

Transformation of lymphoma

Slow-growing (low-grade) lymphoma can sometimes change (transform) into a faster-growing (high-grade or aggressive) type of lymphoma. Faster-growing lymphomas need different treatment.

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What is transformation?

Transformation is when a **slow-growing (low-grade) lymphoma** changes into a **faster-growing (high-grade) lymphoma**. It is important to know if your lymphoma has transformed because transformed lymphoma needs different treatment to low-grade lymphoma.

Most low-grade lymphomas never transform.

If a low-grade lymphoma does transform, it is most likely to develop into a type of high-grade lymphoma called **diffuse large B-cell lymphoma (DLBCL)**. Occasionally, it can transform to other types, such as **Burkitt lymphoma**, **other high-grade B-cell lymphomas** or **Hodgkin lymphoma**.

Very occasionally, people who have a high-grade lymphoma **relapse** in the future with a low-grade lymphoma. Doctors aren't certain why this happens. They think it might be because tiny, undetectable levels of low-grade lymphoma were present at diagnosis, which later caused a relapse. The high-grade lymphoma might have been caused by transformation of low-grade lymphoma at a very early stage.

Why does transformation happen?

Low-grade lymphomas are mostly made up of small, slow-growing cells. These might be mixed in with a few faster-growing cells, or some of the slow-growing cells might mutate (change genetically) over time to become fast-growing. If the number of faster-growing lymphoma cells increases, the lymphoma can begin to behave more like a high-grade lymphoma.

Who might be affected by transformation?

Lymphoma does **not** transform in most people.

Transformation can happen in any type of **low-grade lymphoma** but it is most common in **follicular lymphoma**. Every year, transformation affects around 2 to 3 in every 100 people with follicular lymphoma.

Other types of low-grade lymphoma transform less frequently. Types of lymphoma that sometimes transform include:

- **chronic lymphocytic leukaemia or small lymphocytic lymphoma (CLL/SLL)** (this transformation is called Richter syndrome)
- marginal zone lymphomas (including **gastric MALT lymphoma**, **non-gastric MALT lymphoma**, **nodal marginal zone lymphoma** and **splenic marginal zone lymphoma**)
- **Waldenström's macroglobulinaemia** and other lymphoplasmacytic lymphomas
- a slow-growing type of Hodgkin lymphoma called **nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL)**.

Scientists are trying to identify changes in lymphoma cells that can help them work out who is most at risk of transformation. At the moment, there is no reliable way of predicting whether or not lymphoma is likely to transform in individual people, although there are some factors that might increase your risk. These include the level of certain chemicals in your blood, more widespread lymphoma, and older age.

Nothing you do (or have done) can make transformation more or less likely to happen.

Can treatment affect the risk of transformation?

There is no clear evidence that any of the treatments for low-grade lymphomas (for example, **chemotherapy** or **antibody therapy**) increase or decrease the risk of the lymphoma transforming.

Some studies have suggested that early treatment of the lymphoma could reduce the risk of transformation. Other studies have found that early treatment has no effect on the risk of transformation. However, it might affect the treatment options that are available if transformation does occur.

At present, doctors think there is no difference in the risk of transformation between people who have an initial period of **active monitoring ('watch and wait')** for low-grade lymphoma and people who have treatment straightaway.

When might transformation happen?

Transformation is possible at any time after diagnosis. However, in most cases, transformation **never** happens.

Occasionally, low-grade lymphoma has already transformed when it is diagnosed. In this case, your tests might show that you have a mixture of high-grade and low-grade lymphoma.

In a few people, lymphoma might transform within months of diagnosis. In others, lymphoma might transform many years later. Some research suggests that the risk of lymphoma transforming becomes lower around 15 to 20 years after diagnosis.

Your medical team check for **signs of transformation** at all your appointments.

Symptoms of transformed lymphoma

If your lymphoma transforms, it might affect the same part of your body as before, or a different part. The symptoms you experience depend on where the lymphoma is growing. The most common signs and symptoms of transformed lymphoma include:

- swollen **lymph nodes** that are growing quickly

- rapid swelling of your liver or your **spleen** (an organ of your immune system)
- weight loss, night sweats or fevers (**'B symptoms'**)
- high levels of certain chemicals found on **blood tests**.

Your medical team check for signs of transformation at all your appointments. If you don't have symptoms, your lymphoma is very unlikely to have transformed.

If you think your lymphoma might have transformed, contact your medical team straightaway. You don't have to wait for your next appointment.

The symptoms of transformed lymphoma can be similar to signs that your lymphoma has come back (**relapsed**). Relapsed lymphoma and transformed lymphoma need different treatment so it is important for your medical team to know which you have. If they think your lymphoma might have transformed, they are likely to perform a **PET/CT scan** and a **biopsy** to confirm it.

I had severe back pain that my lymphoma team and I thought was possibly related to spinal surgery I had the previous year. However, blood tests and an MRI scan confirmed that lymphoma had damaged several vertebrae in my spine. I was told that my low grade lymphoma had transformed into diffuse large B cell lymphoma (DLBCL). I found the diagnosis overwhelming.

Nuala, whose lymphoma transformed in 2009

Outlook

Transformed lymphoma can be difficult to treat but treatment options are improving all the time. Many people can be successfully treated.

Your individual outlook varies greatly depending on your individual circumstances. Your medical team are best placed to advise you on your outlook. They can use the results of your tests and other individual factors (for example, your age, the exact type of lymphoma you have and what treatment you've already had) to help them judge how likely you are to respond to a particular treatment.

If you choose to research survival statistics, be cautious. Survival statistics don't tell you what your individual outlook is – they only tell you how a group of people with a similar diagnosis did over a period of time. They are usually measured at least 5 or 10 years after treatment. This means that statistics only tell you how people did in the past. Those people might not have received the same treatment as you. The outlook for transformed lymphoma is much better now than it was before **antibody therapies** were available to treat lymphoma.

Treatment

There is no standard treatment for transformed lymphoma. Your medical team recommends the most appropriate treatment for you based on:

- the **type** and **stage** of the transformed lymphoma
- the treatment you've already had and how you responded to it
- your age
- the results of your tests and scans
- your preferences.

If you haven't had it before, you are likely to be offered the standard **chemotherapy** for the type of high-grade lymphoma your lymphoma has transformed into. For most types of transformed lymphoma, this is combined with **antibody therapy** ('chemo-immunotherapy' – for example, **R-CHOP**).

If you've already had the standard chemotherapy or chemo-immunotherapy regimen for your type of lymphoma, you might be offered a stronger **chemotherapy regimen**. If you respond to this and you're fit enough, your medical team might suggest a **self (autologous) stem cell transplant**. Stem cell transplants are intensive forms of treatment and are not suitable for everyone.

I was started on R-CHOP, which was higher dose chemotherapy than I'd had before, plus methotrexate. I then had a high-dose chemotherapy regimen called BEAM before having an autologous stem cell transplant. I took a long time to recover. One of my daughters was pregnant with our first grandchild and I remember saying to the physiotherapists, 'I've got to be able to hold a baby!' It gave me a very specific goal to aim for.

Nuala, whose lymphoma transformed in 2009

If you need more than one course of treatment for transformed lymphoma, you might be offered a **donor (allogeneic) stem cell transplant**, **CAR T-cell therapy**, or your consultant might ask if you'd like to take part in a **clinical trial**.

Research and targeted treatments

Scientists are testing many different **targeted treatments** in **clinical trials** for lymphoma. Although many of these trials are not open to people with transformed lymphoma, a few are.

Some of the treatments that are being tested in people with transformed lymphoma include:

- **Antibody therapies** that bind to two different targets (one on lymphoma cells and one on T cells, which helps the T cells find and destroy the lymphoma cells). These are called 'bispecific' antibodies.
- **Antibody–drug conjugates** (antibodies joined to chemotherapy drugs). The antibody sticks to a protein on the surface of lymphoma cells and carries the chemotherapy drug directly to it.
- **CAR T-cell therapy**, which involves modifying your own immune cells to recognise and destroy lymphoma cells.
- **Cell signal blockers**, such as **ibrutinib** and **idelalisib**, which block signals that B cells send to help them divide or stay alive.
- Immunomodulators such as **lenalidomide**, which change how your immune system works.
- Programmed cell death inducers such as **venetoclax**, which block proteins that keep lymphoma cells alive.
- **Checkpoint inhibitors** such as pembrolizumab, which stop lymphoma cells hiding from your immune system.

Some of these might be available to you through a clinical trial. Speak to your doctor if you are interested in taking part in a clinical trial. To find out more about clinical trials or to search for a trial that might be suitable for you, visit [Lymphoma TrialsLink](#).

References

The full list of references for this page is available on our website. Alternatively, email publications@lymphoma-action.org.uk or call 01296 619400 if you would like a copy.

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