

Liver Cancer and Tumours



Canadian Liver Foundation
Fondation canadienne du foie

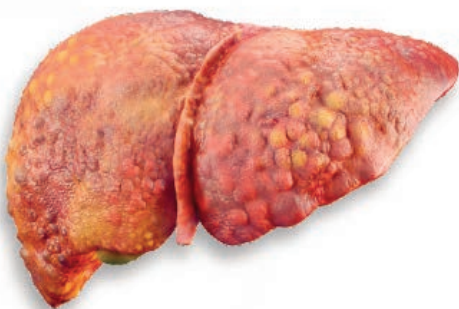
*Bringing liver research to life
Donner vie à la recherche sur le foie*

What causes liver cancer?

Many factors may play a role in the development of cancer. Because the liver filters blood from all parts of the body, cancer cells from elsewhere can lodge in the liver and start to grow. Cancers that begin in the gut often spread to the liver. In addition, after injury has occurred in the liver, the liver cells can regenerate. Sometimes the regeneration is associated with changes (mutations) in the liver cells that have been linked to the development of liver cancers.



NORMAL LIVER



LIVER WITH TUMORS

How are liver tumours classified?

There are many types of liver tumours, only some of which are cancers.

The most important classification is whether the tumours are benign (relatively harmless) or malignant (cancer, i.e., capable of spreading from the liver and thus more serious).

BENIGN TUMOURS

Hemangioma is the most common type of benign liver tumour. It is an abnormal growth of blood vessels of the liver that begins in the fetus. Between 10% and 20% of people in Canada have hemangiomas in the liver. Most people with hemangiomas have no symptoms and require no treatment. Some hemangiomas may rarely enlarge and some may bleed in which case they may require surgical removal.

Hepatic adenomas are benign tumours of liver cells. Most do not cause symptoms and do not require treatment. Some, however, have the potential to become cancers. Often doctors will suggest a biopsy to assess the potential for cancer development. If they are large, they may cause pain or blood loss and may need to be removed. Hepatic adenomas occur more frequently in women and seem to be triggered in some cases by the birth control pill or by pregnancy.

Focal nodular hyperplasia (FNH) is a tumour-like growth of several cell types. Although FNH tumours are benign, it can be hard to distinguish them from liver cancers.

MALIGNANT TUMOURS

The most common form of primary liver cancer (cancer that starts in the liver) in adults is called **hepatocellular carcinoma (HCC)**. It is a cancer of liver cells.

This type of cancer can have different growth patterns. Some begin as a single tumour that grows larger. It may spread to other parts of the liver in later stages of the disease.

Liver cancer may also develop in more than one site in the liver and may grow into multiple tumours. This pattern is most often seen in people with liver cirrhosis (scarring).

Another type of liver cancer is called **cholangiocarcinoma**. It originates in the small bile ducts which are tubes that carry bile from the liver to the gallbladder.

In children the most common liver cancer is called **hepatoblastoma**. Hepatoblastomas are usually diagnosed within the first three years of life and are rarely found beyond the age of five. Hepatoblastomas are also reported to occur more frequently in males than in females. This cancer is caused by rapid growth of immature or abnormal cells that no longer have the specialized function of normal liver cells.

Most often, however, when cancer occurs in the liver, it did not start there, but spread to the liver from a cancer that began somewhere else in the body. These types of cancers are named after the place where they began (primary site) and are considered secondary liver cancers or cancer metastases. For example, cancer that started in the lung and spread to the liver is called metastatic lung cancer with spread to the liver. Secondary liver cancers are 30 times more common than primary liver cancers.

What are the risk factors associated with liver cancer?

In the absence of chronic liver disease, liver cancer is rare. However, in patients with an underlying liver disease, liver cancer may be quite common. The exact cause of liver cancer is not known, but scientists have identified many risk factors that can make someone more likely to develop liver cancer:

- Among those with **chronic liver disease**, men are more likely to develop liver cancer than are women. The reason for this is unknown.
- **Chronic viral infection** of the liver with either hepatitis B or hepatitis C may lead to the development of cancer.
- Certain types of **inherited liver disease** such as hemochromatosis, which results in accumulation of too much iron in the liver, as well as alpha-1 antitrypsin deficiency, and tyrosinemia can lead to the development of liver cancer later in life.

- **Cirrhosis** is the formation of scar tissue in the liver. This can often lead to cancer. Major causes of liver cirrhosis include alcohol use, chronic hepatitis B and C, and non-alcoholic steatohepatitis (NASH). Most causes of cirrhosis are also associated with the development of liver cancer.
- Excessive **alcohol** consumption is a known risk factor for the development of alcoholic cirrhosis and liver cancer.
- **Obesity** increases the risk of liver cancer in those patients in whom it causes liver disease.
- **Tobacco** use increases the risk of liver cancer if you already have a chronic liver disease.
- Long-term use of **anabolic steroids** can increase the risk of liver cancer.

What is the incidence of primary liver cancers?

Primary liver cancers account for less than 1% of all cancers in North America whereas, in Africa, Southeast Asia, and China, they may account for up to 50% of cancers. The high prevalence of people carrying the hepatitis B virus and having liver cirrhosis may account for this geographic discrepancy. Worldwide, primary liver cancers are the third most common cause of cancer death.

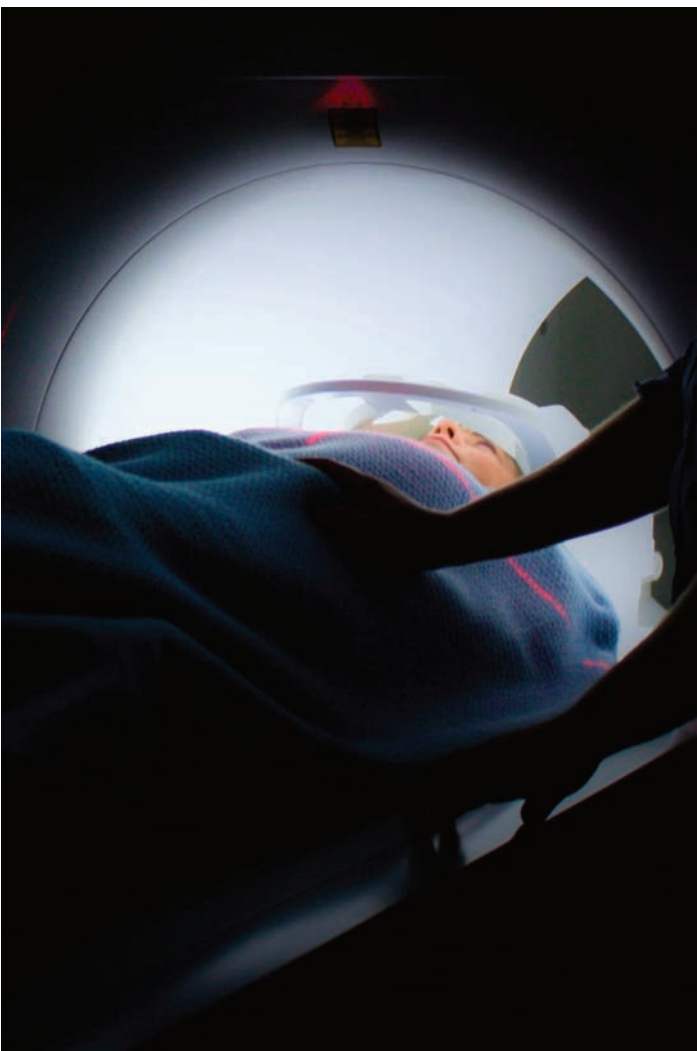
What are the symptoms of liver cancer?

In the early stages, liver cancer does not cause symptoms. Some common symptoms of advanced liver cancer include:

- weight loss
- loss of appetite
- abdominal pain
- jaundice
- fluid in the abdomen

How is liver cancer detected?

- ultrasound of the abdomen
- blood test to check for increased levels of alpha-fetoprotein (AFP)
- computer tomography scan (CT)
- magnetic resonance imaging (MRI)
- removing a sample of tissue of the liver nodule or mass (biopsy)



Are there treatments for primary liver cancer (HCC)?

The treatment of HCC depends on the extent of tumour spread (stage), the speed of tumour growth, and the overall health conditions. Staging (determining the stage of tumours) is often done by imaging of the body, including CT scans, MRIs, and bone scans. Small primary cancers of the liver are curable. Cure rates generally decrease as the tumour size increases. Treatment of liver cancer may involve surgery, radiation therapy and chemotherapy or liver transplantation.

SURGERY

Surgery can remove a small liver tumour through a procedure known as resection, in which a piece of the liver containing the tumour is removed. If all of the cancer can be removed, a patient has a good outlook for survival. If the cancer is too large, is found in many different parts of the liver, or has spread beyond the liver, it may not be possible to remove it completely. For many people with cirrhosis, there is an insufficient amount of healthy liver to allow the removal of even a small part of the liver. In this case, surgery is not an option.

TUMOUR ABLATION

Ablation is a form of localized treatment which refers to methods that destroy the tumour without removing it.

This method can cure small localized primary liver cancer. Examples include destroying the tumour by using high-energy radio waves and heating cancer cells (radiofrequency ablation, or RFA), freezing it with a very cold metal probe (acetic acid ablation or cryoablation), or injecting alcohol directly into the tumour to kill cancer cells (percutaneous ethanol ablation).

EMBOLIZATION

Alternatively, the blood supply to the cancer can be reduced by blocking the artery that feeds the cancer or by injecting materials that plug the artery. This is called embolization, another form of localized treatment. This can be achieved with chemoembolization or radioembolization (described on the next page). Because this kind of treatment often reduces blood supply to the normal liver tissue, it can be dangerous for people with diseases such as hepatitis or cirrhosis.

Chemoembolization involves combining embolization with the delivery of strong anti-cancer drugs (chemotherapy) to kill tumour cells locally. This is referred to as transcatheter arterial chemoembolization (TACE). Chemoembolization prolongs life in patients in whom cure is not possible.

Radioembolization involves combining embolization with the delivery of beads filled with radiation to kill tumour cells locally. This treatment is sometimes referred to as transarterial radioembolization (TARE).

RADIATION THERAPY

Radiation therapy is a treatment that uses high-energy rays (such as x-rays) to kill or shrink cancer cells. This type of treatment may be used to shrink a liver tumour or to provide relief from symptoms, but it does not cure the liver cancer. Studies to show that radiation therapy prolongs life have not yet been done.

CHEMOTHERAPY

Chemotherapy refers to the use of drugs to kill cancer cells. Usually, the drugs are given into a vein or by mouth. Liver cancer does not respond well to most conventional systemic chemotherapy drugs.

TARGETED DRUG THERAPY

These medications target specific abnormalities within the cancer cells. Their use is limited in patients who remain active and well, and who do not have liver failure. For example, sorafenib is one of the targeted drug therapies that has been approved for use in the treatment of primary liver cancer, prolonging survival in patients whose cancer is not curable. Other examples include lenvatinib.

IMMUNOTHERAPY

Immunotherapies act on specific parts of the immune system to better fight cancer cells. These medications are not considered as first-line therapy for the treatment of primary liver cancer (HCC). Examples include nivolumab, and regorafenib. There are also other medications which are undergoing studies for their role in the treatment of HCC.

Are people with liver cancer considered for transplantation?

Most cancers of the liver begin elsewhere in the body and are spread to the liver. These cancers are not curable through liver transplantation. Tumours that originate in the liver are usually detected in an advanced stage. They are also rarely cured by a liver transplant. If the primary liver cancer (HCC) is small and confined to the liver, a liver transplant may be considered.



Are there treatments for secondary liver cancers?

The liver is involved in approximately one-third of all cancers and often those that begin in the gastrointestinal tract, colon, pancreas, stomach, breast and lung. The risk factors involved in this type of liver cancer are numerous given that the cancers originate elsewhere. The prognosis for patients with secondary liver tumours depends on the primary site of malignancy. In general, patients do not live longer than one year from the diagnosis of cancer spreading to the liver (hepatic metastases). Treatments for secondary liver cancers remain unsatisfactory but include surgery, chemotherapy, immunotherapy, and embolization.



Can primary liver cancer be prevented?

Prevention is the best defence against primary liver cancer. Worldwide, the most common risk factors for primary liver cancer are chronic hepatitis B and C infections. Therefore, the prevention of these forms of liver disease is important. The Canadian Liver Foundation recommends that all children, as well as adults at high risk should be vaccinated against hepatitis B.

Since there is no vaccine against hepatitis C, it is important to prevent the spread of this disease, and to identify and assess all those who are already infected with the hepatitis C virus for treatment. The Canadian Liver Foundation recommends that people with risk factors and all adults born between 1945 and 1975 should get tested for hepatitis C.

Alcohol consumption should be limited to no more than one to two standard drinks per day. Drinking alcohol every day, as well as binge drinking can be harmful to your liver. If you already have a liver disease, the safest amount of alcohol is no alcohol at all.

It is important to maintain a well-balanced diet and introduce exercise into your daily routine.

People at high risk of liver cancer should be checked by their doctor regularly to increase the chances of early detection. Early detection of small liver cancers greatly enhances the chances of being cured by using techniques such as radiofrequency ablation. Everyone who is at risk of developing primary liver cancer should undergo regular checkups by ultrasonography at six-month intervals. The discovery of abnormal screening ultrasound results should prompt a visit to a liver specialist.

What does the future hold?

The Canadian Liver Foundation funds research into the causes, diagnosis, prevention and treatment of all forms of liver disease including liver cancer. Scientists are looking for the causes of liver cancer, ways to prevent it and methods to improve treatments. Prevention of new viral hepatitis infections and better treatments for chronic hepatitis could prevent about half of liver cancer cases worldwide

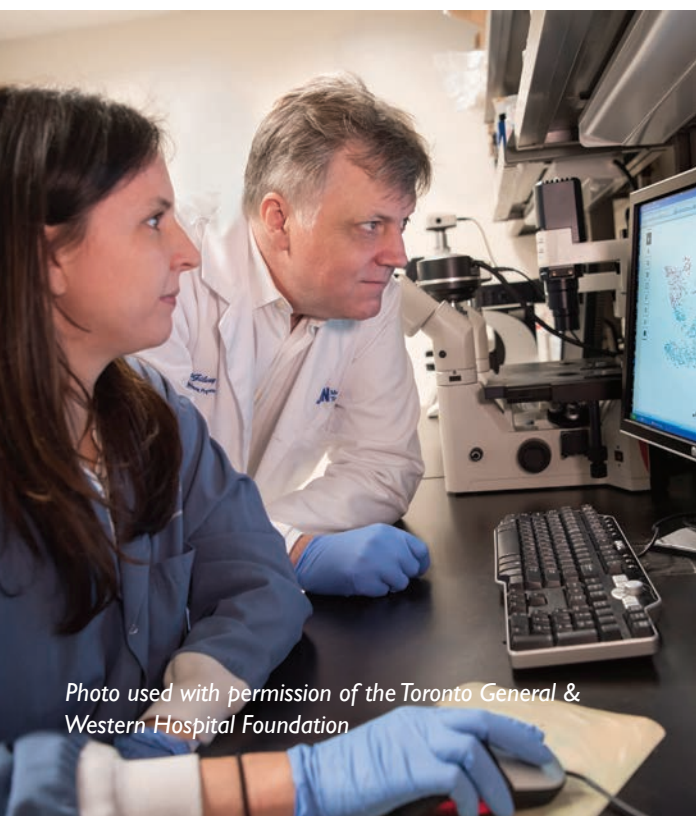


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SUPPORT SERVICES AND PALLIATIVE CARE

*The Canadian Liver Foundation provides support and information to individuals and families coping with liver disease through our national help line, website **liver.ca**, community outreach and educational programs.*

*If you are looking for a place to turn for answers after diagnosis, to help you understand your disease or to learn more about your liver, please contact us by phone: **1 (800) 563-5483** or email: **clf@liver.ca**.*

*Palliative care is the specialized care focused on providing relief of symptoms from serious illness, aiming to help people with cancer feel better. It can also help improve the quality of life of family members. For more information about palliative care and how to access it, please visit **www.liver.ca** or call the CLF National Help Line at **1 (800) 563-5483**.*

CANADIAN LIVER FOUNDATION

1 in 4 Canadians may be affected by liver disease, including everyone from newborn babies to older adults.

Founded in 1969 the Canadian Liver Foundation (CLF) is the only national charity in Canada focused on liver health, and the main source of non-profit funding for liver health research.

Today, we are *bringing liver research to life* by raising funds to promote liver health, improve public awareness, fund research and provide support to individuals affected by liver disease.

To support liver research visit **liver.ca/donate**

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