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# **Esophagus Cancer Causes, Risk Factors, and Prevention**

Learn about the risk factors for esophagus cancer and what you might be able to do to help lower your risk.

#### **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 esophagus cancer.

- Esophageal Cancer Risk Factors
- What Causes Esophageal 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 Esophageal Cancer Be Prevented?

# **Esophageal Cancer Risk Factors**

- Age
- Sex

- Tobacco and alcohol
- Gastroesophageal reflux disease
- Barrett's esophagus
- Obesity
- Diet
- Physical inactivity
- Achalasia
- Tylosis
- Plummer-Vinson syndrome
- Injury to the esophagus
- History of certain other cancers
- Human papillomavirus (HPV) infection

A risk factor is anything that increases 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.

Scientists have found several factors that can affect your risk of esophageal cancer. Some are more likely to increase the risk for adenocarcinoma of the esophagus and others for squamous cell carcinoma of the esophagus.

But having a risk factor, or even many, does not mean that you will get esophageal cancer. And some people who get the disease may not have any known risk factors.

#### Age

The chance of getting esophageal cancer increases with age. Fewer than 15% of cases are found in people younger than age 55.

#### Sex

Men are more likely than women to get esophageal cancer.

#### Tobacco and alcohol

The use of <u>tobacco products</u><sup>1</sup>, including cigarettes, cigars, pipes, and chewing tobacco, is a major risk factor for esophageal cancer. The more a person uses tobacco and the longer it is used, the higher the cancer risk.

Someone who smokes a pack of cigarettes a day or more has at least twice the chance of getting adenocarcinoma of the esophagus than a nonsmoker, and the risk does not go away if tobacco use stops. The link to squamous cell esophageal cancer is even stronger, but this risk does go down for people who quit tobacco.

Drinking <u>alcohol</u><sup>2</sup> also increases the risk of esophageal cancer. The more alcohol someone drinks, the higher their chance of getting esophageal cancer. Alcohol increases the risk of squamous cell carcinoma more than the risk of adenocarcinoma.

Smoking combined with drinking alcohol raises the risk of the squamous cell type of esophageal cancer much more than using either alone.

#### Gastroesophageal reflux disease

The stomach normally makes strong acid and enzymes to help digest food. In some people, acid can escape from the stomach up into the lower part of the esophagus. The medical term for this is **gastroesophageal reflux disease (GERD**), or just **reflux**. In many people, reflux causes symptoms such as heartburn or pain that seem to come from the middle of the chest. In some, though, reflux doesn't cause any symptoms at all.

People with GERD have a slightly higher risk of getting adenocarcinoma of the esophagus. This risk seems to be higher in people who have more frequent symptoms. But GERD is very common, and most of the people who have it *do not* go on to develop esophageal cancer. GERD can also cause Barrett's esophagus (discussed below), which is linked to an even higher risk.

## Barrett's esophagus

If reflux of stomach acid into the lower esophagus goes on for a long time, it can damage the inner lining of the esophagus. This causes the squamous cells that normally line the esophagus to be replaced with gland cells. These gland cells usually look like the cells that line the stomach and the small intestine, and are more resistant to stomach acid. This condition is known as Barrett's (or Barrett) esophagus.

The longer someone has reflux, the more likely it is that they will develop Barrett's esophagus. Most people with Barrett's esophagus have had symptoms of heartburn, but many have no symptoms at all. People with Barrett's esophagus are at a much higher risk than people without this condition to develop adenocarcinoma of the esophagus. Still, most people with Barrett's esophagus do not get esophageal cancer.

The gland cells in Barrett's esophagus can become more abnormal over time. This can

result in *dysplasia*, a pre-cancerous condition. Dysplasia is graded by how abnormal the cells look under the microscope. Low-grade dysplasia looks more like normal cells, while high-grade dysplasia is more abnormal. High-grade dysplasia is linked to the highest risk of cancer.

### **Obesity**

People who are overweight or obese<sup>3</sup> (very overweight) have a higher chance of getting

People with achalasia have a risk of esophageal cancer that is many times normal. On average, the cancers are found about 15 to 20 years after the achalasia began.

#### **Tylosis**

This is a rare, inherited disease that causes extra growth of the top layer of skin on the palms of the hands and soles of the feet. People with this condition also develop small growths (papillomas) in the esophagus and have a very high risk of getting squamous cell cancer of the esophagus.

People with tylosis need to be watched closely to try to find esophageal cancer early. Often this requires regular monitoring with an upper endoscopy (described in <u>Tests for Esophagus cancer</u>)<sup>4</sup>.

#### **Plummer-Vinson syndrome**

People with this rare syndrome (also called *Paterson-Kelly syndrome*) have webs in the upper part of the esophagus, typically along with anemia (low red blood cell counts) due to low iron levels, tongue inflammation (glossitis), brittle fingernails, and sometimes a large spleen.

A web is a thin piece of tissue extending out from the inner lining of the esophagus that causes an area of narrowing. Most esophageal webs do not cause any problems, but larger ones can cause food to get stuck in the esophagus, which can lead to problems swallowing and chronic irritation in that area from the trapped food.

About 1 in 10 people with this syndrome eventually develop squamous cell cancer of the esophagus or cancer in the lower part of the throat (hypopharynx).

#### Injury to the esophagus

Lye is a chemical found in strong industrial and household cleaners such as drain cleaners. Lye is a corrosive agent that can burn and destroy cells. Accidentally drinking a lye-based cleaner can cause a severe chemical burn in the esophagus. As the injury heals, the scar tissue can cause an area of the esophagus to become very narrow (called a *stricture*). People with these strictures have an increased risk of squamous cell esophageal cancer, which often occurs many years (even decades) later.

## History of certain other cancers

People who have had certain other cancers, such as lung cancer, mouth cancer, and throat cancer have a high risk of getting squamous cell carcinoma of the esophagus as well. This may be because these cancers can also be caused by smoking.

#### **Human papillomavirus (HPV) infection**

<u>HPV</u><sup>5</sup>is a group of more than 100 related viruses. They are called papillomaviruses because some of them cause a type of growth called a papilloma (or wart). Infection with certain types of HPV is linked to a number of cancers, including throat cancer, anal cancer, and cervical cancer.

Signs of HPV infection have been found in up to one-third of esophagus cancers from people in parts of Asia and South Africa. But signs of HPV infection have not been found in esophagus cancers from people in the other areas, including the US. HPV is a rare cause of esophageal cancer.

#### **Hyperlinks**

- 1. www.cancer.org/cancer/risk-prevention/tobacco.html
- 2. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/alcohol-use-and-cancer.html</u>
- 3. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/body-weight-and-cancer-risk.html</u>
- 4. <a href="https://www.cancer.org/cancer/types/esophagus-cancer/detection-diagnosis-staging/how-diagnosed.html">www.cancer.org/cancer/types/esophagus-cancer/detection-diagnosis-staging/how-diagnosed.html</a>
- 5. www.cancer.org/cancer/risk-prevention/hpv.html

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Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2016, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975\_2016/, based on November 2018 SEER data submission, posted to the SEER web site, April 2019.

# What Causes Esophageal Cancer?

- Inherited gene mutations
- Acquired gene mutations

We do not yet know exactly what causes most esophageal cancers. However, there are certain risk factors that make getting esophageal cancer more likely.(See Esophageal Cancer Risk Factors<sup>1</sup>.)

Scientists believe that some risk factors, such as the use of <u>tobacco</u><sup>2</sup> or <u>alcohol</u><sup>3</sup>, may cause esophageal cancer by damaging the DNA in cells that line the inside of the esophagus. Long-term irritation of the lining of the esophagus, as happens with reflux, Barrett's esophagus, achalasia, Plummer-Vinson syndrome, or scarring from swallowing lye, may also lead to DNA damage.

Cancer is caused by changes in the DNA inside our cells. DNA is the chemical in each of our cells that makes up our *genes* – which control 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.

- Certain genes that help cells grow, divide, and stay alive are called oncogenes.
- Genes that help keep cell division under control or cause cells to die at the right time are called *tumor suppressor genes*.

Cancers can be caused by DNA mutations (changes) that turn on oncogenes or turn off tumor suppressor genes. This leads to cells growing out of control. Changes in many different genes are usually needed to cause esophageal cancer.

The DNA of esophageal cancer cells often shows changes in many different genes. However, it's not clear if there are specific gene changes that can be found in all (or most) esophageal cancers.

For more about how genes changes can lead to cancer, see Genes and Cancer<sup>4</sup>.

## Inherited gene mutations

Some DNA mutations can be passed on in families and are found in all of a person's

cells. These are called *inherited* mutations. A very small number of esophageal cancers are caused by inherited gene mutations. Some of these DNA changes and their effects on the growth of cells have been discovered and are being studied further. For example:

- Tylosis with esophageal cancer (sometimes called Howel-Evans syndrome) is caused by inherited changes in the *RHBDF*2 gene. People with changes in this gene are more at risk of developing the squamous cell type of esophageal cancer.
- **Bloom syndrome** is caused by changes in the *BLM* gene. The *BLM* gene is important in making a protein that stabilizes DNA as a cell divides. Without this protein, the DNA can become damaged, which can lead to cancer. People with Bloom syndrome are at a higher risk of developing squamous cell esophageal cancer, as well as AML, ALL, and other cancers involving the lymph system. For this syndrome, an abnormal gene is usually inherited from both parents, not just one.
- Fanconi anemia is a rare syndrome that involves abnormal genes that cannot repair damaged DNA. Mutations (changes) in certain *FANC* genes can lead to a higher risk of many cancers including AML and squamous cell cancer of the esophagus.
- Familial Barrett's Esophagus is a syndrome that includes families with Barrett's esophagus and adenocarcinoma of the esophagus and GE junction. The exact genes associated with this are still being studied.

Special genetic tests can find some of the gene mutations linked to these inherited syndromes. If you have a family history of esophageal cancer or other symptoms linked to these syndromes, you may want to ask your doctor about genetic counseling and genetic testing. The American Cancer Society recommends discussing genetic testing with a qualified cancer genetics professional before any genetic testing is done. For more on this, see <u>Understanding Genetic Testing for Cancer</u><sup>5</sup> and <u>What Happens during Genetic Testing for Cancer</u>?

## **Acquired gene mutations**

Most gene mutations that lead to cancer are *acquired* mutations. They happen during a person's lifetime and are not passed on to their children.

In most cases of esophageal cancer, the DNA mutations that lead to cancer are acquired during a person's life rather than having been inherited.

Certain risk factors, such as tobacco and alcohol use, probably play a role in causing

these acquired mutations, but so far it's not known what causes most of them.

## **Hyperlinks**

1. www.cancer.org/cancer/risk-prevention/tobacco.html

## **Can Esophageal Cancer Be Prevented?**

- Avoid tobacco and alcohol
- Watch your diet, body weight, and physical activity
- Get treated for reflux or Barrett's esophagus

Not all esophageal cancers can be prevented, but the risk of developing this disease can be greatly reduced by avoiding certain risk factors<sup>1</sup>.

#### Avoid tobacco and alcohol

In the United States, the most important lifestyle risk factors for cancer of the esophagus are the use of <u>tobacco</u><sup>2</sup> and <u>alcohol</u><sup>3</sup>. Each of these factors alone increases the risk of esophageal cancer many times, and the risk is even greater if they are combined. Avoiding tobacco and alcohol is one of the best ways of limiting your risk of esophageal cancer. If you or someone you know would like to quit tobacco, call us at 1-800-227-2345 or see <u>Stay Away from Tobacco</u><sup>4</sup>.

#### Watch your diet, body weight, and physical activity

Following a healthy eating pattern and staying at a healthy weight are also important. A diet rich in fruits and vegetables may help lower esophageal cancer risk. Obesity has been linked with esophageal cancer, particularly the adenocarcinoma type, so staying at a healthy weight may also help limit the risk of this disease. Being physically active may also reduce your risk of esophageal cancer.

For more on this, read our <u>American Cancer Society Guidelines for Diet and Physical Activity for Cancer Prevention<sup>6</sup>.</u>

## Get treated for reflux or Barrett's esophagus

Treating people with reflux may help prevent Barrett's esophagus and esophageal cancer. Often, reflux is treated with changes in diet and lifestyle (for example, weight loss for overweight individuals), as well as drugs called H2 blockers or proton pump inhibitors (PPIs). Surgery might also be an option for treating reflux if the reflux is not controlled with diet, lifestyle changes, and medicines.

People at a higher risk for esophageal cancer, such as those with Barrett's esophagus, are often watched closely by their doctors with endoscopies to look for signs that the

cells lining the esophagus have become more abnormal. (See <u>Can Esophageal Cancer Be Found Early?</u><sup>7</sup>) If dysplasia (a pre-cancerous condition) is found, the doctor may recommend treatments to keep it from developing into esophageal cancer.

For those who have Barrett's esophagus, daily treatment with a PPI might lower the risk of developing cell changes (dysplasia) that can turn into cancer. If you have chronic heartburn (or reflux), tell your doctor. Treatment can often improve symptoms and might prevent future problems.

Some studies have found that the risk of cancer of the esophagus is lower in people with Barrett's esophagus who take aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen. However, taking these drugs every day can lead to problems, such as kidney damage and bleeding in the stomach. For this reason, most doctors don't advise that people take NSAIDs to try to prevent esophageal cancer. If you are thinking of taking an NSAID regularly, discuss the potential benefits and risks with your doctor first.

### **Hyperlinks**

- 1. www.cancer.org/cancer/risk-prevention/tobacco.html
- 2. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/alcohol-use-and-cancer.html</u>
- 3. www.cancer.org/cancer/risk-prevention/tobacco.html
- 4. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/body-weight-and-cancer-risk.html</u>
- 5. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/acs-guidelines-nutrition-physical-activity-cancer-prevention.html</u>
- 6. <u>www.cancer.org/cancer/types/esophagus-cancer/detection-diagnosis-staging/detection.html</u>

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