, and how long the hospital stay is. It may be helpful for you to ask someone who has had a liver biopsy how it was, and if they recommend the doctor who did it.

Cirrhosis can be diagnosed without a liver biopsy. Health care providers can use a combination of blood tests instead. Some liver specialists, particularly in Europe, are also using a machine called FibroScan that looks at liver stiffness using sound waves. It is difficult to diagnose mild or moderate liver disease without doing a biopsy, however, and FibroScan is not widely available in most countries. Liver biopsy is not always necessary. Sometimes, people do not get a

biopsy before starting HCV treatment. Often, this is because of the cost, or because there is no experienced doctor available to perform one. Liver damage from HCV can develop faster in HIV-positive people, so some health care providers think it is a good idea to go ahead and treat co-infected people whether or not they have had a biopsy.

SECTION 5. TREATMENT FOR PEOPLE WHO USE DRUGS OR ALCOHOL USERS AND TREATMENT ISSUES FOR HIV/HCV COINFECTION

Some doctors may refuse, or be reluctant to treat, people who are using illicit drugs and alcohol—even when they need treatment and are ready and willing to undergo therapy.

Drug Use

Although many doctors think that it is not possible to treat HCV in people who are using drugs, several studies have shown otherwise. These studies found that people who use drugs could be successfully treated for HCV, when their side effects were treated and when counseling from peers and mental health staff, methadone or buprenorphine, clean injection equipment and addiction treatment were available on request. Access to clean injection equipment is also critical to help prevent reinfection.

Alcohol Use

Studies have found that both lifetime and recent alcohol use among people with HCV undergoing treatment can reduce the chance of being cured of the virus. However, many of these studies involved people being treated with non-pegylated interferon, which is considered inferior and harder to take compared with the current standard of care. Plus, the studies didn't measure adherence. In fact, a more recent study suggests that poor treatment adherence, not alcohol consumption, worsens treatment outcomes.

Marijuana

Marijuana may have both positive and negative health effects for people with HCV. Daily marijuana use may increase fat buildup in liver cells (*steatosis*), which can worsen fibrosis, according to one study. Researchers have also found that some people with HCV who have used marijuana daily for many years have more serious liver damage than those who don't use the drug or use it occasionally, although other studies have not confirmed this finding. Modest marijuana use may be beneficial for some people undergoing HCV treatment. In

one study, it helped to reduce side effects, which allowed more people to complete treatment—and be cured of the virus—compared with those who didn't.

There are many new treatments for HCV being studied; hopefully, some people will be able to get access to HCV treatment through clinical trials, but it is important to learn about the risks and benefits of the trial first. Some trials are better than others.

HCV and HIV Treatment Issues for HIV/HCV-Coinfected People:

Ideally, all HIV-positive people should be tested for HCV and offered treatment if needed. HCV progresses more quickly in people who are also HIV-positive, so access to HCV treatment is especially important for people with coinfection. Coinfected people with a CD4 cell count of more than 500 cells/mm³ may treat HCV first, but most people start HIV treatment before treating HCV, because many people don't find out that they are HIV-positive until after their CD4 count is below 200 cells/mm³. HIV treatment can keep the immune system healthy, which slows HCV progression. There is not very much information on how safe HCV treatment is or how well it works for people with less than 200 CD4 cells/mm³ who are also taking ART. This is an important question, because people with low CD4 cell counts are at higher risk for liver damage from HCV.

PEG-IFN and CD4 Cell Count; PEG-IFN can lower the absolute CD4 cell count (but not the percentage of CD4 cells), even when someone is on ART. This can be frightening, but it is temporary. The CD4 cell count goes back up after stopping PEG-IFN.

Antiretrovirals (ARVs) and Liver Toxicity:

Many ARVs are broken down by the liver. Some ARVs are more harmful to the liver than others, especially when a person is coinfecting with HCV. Liver toxicity is more likely for coinfecting people with serious liver scarring. Having liver enzyme levels checked regularly is very important for coinfecting people who are taking ARVs, because these can pick up liver problems caused by HIV drugs or other causes. Although all drugs used to treat HIV may cause liver problems, some are more likely to cause damage than others. Nevirapine, a non-nucleoside reverse transcriptase inhibitor, should not be used in women with a CD4 cell count above 250 cells/mm³ and men with a CD4 cell count above 400 CD4 cells/mm³. Darunavir, an HIV protease inhibitor, can be toxic to the liver. Careful monitoring of liver enzyme levels is recommended for people using this

drug. Curing HCV treatment can lower the risk of liver toxicity from ARVs by slowing or stopping liver scarring.

Drug Interactions:

Some ARVs should not be used during HCV treatment because they interact with ribavirin, telaprevir, or boceprevir. Didanosine (ddI; Videx) should not be used with ribavirin because the combination can cause lactic acidosis (when lactic acid builds up in the blood), and pancreatitis; both conditions can be life-threatening. Using ddI during HCV treatment has caused liver failure in people with cirrhosis.

Zidovudine (AZT; ZDV; zidovudine; Retrovir) can cause anemia, as can ribavirin. The combination increases the risk of anemia, so AZT should be avoided during HCV treatment.

Stavudine (d4T; Stavir) may cause fat loss (called *lipoatrophy*), and increase weight loss when used during HCV treatment. When possible, d4T should not be used during HCV treatment. Note that some of these medications may be combined with other HIV medications in single-tablet formulations (also called *fixed-dosed combinations*). The names of these fixed-dose combinations may be different from those listed above. HIV protease inhibitors boosted with ritonavir should not be taken at the same time as boceprevir. Telaprevir can, however, be taken at the same time as ritonavir-boosted atazanavir.

Efavirenz (also known as EFV or Sustiva; it is also found in the fixed-dose combination tablet Atripla) should not be taken at the same time as boceprevir. It can, however, be taken at the same time as telaprevir as long as the dose of telaprevir is increased to 1,125 mg, three times per day.

It is very important that health care providers know all of the medication a person with HCV or HIV is taking to make sure there are no drug interactions. These can greatly increase the risk of side effects and make HCV or HIV treatment less effective. A complete listing of drug-drug interactions is available at: [www.hep-druginteractions.org.]