



# Non-Hodgkin Lymphoma 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 non-Hodgkin lymphoma.

- [Non-Hodgkin Lymphoma Risk Factors](#)
- [What Causes Non-Hodgkin Lymphoma?](#)

## Prevention

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

- [Can Non-Hodgkin Lymphoma Be Prevented?](#)

## Non-Hodgkin Lymphoma Risk Factors

A risk factor is something 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.

But having a risk factor, or even many risk factors, does not mean that you will get the disease. And many people who get the disease may have few or no known risk factors.

Researchers have found several factors that can affect a person's chance of getting non-Hodgkin lymphoma (NHL). There are many types of lymphoma, and some of these factors have been linked only to certain types.

## **Age**

Getting older is a strong risk factor for lymphoma overall, with most cases occurring in people in their 60s or older. But some types of lymphoma are more common in younger people.

## **Gender**

Overall, the risk of NHL is higher in men than in women, but there are certain types of NHL that are more common in women. The reasons for this are not known.

## **Race, ethnicity, and geography**

In the United States, whites are more likely than African Americans and Asian Americans to develop NHL.

Worldwide, NHL is more common in developed countries, with the United States and Europe having some of the highest rates. Some types of lymphoma are linked to certain infections (described further on) that are more common in some parts of the world.

## **Exposure to certain chemicals and drugs**

Some studies have suggested that chemicals such as benzene and certain herbicides and insecticides (weed- and insect-killing substances) may be linked to an increased risk of NHL. Research to clarify these possible links is still in progress.

Some chemotherapy drugs used to treat other cancers may increase the risk of developing NHL many years later. For example, patients who have been treated for Hodgkin lymphoma have an increased risk of later developing NHL. But it's not totally clear if this is related to the disease itself or if it is an effect of the treatment.

Some studies have suggested that certain drugs used to treat rheumatoid arthritis (RA), such as methotrexate and the tumor necrosis factor (TNF) inhibitors, might increase the risk of NHL. But other studies have not found an increased risk. Determining if these drugs increase risk is complicated by the fact that people with RA, which is an autoimmune disease, already have a higher risk of NHL (see below).

## Radiation exposure

Studies of survivors of atomic bombs and nuclear reactor accidents have shown they have an increased risk of developing several types of cancer, including NHL, [leukemia](#), and [thyroid cancer](#).

Patients treated with radiation therapy for some other cancers, such as [Hodgkin lymphoma](#), have a slightly increased risk of developing NHL later in life. This risk is greater for patients treated with both radiation therapy and chemotherapy.

## Having a weakened immune system

People with weakened immune systems have an increased risk for NHL. For example:

- People who receive organ transplants are treated with drugs that suppress their immune system to prevent it from attacking the new organ. These people have a higher risk of developing NHL.
- The [human immunodeficiency virus \(HIV\)](#) can weaken the immune system, and people infected with HIV are at increased risk of NHL.
- In some genetic (inherited) syndromes, such as ataxia-telangiectasia (AT) and Wiskott-Aldrich syndrome, children are born with a deficient immune system. Along with an increased risk of serious infections, these children also have a higher risk of developing NHL.

## Autoimmune diseases

Some autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus (SLE or lupus), Sjogren (Sjögren) disease, celiac disease (gluten-sensitive enteropathy), and others have been linked with an increased risk of NHL.

In autoimmune diseases, the immune system mistakenly sees the body's own tissues as foreign and attacks them, as it would a germ. Lymphocytes (the cells from which lymphomas start) are part of the body's immune system. The overactive immune system in autoimmune diseases may make lymphocytes grow and divide more often than normal. This might increase the risk of them developing into lymphoma cells.

## Certain infections

Some types of infections may raise the risk of NHL in different ways.

## **Infections that directly transform lymphocytes**

Some viruses can directly affect the DNA of lymphocytes, helping to transform them into cancer cells:

- Infection with human T-cell lymphotropic virus (HTLV-1) increases a person's risk of certain types of T-cell lymphoma. This virus is most common in some parts of Japan and in the Caribbean region, but it's found throughout the world. In the United States, it causes less than 1% of lymphomas. HTLV-1 spreads through sex and contaminated blood and can be passed to children through breast milk from an infected mother.
- Infection with the Epstein-Barr virus (EBV) is an important risk factor for Burkitt lymphoma in some parts of Africa. In developed countries such as the United States, EBV is more often linked with lymphomas in people also infected with HIV, the virus that causes AIDS. EBV has also been linked with some less common types of lymphoma.
- Human herpes virus 8 (HHV-8) can also infect lymphocytes, leading to a rare type of lymphoma called primary effusion lymphoma. This lymphoma is most often seen in patients who are infected with HIV. HHV-8 infection is also linked to another cancer, [Kaposi sarcoma](#). For this reason, another name for this virus is *Kaposi sarcoma-associated herpes virus* (KSHV).

## **Infections that weaken the immune system**

Infection with human immunodeficiency virus (HIV), also known as the AIDS virus, can weaken the immune system. HIV infection is a risk factor for developing certain types of NHL, such as primary CNS lymphoma, Burkitt lymphoma, and diffuse large B-cell lymphoma.

## **Infections that cause chronic immune stimulation**

Some long-term infections may increase a person's risk of lymphoma by forcing their immune system to be constantly active. As more lymphocytes are made to fight the infection, there is a greater chance for mutations in key genes to occur, which might eventually lead to lymphoma. Some of the lymphomas linked with these infections actually get better when the infection is treated.

- *Helicobacter pylori*, a type of bacteria known to cause stomach ulcers, has also been linked to mucosa-associated lymphoid tissue (MALT) lymphoma of the stomach.
- *Chlamydomphila psittaci* (formerly known as *Chlamydia psittaci*) is a type of bacteria that can cause a lung infection called *psittacosis*. It has been linked to MALT lymphoma in the tissues around the eye (called *ocular adnexal marginal zone lymphoma*).
- Infection with the bacterium *Campylobacter jejuni* has been linked to a type of MALT lymphoma called *immunoproliferative small intestinal disease*. This type of lymphoma, which is also sometimes called *Mediterranean abdominal lymphoma*, typically occurs in young adults in eastern Mediterranean countries.
- Long-term infection with the hepatitis C virus (HCV) seems to be a risk factor for certain types of lymphoma, such as splenic marginal zone lymphoma.

## Body weight and diet

Some studies have suggested that [being overweight or obese](#) may increase your risk of NHL. Other studies have suggested that a diet high in fat and meats may raise your risk. More research is needed to confirm these findings. In any event, [staying at a healthy weight and eating a healthy diet](#) have many known health benefits outside of the possible effect on lymphoma risk.

## Breast implants

Although it is rare, some women with breast implants develop a type of anaplastic large cell lymphoma (ALCL) in their breast. This seems to be more likely with implants that have textured surfaces (as opposed to smooth surfaces).

- [References](#)

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Last Medical Review: May 31, 2016 Last Revised: March 24, 2017

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## What Causes Non-Hodgkin Lymphoma?

Researchers have found that non-Hodgkin lymphoma (NHL) is linked with a number of [risk factors](#), but the cause of most lymphomas is not known. This is complicated by the fact that lymphomas are actually a diverse group of cancers.

Still, scientists have made a lot of progress in understanding how certain changes in DNA can cause normal lymphocytes to become lymphoma cells. DNA is the chemical in our cells that makes up our genes, which control how our cells function. We look like our parents because they are the source of our DNA. But DNA affects more than just how we look.

Some genes control when cells grow, divide, and die:

- Genes that help cells grow, divide, and stay alive are called *oncogenes*.
- Genes that help keep cell division under control or make cells 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.

Some people inherit DNA mutations from a parent that increase their risk for some types of cancer. But NHL is not one of the cancer types often caused by these inherited mutations. In other words, having a family history of lymphoma does not seem to increase your risk of lymphoma.

Gene changes related to NHL are usually acquired during life, rather than being

inherited. Acquired gene changes can result from exposure to radiation, cancer-causing chemicals, or infections, but often these changes occur for no apparent reason. They seem to happen more often as we age, which might help explain why most lymphomas are seen in older people.

For some types of lymphoma, some of the gene changes that led to the lymphoma are now known. For example, in follicular lymphoma, the cells often have an exchange of DNA (known as a *translocation*) between chromosomes 14 and 18, which turns on the BCL-2 oncogene. (Chromosomes are long strands of DNA in each cell.) This oncogene stops the cell from dying at the right time, which can lead to lymphoma.

Scientists are learning much about the exact gene changes involved in the different types of NHL. This information is being used to develop more accurate [tests to detect and classify certain types of lymphoma](#). Hopefully, these discoveries can be used to develop new [treatments](#) as well.

While researchers are beginning to understand some of the gene changes that can lead to NHL, they still do not know why many of these gene changes develop, especially in people with no apparent risk factors.

Lymphocytes (the cells from which lymphomas start) are immune system cells, so it's not surprising that changes in the immune system seem to play an important role in many cases of lymphoma:

- People with **immune deficiencies** (due to inherited conditions, treatment with certain drugs, organ transplants, or HIV infection) have a much higher chance of developing lymphoma than people without a weakened immune system.
- People with certain **autoimmune diseases** (where the immune system constantly attacks a certain part of the body) have an increased risk of lymphoma.
- People with certain **chronic infections** are also at increased risk, probably because the immune system is constantly making new lymphocytes to fight the infection, which increases the chances for mistakes in their DNA.
- [References](#)

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## Can Non-Hodgkin Lymphoma Be Prevented?

There is no sure way to prevent non-Hodgkin lymphoma (NHL). Most people with NHL have no [risk factors](#) that can be changed, so there is no way to protect against these lymphomas. But there are some things you can do that might lower your risk for NHL, such as limiting your risk of certain infections and doing what you can to maintain a healthy immune system.

Infection with HIV, the virus that causes AIDS, is known to increase the risk NHL, so one way to limit your risk is to avoid known risk factors for HIV, such as intravenous drug use or unprotected sex with many partners. You can read more about HIV infection in [HIV, AIDS, and Cancer](#).

Preventing the spread of the human T-cell lymphotropic virus (HTLV-1) could have a great impact on non-Hodgkin lymphoma in areas of the world where this virus is common, such as Japan and the Caribbean region. The virus is rare in the United States but seems to be increasing in some areas. The same strategies used to prevent HIV spread could also help control HTLV-1.

*Helicobacter pylori* infection has been linked to some lymphomas of the stomach. Treating *H. pylori* infections with antibiotics and antacids may lower this risk, but the benefit of this strategy has not been proven yet. Most people with *H. pylori* infection have no symptoms, and some have only mild heartburn. More research is needed to find the best way to detect and treat this infection in people without symptoms.

Some lymphomas are [caused by treatment of other cancers](#) with radiation and chemotherapy or by the use of immune-suppressing drugs to avoid rejection of transplanted organs. Doctors are trying to find better ways to treat cancer and organ transplant patients without increasing the risk of lymphoma as much. But for now, the benefits of these treatments still usually outweigh the small risk of developing lymphoma many years later.



Some studies have suggested that [being overweight or obese](#) may increase your risk of non-Hodgkin lymphoma. Other studies have suggested that a diet high in fat and meats may raise your risk. [Staying at a healthy weight and eating a healthy diet](#) may help protect against lymphoma, but more research is needed to confirm this.

- [References](#)

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Last Medical Review: May 31, 2016 Last Revised: May 31, 2016

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