

OVERVIEW OF HEPATITIS C

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Introduction

Hepatitis C virus (HCV) infection is a leading cause of chronic liver disease across the globe. HCV is estimated to affect 4 to 5 million people in the United States and 180 million people worldwide.¹⁻⁴ The estimated number of HCV-infected people in the United States is based on population surveys. The prevalence of hepatitis C in high-risk populations has not been thoroughly studied. Therefore, many hepatitis C experts believe the true number of people infected with HCV is higher than the stated estimates.³

At least 1 out of every 50 people in the United States has been infected with the hepatitis C virus.

Nearly two decades after the discovery of HCV, our knowledge about the natural history of *chronic hepatitis C* is still limited. Studies have provided varying estimates of the risk of disease progression with chronic hepatitis C. Typically, chronic hepatitis C is slowly progressive.

An estimated 15% to 45% of people infected with HCV clear the virus from their body without treatment. Another 25% have no *symptoms*, and have consistently normal levels of *liver enzymes* called aminotransferases. This means that approximately 40% to 70% of people infected with HCV either recover or do not develop symptoms.⁵ These facts indicate there are people whose *immune systems* are capable of getting rid of HCV. However, for reasons we do not yet understand, others' immune systems allow the virus to persist, leading to potentially serious consequences.

Unlike many chronic viruses, hepatitis C is potentially curable with antiviral treatment.

The Course of Chronic Hepatitis C

Several factors influence the course of chronic hepatitis C. The most significant of these factors include:

- **Age at infection** — Persons infected after age 40 may have disease that is more progressive.⁶⁻⁹
- **Alcohol consumption** — *Alcohol* has serious negative effects on people infected with HCV.⁸
- **Sex** — Overall, women (especially those under age 50) do significantly better than men^{10,11} with less severity of infection.¹² Women also appear to *spontaneously clear* the hepatitis C virus more frequently than men do.¹³⁻¹⁵
- **Coinfection with *hepatitis B virus (HBV)* and/or *human immunodeficiency virus (HIV)*** — Coinfection with one or both of these viruses leads to faster hepatitis C disease progression.¹⁶ Rapid progression is also seen in people with organ transplants taking immunosuppressant medications.
- **Fatty liver** — The presence of fat in the liver is associated with higher degrees of *fibrosis*.¹⁷
- **Iron** — Increased iron in the liver can accelerate progression of HCV or lead to decreased *interferon* response or *cure*.¹⁸⁻²⁰

Hepatitis C genotype and viral load do not predict disease progression.

Viral characteristics such as HCV type (*genotype*) and *viral load* (the amount of virus present in the blood) do not seem to affect the course of the disease. However, these factors are used to determine the length of treatment, and to predict the chance of treatment response.⁶

HCV was once thought to affect only the liver. We now know it can affect nearly any organ in the body. In other words, hepatitis C is a systemic disease. As you read *Chapter 5, Signs and Symptoms that May be Associated with Hepatitis C*, you may find some of the symptoms you thought were caused by something else may actually be caused by HCV. This is important because knowing why you are having a symptom is often the first step in making it less troublesome.

How Hepatitis C Is Diagnosed

Screening: Hepatitis C Antibody Tests

Hepatitis C is diagnosed with a blood test. Most people are initially tested for *HCV antibodies* in the blood. The immune system produces *antibodies* to foreign objects such as viruses and bacteria. When someone is infected with HCV, the body begins producing antibodies specifically designed to search out and destroy HCV.

An HCV antibody test is not currently included in most routine physicals. A doctor generally orders the test only if liver disease is suspected, or if the patient has a history of potential exposure to the hepatitis C virus. Hepatitis C screening is routinely performed on all donated blood.

HCV antibody tests are not always completely accurate. This is especially true in people with a weakened immune system. People with a weakened immune system might not produce enough antibodies to be detected by the antibody test. People with normal immune systems also sometimes have a negative antibody test despite being infected with HCV. This is because in some people, HCV antibodies might not be detected for up to one year after the initial infection.²¹ If there is any doubt about the results of the HCV antibody test, people are given another test that detects the HCV virus itself in the blood.

Confirming Hepatitis C: Viral Testing

A diagnosis of current infection with the hepatitis C virus is usually confirmed by testing for the presence of the virus itself in the blood. This type of testing is known as nucleic acid testing or NAT. Different NAT methods are used by different laboratories. Examples of these methods include *polymerase chain reaction (PCR)*, *transcription mediated amplification (TMA)*, and *branched chain deoxyribonucleic acid (b-DNA)*.²²

Most doctors believe NAT is the most effective way to confirm a diagnosis of HCV. Other tests, such as the *recombinant immunoblot assay (RIBA)*, were originally designed for the blood banking industry, but are sometimes used to confirm an HCV diagnosis.²³

Anyone suspected of having HCV should have liver *enzyme* tests (*ALT* and *AST*) to check for liver damage. Blood tests for liver function should also be performed. The initial work up for hepatitis C should start with a complete history and physical examination. Initial blood tests typically include:

HCV genotype	<i>BUN</i> and <i>creatinine</i>	<i>TSH</i>	<i>electrolytes</i>
PT-INR	<i>total protein</i> and <i>albumin</i>	<i>urinalysis</i>	uric acid
<i>CBC</i> with differential	AST, ALT, Alk Phos, GGT	ron, <i>TIBC</i> , and <i>ferritin</i>	<i>glucose</i>
<i>total bilirubin</i>	uric acid	<i>total cholesterol</i> and <i>triglycerides</i>	HDL, LDL, VLDL

For more information on laboratory tests, see *Chapter 6, Laboratory Tests and Procedures*.

Acute Phase Hepatitis C

The first six months after being infected with HCV is called *acute phase hepatitis C*. After infection, there is a period of 7 to 8 weeks before there is a rise in liver enzymes. HCV antibodies are usually detectable in the blood 3 to 12 weeks after infection. The virus itself is usually detectable in the blood within 1 to 3 weeks after infection.^{24,25}

Most people acutely infected with HCV are *asymptomatic* meaning they do not have any symptoms of disease. However, 25% to 35% of infected people experience a mild illness with vague and *nonspecific* symptoms.

Fifteen percent to 45% of people infected with HCV appear to clear the virus on their own without developing any *secondary condition* or result from the infection. Experts believe clearing the virus is at least partially related to the amount of virus in the initial infection.²⁶⁻²⁹ Other factors are also likely to be involved. The process of *spontaneous clearance* is not well understood, and is an area of active medical research.

Patients diagnosed with acute hepatitis C infection and rising viral levels are often considered candidates for immediate treatment with interferon and ribavirin.

If your body does not rid itself of HCV within six months after infection, you are considered to be in the chronic phase of hepatitis C.

Chronic Phase Hepatitis C Infection

The course of chronic phase hepatitis C is usually that of slow disease progression. Most people have no physical *signs* or symptoms of HCV infection during the first 10 to 20 years after infection. Some have only vague, mild symptoms that come and go without presenting much difficulty.

The rate of disease progression in chronic hepatitis C differs from one person to another. The rate at which a person's hepatitis C will progress cannot be accurately determined by the liver enzyme levels, viral load, or HCV genotype.^{30,31} It has been noted that people with normal liver enzymes and low viral load usually have milder liver disease with lower-grade liver *inflammation*. However, even these people occasionally develop *fibrosis* or *cirrhosis*. The inability to accurately predict disease progression makes it difficult for healthcare providers to identify people who are most likely to benefit from treatment.

Why Liver Biopsies Are Performed and How They Are Used

Many healthcare providers believe a *liver biopsy* to be the best way to identify those most likely to have progressive hepatitis C disease. This is the group of people most likely to gain the greatest benefit from curative treatment.

A liver biopsy gives your healthcare provider a great deal of information about your liver including:

- the amount of inflammation present
- the presence and amount of fibrosis (scarring)
- the presence and amount of cirrhosis
- the presence and amount of fat
- other causes of chronic liver disease such as too much iron or medication toxicity
- the need for *liver cancer* screening

A liver biopsy can also help your healthcare provider decide if and when an evaluation for a liver transplant is needed. Your healthcare provider uses the information from a liver biopsy to help predict the rate of your disease progression, and to determine whether you are likely to benefit from treatment. Studies have shown that hepatitis C progresses

slowly in people with mild liver inflammation and no fibrosis. For people with fibrosis, hepatitis C is generally more rapidly progressive.¹²

A number of new tests are being developed to measure the amount of scar tissue in the liver has without a liver biopsy. These tests are called as noninvasive liver fibrosis tests and include specific products such as FibroSURE™, FIBROSpect™, and FibroScan™. To date, none of these tests have been approved for use in the United States by the Food and Drug Administration, although applications are pending. The decision whether to use a noninvasive liver fibrosis test is something each patient should decide carefully with his/her doctor. As treatments become more effective, the role of liver biopsy and other tests to assess liver fibrosis in the management of hepatitis C may change.

Liver biopsy remains the “gold standard” for determining disease status in hepatitis C patients.

Your healthcare provider will consider a number of factors before suggesting a change from monitoring hepatitis C to treating with curative intent therapy. These factors typically include age, general health, likelihood of response to treatment, and other illnesses you may have such as *HIV*, heart disease, kidney disease, and others. Other considerations are also taken into account such as the length of therapy required, cost, frequency of monitoring, past medical history, side effects, and your ability to take the medication as directed. Your healthcare provider should discuss all *contraindications* to any therapy he or she recommends to you.

For more information about liver biopsy results, see *Chapter 4.1, Liver Disease Progression*.

HCV Genotype

The hepatitis C family of viruses is divided into groups called genotypes. There are 6 known genotypes and more than 90 subtypes of the hepatitis C virus.³² The types are numbered 1 through 6, and the subtypes are labeled a, b, c, and so on, in order of their discovery.

Presently, *genotype testing* is used to determine the duration of *interferon-based treatment*, to help healthcare providers advise people about their potential treatment response, and for research purposes. Genotype testing is an important part of standard, western medical care for people with HCV infection who are being counseled about interferon-based treatment. The reason is that researchers have found certain strains of HCV are more likely to respond to interferon-based treatment than others are. Further, some strains respond more quickly than others do and require a shorter treatment interval. Therefore, it is very important to know the genotype and subtype of HCV with which you are infected. If you are infected with one of the strains that is hard to treat, your healthcare provider may advise a longer than normal course of treatment to see if you might eventually respond.

You may hear the term *quasispecies* in relation to HCV genotype. Quasispecies occur because HCV mutates freely, causing diverse genetic strains in each infected person. The longer you have been infected with HCV, the more likely you are to have a number of quasispecies of HCV in your body. One small study found changes in quasispecies were associated with levels of the liver enzyme ALT during the acute phase of infection. This finding suggests that the formation of quasispecies might be related to the severity of HCV infection.³³ Additional research is need to clarify the role of quasispecies in hepatitis C disease management and treatment.

Researchers are working to discover why different HCV genotypes respond differently to interferon-based treatment. Currently, genotypes 1a and 1b account for 65% to 75% of chronic HCV in the United States. While genotypes 1a and 1b experience the lowest response rate to interferon-based treatment, you should not allow your genotype alone to deter you from treatment. People with all genotypes have cleared the virus. Remember, your genotype does not determine how your disease will progress.

The *sustained response* rate for genotype 1 following treatment with *pegylated* interferon and *ribavirin* is approximately 40%.^{34,35} However, for patients who adhere to a full year of treatment at full dose, the viral response rate or “cure” can be up to 50%.³⁶ With genotype 2 or 3, response rates with pegylated interferon plus ribavirin can increase from an average of 70% to 80% up to 90% with strict adherence and full dose therapy.³⁷⁻⁴⁰

The duration of interferon-based therapy varies depending on genotype, and is another area of ongoing medical research. See *Chapter 8, Western (Allopathic) Medicine* for additional information on duration of interferon-based therapy.

No studies are available to date showing that genotype influences symptom or disease response to *complementary and alternative medicine (CAM)* treatments. Further, there are no data to date proving that CAM therapies cure HCV disease (that is, clear the virus from the body).

Liver Failure

Liver failure is a common cause of death in the United States, claiming more than 30,000 lives each year.⁴¹ Hepatitis C is a common cause of liver failure and is a very serious, growing public health problem.⁴² While the number of new HCV infections has declined in the United States, it is believed that the number of people who will develop complications of advanced liver disease will increase over the next 10 to 20 years.^{42,43} Approximately 20% to 30% of people with chronic hepatitis C will develop cirrhosis over a 20 to 30 year period. Ten percent of those who develop cirrhosis will eventually progress to end-stage liver disease.^{44,45,46}

It is important to remember that a diagnosis of cirrhosis is not a death sentence! Even if you have a cirrhotic liver, unless you develop complications, you can live a long, productive life. Nonetheless, people with cirrhosis should discuss the need for liver cancer screening with their medical practitioners.

Liver Transplantation

Liver failure due to chronic hepatitis C is the most common reason for liver transplantation in the United States. There are currently almost 17,000 people waiting for a liver transplant in this country, but only about 6,000 livers are available for transplant each year.⁴⁷

Evidence to date shows that all patients with chronic HCV infect their new liver shortly after transplantation. *Clinical trials* are currently underway to try to interrupt this process.^{48,49} However, at this time, HCV infection of a transplanted liver is expected, and therefore, ongoing disease monitoring and discussion about treatment must take place for all liver transplant patients.^{50,51}

Liver transplant patients must take medicines called antirejection drugs to keep the body from rejecting the new organ. Antirejection drugs suppress the immune system. This can cause HCV disease to progress faster than it would otherwise. Your healthcare provider will work closely with you to decide if you should consider using *antiviral* therapy after your liver transplant.

It is very important to talk with your healthcare providers about all treatments and/or supplements you are taking or are considering taking. This information is important in making recommendations regarding liver transplantation.

How Hepatitis C Is Transmitted

Blood-to-Blood Contact

HCV is transmitted from one person to another through blood-to-blood contact. In other words, a person is infected with the hepatitis C virus only if their blood system comes into contact with another person's HCV-infected blood. Blood-to-blood contact occurs in a variety of ways, some very obvious and others you may not have considered.

Examples of blood-to-blood contact that can lead to HCV transmission include:

- receiving blood or blood products prior to 1992
- sharing drug paraphernalia, even once
- being stuck by a used blood needle
- being on kidney dialysis
- having a tattoo or body piercing done in an unsterile environment
- having sexual activity that involves contact with blood
- having a job that exposed you to blood
- sharing personal care items (razors, toothbrushes, nail clippers, etc.) with others
- having been incarcerated
- having been in combat in the military

Pregnancy and Breast Feeding

The Centers for Disease Control and Prevention (CDC) report that the risk of transmission of HCV from an infected mother to her infant at birth is approximately 4% (that is, the baby is infected in 4 out of every 100 births to mothers with chronic hepatitis C). In mothers who have both HCV and HIV, the risk of transmitting hepatitis C to the baby goes up to approximately 19%. There is currently no medication to prevent the transmission of hepatitis C from a mother to her baby.

CDC states that there is no evidence that hepatitis C is spread through breast milk. However, nursing mothers should consult with their doctor if there are breaks in the skin and/or bleeding of the nipples associated with breastfeeding.

Sexual Intercourse and Other Sexual Activity

Hepatitis C is rarely transmitted through sexual intercourse though it does occur. Among the general population, a rate of sexual transmission of 3% or less is considered accurate by most experts.⁵² However, increased levels of risk have been reported^{53,54} in association with:

- multiple sexual partners
- activity that involves blood-to-blood exposure
- the presence of a sexually transmitted infection
- coinfection with HIV have been reported to be important factors in new hepatitis C infections. CDC states there is no evidence of HCV transmission associated with oral sex.

In general, most experts agree that sexual transmission of HCV through intercourse plays a role in the ongoing spread of the disease, but that this route of transmission is uncommon overall.

If you have any questions about the sexual transmission of hepatitis C, talk with your doctor. All people, regardless of health challenges, are sexual beings and your doctor understands that sexual health is an important component of your overall health.

Summary

The decision to begin any hepatitis C treatment is a big step. Only you know if you are ready to take that step. Once you have decided on your treatment goals, discuss all of your options and concerns with your healthcare providers. It is often helpful to get a second opinion, or even a third. Choosing healthcare providers you are comfortable speaking with will help you work together as a team.

Making treatment decisions that fit your goals, personality, and lifestyle will make your choices easier to incorporate into your life.

Taking steps to enhance your general health by doing things such as eating a healthy diet, stopping all alcohol consumption, and attaining a normal body weight are important parts of your treatment plan. Exercise, spiritual practices, massage, acupuncture, herbs, and other complementary therapies can all have a role in attaining better health.

We know a great deal about hepatitis C. However, there is even more we do not yet know. Good *clinical* research is needed in all areas of hepatitis C management including western medicine, naturopathy, traditional Chinese medicine, Ayurveda, homeopathy, nutritional support, and other complementary therapies. This research will lead to the next advances in the care of those living with hepatitis C.

Therapy for hepatitis C is evolving rapidly. As a result, treatment recommendations are likely to change every few years. We anticipate new approaches in the near future that will improve the effectiveness of treatment for those living with HCV.

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