



# Hepatitis B

## 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, 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 B

Hepatitis B is one of many viruses that can damage the liver. After exposure to the hepatitis B virus, infection begins as acute hepatitis B. Although many people will eliminate the virus and develop lasting immunity, some will develop ongoing infection, known as chronic hepatitis B. Approximately 30% of the global population shows evidence of past or present infection, but only about 5% of these individuals develop chronic hepatitis B. Fewer than 1% of those living in Canada have chronic hepatitis B.

## Spreading Hepatitis B

The hepatitis B virus (HBV) is transmitted through blood-to-blood contact, unprotected sexual activity with an infected person (the virus is found in semen and vaginal fluid), and can be passed from mothers with hepatitis B to their newborns at the time of birth. Blood-to-blood contact may occur through sharing of personal hygiene items (such as razors and toothbrushes), sharing of drug paraphernalia, and through contact with open

wounds. Although the virus is sometimes detected in saliva, the risk of transmitting the virus through contact with saliva that is not visibly bloody is exceedingly low, and the virus does not spread through sharing of utensils, kissing, hugging, or other casual contact.

## Chronic Hepatitis B

The risk of developing chronic hepatitis B if exposed as a newborn is relatively high (unless vaccination occurs at time of birth), but it is very low if exposed as an adult. Many individuals learn of their hepatitis B infection only at the time of routine screening or as part of investigating the cause of other abnormal lab tests.

The way a person's immune system interacts with the virus differs between individuals and over time. This means that some people will go on to develop chronic hepatitis B infection that might persist for many years with little or no damage to their liver, while others might incur damage to the liver. In some people, the immune system attacks hepatitis B infected liver cells in an attempt to eliminate the virus, resulting in liver inflammation and irritation. Appropriate monitoring of individuals affected with chronic hepatitis B is necessary to identify those at risk of ongoing liver damage and to offer treatment when necessary.

While there is no cure for hepatitis B at this time, there are excellent treatments available, as well as clear strategies to prevent HBV infection, decrease complications, and to avoid further spread of this disease.

## Symptoms

Hepatitis B infection will often be silent. That is, many people who have hepatitis B do not have any symptoms but, for those who do, symptoms are generally nonspecific, such as

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mild fatigue or discomfort in the abdomen. Over many years, inflammation in the liver caused by the hepatitis B virus may cause scar tissue to form. If very advanced, the amount of scar tissue in the liver may reach the level termed cirrhosis, which 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 worsening fatigue, fluid accumulation in the abdomen (ascites), bleeding from veins in the esophagus or stomach (varices), and confusion (encephalopathy). Hepatitis B may increase your risk of developing liver cancer. Early diagnosis of hepatitis B infection, appropriate monitoring, and treatment if indicated, will prevent the spread of the disease, and decrease the chance of complications.

## Diagnosis and Screening

A number of blood tests for diagnosing hepatitis B are available that, in combination, help determine whether a person has been infected with the hepatitis B virus and how their immune system is responding to it.

Screening for hepatitis B is recommended for people who have one or more of the risk factors described above, as well as pregnant women and those who have abnormalities in liver enzyme tests. In many areas of the world, hepatitis B is quite common and testing should be done for those people who were born in areas including, but not limited to, Asia, Africa, South Pacific Islands, much of the Middle East, Eastern Europe, and Central and South America. If you believe you may be at risk, talk to your healthcare provider.

## Investigations

If you are newly diagnosed with hepatitis B infection, it is important to see a healthcare provider with specialized knowledge in that area. This might be a nurse, family doctor, or specialist (hepatologist or gastroenterologist), who will conduct initial investigations to determine how many copies of the hepatitis B virus are in the blood (viral load), the phase of infection, extent or stage of the underlying disease, and to rule out other liver diseases that can co-exist. Most of this information can be obtained through physical examination, blood tests, and imaging of the abdomen (usually ultrasound).

Liver biopsy – which involves the use of a needle to take a sample of liver tissue so that a physician can examine it under a microscope – can be helpful in determining how much inflammation the virus is causing, and how much, if any, scar tissue is present. Staging is the process of determining the amount of scar tissue (fibrosis) in the liver and, in the past, liver biopsy was the only tool used. A normal liver with no scar tissue present is stage 0. A combination of increasing amounts of scar tissue in the liver and a change in its pattern increases

the classification to a higher stage. Stage 1 is minimal scar tissue and stage 4 is cirrhosis. Although biopsy is a safe procedure, it is an invasive one, and accordingly carries some risks, including bleeding and pain while recovering from the procedure. One of the drawbacks of liver biopsy, other than its invasive nature, is the fact that it samples only a very small portion of a large organ and, in some circumstances, might not show the same degree of damage as is present in other parts of the liver.

## 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. It is a technique used to measure 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 on 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

Not everyone who has hepatitis B requires treatment with medication. However, because the activity of the virus and the way it interacts with the immune system may change over time, everyone should undergo periodic monitoring. Some people require therapy, some require monitoring for liver cancer, and all should have long-term follow-up.

## Alcohol

Drinking excessive amounts of alcohol may put a person with hepatitis B at additional risk of disease progression and liver cancer. While a safe level of alcohol consumption is difficult to define, and may differ from person to person, limiting intake to no more than 1-2 drinks per day (one drink is 5oz/148 mL of wine, 1.5oz/44 mL of spirits, or 355 mL of beer) and not

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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. Discuss this issue with your healthcare provider.

### **Other Medical Conditions**

Medical conditions that require treatment with drugs that affect the immune system, such as chemotherapy for cancer, can also affect the activity of hepatitis B in someone infected with the virus. In these situations, knowing a person's hepatitis B status before starting these therapies is important so that close monitoring or, in some circumstances, treatment for hepatitis B can be initiated.

### **Medications**

Current therapies for hepatitis B are very effective at halting the damage caused by the virus and controlling the viral load. In addition, medications have the ability to stimulate the immune system to create antibodies against the virus in some circumstances, which may also help in controlling its activity. There is evidence that long-term treatment (years) can result in reversal of scar tissue in the liver. Treatment may also decrease the risk of developing liver cancer for some individuals.

There are other circumstances where hepatitis B therapy may be appropriate, including in some pregnant women with high viral loads, in order to decrease the risk of mother-to-newborn transmission at the time of birth.

There are two main types of therapy for hepatitis B, interferon and oral nucleoside/nucleotide analogues.

### **Interferon**

Interferons are a family of proteins that are released by the body's cells to help fight off viral infections. Administering interferon can be effective at controlling hepatitis B infection in certain situations. While used relatively infrequently, pegylated interferon alpha-2a (Pegasys®) represents the standard of care for interferon-based therapy in hepatitis B and is given by subcutaneous injection once a week. Standard treatment duration with pegylated interferon is between 24-48 weeks, during which time the medication changes the way the patient's immune system interacts with the hepatitis B virus.

The main benefit of interferon-based treatment is that it is given for a finite period. This may avoid the need to be on medication long-term and can be particularly useful for women of childbearing age who may wish to avoid being on long-term medications.

The main considerations from a patient perspective when considering interferon-based treatment are the associated side effects and method of administration. Although easy and safe to administer, many patients do not prefer the delivery of

medication via injection. Patients should discuss with their treating physician whether interferon is a suitable treatment option.

### **Oral Anti-Viral Agents**

Current oral anti-viral agents are therapies (known as nucleoside/nucleotide analogues) that resemble the building blocks of the hepatitis B virus. Administering these medications allows them to integrate into new growing copies of the virus. However, after they are incorporated, they interfere with the copying process and the virus is unable to replicate.

A number of nucleoside/nucleotide analogues are currently in use, with varying chemical structures, potency, and ability for the hepatitis B virus to become resistant to their effects. The newest and most effective agents with the highest barriers to resistance include entecavir (Baraclude®), tenofovir alafenamide fumarate (Vemlidy®), and tenofovir disoproxil fumarate (Viread®). Lamivudine (Heptovir®), remains a commonly used option in some jurisdictions. All of these medications are in tablet form and are for oral, once-a-day use. Some have been proven safe for use in pregnancy. Most of these drugs have generic versions as well.

In addition to being highly effective, the oral nucleoside/nucleotide analogues have the benefits of easy administration and mild or few side effects. Occasionally, patients may experience nausea and stomach upset. One of the main differences between these medications and interferon is that treatment with oral nucleoside/nucleotide analogues is usually long-term (years).

### **Hepatitis B and Liver Cancer**

Some individuals infected with HBV have an increased risk of developing liver cancer (hepatocellular carcinoma). Identifying who is at the highest risk of developing liver cancer is important so that healthcare professionals can take steps to monitor the patient appropriately and detect any disease at an early stage.

Fortunately, if detected early, there are many effective therapies available. It might be beneficial for some patients to have regular abdominal imaging with ultrasound every six months to screen for liver cancer. However, not everyone with hepatitis B needs to have regular ultrasound surveillance and patients should discuss this with their healthcare providers.

### **Hepatitis B Vaccine**

The hepatitis B vaccine is an effective way to protect an individual against contracting the virus. As mentioned, the chances of developing chronic hepatitis B, if exposed as a newborn, are relatively high, but if exposed as an adult, are very low; therefore, the most effective way to use the vaccine to prevent the spread of hepatitis B is to vaccinate at birth. Adults

