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 gallbladder cancer.

- What Are the Risk Factors for Gallbladder Cancer?
- Do We Know What Causes Gallbladder 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 Gallbladder Cancer Be Prevented?

What Are the Risk Factors for Gallbladder Cancer?

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 having a risk factor, or even several risk factors, does not mean that a person will get the disease. And many 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 gallbladder cancer. Many of these are related in some way to chronic
inflammation (irritation and swelling) in the gallbladder.

**Gallstones**

Gallstones are the most common risk factor for gallbladder cancer. Gallstones are pebble-like collections of cholesterol and other substances that form in the gallbladder and can cause chronic inflammation. At least 3 out of 4 people with gallbladder cancer have gallstones when they are diagnosed. But gallstones are very common, and gallbladder cancer is quite rare, especially in the United States. Most people with gallstones never develop gallbladder cancer.

**Porcelain gallbladder**

Porcelain gallbladder is a condition in which the wall of the gallbladder becomes covered with calcium deposits. It sometimes occurs after long-term inflammation of the gallbladder (cholecystitis), which can be caused by gallstones. People with this condition have a higher risk of developing gallbladder cancer (possibly because both conditions can be related to inflammation).

**Female gender**

In the United States, gallbladder cancer occurs more than twice as often in women. Gallstones and gallbladder inflammation are important risk factors for gallbladder cancer and are also much more common in women than men.

**Obesity**

Patients with gallbladder cancer are more often overweight or obese than people without this disease. Obesity is also a risk factor for gallstones, which might help explain this link.

**Older age**

Gallbladder cancer is seen mainly in older people, but younger people can develop it as well. The average age of people when they are diagnosed is 72. More than 2 out of 3 people with gallbladder cancer are 65 or older when it is found.
Ethnicity and geography

In the United States, the risk of developing gallbladder cancer is highest among Mexican Americans and Native Americans. They are also more likely to have gallstones than members of other ethnic and racial groups. The risk is lowest among African Americans. Worldwide, gallbladder cancer is much more common in India, Pakistan, and Central European and South American countries than it is in the United States.

Choledochal cysts

Choledochal cysts are bile-filled sacs that are connected to the common bile duct, the tube that carries bile from the liver and gallbladder to the small intestine. (Choledochal means having to do with the common bile duct.) The cysts can grow large over time and may contain as much as 1 to 2 quarts of bile. The cells lining the sac often have areas of pre-cancerous changes, which increase a person’s risk for gallbladder cancer.

Abnormalities of the bile ducts

The pancreas is another organ that releases fluids through a duct into the small intestine to help digestion. This duct normally meets up with the common bile duct just as it enters the small intestine. Some people have an abnormality where these ducts meet that lets juice from the pancreas reflux (flow backward) into the bile ducts. This backward flow also prevents the bile from being emptied through the bile ducts as quickly as normal. People with these abnormalities are at higher risk of gallbladder cancer. Scientists are not sure if the increased risk is due to the action of the pancreatic juice or is possibly due to the ducts being exposed longer to damaging substances in the bile itself.

Gallbladder polyps

A gallbladder polyp is a growth that bulges from the surface of the inner gallbladder wall. Some polyps are formed by cholesterol deposits in the gallbladder wall. Others may be small tumors (either cancerous or benign) or may be caused by inflammation. Polyps larger than 1 centimeter (almost a half inch) are more likely to be cancer, so doctors often recommend removing the gallbladder in patients with gallbladder polyps that size or larger.
Primary sclerosing cholangitis

In primary sclerosing cholangitis (PSC), there is inflammation and scarring of the bile ducts. People with this disease have an increased risk of cancer of the gallbladder and bile ducts. Many people with PSC also have ulcerative colitis, a type of inflammatory bowel disease.

Industrial and environmental chemicals

It is not clear if exposure to certain chemicals in the workplace or the environment increases the risk of gallbladder cancer. This is hard to study because this cancer is not common. Some studies in lab animals have suggested that chemical compounds called nitrosamines may increase the risk of gallbladder cancer. Other studies have found that gallbladder cancer might occur more in workers in the rubber and textile industries than in the general public. More research is needed in this area to confirm or refute these possible links.

Typhoid

People chronically infected with salmonella (the bacterium that causes typhoid) and those who are carriers of the disease are more likely to get gallbladder cancer than those not infected. This is probably because the infection can cause gallbladder inflammation. But typhoid is rare in the United States.

Family history

Most gallbladder cancers are not found in people with a family history of the disease. A history of gallbladder cancer in the family seems to increase a person’s chances of developing this cancer, but the risk is still low because this is a rare disease.

- References

See all references for Gallbladder Cancer

Do We Know What Causes Gallbladder Cancer?

Researchers have found several risk factors that make a person more likely to develop gallbladder cancer. (See “What are the risk factors for gallbladder cancer?”) They are also beginning to understand how some of these risk factors might lead to gallbladder cancer.

Chronic gallbladder inflammation is a common link among many of the risk factors for gallbladder cancer. For example, when someone has gallstones, the gallbladder may release bile more slowly. This means that cells in the gallbladder are exposed to the chemicals in bile for longer than usual. This could lead to irritation and inflammation.

In another example, abnormalities in the ducts that carry fluids from the gallbladder and pancreas to the small intestine might allow juices from the pancreas to flow backward (reflux) into the gallbladder and bile ducts. This reflux of pancreatic juices might inflame and stimulate growth of the cells lining the gallbladder and bile ducts, which might increase the risk of gallbladder cancer.

Scientists are starting to understand how risk factors such as inflammation might lead to certain changes in the DNA of cells, making them grow abnormally and form cancers. DNA is the chemical in each of our cells that makes up our genes (the instructions for how our cells function). We usually look like our parents because they are the source of our DNA. But DNA affects more than how we look.

Some genes control when cells grow, divide into new cells, and die. Genes that help cells grow, divide, and stay alive 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 (mutations) that turn on oncogenes or turn off tumor suppressor genes. Changes in several different genes are usually needed for a cell to become cancerous.

Some people inherit DNA mutations from their parents that greatly increase their risk for certain cancers. But inherited gene mutations are not thought to cause very many gallbladder cancers.
Gene mutations related to gallbladder cancers are usually acquired during life rather than being inherited. For example, acquired changes in the \textit{TP53} tumor suppressor gene are found in many cases of gallbladder cancer. Other genes that may play a role in gallbladder cancers include \textit{KRAS}, \textit{BRAF}, \textit{CDKN2}, and \textit{HER2}. Some of the gene changes that lead to gallbladder cancer might be caused by chronic inflammation. But sometimes what causes these changes is not known. Many gene changes might just be random events that sometimes happen inside a cell, without having an outside cause.

- References
  See all references for Gallbladder Cancer

Can Gallbladder Cancer Be Prevented?

There is no known way to prevent most gallbladder cancers. Many of the known risk factors for gallbladder cancer, such as age, gender, ethnicity, and bile duct abnormalities, are beyond our control. But there are things you can do that might lower your risk.

Getting to and staying a healthy weight is one important way a person may reduce their risk of gallbladder cancer, as well as several other cancers. The American Cancer Society recommends that people try to stay at a healthy weight throughout life by being active and eating a healthy diet, with mostly plant foods. This includes at least 2½ cups of vegetables and fruits every day. Choose whole-grain breads, pastas, and cereals instead of refined grains. Eat fish, poultry, or beans and limit how much processed meat and red meat you eat. To learn more, see the \textit{American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention}.

Since gallstones are a major risk factor, removing the gallbladders of all people with gallstones would prevent many of these cancers. But gallstones are very
common, and gallbladder cancer is quite rare, even in people with gallstones. Most doctors don’t recommend people with gallstones have their gallbladder removed unless the stones are causing symptoms or other problems. This is because the possible risks and complications of surgery probably don’t outweigh the possible benefit. Some doctors might advise removing the gallbladder if long-standing gallstone disease has resulted in a porcelain gallbladder.

- References
See all references for Gallbladder Cancer


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