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Chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL)

This information is about chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL). CLL and SLL are different forms of the same illness. They are often grouped together as a type of slow-growing (low-grade or indolent) non-Hodgkin lymphoma.

On this page

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 is CLL/SLL?

Chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL) are slow-growing types of blood cancer. They develop when white blood cells called **lymphocytes** grow out of control. Lymphocytes are part of your **immune system**. They travel around your body in your **lymphatic system**, helping you fight infections. There are two types of lymphocyte: **T lymphocytes (T cells)** and **B lymphocytes (B cells)**.

CLL and SLL are different forms of the same illness. They develop when B cells that don't work properly build up in your body.

- In CLL, the abnormal B cells build up in your blood and **bone marrow**. This is why it's called 'leukaemia' – after 'leucocytes': the medical name for white blood cells.
- In SLL, the abnormal B cells mainly build up in your **lymph nodes**. This is why it's called lymphoma'.

CLL and SLL are slow-growing (low-grade or 'indolent') cancers. Many doctors group them together as a type of **non-Hodgkin lymphoma**. They usually behave like a long-term (chronic) condition that needs treatment from time-to-time to keep it under control.

CLL and SLL are treated in the same way. In this information, we use the term 'CLL' to refer to both, except where there are important differences.

Who gets CLL?

Between 3,800 and 4,500 people are diagnosed with CLL every year in the UK – more than 10 people each day. It affects nearly twice as many men as women. It is more common in people over 60, with an average age at diagnosis of 72 years. CLL is rare in young people.

In most cases, there is no known **cause** of CLL. People who have a close relative (parent, brother, sister or child) with CLL have a higher chance of developing it themselves, but the risk is still very low.

Monoclonal B-lymphocytosis

Sometimes, **blood tests** reveal a low level of abnormal B cells in people who have normal blood counts and do not have swollen lymph nodes or any other symptoms. This condition is called monoclonal B-lymphocytosis (MBL).

MBL is fairly common in people over 60. Most people never know they have it and it does not usually cause any problems. However, each year around 1 to 2 in every 100 people with MBL go on to develop CLL. This is more likely to happen in people who have a higher number of abnormal B cells in their blood (sometimes called ‘high-count MBL’).

People with high-count MBL usually have blood tests every so often to check their level of abnormal cells.

Symptoms of CLL

Most people have no **symptoms** when they are diagnosed with CLL. It’s usually found by chance when doctors notice high levels of lymphocytes on a blood test done for another reason.

As more abnormal B cells build up, you might start to develop symptoms, although some people never do. Any symptoms tend to be mild at first and gradually get worse over a period of months or years as more abnormal cells build up. You might feel generally unwell, with symptoms like:

- fatigue (extreme tiredness)
- weight loss
- fevers
- night sweats
- flu-like symptoms.

The abnormal cells can collect in your **lymph nodes**, causing them to swell. You might feel these as lumps. They can develop anywhere in your body but are most often found in your neck, armpit or groin. If abnormal cells build up in your **spleen** (an organ in your lymphatic system), you might feel pain or even a lump at the top-left of your tummy (abdomen).

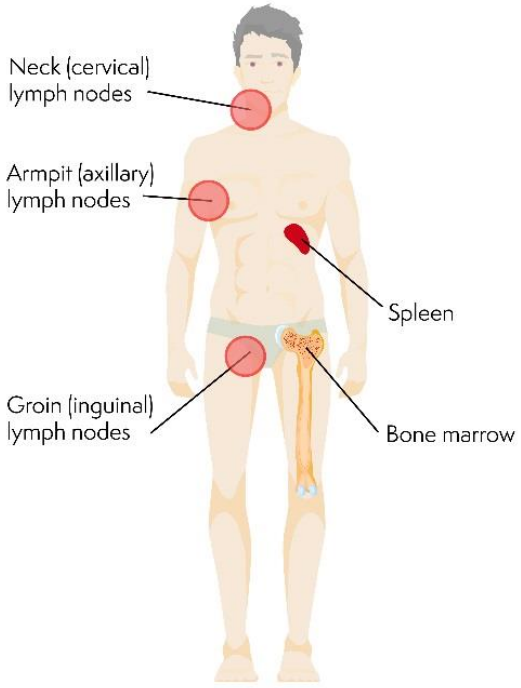


Figure: Parts of the body where CLL is often found

If lymphoma cells build up in your bone marrow, they can take up the space needed for healthy blood cells to develop. This means your body might not be able to make enough blood cells and you might develop low blood counts:

- **anaemia** (low red blood cells), which can make you feel tired, breathless or dizzy
- **thrombocytopenia** (low platelets), which makes you more likely to bruise and bleed
- **neutropenia** (low neutrophils – a type of white blood cell), which might make you pick up infections more easily than usual, and can make it harder to get rid of them.

Some people with CLL develop low blood counts due to an autoimmune reaction. This is when your body makes **antibodies** that attack your own cells. If the antibodies stick to blood cells, they can cause:

- low red blood cells (**autoimmune haemolytic anaemia**, or AIHA)
- low platelets (**immune thrombocytopenic purpura**, or ITP).

Low blood counts due to autoimmune conditions need different treatment from low blood counts caused by too many abnormal cells in your bone marrow.

CLL can also cause **fatigue** and recurrent infections.

Diagnosis and staging

CLL can be diagnosed on a blood test. SLL is usually diagnosed by taking a sample of cells from a swollen lymph node to look at under a microscope. This is called a lymph node **biopsy**. A doctor either uses a hollow needle to remove a ‘core’ of tissue from a lymph node (a ‘needle core biopsy’), or removes the whole node. Both types of biopsy are done under anaesthetic so you won’t feel any pain. This is usually a local anaesthetic, but occasionally you might have a general anaesthetic.

Your blood and biopsy samples are examined by an expert CLL or lymphoma **pathologist**. The pathologist looks at the samples under a microscope and tests the abnormal B cells to find out if they have certain genetic changes. Some genetic changes mean CLL is likely to grow faster and need a different type of treatment. These are called ‘high-risk’ genetic changes. Your medical team uses the information from your blood tests and biopsy to help choose the most appropriate **treatment** for you.

You also have **blood tests** to look at your general health, measure your antibody levels, and find out how well your kidneys and liver are working. If you are starting treatment, you might have blood tests to check if you have any viral infections that could flare up during treatment.

If you have low blood counts, you might have a test to check for lymphoma cells in your bone marrow (a **bone marrow biopsy**). You might also have a bone marrow biopsy when you finish treatment, to check how well your CLL has responded. However, this isn’t always needed.

If you have symptoms and you need to start treatment, you might have a **CT scan** to find out where the CLL is in your body. You might have another CT scan after any treatment to check how well you have responded to it.

You usually have your tests done as an outpatient. It takes a few weeks to get all the results. **Waiting for test results** can be a worrying time, but it is important for your medical team to have all the information they need so they can plan the most appropriate **treatment** for you.

Staging of CLL

Your medical team uses the results of your tests and scans to work out how widespread your CLL is and how it is affecting you. This is called staging.

Staging of SLL is the same as for other types of non-Hodgkin lymphoma. CLL is staged differently because it generally affects your blood rather than your lymph nodes. There are two main ways to stage CLL: the Binet system and the Rai system.

The Binet system

- Stage A: You have fewer than three areas of 'lymphoid swelling' (swollen liver or spleen, or swollen lymph nodes in your neck, armpits or groin).
- Stage B: You have three or more areas of lymphoid swelling.
- Stage C: You have a low red blood cell count (anaemia), a low platelet count (thrombocytopenia) or both.

The Rai system

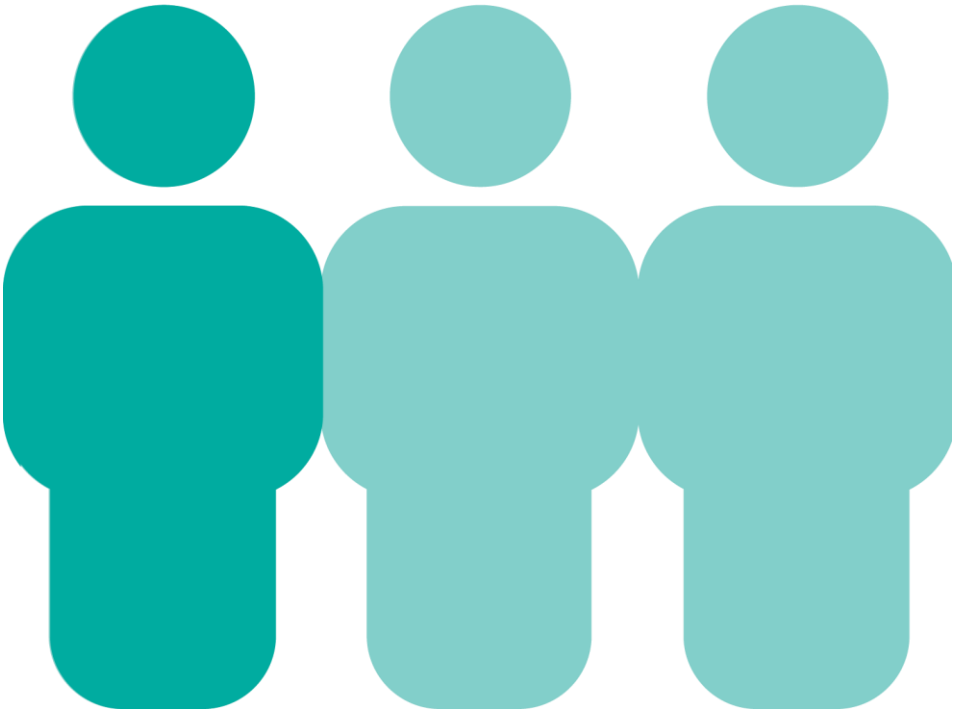
- Stage 0: You have a high lymphocyte count.
- Stage I: You have a high lymphocyte count and swollen lymph nodes.
- Stage II: You have a high lymphocyte count and a swollen liver or spleen, with or without swollen lymph nodes.
- Stage III: You have a high lymphocyte count and a low red blood cell count (anaemia), with or without swollen lymph nodes or a swollen liver or spleen.
- Stage IV: You have a high lymphocyte count and low platelets (thrombocytopenia), with or without swollen lymph nodes, a swollen liver or spleen, or anaemia.

Staging is important because it helps your medical team plan the best treatment for you.

Outlook

CLL usually grows very slowly and there are lots of effective treatment options. They generally aim to keep the lymphoma under control rather than curing it.

Most people live with CLL for many years, with some periods when they need treatment, and other periods when they don't. It is hard to predict how long it might be before you start treatment.



- Around 1 in 3 people need treatment soon after their diagnosis.
- Around 1 in 3 people need treatment at some point in the future.
- Around 1 in 3 people never need treatment.

In general, people with CLL at a lower stage have a better outlook than those with more advanced CLL. Some people have particular genetic changes in their lymphoma cells that mean it grows faster and is likely to need more frequent treatment. Your doctor is best placed to advise you on your outlook based on your individual circumstances and test results.

Rarely, CLL **transforms** (changes) into a faster-growing type of lymphoma. This is known as 'Richter transformation'. It happens to about 1 in every 100 people with CLL each year. Most of these cases transform to a type of **diffuse large B-cell lymphoma (DLBCL)** but they can occasionally transform to **Hodgkin lymphoma** or other **non-Hodgkin lymphomas**. Transformed CLL is more difficult to treat.

Treatment

CLL is slow-growing and there is rarely an urgent need for treatment. Some people might not need treatment for many years. Your medical team will consider carefully whether you need treatment straightaway and what treatment is best for you.

If you need treatment, there are several different options. The treatment your medical team recommends depends on:

- the stage of your CLL
- how it is affecting you
- the particular genetic changes in your CLL cells
- any other illnesses you have
- your preferences
- the potential **side effects**, long-term or **late effects** (health problems that develop months or years after treatment) of the treatment.

Depending on your individual circumstances, you might need several different treatments during your illness. Treatment aims to reduce your symptoms and keep the CLL under control for as long as possible with as few side effects as possible. Most people have long periods of feeling well between courses of treatment. For some of the newer types of treatment, you might take tablets to treat the CLL for a number of years.

Active monitoring (watch and wait)

Most people don't have any symptoms when they are first diagnosed with CLL. If the CLL is not causing problems, you do not need treatment straightaway. Instead, your medical team monitors you periodically until you need treatment. This is called **active monitoring or watch and wait**.

Research shows that there is no benefit to starting treatment before you need it. All treatment also carries a risk of causing **side effects**, so doctors often advise delaying treatment for as long as possible.

If you are worried about your health at any time, contact your GP or medical team. You don't have to wait for your next appointment.

You are likely to start **treatment** if:

- your symptoms get worse or become difficult to cope with
- your lymph nodes, spleen or liver become swollen enough to cause you symptoms
- you develop low blood counts
- the number of abnormal lymphocytes in your blood rises very quickly
- you have **autoimmune anaemia** or **thrombocytopenia** that is not responding to treatment.

When you finish your treatment, you go back onto active monitoring.

Treatment for people without high-risk genetic changes

There are a number of different ways that CLL can now be treated. For many years people with CLL who do **not** have high-risk genetic changes have been treated with **chemotherapy** combined with **antibody therapy** (for example **rituximab**) as their first treatment. This is sometimes called chemo-immunotherapy. While chemo-immunotherapy is often a very effective treatment for CLL, it can cause a range of side effects and complications.

There are now a number of non-chemotherapy approaches to treat CLL. These are **targeted drugs** that you take as a tablet. They are sometimes combined with **antibody therapy**. Studies have shown that these newer treatments can be more effective than chemotherapy at keeping CLL in remission. The tablets are also commonly better tolerated than chemotherapy. They include drugs such as **ibrutinib**, acalabrutinib and **venetoclax**.

The antibody most commonly used in first-line treatment for CLL is called **obinutuzumab**. It can sometimes be combined with one of the newer tablet medications.

The different treatments that are approved for CLL within the UK are changing rapidly. As more options become available, it is important that you discuss these choices with your CLL doctor. This will allow you to choose the treatment that is best suited to your needs.

In addition to these options, your medical team might ask you if you'd like to take 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**.

> **I was treated as part of a clinical trial. The researchers won't know if it was better than standard treatment for many years but I felt I was doing my bit by taking part.**
>
> Michael, diagnosed with SLL at 63

Treatment for people with high-risk genetic changes

CLL that has high-risk genetic changes doesn't usually respond well to chemotherapy. However, there are several **targeted drugs** that can be very effective.

The most common treatment is **ibrutinib**. This is a type of targeted drug that blocks the signals that B cells send to help them stay alive and divide. You have it as a tablet that you take every day unless your lymphoma stops responding or you develop troublesome side effects.

If ibrutinib is not suitable for you, your medical team might suggest a different cell signal blocker called **idelalisib**, usually combined with rituximab. Other treatment options include idelalisib on its own, or a different targeted drug called **venetoclax**.

Other treatment options

Radiotherapy is sometimes used to treat SLL that is only affecting one part of your body. In this case, it can sometimes cure the lymphoma. Radiotherapy is not often used for CLL but might occasionally be used to shrink large lymph nodes if other treatments are not suitable or have not worked for you.

Treatment or prevention of symptoms

As well as treatments to control your lymphoma, you might have treatments to help relieve your symptoms or prevent infections. These might include:

- antibiotics, antifungal and antiviral drugs to prevent or treat infections
- vaccinations against flu and pneumonia
- **growth factor (G-CSF) injections** to boost your white blood cell count
- **immunoglobulin replacement therapy** to strengthen your immune system if your level of natural antibodies is low
- **red blood cell transfusions or platelet transfusions** to treat low blood counts
- treatments for **autoimmune haemolytic anaemia** and **immune thrombocytopenic purpura**.

Contact your medical team straightaway if you have any **symptoms of infection**. It is important that you get prompt treatment.

Follow-up

After treatment with chemotherapy, most people go back onto **active monitoring** if their CLL is under control. If you are taking one of the newer tablet treatments, you might stay on treatment for a number of years. You have clinic appointments and blood tests to make sure your CLL is under control.

As part of your follow-up, your medical team check your general health and look for any signs that your CLL might be becoming more active again. This usually happens quite slowly. Your medical team check for changes in your blood test results, and whether you develop any new symptoms or new swollen lymph nodes.

Rarely, CLL can change to a more aggressive condition. If your doctor thinks this might have happened, they might arrange for you to have a **PET/CT scan** and another **biopsy**.

Relapsed and refractory CLL

Treatment for CLL is often effective. However, at some point it usually comes back (**relapses**) and needs more treatment. Occasionally, CLL doesn't respond well to your first treatment. This is called 'refractory' CLL. It is usually treated the same way as relapsed CLL. Some people with CLL need several courses of treatment during their illness.

The length of **remission** after successful treatment can vary a lot, so it can be difficult to predict how long it might be before you need more treatment. Some people stay in remission for several years but others need more treatment sooner. As new and more effective treatments for CLL become available, remissions are generally getting longer.

Treatment for relapsed or refractory CLL

When you need more treatment, your doctor considers the same factors as for your first treatment but also takes into account:

- what treatment you had before
- how well you responded to your previous treatment
- how your previous treatment affected you.

There are lots of different treatments available for CLL. If your CLL relapses, your medical team are likely to recommend a different treatment than you had before. Treatment options might include drugs such as **ibrutinib**, **venetoclax**, **idelalisib,** or another new **targeted drug**, possibly as part of a **clinical trial**.

Rarely, your medical team might suggest an **allogeneic stem cell transplant**. This is an intensive form of treatment and is only suitable for people who are fit enough. Your medical team might suggest it if your CLL has not responded to chemo-immunotherapy or **cell signal blockers** (for example, ibrutinib or idelalisib).

Treatment for transformed CLL

Transformed CLL can be difficult to treat. It does not usually respond well to treatment. Many people with transformed CLL are older and have had several previous courses of treatment so might not be fit enough for intensive treatment. The most likely treatment is **chemotherapy**, possibly followed by a **donor (allogeneic) stem cell transplant** if you are fit enough. If you are not fit enough for chemotherapy, you might be able to enter a **clinical trial** or you might consider **palliative care**, where you have treatment to control your symptoms.

Research and targeted treatments

Scientists are testing many different **targeted treatments** in **clinical trials** for CLL, including some treatments that are already approved for other types of lymphoma. New types of treatment that are being tested in people with CLL include:

- New **cell signal blockers**, such as acalabrutinib and zanubrutinib, which block signals that B cells send to help them divide or stay alive. These work in a similar way to ibrutinib.
- **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.
- **CAR T-cell therapy**, which involves genetically modifying your own T cells so they can recognise and kill lymphoma cells.

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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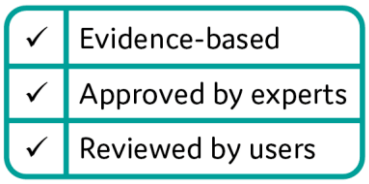

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