

Causes and risk factors for lymphoma

In most cases of lymphoma there is no known cause. There are, however, several risk factors which are associated with developing lymphoma.

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We have separate information about the topics in **bold font**. Please get in touch if you'd like to request copies or if you would like further information about any aspect of lymphoma. Phone 0808 808 5555 or email information@lymphoma-action.org.uk.

What causes lymphoma?

If you have lymphoma, it's not because of anything you did or didn't do. You can't catch lymphoma and you can't give it to anybody else.

Lymphoma is a type of cancer that develops when white blood cells called **lymphocytes** grow out of control. This happens if the DNA inside a lymphocyte changes in a way that stops it responding to signals. This means that the lymphocyte divides in an abnormal way or does not die when it should.

DNA changes (mutations) happen all the time. Most of the time they're completely harmless but sometimes they can affect critical genes. If more than one critical gene is affected in a certain combination, it can lead to cancer, such as lymphoma.

One DNA change on its own is not usually enough to cause lymphoma. It takes a number of different changes before a cancer starts to grow. In most cases, it's not known what causes these changes. Most of them probably happen by chance, although in some cases a cause can be identified. There are also some factors that might make you more likely to develop the DNA changes that lead to lymphoma. These are called 'risk factors'. Most risk factors for cancer work by increasing the rate of natural mutation events.

Most people who develop lymphoma have none of these risk factors and the cause is unknown.

Causes and risk factors

In medical terms, a cause is something that leads to an illness. Without the cause, the illness doesn't happen. Removing the cause can often cure the illness.

A risk factor is not the same as a cause. A risk factor is something that might increase your chance of getting an illness. A risk factor means there is a link (or 'association') between the factor and the illness. Other factors – or even pure chance – could be involved. Removing the risk factor might not affect the illness.

For example, there is an association between eczema and T-cell skin lymphoma. This doesn't necessarily mean that eczema causes skin lymphoma. In fact, eczema and skin lymphoma often look very similar. The association might simply be that it

is not possible to tell the difference between early T-cell skin lymphoma and eczema.

Causes of lymphoma

In most cases, there is no known cause for lymphoma. However, for a few types of lymphoma, scientists have identified a cause:

- Most cases of gastric **MALT lymphoma** are caused by a common bacterial infection called *Helicobacter pylori*. Usually, *Helicobacter pylori* causes stomach ulcers and indigestion. It is easily treated. Most people with *Helicobacter pylori* infection do **not** get lymphoma, but almost all people who get gastric MALT lymphoma have *Helicobacter pylori* infection. Treating the infection usually causes regression of the lymphoma and may even cure the lymphoma.
- **Breast implant-associated anaplastic large cell lymphoma** (BIA-ALCL) is caused by having textured breast implants. Although it develops in the breast, BIA-ALCL is a type of lymphoma, not a type of breast cancer. It is more common in people with implants that have a rough, textured surface than people with smooth implants. Scientists think it might be caused by an inflammatory reaction to the implant. It typically develops 8 to 10 years after having the implant but it can develop sooner or later than this. Most people with breast implants do **not** develop BIA-ALCL – but everyone who develops BIA-ALCL has had breast implants. In many cases, removing the breast implants cures the lymphoma and no further treatment is needed.

Risk factors for lymphoma

There are several risk factors linked to lymphoma. Some of these increase your chance of developing lymphoma, or particular types of lymphoma.

Having one or more risk factors for lymphoma does **not** mean you will develop it. It means you are a bit more likely to develop lymphoma than someone with no risk factors. Even if you have risk factors, your chance of developing lymphoma is usually still very small.

Risk factors for lymphoma include:

- **age**
- **gender**

- **family history**
 - **certain infections**
 - **a lowered immune system**
 - **autoimmune conditions**
 - **other conditions**
 - **additional possible factors.**
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Age

Lymphoma can develop at any age, but most types of **non-Hodgkin lymphoma** are more common in older people. This is because genetic changes in your cells (mutations) tend to build up throughout your life. Some of these changes can lead to lymphoma. **Hodgkin lymphoma**, however, is most common in people aged between 15 and 34, or over 60.

Gender

Lymphoma is slightly more common in males than females.

Family history

Lymphoma is not passed on from parent to child (inherited).

Most people who have a close family member with lymphoma or another **blood cancer** do **not** develop lymphoma themselves. However, your risk of developing lymphoma is slightly higher if you have a close relative (parent, brother or sister, or child) who has had lymphoma or another type of blood cancer. This might be due to lots of small inherited genetic changes that all increase your risk of lymphoma slightly.

Infections

Lymphoma is not infectious. You cannot catch lymphoma and you cannot pass it on to someone else.

However, there are some infections that can increase your chance of developing lymphoma. There are a few reasons for this:

- Some viruses infect lymphocytes (the type of cell that grows out of control if you have lymphoma). Occasionally, these viruses can cause changes to the DNA of the cells so they become cancerous.
- Some infections make your immune system too active. This means your body is constantly making new lymphocytes, which increases the chance of changes developing in their DNA. Occasionally, these DNA changes can lead to lymphoma.
- Some infections weaken your immune system. This makes it harder for your body to fight off other infections, including infections that might be linked to lymphoma.

Many of the infections linked to lymphoma are very common. Most people who have these infections do **not** get lymphoma. Scientists don't know why some people who have certain infections get lymphoma while most don't.

Viral infections

A number of different viral infections have been linked to lymphoma. However, the majority of people who have them never get lymphoma. They include:

- **Epstein–Barr virus (EBV):** EBV is a very common virus that can cause **glandular fever**. It infects **B lymphocytes**. About 9 in 10 adults have been infected with EBV but many people don't know they've had it. After you've been infected with EBV, it stays in your body, but it is normally kept under control by your **immune system**. People who have been infected with EBV have a higher chance of developing several types of lymphoma, including **Hodgkin lymphoma, Burkitt lymphoma, HIV-associated lymphoma, post-transplant lymphoproliferative disorder (PTLD)** and some **T-cell lymphomas**. However, the vast majority of people who have had EBV never get lymphoma.
- **Hepatitis C virus (HCV):** HCV is a virus that infects the liver. It can increase your chance of developing several types of lymphoma. It has been linked to **nodal marginal zone lymphoma, splenic marginal zone lymphoma, lymphoplasmacytic lymphoma, and diffuse large B-cell lymphoma (DLBCL)**. However, the vast majority of people who have had HCV never get lymphoma. Effective treatments for HCV are available.

- **Human immunodeficiency virus (HIV):** HIV weakens your immune system, making it harder for your body to fight infections. As some infections are linked to developing lymphoma, having HIV also increases your risk of developing some types of lymphoma.
- **Human herpesvirus 8 (HHV-8):** HHV-8 infects lymphocytes. It is linked with a very rare form of lymphoma called **primary effusion lymphoma (PEL)**. PEL mainly affects young people with HIV but it can develop in people with other immune system disorders or liver disease.
- **Human T-lymphotropic virus type 1 (HTLV-1):** HTLV-1 infects **T lymphocytes**. It is a rare infection in the UK, and does not usually cause any symptoms. It is strongly linked to a very rare lymphoma called **adult T-cell leukaemia/lymphoma**.

Bacterial infections

Some bacterial infections have also been linked to lymphoma. However, the majority of people who have them never get lymphoma. They include:

- ***Helicobacter pylori***, which can cause gastric MALT lymphoma.
- ***Chlamydia psittaci***, which causes a rare lung infection called psittacosis. It is spread by birds, including pet birds like parrots. Infection with *Chlamydia psittaci* is linked to **MALT lymphoma** in the tear ducts and around the eyes.
- ***Campylobacter jejuni***, a common cause of **food poisoning**. It has been linked to **MALT lymphoma** in the small bowel.
- ***Borrelia burgdorferi***, the bacteria that causes **Lyme disease**, an infection spread by ticks, might be linked to **MALT lymphoma** in the skin.
- ***Moraxella catarrhalis***, a bacteria that can cause chest infections, is linked to an **uncommon form of Hodgkin lymphoma**.

Lowered immune system

If you have a lowered immune system, you are less able to fight infections. This includes infections that increase your chance of developing lymphoma. There are two particular conditions that lower your immune system and have a higher risk of lymphoma. These are:

- **Human immunodeficiency virus (HIV):** HIV infects a particular type of **T lymphocyte** called a helper T cell. Helper T-cells activate other cells in your

immune system. Without them, your immune system can't work properly and you are less able to fight infections. This includes infections that are linked to lymphoma. People who have HIV have a higher risk of developing types of lymphoma such as **Burkitt lymphoma**, **diffuse large B-cell lymphoma** (DLBCL), **Hodgkin lymphoma** and very rare types of lymphoma such as **primary effusion lymphoma** (PEL) and **plasmablastic lymphoma**.

- **Post-transplant lymphoproliferative disorders** (PTLDs): These are lymphomas that can develop in people who are taking medicines to dampen their immune system after a transplant. This could be an organ transplant or a **donor (allogeneic) stem cell transplant**. PTLD can lead to several different types of lymphoma, including **diffuse large B-cell lymphoma** (DLBCL), **Burkitt lymphoma**, **T-cell lymphomas** or **Hodgkin lymphoma**. **PTLD is uncommon**. Most people who have had transplants do **not** develop PTLD.
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Autoimmune conditions

Autoimmune conditions are illnesses that develop when your immune system mistakenly attacks your own body.

Most people with autoimmune conditions do **not** develop lymphoma. However, some autoimmune conditions are linked to a higher chance of developing certain types of lymphoma. This might be because autoimmune conditions can cause long-term activation of the immune system. Another possible reason is that people with autoimmune conditions are likely to be on medicines that dampen their immune system. Both of these factors can contribute to the development of lymphoma.

Several autoimmune disorders might increase your chance of developing lymphoma.

- **Sjögren's syndrome** increases the risk of developing **splenic marginal zone lymphoma**, **MALT lymphoma** affecting the spit (salivary) glands or lungs, **diffuse large B-cell lymphoma** (DLBCL), and **Waldenström's macroglobulinaemia**.
- **Hashimoto's thyroiditis** increases the risk of **MALT lymphoma** affecting the thyroid gland.

- Refractory **coeliac disease** is strongly linked to **enteropathy-associated T-cell lymphoma** (EATL). However, EATL is very rare even in people who have coeliac disease.
 - **Rheumatoid arthritis** and **systemic lupus erythematosus** are both linked to **splenic marginal zone lymphoma** and **diffuse large B-cell lymphoma** (DLBCL). Rheumatoid arthritis is also strongly linked to a type of chronic leukaemia affecting lymphocytes, called **T-cell large granular lymphocytic leukaemia**.
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Other conditions

Monoclonal gammopathy of unknown significance (known as 'MGUS') is a non-cancerous condition where the body makes an abnormal antibody, called a monoclonal protein or paraprotein. MGUS does not cause any symptoms and is usually diagnosed when tests are performed to investigate other problems.

There are three types of MGUS named according to the type of protein involved (IgM, non-IgM and 'light chain'). A very small number of people with an IgM MGUS can go on to develop a low-grade (slow-growing) lymphoma, such as Waldenström's macroglobulinaemia or a marginal zone lymphoma.

The **IgM MGUS information sheet**, created by Charlotte Bloodworth and Dr Simona Gatto from University Hospital of Wales, Cardiff and Dr Shirley D'Sa from University College London Hospital, provides additional information.

Additional possible factors

Many studies have looked at other possible causes of lymphoma. Sometimes one or two studies suggest a possible link, but others find something different. As most types of lymphoma are rare, it can be difficult to work out whether or not a factor increases your chance of developing it or not.

Previous cancer treatment

Some treatments, such as chemotherapy drugs or CAR-T cell therapy, used to treat other types of cancer, including other blood cancers, might increase your chance of developing lymphoma in the future. Exposure to radiation, including radiotherapy for other cancers, might also increase your risk of developing lymphoma.

However, most people who've been treated for another cancer do **not** develop lymphoma.

Weight

Having a **body mass index** of over 30 (obesity) increases your risk of developing many types of cancer, including **Hodgkin lymphoma**, **non-Hodgkin lymphoma** and **chronic lymphocytic leukaemia** (CLL).

Keeping a **healthy lifestyle** by maintaining a healthy weight, exercising regularly and eating a **healthy diet** can reduce your risk of many health problems. Cancer Research UK has more information on **reducing your risk of developing cancers** by following a healthy lifestyle.

Chemicals

Being around high levels of industrial chemicals, solvents, **weedkillers** and insecticides are possible risk factors for developing lymphoma. Hair dyes might also be a risk factor, although modern hair dyes seem to be safer than those used in the past (pre-1980s). However, the evidence on all these chemicals is limited and scientists aren't sure if there is a link with lymphoma or not.

Working in a job where you're exposed to high levels of these chemicals (for example, crop farming, hairdressing, painting and decorating, or working in the rubber manufacturing industry) might slightly increase your risk of developing lymphoma. Most people who work in these occupations do **not** develop lymphoma.

References

The full list of references for this page is available on our website. Alternatively, email publications@lymphoma-action.org.uk or call 01296 619409 if you would like a copy.

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