Liver Cancer Causes, Risk Factors, and Prevention

Risk Factors

A risk factor is anything that affects your chance of getting a disease such as cancer. Learn more about the risk factors for liver cancer.

- Liver Cancer Risk Factors
- Do We Know What Causes Liver Cancer?

Prevention

There is no way to completely prevent cancer. But there are things you can do that might lower your risk. Learn more.

- Can Liver Cancer Be Prevented?

Liver Cancer Risk Factors

A risk factor is anything that affects your chance of getting a disease, such as cancer. Different cancers have different risk factors. Some risk factors, like smoking, can be changed. Others, like a person's age or family history, can't be changed.

But risk factors don't tell us everything. Having a risk factor, or even several risk factors,
does not mean that you will get the disease. And some people who get the disease may have few or no known risk factors.

Scientists have found several risk factors that make a person more likely to develop hepatocellular carcinoma (HCC).

**Gender**

Hepatocellular carcinoma is much more common in males than in females. Much of this is probably because of behaviors affecting some of the risk factors described below. The fibrolamellar subtype of HCC is more common in women.

**Race/ethnicity**

In the United States, Asian Americans and Pacific Islanders have the highest rates of liver cancer, followed by American Indians/Alaska Natives and Hispanics/Latinos, African Americans, and whites.

**Chronic viral hepatitis (Hep-B or Hep-C)**

Worldwide, the most common risk factor for liver cancer is chronic (long-term) infection with hepatitis B virus (HBV) or hepatitis C virus (HCV). These infections lead to cirrhosis of the liver (see above) and are responsible for making liver cancer the most common cancer in many parts of the world.

In the United States, infection with hepatitis C is the more common cause of HCC, while in Asia and developing countries, hepatitis B is more common. People infected with both viruses have a high risk of developing chronic hepatitis, cirrhosis, and liver cancer. The risk is even higher if they are heavy drinkers (at least 6 standard drinks a day).

HBV and HCV can spread from person to person through sharing contaminated needles (such as in drug use), unprotected sex, or childbirth. They can also be passed on through blood transfusions, although this is very rare in the United States since the start of blood product testing for these viruses. In developing countries, children sometimes contract hepatitis B infection from prolonged contact with family members who are infected.

HBV is more likely to cause symptoms, such as a flu-like illness and a yellowing of the eyes and skin (jaundice). But most people recover completely from HBV infection within a few months. Only a very small percentage of adults become chronic carriers (and
have a higher risk for liver cancer). Infants and small children who become infected have a higher risk of becoming chronic carriers.

HCV, on the other hand, is less likely to cause symptoms. But most people with HCV develop chronic infections, which are more likely to lead to liver damage or even cancer.

Other viruses, such as the hepatitis A virus and hepatitis E virus, can also cause hepatitis. But people infected with these viruses do not develop chronic hepatitis or cirrhosis, and do not have an increased risk of liver cancer.

**Cirrhosis**

Cirrhosis is a disease in which liver cells become damaged and are replaced by scar tissue. People with cirrhosis have an increased risk of liver cancer. Most (but not all) people who develop liver cancer already have some evidence of cirrhosis.

There are several possible causes of cirrhosis. Most cases in the United States occur in people who abuse alcohol or have chronic HBV or HCV infections.

**Non-alcoholic fatty liver disease**

Non-alcoholic fatty liver disease, a condition in which people who consume little or no alcohol develop a fatty liver, is common in obese people. People with a type of this disease known as *non-alcoholic steatohepatitis* (NASH) might go on to develop cirrhosis.

**Primary biliary cirrhosis**

Some types of autoimmune diseases that affect the liver can also cause cirrhosis. For example, there is also a disease called *primary biliary cirrhosis (PBC)*. In PBC, the bile ducts in the liver are damaged and even destroyed which can lead to cirrhosis. People with advanced PBC have a high risk of liver cancer.

**Inherited metabolic diseases**

Certain inherited metabolic diseases can lead to cirrhosis.

People with *hereditary hemochromatosis* absorb too much iron from their food. The iron settles in tissues throughout the body, including the liver. If enough iron builds up in the liver, it can lead to cirrhosis and liver cancer.
Heavy alcohol use

Alcohol abuse is a leading cause of cirrhosis in the United States, which in turn is linked with an increased risk of liver cancer.

Obesity

Being obese (very overweight) increases the risk of developing liver cancer. This is probably because it can result in fatty liver disease and cirrhosis.

Type 2 diabetes

Type 2 diabetes has been linked with an increased risk of liver cancer, usually in patients who also have other risk factors such as heavy alcohol use and/or chronic viral hepatitis. This risk may be increased because people with type 2 diabetes tend to be overweight or obese, which in turn can cause liver problems.

Certain rare diseases

Diseases that increase the risk of liver cancer include:

- Tyrosinemia
- Alpha1-antitrypsin deficiency
- Porphyria cutanea tarda
- Glycogen storage diseases
- Wilson disease

Aflatoxins

These cancer-causing substances are made by a fungus that contaminates peanuts, wheat, soybeans, ground nuts, corn, and rice. Storage in a moist, warm environment can lead to the growth of this fungus. Although this can occur almost anywhere in the world, it is more common in warmer and tropical countries. Developed countries such as the United States and those in Europe regulate the content of aflatoxins in foods through testing.

Long-term exposure to these substances is a major risk factor for liver cancer. The risk is increased even more in people with hepatitis B or C infections.
Vinyl chloride and thorium dioxide (Thorotrast)

Exposure to these chemicals raises the risk of angiosarcoma of the liver (see What is liver cancer?). It also increases the risk of developing cholangiocarcinoma and hepatocellular cancer, but to a far lesser degree. Vinyl chloride is a chemical used in making some kinds of plastics. Thorotrast is a chemical that in the past was injected into some patients as part of certain x-ray tests. When the cancer-causing properties of these chemicals were recognized, steps were taken to eliminate them or minimize exposure to them. Thorotrast is no longer used, and exposure of workers to vinyl chloride is strictly regulated.

Anabolic steroids

Anabolic steroids are male hormones used by some athletes to increase their strength and muscle mass. Long-term anabolic steroid use can slightly increase the risk of hepatocellular cancer. Cortisone-like steroids, such as hydrocortisone, prednisone, and dexamethasone, do not carry this same risk.

Arsenic

Drinking water contaminated with naturally occurring arsenic, such as that from some wells, over a long period of time increases the risk of some types of liver cancer. This is more common in parts of East Asia, but it might also be a concern in some areas of the United States.

Infection with parasites

Infection with the parasite that causes schistosomiasis can cause liver damage and is linked to liver cancer. This parasite is not found in the US, but infection can occur in Asia, Africa, and South America.

Tobacco use

Smoking increases the risk of liver cancer. Former smokers have a lower risk than current smokers, but both groups have a higher risk than those who never smoked.

Factors with unclear effects on liver cancer risk
Birth control pills

In rare cases, birth control pills, also known as oral contraceptives, can cause benign tumors called hepatic adenomas. But it is not known if they increase the risk of hepatocellular cancer. Some of the studies that have looked at this issue have suggested there may be a link, but most of the studies were not of high quality and looked at types of pills that are no longer used. Current birth control pills use different types of estrogens, different estrogen doses, and different combinations of estrogens with other hormones. It is not known if the newer pills increase liver cancer risk.

References

See all references for Liver Cancer (https://www.cancer.org/content/cancer/en/cancer/liver-cancer/references.html)

Do We Know What Causes Liver Cancer?

Although several risk factors for hepatocellular cancer are known (see Liver Cancer Risk Factors), exactly how these may lead normal liver cells to become cancerous is only partially understood.

Cancers develop when a cell’s DNA is damaged. DNA is the chemical in each of our cells that makes up our genes – the instructions for how our cells function. Some genes have instructions for controlling when cells grow, divide into new cells, and die.

- Some genes that tell cells to grow and divide are called oncogenes.
- Genes that slow down cell division or cause cells to die at the right time are called tumor suppressor genes.

Cancers can be caused by DNA changes that turn on oncogenes or turn off tumor
suppressor genes. Several different genes usually need to have changes for a cell to become cancerous.

Certain chemicals that cause liver cancer, such as aflatoxins, are known to damage the DNA in liver cells. For example, studies have shown that aflatoxins can damage the \textit{TP53} tumor suppressor gene, which normally works to prevent cells from growing too much. Damage to the \textit{TP53} gene can lead to increased growth of abnormal cells and formation of cancers.

Infection of liver cells with hepatitis viruses can also damage DNA. These viruses have their own DNA, which carries instructions on how to infect cells and produce more viruses. In some patients, this viral DNA can insert itself into a liver cell's DNA, where it may affect the cell's genes. But scientists still don't know exactly how this might lead to cancer.

Liver cancer clearly has many different causes, and there are undoubtedly many different genes involved in its development. It is hoped that a more complete understanding of how liver cancers develop will help doctors find ways to better prevent and treat them.

References

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Can Liver Cancer Be Prevented?

Many liver cancers could be prevented by reducing exposures to known risk factors for this disease.

\textbf{Avoiding and treating hepatitis infections}
Worldwide, the most significant risk factor for liver cancer is chronic infection with hepatitis B virus (HBV) and hepatitis C virus (HCV). These viruses can spread from person to person through sharing contaminated needles (such as in drug use) and through unprotected sex, so some of these cancers may be prevented by not sharing needles and by using safer sex practices (such as consistent use of condoms).

A vaccine to help prevent HBV infection has been available since the early 1980s. The US Centers for Disease Control and Prevention (CDC) recommends that all children, as well as adults at risk get this vaccine to reduce the risk of hepatitis and liver cancer.

There is no vaccine for HCV. Preventing HCV infection, as well as HBV infection in people who have not been immunized, is based on understanding how these infections occur. These viruses can be spread through sharing contaminated needles (such as in drug use), unprotected sex, and through childbirth.

Blood transfusions were once a major source of hepatitis infection as well. But because blood banks in the United States test donated blood to look for these viruses, the risk of getting a hepatitis infection from a blood transfusion is extremely low.

People at high risk for HBV or HCV should be tested for these infections so they can be watched for liver disease and treated if needed.

According to the CDC, you are at risk of having hepatitis B if you:

- Have sex with someone who is infected
- Have multiple sex partners
- Have a sexually transmitted disease
- Are a man who has sex with other men
- Inject drugs
- Live with a person who has chronic HBV
- Travel to countries where many people have HBV
- Are exposed to blood on the job
- Get long-term hemodialysis

A baby born to a mother that is infected with HBV is also at risk for being infected.

The CDC recommends that you get tested for HCV if any of the following are true:

- You were born from 1945 through 1965 (this is because most of the people in the US that are infected with HCV were born in these years)
• You ever injected drugs (even just once or a long time ago)
• You needed medicine for a blood clotting problem before 1987
• You received a blood transfusion or organ transplant before July 1992 (when blood and organs started being screened for HCV)
• You are on long-term hemodialysis
• You are infected with HIV

Treatment of chronic HCV infection can eliminate the virus in many people.

A number of drugs are used to treat chronic HBV. These drugs reduce the number of viruses in the blood and lessen liver damage. Although they do not cure the disease, they lower the risk of cirrhosis and might lower the risk of liver cancer, as well.

**Limiting alcohol and tobacco use**

Drinking alcohol can lead to cirrhosis, which in turn, can lead to liver cancer. Not drinking alcohol or drinking in moderation could help prevent liver cancer.

Since smoking also increases the risk of liver cancer, not smoking will also prevent some of these cancers. If you smoke, quitting will help lower your risk of this cancer, as well as many other cancers and life-threatening diseases.

**Getting to and staying at a healthy weight**

Avoiding obesity might be another way to help protect against liver cancer. People who are obese are more likely to have fatty liver disease and diabetes, both of which have been linked to liver cancer.

**Limiting exposure to cancer-causing chemicals**

Changing the way certain grains are stored in tropical and subtropical countries could reduce exposure to cancer-causing substances such as aflatoxins\(^1\). Many developed countries already have regulations to prevent and monitor grain contamination.

Most developed countries also have regulations to protect consumers and workers from certain chemicals known to cause liver cancer. For example, the US Environmental Protection Agency (EPA) limits the allowable level of arsenic\(^2\) in drinking water in the United States. But this may continue to be a problem in areas of the world where naturally occurring arsenic commonly gets into drinking water.
Treating diseases that increase liver cancer risk

Certain inherited diseases\(^3\) can cause cirrhosis of the liver, increasing a person’s risk for liver cancer. Finding and treating these diseases early in life could lower this risk. For example, all children in families with hemochromatosis should be screened for the disease and treated if they have it. Treatment regularly removes small amounts of blood to lower the amount of excess iron in the body.

References

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