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NOTES ON HEPATITIS

What you need to know about Hepatitis

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NOTES ON HEPATITIS

Hepatitis A

What is it? How is it transmitted?

Hepatitis A is caused by the hepatitis A virus (HAV). HAV is spread from one person to another when the feces (shit) of someone with the virus gets into another person's mouth. There are a number of ways that this can happen:

- Eating food – particularly food that is raw or not thoroughly cooked (shellfish, for example) – that has been handled or prepared by someone who has hepatitis A.
- Drinking water or ice that is contaminated with feces.
- Engaging in oral-anal sex ("rimming") with someone who has hepatitis A.
- Rarely, HAV can also be spread through blood-to-blood exposure (sharing intravenous drug injection equipment, for example).

Hepatitis A is an acute form of hepatitis, meaning that it does not cause long-term (chronic) infection. If you have had hepatitis A once, you cannot be infected with the virus again. However, you can still be infected with other hepatitis viruses ([hepatitis B virus](#) and [hepatitis C virus](#), for example).

People with HIV are not at greater risk of becoming infected with HAV than anyone else. However, some studies suggest that people with HIV are more likely to experience prolonged symptoms of hepatitis A, meaning that it might take longer for someone who is HIV-positive to recover fully from hepatitis A.

Another important issue to consider is that many people with HIV are taking anti-HIV medications that can be toxic to the liver. Some of these medications can make symptoms of hepatitis A worse. In turn, it might be necessary to stop all anti-HIV medications until the hepatitis A has run its course or until liver enzyme levels have returned to normal. If you are HIV-positive, are taking anti-HIV medications, and develop hepatitis A, do not stop your anti-HIV medications without first discussing it with your doctor.

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What are the symptoms?

Not everyone who is infected with HAV will experience noticeable symptoms. For example, many babies and young children infected with HAV do not experience any symptoms of infection. Symptoms are much more likely to occur in older children, adolescents, and adults.

Symptoms of hepatitis A (and acute hepatitis in general) can include:

- Yellowing of the skin and whites of the eyes (jaundice)
- Feeling tired and rundown ([fatigue](#))
- Pain in the upper-right abdomen
- Loss of appetite
- Weight loss
- Fever
- [Nausea](#)
- [Diarrhea](#)
- [Vomiting](#)
- Dark urine and/or pale stool
- Joint pain

HAV infection can also cause enzymes produced by the liver to increase above normal levels in the bloodstream. The most important liver enzymes are alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Elevated enzyme levels indicate that the liver is not functioning properly and that there may be a risk of permanent liver damage. With hepatitis A, liver enzyme levels can be temporarily elevated, but this rarely leads to long-term liver problems. Both of these enzymes are measured as part of a standard Chem-Screen (CS) Test, which people on anti-HIV treatments usually have done on a regular basis, along with their other blood tests. To see a sample of this test, go to [Understanding Your Chem-Screen \(CS\) Test](#).

It can take the immune system up to eight weeks to clear HAV from the body. If symptoms occur, they usually do so within two to four weeks after being infected. The symptoms of hepatitis A can last anywhere from a week to more than a month. Approximately 15% of people with hepatitis A experience symptoms that last between six to nine months.

About one out of 100 people infected with HAV may experience a quick and severe (fulminant) infection, which – very rarely – can lead to liver failure and death.

How is it diagnosed?

Hepatitis A can be diagnosed using blood tests. Your healthcare provider can order these tests if you have symptoms of hepatitis A or if you want to know if you were infected with HAV in the past.

The blood test looks for two different types of antibodies to the virus. First it looks for IgM antibodies, which are produced by the immune system five to ten days before symptoms appear and usually disappear within six months. It also looks for IgG antibodies, which replace IgM antibodies and protect against future HAV infection.

- If the blood test shows that you are negative for both IgM and IgG antibodies, you probably have never been infected with the virus and should consider getting the HAV vaccine.
- If you are positive for IgM antibodies and negative for IgG antibodies, HAV infection most likely took place within the past six months and is either in the process of being cleared by the immune system or getting worse.
- If you are negative for IgM antibodies and positive for IgG antibodies, either you were infected with HAV some time in the past or you have been vaccinated against hepatitis A; in either case, you are now immune to the virus.

How is it treated?

The usual treatment for hepatitis A is bed rest. It is also important to drink plenty of fluids, particularly if you are experiencing diarrhea or vomiting. Over-the-counter pain relievers, such as ibuprofen (Advil®, Motrin®, etc.), can help manage some of the symptoms of hepatitis A, although it's best to consult with your healthcare provider before using any medications.

If you think that you may have recently been exposed to HAV – for example, if somebody in your household has been diagnosed with hepatitis A – you can talk to your doctor about receiving an injection of **immune globulin** (also called gamma globulin). Immune globulin contains high levels of antibodies to HAV, which can help prevent the disease if you have been exposed to the virus. Immune globulin needs to be given within two to six weeks after possible exposure to HAV. People who receive immune globulin to prevent active hepatitis A should also receive the hepatitis A vaccine (discussed in the next section).

How can it be prevented?

The best way to prevent hepatitis A is to be vaccinated. Two HAV vaccines are available: Havrix® and VAQTA®. Both of these vaccines require two injections, usually administered six months apart. If side effects from the hepatitis A vaccine occur, they are usually mild and may include soreness at the injection site and mild flu-like symptoms. A combination vaccine for HAV and [hepatitis B virus](#) (Twinrix®) is also available.

The HAV vaccine is very effective. More than 99% of people who are vaccinated develop immunity against the virus and will never get HAV even if they are exposed to it. There is some concern that people with HIV with suppressed immune systems are less likely to benefit from the vaccine, so it is best to get the vaccine when T-cell counts are within healthy ranges.

If you do not think you were ever infected with hepatitis A, talk to your healthcare provider about the vaccine. Because people with HIV often experience worse symptoms of HAV infection and the liver plays such an important role in breaking down anti-HIV medications, the hepatitis A vaccine is strongly recommended for people with HIV. Getting vaccinated is especially important for people who are also infected with [hepatitis B](#) or [hepatitis C](#).

Even if you haven't been vaccinated against hepatitis A, there are things you can do to prevent HAV infection:

- Avoid water that could be contaminated with fecal matter.
- Avoid undercooked or raw shellfish.
- Always wash your hands with soap and water after using the bathroom, changing a diaper, and before preparing and eating food.
- Use a latex barrier – such as a dental dam – for oral-anal sex ("rimming").

HEPATITIS B – HbsAg

What is it? How is it transmitted?

Hepatitis B is caused by the hepatitis B virus (HBV). HBV is a noncytopathic virus. This means that the virus, itself, does not cause direct damage to liver cells. Instead, it is the immune system's aggressive response to the virus that usually leads to inflammation and damage to the liver (hepatitis). However, HBV can cause damage to the genetic material inside liver cells. This can lead to liver cancer which, like hepatitis, can also be fatal.

People who have not been infected with HBV can be vaccinated against the virus to prevent infection.

HBV is very similar to HIV in the ways it is transmitted: through direct blood-to-blood contact and through sexual activity. However, blood levels of HBV are much higher than for HIV or the [hepatitis C](#) virus, making this virus much easier to transmit in certain situations (e.g., from mother to child during delivery).

HBV is present in blood, semen, and vaginal fluids and is transmitted primarily through sexual activity. Another major transmission route is sharing injection drug equipment (including needles, cookers, tourniquets) and, to a lesser extent, non-injection drugs (cocaine straws and crack pipes) due to the possibility of exposure to blood. Pregnant women who have hepatitis B can also transmit the virus to their babies, most likely during birth.

The number of new hepatitis B infections in the U.S. has declined from about 260,000 a year in the 1980s to about 73,000 in 2003, with the greatest decline occurring in children and adolescents due to routine HBV vaccination.

What happens when someone is infected with HBV?

Soon after HBV enters the body, it infects cells in the liver called hepatocytes. In response to this infection, the immune system targets the virus and targets the hepatocytes already infected with the virus. This causes inflammation of the liver (hepatitis).

HBV can cause acute hepatitis, meaning short-term inflammation of the liver, until the immune system is able to clear the virus from the body, usually within six months of becoming infected with the virus. However, HBV can become a chronic infection. This means that the immune system is not able to get rid of the virus within six months after infection. In other words, the virus continues to reproduce in the person's liver for several months or years after infection. This can increase the risk of liver damage and liver cancer. What's more, someone with chronic HBV infection can transmit the virus to others.

Less than 10% of adults infected with HBV go on to experience chronic HBV infection. Babies infected with HBV around the time of birth go on to experience chronic HBV infection approximately 90% of the time, which is why it is important that pregnant

women know whether or not they are infected with the virus before giving birth. Medication can be given to the baby after birth to help prevent hepatitis B. Young children who are infected with HBV have a 25% to 50% risk of developing chronic hepatitis B. With adults, the risk of developing chronic HBV infection depends on the health of the immune system. For example, patients with impaired immune responses who are recovering from organ transplants, undergoing chemotherapy, undergoing dialysis for kidney problems, receiving steroid therapy to suppress the immune system, *or are HIV-positive* are more likely to develop chronic HBV infection than patients with normal immune responses. In other words, HIV-positive people are more likely to develop chronic HBV infection after being infected with the virus than HIV-negative people (with healthy immune systems).

What are the symptoms?

Not everyone who is infected with HBV will experience symptoms of acute hepatitis – between 30% and 40% of people infected with the virus do not experience any noticeable symptoms. If symptoms *do* occur, they usually do so within four to six weeks after being infected and can last anywhere from one or two weeks to several months.

The symptoms of acute hepatitis B can include:

- Yellowing of the skin, whites of the eyes, and under the fingernails (jaundice)
- Dark urine and/or pale stool
- Feeling tired and rundown ([fatigue](#))
- Fever
- Abdominal pain
- Loss of appetite
- [Nausea](#)
- [Diarrhea](#)
- Joint pain

If the immune system is not able to control acute HBV infection within six months, symptoms of chronic hepatitis B are possible. Not everyone with chronic hepatitis B experiences symptoms. Some people with chronic hepatitis B experience occasional symptoms, while others experience symptoms that never seem to go away.

Symptoms of chronic hepatitis B can include those typically seen in acute hepatitis B. They tend to be mild to moderate in intensity and typically come and go. Other symptoms can occur, particularly in people who have been dealing with chronic hepatitis B for many years. Additional symptoms include rash, hives (urticaria), arthritis, and burning/tingling in the arms and legs ([polyneuropathy](#)).

Less than 1% of people infected with HBV may experience a quick and severe (fulminant) infection, which – very rarely – can lead to liver failure and death. Symptoms of hepatitis, whether acute or chronic, should always be brought to the attention of a healthcare provider.

What laboratory tests do I need to know about?

There are laboratory tests to diagnose HBV infection and laboratory tests to monitor people with chronic hepatitis B.

Hepatitis B is first diagnosed using a blood test that looks for certain antigens (fragments of HBV) and antibodies (produced by the immune system in response to HBV). Initial blood tests to diagnose HBV infection look for one antigen – HBsAg (the

hepatitis B surface antigen) and two antibodies – anti-HBs (antibodies to the HBV surface antigen) and anti-HBc (antibodies to the HBV core antigen). There are actually two types of anti-HBc antibodies produced: IgM antibodies and IgG antibodies. IgM antibodies are produced early in the course of infection. IgG antibodies are produced later in the course of infection and replace IgM antibodies.

The blood test used to check for HBV infection can be quite confusing, given that a number of different combinations of antigens and antibodies are possible and can mean different things. Here's a look at the most important test results to know:

Hepatitis B status	HBsAg	Anti-HBc (total)	Anti-HBc (IgM)	Anti-HBs
Never infected with the virus (consider getting the vaccine).	Negative	Negative	Negative	Negative
Infection likely took place over the last six months and is still active.	Positive	Positive	Positive	Negative
Infection likely took place over the past six months and is in the process of clearing. A false-positive is another possibly (HIV-positive people with this particular test result should have their HBV viral load checked).	Negative	Negative	Positive	Negative
Infection likely took place more than six months ago and has been successfully controlled by the immune system.	Negative	Positive	Negative	Positive
The vaccine was successfully given to prevent HBV infection.	Negative	Negative	Negative	Positive
Chronic HBV infection.	Positive	Negative	Positive	Negative

Depending on these results, additional diagnostic tests may be necessary. Somebody who has never been infected with HBV or has been vaccinated against the virus does not require any additional testing. Someone who was recently infected with HBV and has acute hepatitis B may want to get another blood test after six months have passed to make sure that the necessary immune response has occurred. People with chronic HBV infection require additional testing to learn more about their hepatitis B.

If you have chronic hepatitis B, your healthcare provider will usually order additional tests to determine if the infection is active:

Additional Tests	
◆	HBeAg and anti-HBe: HBeAg is the hepatitis B envelope antigen, and anti-HBe are the antibodies produced against this antigen. If HBeAg is detectable in a blood sample, this means that the virus is still active in the liver (and can be transmitted to others). If HBeAg is negative and anti-HBe is positive, this generally means that the virus is inactive. However, this is not always the case. Some people with chronic hepatitis B – especially those who have been infected with HBV for many years – may have what is known as a "precore mutant" of HBV. This can cause HBeAg to be negative and anti-HBe to be positive, even though the virus is still active in the liver.
◆	HBV viral load: Similar to the technology used to measure the amount of HIV in the bloodstream, viral load testing can determine if HBV is reproducing in the liver. In a person with detectable HBeAg, an HBV viral load greater than 100,000 indicates that the virus is active and has the greatest potential to cause damage to the liver. Similarly, in a person with an HBV precore mutant, an HBV viral load of greater than 10,000 indicates that the virus is active and has the potential to cause damage to the liver. Generally speaking, if the HBV viral load is above these numbers, treatment is considered necessary. However, some experts believe that hepatitis B should be treated at <i>any</i> viral load, given that there is a risk of liver cancer developing even when the HBV viral load is low.

<p>◆ Liver Function Tests: One of the most important liver enzymes to look for is alanine aminotransferase (ALT), sometimes called SGPT on lab reports. An elevated ALT level indicates that the liver is not functioning properly and that there is a risk of permanent liver damage. During acute hepatitis B infection, ALT levels can be temporarily elevated, but this rarely leads to long-term liver problems. In chronic hepatitis B, ALT levels can either be periodically or consistently increased, indicating a higher risk of long-term liver damage.</p>
<p>◆ HBV Genotype: There are actually eight different types – or "genotypes" – in the world. The differences between the eight genotypes are based on differences in HBV's genetic structure. HBV genotypes B and C are common in Asia, whereas genotypes A and D occur frequently in Europe. Genotypes F and H are found in Central and South America. In the United States, we see genotypes A, B, C, and D. There is still some debate regarding whether it is important to know a patient's HBV genotype. However, studies have demonstrated that patients with HBV genotypes A or B are likely to have better responses to some treatments than patients with genotypes C or D. In turn, finding out the HBV genotype may have some value when choosing treatments for hepatitis B.</p>
<p>◆ Imaging: Magnetic resonance imaging (MRI) and "triple-phase" computed tomography (CT or CAT) scans are becoming more common, painless tests to look for changes in the liver, most notably liver cancer tumors. Some experts suggest that triple-phase CT and MRI are the best way to look for tumors in people who have cirrhosis of the liver.</p>
<p>◆ Ultrasound: Like MRI and CT scans, ultrasound can be used to look for liver cancer tumors. Some experts suggest that ultrasound is an effective screening tool in people who do not have cirrhosis of the liver.</p>
<p>◆ Alpha-fetoprotein (AFP): This test looks for high levels of AFP, a protein that is produced by cancerous liver cells. AFP is not a very sensitive test. In turn, it is often used if imaging or ultrasound suggests that liver cancer tumors are present.</p>
<p>◆ Liver biopsy: Unfortunately, blood tests and imaging do not tell the whole story regarding the health of the liver. In turn, a liver biopsy may be needed to look for evidence of cirrhosis and liver cancer.</p> <p>A liver biopsy is usually performed on an outpatient basis in a hospital. Sometimes, a trained healthcare provider – such as a hepatologist or a gastroenterologist – can perform a liver biopsy in his or her office. An ultrasound is sometimes used to identify the best location to make the biopsy. The patient lies on his or her back or slightly to the left side. The area of the skin where the biopsy will be done is carefully cleaned. Then, a local anesthetic agent is used to numb the skin and tissue below. A specially designed thin needle is inserted through the skin. At this point, the physician will instruct the patient to take a deep breath in and out, and to hold it for about five seconds. The needle is inserted into and out of the liver. This takes only one or two seconds. A slender piece of liver tissue is removed with the needle and is then processed in a laboratory. The entire procedure from start to finish lasts only 15 to 20 minutes. The patient then has to lie still for several hours to avoid the possibility of internal bleeding. There may be some discomfort in the chest or shoulder, but this is almost always temporary.</p> <p>There is still some debate regarding the value of liver biopsies. Some experts argue that they can be useful in figuring out how best to treat hepatitis B, whereas others argue that treatment decisions (including when to start and which medications to use) can be made using blood tests.</p>

How is hep B different for people with HIV?

Although healthy adults who are infected with HBV have a less than 10% chance of seeing the infection develop into chronic hepatitis B, when an HIV-positive adult is infected, this risk jumps to almost 25%. In other words, people with HIV are more likely to develop chronic hepatitis B as a result of HBV infection than HIV-negative people with strong immune systems.

A number of reports have also suggested that, as HIV disease progresses, the body's immune response to HBV gradually decreases or is sometimes lost. This can cause the virus to become active again after being inactive, which can once again increase the risk of liver damage.

It is not entirely understood what impact HIV has on the severity of chronic HBV infection. There have been a number of reports showing that people infected with both viruses have higher HBV viral loads and more cirrhosis, regardless of immune system status. There are also data from studies suggesting that people with HIV with chronic hepatitis B are more than twice as likely as their HIV-negative counterparts to experience liver failure, thus requiring consideration of a liver transplant. It is not yet known if people with HIV with chronic hepatitis B are at a higher risk of liver cancer than their HIV-negative peers, but given the strong link between HBV and liver cancer, this would seem to be likely.

As discussed in the next section, people co-infected with HIV and chronic hepatitis B need to be careful when choosing treatments for both infections.

How is it treated?

People with acute hepatitis B do not require treatment. Bed rest, drinking lots of fluids, and over-the-counter pain relievers (products containing ibuprofen, such as Motrin® and Advil®, are considered to be safer than products containing acetaminophen, such as Tylenol®, in people with acute hepatitis) are usually all that is needed for someone who is experiencing symptoms because of acute hepatitis B.

Treatment is only recommended for people with chronic hepatitis B. The goal of therapy is to reduce HBV viral load to undetectable levels and to return liver enzymes to normal levels, with the intent of getting rid of both HBeAg and HBsAg. If these antigens are cleared from the bloodstream, the virus is less likely to rebound once treatment is stopped.

There is still some debate regarding the best time to begin anti-HBV treatment. Many experts argue that treatment should be started when the HBV viral load is high or ALT levels are increased. Other experts argue that it doesn't matter what the HBV viral load is – if it's detectable it should be treated, given that any sign of active viral replication can mean an increased risk of liver cancer.

There are several treatments approved for the management of chronic hepatitis B:

Treatments for Chronic Hepatitis B Infection

Interferon-alfa Interferon-alfa mimics naturally occurring interferon-alfa, the body's own antiviral. Standard versions of interferon-alfa (**Roferon A®**, **Intron A®**) have been approved for several years for the treatment of chronic hepatitis B. Pegylated interferon-alfa – a drug that contains microscopic waxy particles (polyethylene glycol) linked to an interferon molecule – is now the preferred version of interferon-alfa for the treatment of hepatitis B. Roche's **Pegasys®** has been approved for the treatment of chronic HBV and Schering-Plough's **Peg-Intron** is currently being studied as a treatment for hepatitis B.

Studies of Pegasys indicated that pegylated interferon-alfa is more effective than standard interferon-alfa for treating HBeAg-positive HBV infection. Studies have demonstrated that pegylated interferon may not be as effective in people with HIV and HBV infection – it is best used while the T-cell count is above 350. Studies have also shown that HBV genotypes A and B respond better to interferon treatment than HBV genotypes C and D. In turn, if interferon-alfa is selected as a treatment for HBV infection, it is recommended that the patient's HBV genotype is checked first.

The Pegasys dose is 180 micrograms, injected subcutaneously (directly under the skin) once a week for a total of 48 weeks. Side effects of interferon-alfa are common and can include: [fatigue](#), joint and muscle aches, low-grade fever and/or chills, headache, [nausea and vomiting](#), skin irritation at the injection site, weight loss, low white and red blood cells, mild hair loss, irritability, [depression](#), and/or suicidal thoughts (rare). These side effects are generally worse during the first few weeks of treatment, especially after the first injection, but usually diminish over time.

Lamivudine (Epivir®, Epivir-HBV): After being approved for the treatment of HIV, the nucleoside analogue lamivudine was also approved for the treatment of chronic hepatitis B. People who are infected only with HBV (and not HIV) take one 100mg lamivudine tablet every day. People who are infected with both HBV and HIV should use the dose typically used for the treatment of HIV: one 300mg tablet (or two 150mg tablets) once a day.

As in HIV, HBV resistance to lamivudine can and does occur. When lamivudine is used alone without other anti-HBV treatments (monotherapy), approximately 25% of people with HIV/HBV develop HBV resistance to the drug within one year. After four years of lamivudine monotherapy use, approximately 90% have HBV strains resistant to the drug. (The percentage developing lamivudine resistance is somewhat lower in people infected with HBV but not HIV.)

Emtricitabine (Emtriva®) is very similar to lamivudine and is known to be active against HBV. Because emtricitabine is also approved for the treatment of HIV, some healthcare providers use it instead of lamivudine to treat both infections at the same time. If an HIV-positive person's regimen contains emtricitabine, there is no need to add lamivudine.

Adefovir dipivoxil (Hepsera®): Adefovir is a nucleotide analogue, which differs slightly in its chemical structure than the nucleoside analogues (lamivudine and entecavir). Originally studied as a potential treatment for HIV, the dose of adefovir needed to treat HIV was associated with kidney problems. For the treatment of HBV, the dose is much lower – one 10mg tablet every day – and carries a much lower risk of kidney-related side effects. In clinical trials, adefovir was found to be an effective treatment for people with chronic hepatitis B starting therapy for the first time and for people who have tried and failed lamivudine in the past.

Adefovir is active against HBV strains that are resistant to lamivudine.

HBV can develop resistance to adefovir, but not as quickly as HBV develops resistance to lamivudine. After four years of HBV monotherapy treatment, approximately 18% of people develop HBV resistance to the drug. After five years of adefovir monotherapy treatment, HBV resistance occurs in approximately 29%. Rates of resistance are likely higher in people who become resistant to lamivudine and then switch to adefovir monotherapy.

It is not clear if people living with HIV and HBV should be treated with adefovir. Adefovir is very similar to [tenofovir \(Viread®\)](#), a drug that is approved for the treatment of HIV and is also active against HBV. If an HIV-positive person's regimen contains tenofovir, there is no need to add adefovir. Early data from at least one clinical trial suggests that tenofovir is even more effective against HBV than adefovir. [Truvada®](#), a once-daily tablet that contains Viread and Emtriva (see above), is frequently prescribed for people living with both HIV and HBV, always in combination with another HIV medication.

Because the adefovir dose used to treat HBV is considered too low to be active against HIV, it has been suggested that adefovir monotherapy can be used by people infected with both viruses to treat HBV before combination antiretroviral therapy is necessary. However, experts caution that this may be a risky choice – it is still possible that there will be a low-level effect of adefovir on HIV, when used as monotherapy for hepatitis B, which may cause HIV to become resistant to adefovir and similar HIV medications (e.g., tenofovir).

Entecavir (Baraclude®): Entecavir is a nucleoside analogue like lamivudine. It was approved in March 2005 for the treatment of chronic hepatitis B. The dose of entecavir will depend on a person's hepatitis B treatment history. For example, if the person is starting a nucleoside analogue for the first time, the entecavir dose is one 0.5-mg tablet per day. If the person has taken Eпивir or Emtriva in the past – and has HBV that is resistant to either of these drugs – the correct entecavir dose is one 1-mg tablet per day.

Very little is known about entecavir's resistance profile. After two years of entecavir monotherapy, no cases of HBV resistance to the drug have been reported. However, long-term follow-up data is needed from studies to better understand if, and how quickly, HBV develops resistance to entecavir.

While entecavir is not specifically approved for people with HIV/HBV coinfection, it has been studied in a trial involving people infected with both viruses. Entecavir was found to be effective, including against HBV resistant to lamivudine.

When entecavir was first approved, it was believed to have no effect on HIV replication. In turn, some experts suggested that it be used, as monotherapy, to treat HBV before combination therapy is prescribed for HIV, without the risk of HIV becoming resistant to the drug (and, in turn, cross resistant to other HIV medications). In early 2007, reports emerged showing that entecavir does have HIV activity and caused HIV drug resistance in some patients. In turn, experts and the U.S. Food and Drug Administration are urging caution if entecavir monotherapy is being considered for the treatment of HBV in HIV-positive patients.

◆ **Telbivudine (Tyzeka™):** Tyzeka is a once-daily anti-HBV treatment approved by the FDA in October 2006.

Tyzeka was studied in a year-long international clinical trial involving 1,367 patients with chronic HBV. Three-quarters of the trial participants were male, and all were 16 years of age or older. The trial produced evidence of antiviral effectiveness, including the suppression of HBV, and improvement in liver inflammation comparable to Eпивir®.

It is not known how well Tyzeka works in people infected with HIV and HBV, nor is it known how well the drug works in people with HBV resistance to other available medications.

Telbivudine is not believed to have any activity against HIV. In turn, some healthcare providers may prescribe it, as monotherapy, to treat HBV before combination therapy is considered necessary for HIV, without the risk of HIV becoming resistant to the drug (and, in turn, cross resistant to other HIV medications). However, due to the emergence of data indicating that entecavir has anti-HIV activity, some experts are urging caution regarding the use of telbivudine as monotherapy in HIV/HBV-coinfected patients until additional studies exploring the effects of the drug on HIV are conducted and completed.

The U.S. Department of Health and Human Services has discussed how best to treat chronic HBV in people who are infected with HIV. These recommendations first appeared in the May 2006 publication of the *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*. The Guidelines list a number of important general recommendations, including being **vaccinated against the hepatitis A virus** (if not already immune to the virus), **avoiding alcohol**, and learning about **methods to prevent the transmission of HBV** to others.

While there is some overlap between the drugs used to treat HIV and HBV (this can make things much easier), it is sometimes necessary to carefully consider which medications to use if it is necessary to treat one infection but not the other. For example, someone may have a very high HBV viral load and elevated liver enzymes, but a healthy T-cell count and low HIV viral load. In

other words, this person may need treatment for his HBV but not his HIV. To help patients and doctors figure out what to do in situations like this, the DHHS makes the following recommendations:

Treating HBV and HIV

Need to treat HIV, but not HBV

Use [tenofovir \(Viread®\)](#) plus [lamivudine \(Epivir®\)](#) or tenofovir plus emtricitabine ([Truvada®](#)) in the anti-HIV drug regimen. Do not use tenofovir without lamivudine or emtricitabine (or vice versa), as this may lead to HBV drug resistance.

Need to treat HIV and HBV

The combination of tenofovir plus lamivudine or emtricitabine should be included in the first anti-HIV drug regimen. Another option might be entecavir (Baraclude) plus either tenofovir, lamivudine, or emtricitabine. Do not use only one drug with anti-HBV activity in an anti-HIV drug combination.

Need to treat HBV, but not HIV

Pegylated interferon monotherapy is an option. It does not lead to the development of drug-resistant HIV or HBV. DHHS also states that entecavir or telbivudine can be used as monotherapy to treat HBV in people infected with HIV who do not yet require combination antiretroviral therapy. However, this recommendation was made before researchers found that entecavir has low-level activity against HBV and may develop resistance to it (and cross-resistance to commonly used HIV medications). Similar concerns have been raised regarding adefovir. Based on these observations, some experts are urging caution when considering entecavir or adefovir monotherapy for the treatment of HBV in HIV-positive people. While telbivudine has not been shown to be active against HIV, some experts are suggesting that, in light of the entecavir resistance discovery, telbivudine be evaluated more closely for anti-HIV activity.

It is very important that people with chronic hepatitis B take their medications exactly as prescribed. Missing doses can cause HBV to become resistant to HBV medications. Prematurely stopping HBV medications can also cause HBV viral load and liver enzymes to quickly increase, which can damage the liver and cause severe symptoms. This can also happen in people who have HBV that develops resistance to the medications they are using. In turn, for people with chronic hepatitis B who are receiving treatment, it is very important to be monitored frequently and carefully by a healthcare provider.

How can it be prevented?

The best way to prevent hepatitis B is to be vaccinated. Two HBV vaccines are available: [Recombivax HB®](#) and [Engerix-B®](#). Both of these vaccines require three injections administered over a six-month period. The side effects of the hepatitis B vaccine are usually mild and may include soreness at the injection site and mild flu-like symptoms. There is also a combined [hepatitis A \(HAV\)](#) and HBV vaccine available ([Twinrix®](#)), which also requires three injections administered over a six-month period but offers the added advantage of providing protection against both viral infections.

The HBV vaccine is generally effective for more than 90% of adults and children who receive all three doses. However, some research suggests that people with HIV are less likely to develop immunity to HBV through vaccination, especially if they have compromised immune systems. So it is best for people with HIV to receive the hepatitis B vaccine when T4 cell counts are within healthy ranges.

If you do not think you were ever infected with hepatitis B, talk to your healthcare provider. The vaccine is recommended for:

- People with HIV
- Men who have sex with other men
- Injection drug users
- People with chronic hepatitis C virus
- Heterosexual adults with more than one sex partner in the last six months or a history of sexually transmitted disease
- People who work in places where there is a risk of infection (such as hospitals and doctors' offices)
- Hemodialysis patients
- People who share living quarters with someone with chronic hepatitis B

Increasingly, universal vaccination against HBV is being recommended for all children.

If you have not been vaccinated against hepatitis B, there are still things you can do to prevent HBV infection. These include using a condom or another type of latex barrier while having sex. If you are an injection drug user and share equipment, cleaning your syringes with bleach will not help you avoid hepatitis B – it's always best to use new needles to prevent the risk of HBV infection. Also, don't share items that may have been contaminated with someone else's blood such as toothbrushes, razors, and needles used for body piercing, tattooing, or acupuncture.

If you have not been vaccinated against hepatitis B and fear that you were recently exposed to HBV – for example, after being poked with a used hypodermic needle or as a result of sexual contact with a person with hepatitis B – it is possible to receive a single injection of hepatitis B immune globulin (HBIG). HBIG is recommended following exposure to hepatitis B virus because it provides immediate, short-term protection against the virus. A dose of the hepatitis B vaccine is given at the same time. Two additional doses of hepatitis B vaccine are given to complete the series and ensure long-term protection.

HEPATITIS C – HVC

What is it?

Hepatitis C is a disease caused by a virus that infects the liver. The virus, called hepatitis C virus (HCV), can cause lifelong infection, cirrhosis (scarring) of the liver, liver cancer, liver failure, and death. [See our lesson called [Risks To Your Liver \(Hepatotoxicity\)](#)]. Nearly 4 million people are infected with HCV in the United States and between 8,000 and 10,000 people die of hepatitis C in this country every year. Worldwide, there are estimated to be 170-200 million people infected with HCV! Fortunately, much progress has been made in terms of treating people who have hepatitis C, including people who are infected with both HIV and HCV.

HCV is a common infection among people living with HIV. It can cause liver disease faster in people who are also infected with HIV and can make it more difficult to treat HIV correctly. This is why hepatitis C is considered an AIDS-related opportunistic infection, at least in the eyes of the United States Public Health Service and the Infectious Disease Society of America.

It is important for people infected with HIV and HCV to work closely with their healthcare providers in order to safely and effectively treat both infections.

Who is at risk & how is it transmitted?

Hepatitis C is common in people living with HIV. Between one-quarter (25%) and one-third (33%) of all HIV-positive people in the United States are infected with HCV. This means that approximately 350,000 Americans are living with both HIV infection and hepatitis C.

Injection drug users (IDUs), if they share needles with other people, are at the highest risk of being infected with HCV – between 50% and 90% of all IDUs who are infected with HIV are also infected with HCV. This is because both viruses can be spread easily through blood and blood products.

To cause a new infection, HCV must pass from the blood of an infected person into the blood of an uninfected (susceptible) person. In other words, HCV is most easily spread through direct blood-to-blood contact, such as:

- Sharing needles and other equipment (paraphernalia) used to inject drugs.
- Needle-stick injuries and exposure of open wounds or mucous membranes to infected blood. (*Note: The risk of transmission in the healthcare setting is actually quite low – 4% to 10% risk through a needle-stick injury involving a needle previously used in someone infected with HCV.*)
- Blood or blood-product transfusion (especially prior to 1992).

Unlike HIV, it is generally believed that HCV cannot be transmitted through semen or other genital fluids, unless blood is present. Thus, the risk of becoming infected with HCV through unprotected sexual intercourse is low – but it is still possible. As a result, experts recommend that people infected with HCV practice safer sex using a protective barrier (e.g., condoms), especially during intercourse, to protect their partners.

Women who are infected with HCV have a less than 10% chance of passing the virus along to their babies during pregnancy or delivery, although the risk increases if the woman's HCV viral load (the amount of HCV in a measurement of blood) is high. It is unlikely that HCV can be transmitted through breastfeeding or breast milk.

You may be at risk for hepatitis C and should contact your healthcare provider for a blood test if you:

- Were notified that you received blood from a donor who later tested positive for hepatitis C.
- Have ever injected illegal drugs, even if you experimented a few times many years ago.
- Received a blood transfusion or solid-organ transplant before July, 1992.
- Received a blood product for clotting problems before 1987.
- Have ever been on long-term kidney dialysis.
- Have evidence of liver disease (e.g., persistently abnormal liver function tests).
- Have had multiple sexual partners, or sexual contact with an HCV+ person.
- Have an HCV+ mother.

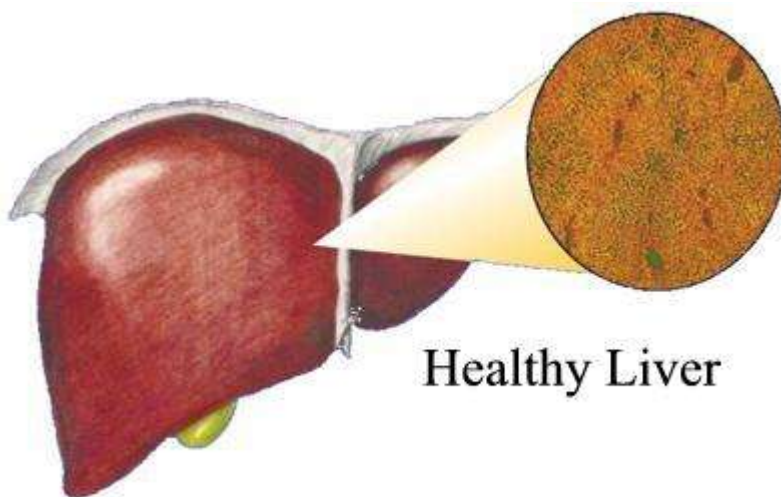
What happens when someone is infected?

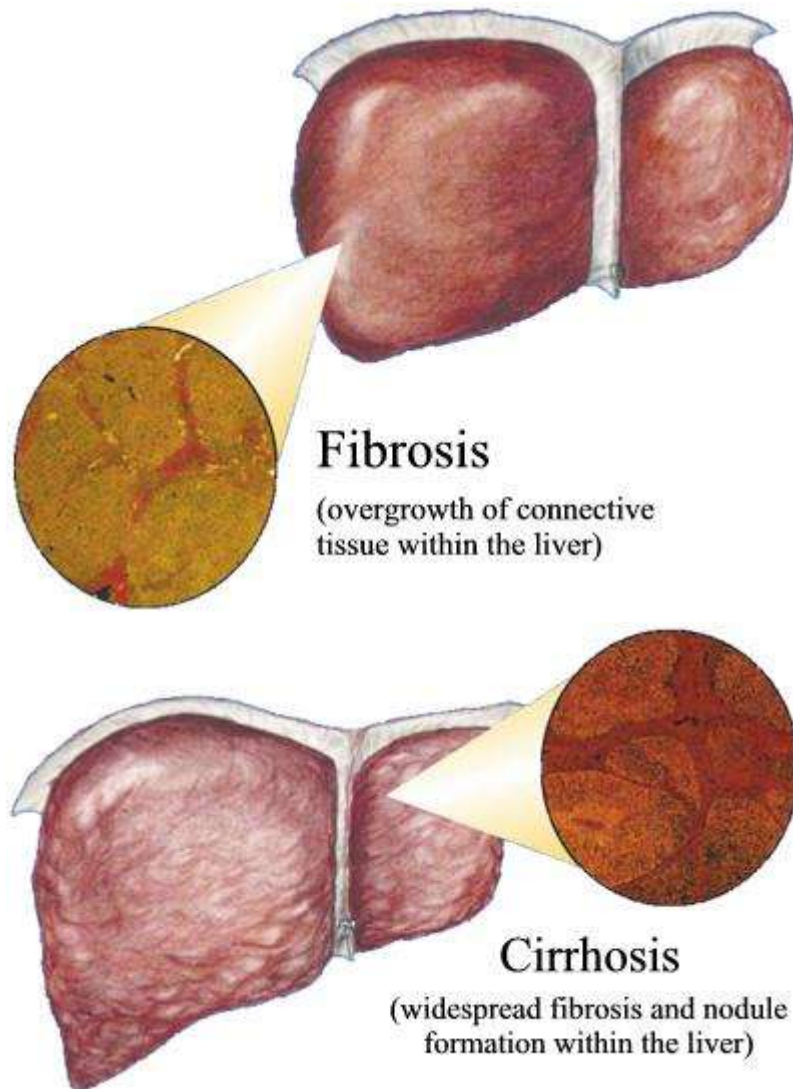
Being infected with HCV does not necessarily mean that liver disease will occur. What's more, it can take several years – decades, in many cases – for HCV to cause life-threatening liver disease.

Soon after HCV enters the body, it infects cells in the liver called hepatocytes. Only a small number of people (approximately 25%) actually experience symptoms of infection, such as **fatigue**, decreased appetite, **nausea**, or jaundice (yellowing of the skin and eyes). However, almost all people infected with HCV experience an increase in their liver enzymes – such as serum alanine aminotransferase (ALT) – which can be detected by a simple blood test. An increase in ALT means that some liver cells are becoming damaged by the HCV infection.

Approximately 15% of people who are infected with HCV are able to clear the virus from their bodies, usually within six months after becoming infected. However, the majority of people (85%) who are infected with HCV have "chronic" hepatitis C – an infection that will stay with them for life. In other words, if 100 people are infected with HCV tomorrow, 15 of them will clear the virus from their bodies within six months, whereas 85 of them will remain infected with the virus.

Of the 85 people with chronic hepatitis C, approximately 20 of them will remain healthy – their liver enzymes will stay normal, even though HCV can be detected in their livers and in their blood, and they will not go on to develop liver disease or experience symptoms of the infection. The remaining 60 to 65 people with chronic hepatitis C will go on to experience some signs and symptoms of liver disease, such as fatigue, nausea, muscle aches, and abdominal pain – usually after 13 to 15 years of being infected with HCV. Approximately 20 to 25 of these people, usually after 20 years of HCV infection, will develop cirrhosis – a scarring of the liver that results from widespread fibrosis (an extreme overgrowth of the liver's connective tissue). Here are some pictures of a healthy liver, then fibrosis, then cirrhosis:





Although cirrhosis is not life threatening, it can affect the way the liver works and increases the risk of liver cancer. Of the 20 to 25 people with HCV who develop cirrhosis, between five and 10 of them will develop liver cancer and possibly liver failure after another five years.

How is it different for people with HIV?

There have been a number of studies showing that HIV can have a negative effect on the way HCV acts in the body. For starters, HIV can increase the chance that someone with chronic HCV infection will experience cirrhosis of the liver. As discussed in the last question, approximately 20 to 25 of every 85 people with healthy immune systems who have chronic HCV infection will go on to develop cirrhosis of the liver within 20 years. If HIV is also present, approximately 30 to 35 of every 85 people will likely experience cirrhosis.

HIV infection can also speed up the rate by which HCV infection causes cirrhosis of the liver. In one study, people infected with both HIV and HCV were twice as likely to have cirrhosis of the liver after 13 years than people only infected with HCV (15% vs. 6%). Similar results have been seen in other studies.

It is also true that people with HIV and HCV are more likely to experience liver failure – which is often fatal, unless a transplant is performed – than people infected only with HCV. In one study, people infected with both viruses were 21-times more likely to die of liver failure than those only infected with HCV.

Another issue to consider is liver health and anti-HIV medicines. Many anti-HIV treatments, including the [protease inhibitors](#) and the [non-nucleoside reverse transcriptase inhibitors](#), are broken down (metabolized) by the liver. This can pose two problems for people infected with both HIV and HCV. First, the liver needs to be healthy in order to process these drugs correctly. If HCV damages the liver, it might not be possible to begin or continue taking life-saving anti-HIV therapy. Second, some of the drugs used to treat HIV can cause liver damage, even in people who aren't infected with HCV. In turn, some anti-HIV drugs might worsen or speed up the liver disease being caused by hepatitis C.

People infected with both HIV and HCV need to work very closely with their healthcare providers. It is important that people infected with both viruses monitor their health carefully.

What are the symptoms?

Many people with chronic hepatitis C have no symptoms of liver disease. That is, they don't necessarily feel or look sick. If symptoms are present, they are usually mild, aren't very specific (some people simply say they're feeling "blah"), and tend to come and go. These symptoms may include [fatigue](#), pains of the upper-right portion of the gut, [nausea](#), decreased appetite, and muscle and joint pains.

If the hepatitis C begins causing serious liver damage or cirrhosis, symptoms may become more prominent. In addition to fatigue, there may be muscle weakness, poor appetite, nausea, jaundice, weight loss, itching, dark urine, fluid retention, abdominal swelling, and ankle swelling.

How is it diagnosed, & what tests are used?

HCV Antibody Testing: Diagnosing hepatitis C begins with an antibody test, similar to the one used to diagnose HIV infection. Antibodies to HCV can be detected in the blood, usually within two or three months after the virus enters the body. If the HCV antibody test is positive, a second test – either a Western blot assay or a PCR test – is performed to confirm the result.

If a person is positive for HCV antibodies, he or she has been exposed to the virus in the past. As discussed above, however, approximately 15% of people who are initially infected with the virus are able to clear the virus from their bodies, usually within six months of exposure. The next step is to look for the actual virus in the bloodstream.

HCV Viral Load Testing: To look for HCV, a healthcare provider can request a qualitative PCR test to determine whether or not the virus is in a person's bloodstream. A healthcare provider can also order a *quantitative* PCR or bDNA test – very similar to those used in HIV – to check for the presence of HIV and to figure out the person's HCV viral load (the amount of HCV in a measurement of blood).

The HCV viral load is a very important laboratory test. Unlike viral load testing for HIV, which can help determine how fast someone may develop AIDS, the HCV viral load test cannot determine if or when someone with hepatitis C will develop cirrhosis
Courtesy: [E.F.I. Health Inc...](#) Visit: www.efihealth.org

or liver failure. However, the HCV viral load can help determine how likely it is someone will respond to treatment. As a rule of thumb, the lower the HCV viral load, the better someone's chances that he or she will respond to anti-HCV treatment. *Note: HCV viral load numbers are usually much higher than HIV viral load numbers. This can be very confusing. A low HIV viral load is considered to be less than 5,000 copies/mL; a low HCV viral load is considered to be less than 2,000,000 copies/mL.*

HCV viral load testing is often used during treatment to determine how well therapy is working.

Genotypic Testing: Not all hepatitis C viruses are the same. There are 11 different "genotypes" of HCV – meaning that, while they look and act very much the same, their genetic structures differ somewhat from each other. Complicating matters further is the fact that each genotype can be divided into different subtypes. For example, HCV genotype 1 can be divided into subtypes "a" and "b."

In the United States, HCV genotypes 1, 2, and 3 are common. The other eight genotypes are less common in the United States and found mostly in the Middle East, Africa, or Asia.

HCV's genotype does not change the likelihood that someone with hepatitis C will develop cirrhosis or liver failure, nor does it affect the speed by which these liver problems can occur. In other words, the genotype of HCV does not affect disease progression in hepatitis C. However, HCV's genotype can predict the effectiveness of treatments – HCV genotypes 1a and 1b are the most difficult to treat, whereas HCV genotypes 2 and 3 are much more likely to respond completely to treatment, perhaps in a shorter period of time. Unfortunately, HCV genotypes 1a and 1b are the most common among HIV-positive people in the United States.

Knowing the genotype of your HCV can help you and your healthcare provider determine how best to approach treatment when the time comes. This might include decisions about which treatments to use and the length of your treatment.

Liver Function Tests: Because hepatitis C is a disease of the liver, you and your doctor will want to monitor the health of your liver. The easiest way to do this is to have regular blood tests that measure the levels of liver enzymes. When hepatocytes (liver cells) become damaged by HCV, these enzymes can become elevated. Some tests to know:

Liver Function Tests

Alanine aminotransferase (ALT; sometimes listed as "SGPT"): In approximately two-thirds of people with chronic hepatitis C, ALT levels are continuously elevated, reflecting ongoing damage to liver cells. In one-third of people with chronic hepatitis C, ALT levels remain normal, even though they have a detectable HCV viral load. Most of these people will live with HCV infection without any liver-related problems.

Aspartate aminotransferase (AST; sometimes listed as "SGOT"): AST levels are often elevated in people with chronic hepatitis C. However, AST levels are usually lower than ALT levels. If cirrhosis occurs, AST levels can increase higher than ALT levels – a sign that damage to the liver is worsening.

Alkaline phosphatase and gamma glutamyl transpeptidase (GGT or GGTP): These levels are usually normal. However, they may become elevated if hepatitis C progresses to cirrhosis.

Liver Biopsy: Unfortunately, liver enzymes do not tell the whole story regarding the health of the liver. Measuring HCV viral load and liver enzyme levels in the blood cannot determine if – and how much – damage has actually been done to the liver. For this, a liver biopsy is needed. A biopsy allows experts to examine actual tissues taken from the liver. Not only can this determine how healthy the liver really is, but it can also help you and your doctor figure out when to start treatment for hepatitis C.

A liver biopsy is often performed, on an outpatient basis, in a hospital. Sometimes, a trained healthcare provider – such as a hepatologist or a gastroenterologist – can perform a liver biopsy in his or her office. An ultrasound or "echo" machine is sometimes used to identify the best location to make the biopsy. The patient lies quietly on his or her back or slightly to the left side. The area of the skin where the biopsy will be done is carefully cleaned. Then, a local anesthetic agent is used to numb the skin and tissue below. A specially designed thin needle is inserted through the skin. At this point, the physician will instruct the patient to take a deep breath and to hold it for approximately five seconds. The needle is advanced into and out of the liver. This takes only one or two seconds. A slender piece of tissue is removed with the needle, and is then processed through a laboratory. The entire procedure from start to finish lasts only 15 to 20 minutes. The patient will then be instructed to lie still for several hours. There may be some discomfort in the chest or shoulder, but this is usually temporary.

The results of the biopsy are usually available within a week and will be explained to you by your healthcare provider.

When should treatment for be started?

Figuring out if you should begin treatment for hepatitis C – and determining when you should start it – are complicated issues, especially for people infected with HIV and HCV. Because HCV treatment can cause side effects, along with the fact that there is no guarantee that treatment will be completely effective, people with hepatitis C must weigh the risks of therapy against the benefits in deciding if and when treatment should be started.

As a rule of thumb, the National Institutes of Health (NIH) recommend that treatment be started before cirrhosis occurs (this can be determined through a liver biopsy), but only for those who are considered to be at a "high risk" of developing cirrhosis in future. These include patients with:

1. Elevated ALT levels; *and*
2. HCV that is detectable by PCR; *and*
3. A liver biopsy that shows **moderate to severe** signs of "fibrosis," "inflammation," and "necrosis" (cell death).

If these criteria are met, a patient should be offered treatment, regardless of the presence or absence of symptoms, the route of HCV infection, the genotype of HCV, or the HCV viral load.

Extreme caution regarding treatment is recommended under the following circumstances:

1. The patient has severe liver disease, such as "decompensated cirrhosis" (a liver transplant may be the best option for these patients); *or*
2. Normal ALT levels, even if HCV is detectable by PCR; *or*
3. A recent kidney, liver, heart, or other solid-organ transplant; *or*
4. A history of problems that might interfere with the safety or effectiveness of treatment, such as severe depression (which can be made worse by the use of interferon, a mainstay treatment for hepatitis C).

For people who are infected with HIV and HCV, there are additional factors to consider when figuring out if and when to begin HCV treatment. Unfortunately, there are no specific guidelines from the National Institutes of Health or other expert groups in terms of treating both HCV and HIV, so it is very important that people who are infected with both viruses discuss their options – very carefully – with their healthcare provider. Some issues to consider:

- People with HIV and HCV may experience cirrhosis or liver failure faster than people only infected with HCV. In turn, some experts recommend treatment, even if a liver biopsy reveals **mild** signs of "fibrosis," "inflammation," and "necrosis" (as opposed to moderate to severe signs in the general population of people with hepatitis C).
- HCV may increase the risk of liver damage, which can prevent certain anti-HIV medications from being broken down in the body correctly. Because of this, some experts recommend early treatment for HCV, before anti-HIV treatment is indicated (for example, while a person's T-cell count is high and HIV viral load is low).
- Anti-HIV medications may cause side effects of the liver that can worsen a person's hepatitis C. This, too, has some experts recommending treatment to lessen the chance that hepatitis C will cause (more) damage to the liver once anti-HIV medicines are started.

Above all, deciding if and when to start treatment should be individualized. Meaning that, regardless of what "official" guidelines do or don't say, it is up to you and your healthcare provider to figure out what's best for you, based on your own thoughts, concerns, and capabilities.

Can medicines cure HEP C?

The success of treatment can be determined at two time points: at the **end of treatment (ETR)**, either six or 12 months after treatment is started (discussed in the next section); and six months after treatment is discontinued, often referred to as the **sustained response (SR)**. The two tests that are most important at these time points are the liver function tests (e.g., ALT) and the HCV viral load. If a person's liver function tests are normal and HCV viral load is undetectable at the end of treatment, the person is said to have an effective ETR. If a person's liver function tests remain normal and his HCV viral load does not become detectable again after six months of being off treatment, he or she is said to have an effective SR.

If someone is no longer taking treatments for hepatitis C and his or her liver enzymes are normal and no HCV virus is present in the blood, wouldn't this be considered a cure? It all depends on whom you ask. Some experts say that, yes, this is a cure – the vast majority of people who achieve a sustained response as a result of treatment maintain healthy livers for many years after treatment is stopped. However, some experts point out that most patients who achieve an SR still have traces of HCV in their liver that could, over time, become active again.

Only time will tell what an SR really means. Because HCV was only discovered in 1988, our knowledge of how treatments work and what we can expect out of them is still young. However, an ETR is considered to be a good response to treatment and an SR is considered to be an excellent outcome of treatment. Both translate into liver-health improvements that are widely believed to be life-saving and life-enhancing.

But what about people with hepatitis C who don't achieve either an ETR or SR as a result of treatment? According to a few recent studies, treatment has a great deal to offer people with hepatitis C who don't achieve an ETR or SR. Even if they experience only mild improvements in their liver function tests or moderate improvements in their HCV viral load – or see their lab tests worsen after an initial good response during therapy – this usually translates into some long-term benefits. Researchers are still conducting studies to determine what these benefits mean in terms of people with hepatitis C living longer, healthier lives.

What treatments are available?

Treatment options for hepatitis C have improved, remarkably, in recent years. Up until a few years ago, the only treatment was interferon-alfa (Roferon® A; Intron® A; Infergen®), a synthetic version of a naturally occurring hormone that has antiviral and

immune-boosting properties. The drug was considered to be only moderately effective in terms of end-of-treatment responses (ETR) and sustained responses (SR) [these terms are reviewed in the last section] and was associated with a significant number of side effects.

While interferon is still used today, new and improved versions of the drug are available. Pegylated interferon (Pegasys®; PEG-Intron®) contains microscopic fat-like spheres harboring tiny amounts of interferon- α . This allows for once-weekly injections of the drug (standard interferon required daily or three-times-weekly injections). What's more, interferon levels in the bloodstream using pegylated interferon are higher and last longer than standard versions of the drug, thus making interferon more effective against HCV. Although the side effects of pegylated interferon are similar to those seen in people taking standard versions of interferon, the benefit of treatment is much more pronounced in light of the potential risks. At the present time, it is not clear which brand of pegylated interferon is the most effective; a study comparing these two drugs is being developed. Presently, only Pegasys has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of hepatitis C in HIV-positive people.

The pegylated interferon dose depends on the brand used. The dose of PEG-Intron varies according to body weight, whereas the Pegasys dose is the same regardless of weight. Both brands of pegylated interferon are injected subcutaneously (under the skin) once a week.

Additionally, a second antiviral drug was approved by the U.S. Food and Drug Administration (FDA) for the treatment of hepatitis C. Ribavirin (Rebetol®; Copegus®), when combined with either standard interferon or pegylated interferon, increases the chance of an ETR and SR. Because clinical trials have demonstrated that interferon- α (either standard or pegylated) is much more effective when combined with ribavirin (and vice versa), taking both drugs together is now considered to be the standard of care for the treatment of hepatitis C. And because pegylated interferon has been shown to be more effective than standard interferon- α , the usual treatment for hepatitis C – which includes people who are also infected with HIV – is **pegylated interferon plus ribavirin**.

In HCV-positive people (who are not also infected with HIV), more than 50% can expect a sustained response after completing 12 months of treatment. Approximately 45% of people with hepatitis C who have HCV genotype 1 have an SR six months after stopping therapy. And more than 75% of people with hepatitis C who have HCV genotypes 2 or 3 have an SR six months after stopping therapy.

Unfortunately, sustained responses are less likely to occur in people with hepatitis C who also have HIV. Overall, up to 40% of people with HIV and HCV who used pegylated interferon and ribavirin in clinical trials have a sustained response. Among HIV-positive people infected with HCV genotype 1, sustained responses have been seen in as many as 29% of those who completed 12 months of treatment. And among HIV-positive people infected with HCV genotypes 2 or 3, sustained responses have been between 44% and 73%.

For people with HCV, including those also infected with HIV, the success of treatment depends on the HCV genotype. We also know that, the higher the dose of ribavirin (at least 800 mg/day), the more likely it is that therapy will be effective. However, ribavirin has a number of side effects, including anemia (low red blood cells) and leukopenia (low white blood cells), which appear to be worse in HIV-positive people. In turn, it can be challenging to remain on a high enough dose to push HCV viral load undetectable – and to keep it there.

It's possible that HIV-positive people with hepatitis C might benefit from longer courses of treatment. For people with hepatitis C, but not HIV infection, treatment can sometimes be concluded in as little as six months (if the person has HCV genotype 2 or 3)

and usually no longer than 12 months (if the person has HCV genotype 1 or 4). For people with HIV and HCV, many experts believe that it's a good idea to remain on treatment for at least 12 months (regardless of the HCV genotype) and possibly for 18 months (especially for people with HCV genotype 1).

Many people are evaluated after three months (12 weeks) on treatment. If their HCV viral load hasn't dropped significantly, treatment is often stopped since this indicates that they're unlikely to achieve a sustained response. Some people go through treatment more than once if they don't achieve a sustained response the first time. While the likelihood of treatment working a second or third time is relatively low, retreatment definitely works for some people. And some people use low-dose interferon as maintenance therapy following a course of treatment.

Are there any experimental treatments?

Yes. Many of the treatments that are being developed for hepatitis C can be divided into one of three categories:

- Drugs to prevent HCV from binding to liver cells
- Compounds that attack viral enzymes that help HCV to replicate (reproduce)
- Drugs to bolster the immune response to HCV

Unfortunately, very little information is available on particular drugs in development. Most are still in the laboratory stages of development and have yet to be tested in humans. Here is an overview:

Preventing Cellular Infection

Before the virus can infect a cell, HCV must first successfully bind to the cell's membrane. Based on their experiences with other viruses – including rhinovirus, influenza virus, picornavirus, and, we kid you not, the Semliki Forest virus and the foot and mouth disease virus (FMDV) – researchers have stumbled upon several possible approaches that may prevent the binding of HCV to liver cells (hepatocytes). These compounds, which include neutralizing antibodies and fusion inhibitors, are barely out of the test tube, so information about how effective they may be is extremely limited.

Viral Enzyme Targets

Once inside a cell, HCV uses several of its own enzymes to help itself replicate. Thus, finding drugs that stop these enzymes from functioning is a primary goal for many researchers. It is likely that these drugs will be used in combination, both with interferon and each other, in clinical trials.

Protease inhibitors, as their name implies, attack the HCV protease enzyme. Similar to HIV's protease enzyme, HCV protease snips large strands of the virus into smaller pieces during the replication process, allowing them to form into new virus. Unfortunately, there has been very little success producing any anti-HCV protease inhibitors, although many researchers are screening possible candidates.

Helicase is another enzyme used by HCV and is primarily responsible for unwinding the virus' RNA once it is inside a cell. As this is an important step in the life cycle of HCV, **helicase inhibitors** may prove to be effective treatments. Researchers have recently determined the three-dimensional structure of helicase – an important discovery for pharmaceutical companies hoping to produce compounds that will work against it.

Three other classes of drugs include replicase inhibitors, antisense molecules, and ribozymes. **Replicase inhibitors** are being developed to halt the production of new HCV RNA. **Antisense molecules** are receiving much attention, as they have shown to be effective for the treatment of other viral infections, such as CMV. As a potential treatment against HCV, these drugs prevent the virus from producing necessary proteins and prevent HCV RNA from functioning properly. **Ribozymes** do the opposite of protease inhibitors. They cleave RNA at critical places needed by HCV to replicate.

Immune Therapies

Over the past few years, much has been learned about the role of the immune system and its inability to control HCV in the majority of people infected with the virus. People who are either able to clear the virus or control HCV replication for many years have an abundance of "type 1" T-cells (Th1), while people who gradually see their HCV viral load increase and experience liver damage mostly have "type 2" T-cells (Th2). The difference? Th1 T-cells produce vital proteins, called cytokines and chemokines, which program other immune system cells to seek and destroy HCV-infected cells. Th2 T-cells, on the other hand, produce antibodies that can prevent necessary immune system cells from doing their job correctly. The reason for this phenomenon is not known, but one thing is for sure: Th1 T-cells are the ones to have.

One of the advantages of interferon therapy is its ability to shift the immune response in people with chronic viral infections from Th2 to Th1. Some of the other immune-based therapies slated for development include **cytokine therapies** – particularly those that boost Th1 cytokines, such as interleukin-2 (IL-2) and interleukin-12 (IL-12), and those that block Th2 cytokines, including IL-10 and tumor necrosis factor (TNF) – and therapeutic **vaccines**.

If you would like to find out if you are eligible for any clinical trials involving new treatments for HCV, there is an interactive web site run by [ACRIA](#), the AIDS Community Research Initiative of America. Another useful service for finding clinical trials is [AIDSinfo.nih.gov](#), a site run by the U.S. National Institutes of Health. They have "health information specialists" you can talk to at their toll-free number at 1-800-HIV-0440 (1-800-448-0440).

Can HEP C be prevented?

Persons living with HIV who are not already infected with HCV can adopt measures to prevent acquiring HCV. Such measures will also reduce the chance of transmitting their HIV infection to others.

Not injecting or stopping injection drug use would eliminate the chief route of HCV transmission. If you continue injecting drugs, you should be sure to use new, sterile syringes every time you inject – you should never reuse or share syringes, needles, water, or drug preparation equipment.

You should not share toothbrushes or razors with someone you know is infected with HCV. If you are considering a tattoo or body piercing, you should be sure that they are performed by reputable, licensed experts and that strict hygiene procedures are followed (e.g., sterile equipment).

While it is not clear if HCV can be transmitted through sexual activity, it is generally advised that barrier protection (e.g., condoms) be used to reduce the risk of transmitting HIV, HCV, and other sexually transmitted diseases.