



# Hepatitis C

## The Liver

The liver is the largest solid internal organ and it is located underneath the ribcage in the right upper part of the abdomen. Although liver size depends on a person's age, body size and shape, gender, and disease state, it is about the size of a football in most adults. The liver has many important functions. It acts as a filter for the blood. It metabolizes nutrients and other substances such as medications. It stores energy. It synthesizes proteins that are essential for our body to function, including those that help blood to clot when we bleed. Although the liver is a very resilient organ that has the ability to repair itself, it is susceptible to damage from many different sources, including viruses, toxins, inherited conditions, and even our body's own immune system.

## Hepatitis C

Hepatitis C is one of many viruses that can damage the liver. It affects approximately 3% of the global population. In Canada, an estimated 1% of the population have been infected with the hepatitis C virus. Infection begins as acute hepatitis C, and although some will clear the virus on their own, most people (approximately 75%) will develop chronic hepatitis C.

Hepatitis C infection, whether acute or chronic, will often be silent. This means that diagnosis for many people could occur at the time of routine screening or as part of investigating the cause of other abnormal lab tests.

Acute hepatitis C usually passes without consequence. However, in those who go on to develop chronic hepatitis C, years of infection with minimal obvious symptoms, may result in significant damage to the liver. To help individuals with the condition, we must identify those at risk and offer treatment when possible. In Canada, 43% of those infected with the hepatitis C virus (HCV) are current or former injection drug

users and 35% were born outside of Canada.

There are now highly-effective and well-tolerated oral medications available to cure hepatitis C. However, although research is in progress, there is no effective hepatitis C vaccine at this time.

## Spreading Hepatitis C

Hepatitis C is transmitted through activities involving blood-to-blood contact. Common risk factors include being born or having been resident in an area where hepatitis C is more common, injection drug use, and sharing of any drug paraphernalia that may have contamination with blood, whether past or current. Although blood transfusion before 1992 remains an important risk factor, with current screening practices for blood donors, the risk of acquiring hepatitis C from a transfusion today is exceedingly low. Other important risk factors include sharing personal hygiene items such as razors and toothbrushes with another person who is infected, and having piercings and tattoos without appropriate sterilization. In general, the risk of sexual transmission is low, but may be increased with rough sex or anal intercourse. You don't transmit hepatitis C through hugging, kissing, or sharing eating utensils.

## Symptoms

Many individuals with hepatitis C do not have any symptoms, but for those who do, symptoms are generally nonspecific, such as fatigue or discomfort in the abdomen. Over many years, the inflammation in the liver caused by the hepatitis C virus may result in the formation of scar tissue. If very advanced, the amount of scar tissue in the liver may reach a level termed cirrhosis. Cirrhosis refers to a specific pattern and degree of scar tissue in the liver. For patients with cirrhosis, ongoing damage to the liver may eventually result in signs and symptoms such as

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worsening fatigue, fluid accumulation in the abdomen (ascites), bleeding from veins in the esophagus or stomach (varices), and confusion (encephalopathy). Those with hepatitis C and cirrhosis are also at an increased risk of liver cancer.

A major goal in identifying and treating hepatitis C is to cure the disease before cirrhosis and its complications occur.

## Diagnosis and Screening

Testing that identifies antibodies to the hepatitis C virus (anti-HCV) in the blood reveals that the person has a current or past infection. If this test is positive, then another test to look for the presence of the virus in the blood (HCV RNA) should be done to determine if there is a currently active infection.

Screening for hepatitis C is recommended for all individuals in Canada born between 1945 and 1975, as well those who have one or more of the risk factors described above and/or abnormalities in liver enzyme tests. Other people may benefit from testing; if in doubt, ask your healthcare provider.

## Types of Hepatitis C

The hepatitis C virus exists in many different forms. The different types of hepatitis C are known as genotypes. These genotypes number from 1 to 6. Each genotype may have other subtypes, denoted by a lower-case letter (e.g., genotype 1a). The genotype is important because it may help determine the approach to treatment. Genotype distribution varies based on geography. In North America, the most common genotype is 1, followed by genotypes 3 and 2. The hepatitis C viral genotype can be determined using a blood test.

## Investigations

When a person receives a new diagnosis of hepatitis C, it is important that they see a healthcare provider with experience in the area. This may be a nurse, nurse practitioner, family doctor, or specialist (hepatologist or gastroenterologist). Initial investigations will help determine the virus genotype, rule out other underlying causes of liver disease, and determine the extent or stage of the underlying disease. Most of this information can be obtained through physical examination, blood tests, and imaging of the abdomen (usually ultrasound).

Determining the degree of fibrosis (scar tissue) in the liver (also known as staging) can provide important information for healthcare providers to determine necessary treatments. In the past, staging was accomplished only by liver biopsy; an examination involving the use of a needle to take a sample of liver tissue for examination under a microscope. Although biopsy is a safe procedure, it is an invasive one, and accordingly carries some risks, including bleeding and post-procedure pain. One of the drawbacks of conducting a liver biopsy, other than its invasive nature, is the fact that it samples only a very small portion of a

large organ, and thus is susceptible to sampling error.

## Non-invasive Tools to Measure Fibrosis

Liver biopsy remains the gold standard for the staging of liver disease and it is still a good option for many patients. However, healthcare providers are increasingly using other effective tools to determine the degree of fibrosis in the liver. Of the emerging alternative staging methods, the following are the most commonly used in Canada.

**FibroScan®** is a non-invasive tool used to assess the degree of fibrosis in the liver by measuring liver stiffness, which is closely related to the degree of fibrosis in the liver. The scan involves the painless placement of a probe on the surface of the skin and takes only a few minutes to complete. The area sampled is approximately 100 times greater than that seen using a typical liver biopsy. This procedure results in a reliable reading for most people. FibroScan® is available at a number of centres across Canada.

**APRI** (AST-to-Platelet Ratio Index) and **FIB-4** (Fibrosis-4) are non-invasive tools that rely on calculations based on simple blood tests to estimate the degree of fibrosis in the liver.

Regardless of the tool used to estimate fibrosis, expert interpretation is essential in ensuring the information gained is useful in making treatment decisions. In addition, liver biopsy may still provide valuable information that non-invasive tools cannot. Your healthcare provider will be able to determine which tests are best suited to your situation.

## Management

The goal of hepatitis C treatment is to cure the disease by eliminating the virus. Achieving this goal requires a commitment to success from both those infected with HCV and their healthcare providers.

## Pre-Treatment Management

Taking steps to minimize the risk of disease progression and optimize the chances of success once therapy begins are integral to achieving cure in the management of chronic hepatitis C.

## Alcohol

Excessive alcohol consumption is a known risk factor for disease progression. While a safe level of alcohol consumption is difficult to accurately define and may differ from person to person, limiting intake to no more than 1-2 drinks per day (one drink is 5 oz/148 mL of wine, 1.5 oz/44 mL of spirits, or 12 oz/355 mL of beer) and not consuming alcohol every day is a reasonable goal. Those with more advanced liver disease might need to limit intake to a greater degree or even abstain from alcohol completely. Discuss this issue with your healthcare provider.

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## Other Medical Conditions

Pre-existing medical conditions will be unlikely to reduce cure rates, but physicians may need to address them prior to embarking on therapy, especially if there are concerns with drug-to-drug interactions. It is important to have a detailed discussion regarding your medical history with your healthcare provider as part of treatment planning.

## Herbal Therapies

Significant interest exists in herbal preparations that may influence the severity of disease and improve quality of life in hepatitis C. To date, none of these types of preparations have conclusive evidence to recommend their use. Even what is perhaps the most widely used agent, oral milk thistle (or its active extract silymarin), does not have sufficient evidence to suggest benefit, despite research in a well-designed randomized control trial.

## Curative Therapies for Hepatitis C

Current therapy to cure hepatitis C relies on oral antiviral medications taken for 8 to 16 weeks. Injection therapy (interferon) is no longer used. The duration of therapy and the suitable regimen(s) may depend on disease severity and viral genotype. Recent advancements in hepatitis C therapies have boosted cure rates to greater than 95% for nearly all individuals. Remarkably, tolerability has also improved dramatically, typically with only mild side effects if any at all. The following is an overview of most commonly used therapies in Canada.

## Direct Acting Antivirals (DAAs)

The hepatitis C virus replicates by using proteins to make copies of itself. All current generation therapies attack the hepatitis C virus by directly inhibiting proteins that are vital to the virus's ability to replicate. These direct acting antiviral (DAA) medications are in wide use across hepatitis C genotypes. Many different DAAs with unique mechanisms of action are now available for use in combination, typically co-formulated in a single oral tablet.

**Epclusa® (sofosbuvir/velpatasvir):** Epclusa® is a co-formulated single tablet regimen of sofosbuvir (an NS5B nucleotide polymerase inhibitor) and velpatasvir (an NS5a inhibitor). This regimen is currently widely used in Canada for all HCV genotypes, in a 12-week, daily treatment.

**Maviret® (glecaprevir/pibrentasvir):** Maviret® is a co-formulated single tablet regimen of glecaprevir (an NS3/4a protease inhibitor) and pibrentasvir (an NS5a inhibitor). This ribavirin-free regimen is currently widely used in Canada for all HCV genotypes, in an 8- or 12-week, daily treatment. Maviret® is the only pan-genotypic treatment approved for use in patients across all stages of chronic kidney disease.

**Zepatier® (elbasvir/grazoprevir):** Zepatier® is a co-formulated single tablet regimen of elbasvir (an NS5A inhibitor) and grazoprevir (an NS3/4a protease inhibitor). This regimen is currently widely used in Canada for HCV genotypes 1 and 4 in a 12-week, daily treatment. In some specific circumstances, it may be used for 8 or 16 weeks, and may also be combined with sofosbuvir for the treatment of HCV genotype 3.

**Vosevi® (sofosbuvir/velpatasvir/voxilaprevir):** Vosevi® is a co-formulated single tablet regimen of sofosbuvir (an NS5B nucleotide polymerase inhibitor), velpatasvir (an NS5a inhibitor), and voxilaprevir (an NS3/4a protease inhibitor). In Canada, this 12-week, one pill, once daily regimen is typically reserved for re-treatment of the very small proportion of individuals who are not cured following first-line therapy.

## Ribavirin

Ribavirin is an oral antiviral medication that may occasionally be combined with certain direct acting antivirals in specific circumstances to increase rates of cure. Ribavirin is in pill form, taken twice a day.

## Cure Rates

Sustained virologic response (SVR) refers to the inability to detect the hepatitis C virus in the blood 12 and/or 24 weeks after the completion of therapy. If this is achieved, a person is cured of hepatitis C. It is important to note that cure does not protect against re-infection. In addition, if advanced liver fibrosis is present prior to treatment, long-term monitoring including abdominal ultrasound may still be required after virologic cure, in order to screen for liver cancer.

Historically, with older treatment regimens, cure rates would vary significantly based on baseline characteristics including the genotype of hepatitis C, previous treatment experience, and background disease severity. With current generation treatments however, if treatment is optimized, nearly all individuals can expect >95% cure rates, so long as they remain adherent for the full duration of therapy.

Viral hepatitis, including hepatitis C, is a leading cause of morbidity and mortality worldwide. Canada has committed to the World Health Organization's goal of global elimination of hepatitis C as a public health problem by the year 2030. Achieving this will require increased measures to prevent the spread of the hepatitis C virus, as well as increased testing and subsequent treatment with direct acting antivirals when required. Hepatitis C is a curable condition that could soon be a disease of the past if we commit to appropriate action.

## Side Effects of Therapy

Historically, one of the greatest concerns for those seeking treatment for hepatitis C was the side effect profile of the

medications used. This should no longer be the case. Current therapies are extremely well tolerated, typically with only mild side effects that most commonly include fatigue, nausea, and/or headache. Some patients experience no side effects at all.

Other medications (both over-the-counter and prescription) may interact with hepatitis C medications, so patients should discuss any new medications with their healthcare providers.

## Outlook

The future of hepatitis C lies in the education of healthcare providers and the public so that we can identify and consider treatment in all individuals with this curable condition. Now, with broad public access to therapy for all individuals with hepatitis C, the goals include:

- identification of all individuals with hepatitis C through appropriate screening initiatives, including both risk-based screening as well as birth cohort screening of those born between 1945 and 1975
- linkage of all individuals with hepatitis C to experienced care, so all may be considered for treatment
- achieving the World Health Organization's goal to eliminate viral hepatitis as a public health threat by 2030

## Find Out More

Ongoing research continues to reveal more about the symptoms, causes, cures, treatments, and preventative measures associated with gastrointestinal and liver conditions. It would be our pleasure to send you a full information package on this topic. Please view our hepatitis C video at [www.badgut.org](http://www.badgut.org).

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Reach us at [info@badgut.org](mailto:info@badgut.org) with your comments or suggestions to help us make this booklet more valuable for you and other readers.

## About the Gastrointestinal Society

The GI (Gastrointestinal) Society is a registered Canadian charity committed to improving the lives of people with gastrointestinal and liver conditions, supporting research, advocating for appropriate patient access to healthcare, and promoting gastrointestinal and liver health.

Want to learn more on this subject? The *Inside Tract*®, the GI Society's quarterly newsletter, provides the latest on digestive and liver research, disease and disorder treatments (e.g., medications, nutrition), and a whole lot more. If you have any kind of digestive problem, then you will want this timely, informative publication. **Subscribe today!**

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