

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

This information page is about chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL). CLL and SLL are different forms of the same disease and are treated in the same way. 'CLL' is used to refer to both forms of disease, except where there are important differences.

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Quick overview of CLL/SLL

This section is an overview of the information on this page. There is more detail in the sections below.

What is it?

CLL/SLL is a type of cancer that develops from B lymphocytes (white blood cells that fight infection). It is usually slow-growing and behaves like a chronic (long-term) condition; it needs treatment from time-to-time to keep it under control.

What are the symptoms and how is it diagnosed?

Most people have no symptoms when they are diagnosed, but can have high levels of lymphocytes (white blood cells) in their blood or sometimes enlarged lymph nodes (swollen glands). Some people never develop symptoms. Symptoms develop gradually and can include feeling generally unwell, with fatigue (extreme tiredness), fevers, night sweats, weight loss and frequent infections.

CLL is normally diagnosed by looking at abnormal cells from a blood test. People with SLL usually need a biopsy of an enlarged lymph node.

How is it treated?

Before starting treatment, you might be monitored ('active monitoring' or 'watch and wait'). You start treatment when your symptoms become troublesome. Some people never need treatment. The main treatment for CLL is chemo-immunotherapy (chemotherapy with antibody treatment). Targeted drugs are becoming very important for treating CLL, particularly for CLL that is difficult to treat or for CLL that has relapsed (come back) after chemo-immunotherapy. You have active monitoring between courses of treatment.

What is CLL?

CLL and SLL are cancers of the **lymphatic system**. They can develop when lymphocytes (a type of white blood cell that fights infection) grow out of control. CLL has 'leukaemia' in its name because it affects the blood. SLL is another form of the same disease and it mainly affects the lymph nodes (glands), which is why it is called a 'lymphoma'. Both forms of the disease are low-grade (slow-growing) and are often grouped as **non-Hodgkin lymphomas**. CLL and SLL are treated in the same way. On this page, the term 'CLL' is used to refer to both forms of the disease except where there are important differences.

Who gets CLL and what causes it?

Around 3,500 to 4,000 people are diagnosed with CLL every year in the UK – that's around 10 people every day. It affects nearly twice as many men as women. The risk of developing CLL increases with age, 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 with a close relative (parent, brother, sister or child) with CLL are at an increased risk of developing CLL. However, the risk of developing CLL if you have a family member with the disease is still very small. Research has not identified any genes that are associated with developing CLL.

Symptoms

The majority of people have no symptoms when they are diagnosed with CLL. In around 7 in 10 people, CLL is found by chance on a blood test done for another reason.

The abnormal cells in CLL are B cells that are immature (not fully developed) and don't work properly. In the CLL form of the disease, the abnormal cells are found mainly in the blood. In the SLL form, they are found mainly in the lymph nodes or spleen and only at low levels in the blood.

As the abnormal cells build up, **symptoms** can develop. Any symptoms tend to be mild at first and gradually get worse as more abnormal cells build up.

You might feel generally unwell, with symptoms like:

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

As your **immune system** is affected, you might have frequent infections or find it difficult to shake off infections.

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, you might feel pain or even a lump at the top-left of your abdomen (tummy).

CLL cells can build up in your bone marrow (the spongy centre of some of our bones where blood cells are made). This can cause **low blood counts** as the CLL cells take up the space of normal cells. You might develop:

- **anaemia** (low red blood cells), which can cause tiredness and shortness of breath
- **thrombocytopenia** (low platelets), which makes you more likely to bruise and bleed
- **neutropenia** (low neutrophils – a type of white blood cell), which makes you more prone to infection.

Low blood counts in people with CLL can sometimes be due to an autoimmune reaction, where your body produces antibodies that destroy your blood cells, for example:

- low red blood cells can be due to **autoimmune anaemia**
- low platelets can be due to **immune thrombocytopenic purpura (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.

What is monoclonal B-lymphocytosis?

Some people have CLL-like cells at low levels in their blood but have normal blood counts and no other symptoms. This condition is called clinical monoclonal B-lymphocytosis (MBL). Many healthy older people (more than 1 in 10 people) have MBL and may not be aware of it. It does not usually cause any problems.

Most people with MBL do not go on to develop CLL, particularly if the abnormal cells are at a low level. However, evidence suggests that MBL develops first in all people who go on to develop CLL. Around 1–2 of every 100 people diagnosed with MBL develop CLL each year.

People with MBL who are at high risk of developing CLL usually have blood tests every so often to check if the level of abnormal cells is rising.

Diagnosis and staging

CLL is usually first found in blood tests. If there are a large number of lymphocytes in your blood, CLL might be suspected. It is then diagnosed by looking at the lymphocytes in more detail and doing tests on them.

Tests on the abnormal lymphocytes also help your medical team to find out more about the CLL. For example, they can detect certain genetic mutations (changes) that make CLL more difficult to treat.

The SLL form is usually diagnosed by finding abnormal lymphocytes in a **biopsy** of a swollen lymph node.

When you have been diagnosed, you have other tests, for example:

- more **blood tests** to find out about your general health
- a physical examination to check for other signs of CLL such as enlarged lymph nodes or an enlarged spleen.

Some people have other tests, too, such as **X-rays**, a **CT scan** or **bone marrow tests**. These are done to find out if CLL is causing problems in certain parts of the body.

Although **waiting for the results of your tests** can be difficult, your doctor is collecting important information during this time. It is important that your doctor knows exactly how your CLL is affecting you so they can give you the most appropriate treatment.

What does 'stage' mean?

The tests you have are part of 'staging' – working out how widespread your CLL is and how it is affecting you. CLL is staged differently from other types of non-Hodgkin lymphoma because it is mostly found in the blood. The abnormal cells are therefore carried around the body in a different way to types of lymphoma that are mostly found in the lymph nodes. The most common staging system for CLL in the UK is the Binet staging system:

- Stage A – you have fewer than three groups of swollen lymph nodes
- Stage B – you have three or more groups of swollen lymph nodes
- Stage C – you have anaemia (low red blood cells) or thrombocytopenia (low platelets) or both.

Another staging system, the Rai system, might be used. In this system, you are given a stage from 0 (the earliest stage) to 4 (the most advanced stage).

As SLL usually affects lymph nodes rather than blood, it is often **staged** the same way as non-Hodgkin lymphoma.

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

Outlook

Most people with CLL are treated to keep the lymphoma under control, rather than to cure it. There are lots of good treatments for CLL. It can usually be controlled for many years with several courses of treatment.

Survival statistics can be confusing as they don't tell you what your individual outlook is – they only tell you how a group of people with the same diagnosis did over a period of time in the past.

CLL usually grows very slowly and you might have many years between courses of treatment. However, some people have a faster-growing form that is likely to need more frequent treatment. Certain genetic mutations in the cells can make CLL more difficult to treat ('high-risk'). For example, 17p or 11q deletions or TP53 mutations can affect how your CLL is treated.

In general, people with CLL at a lower stage have a better outlook than those with more advanced CLL.

Average expected survival is reported to be around 10 years but this varies a lot between individual people and depends on many factors including the stage of the CLL and how it behaves. The availability of newer targeted drugs is significantly improving the outlook for people with CLL. Some of these new treatments are very effective for people with high-risk genetic mutations and offer alternatives to standard chemo-immunotherapy (chemotherapy with antibody therapy), which does not work well for this type of CLL. As people with CLL generally live for many years, it takes a long time to find out how these newer treatments affect outcomes.

Your doctor is best placed to advise you on your outlook based on your individual circumstances. Your doctor can use the results of your tests and consider other factors, like your age, symptoms, and other conditions you might have to predict how likely you are to respond to a particular treatment. These factors are called 'risk factors'.

Treatment

CLL might not cause problems for many years. Some people never need treatment. Your doctor considers carefully whether you need treatment straightaway and what treatment is best for you. You are likely to need several courses of treatment during your illness. Most people have long periods of feeling well between courses of treatment.

Treatment aims to reduce your symptoms and keep the CLL under control for as long as possible with as few side effects as possible.

CLL is not causing problems for more than three-quarters of people when they are first diagnosed. If the CLL is not causing problems, you do not need treatment straightaway. You might be monitored regularly by your doctor until you need treatment (**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 prefer to delay treatment for as long as possible.

What does active monitoring involve?

Your monitoring might be done at the hospital clinic or with your usual GP, depending on how your CLL behaves and your personal circumstances. You have blood tests and a check-up at each appointment. At first, the appointments may be every 3 months but the time between appointments might increase to once a year if you have early-stage CLL and stay well. The appointments allow your medical team to check for signs of the CLL getting worse. They also give you an opportunity to raise concerns and ask questions.

You are likely to have a physical examination and blood tests. Scans are not usually done unless there is a particular reason for them.

Some people go onto a **self-management** scheme. You are given information on what to look out for and how to look after yourself. You might have blood tests at your GP surgery.

If you are worried about your health at any time, contact your GP or medical team. They can reassure you or arrange an appointment for you to have a check-up.

You might have treatments to keep your symptoms under control while on active monitoring. For example, if you have **autoimmune anaemia** you might be treated with **steroids**.

When does treatment start?

You usually start treatment for the CLL when it worsens, for example:

- your symptoms (for example fevers, night sweats, fatigue or weight loss) become severe
- the numbers of lymphocytes in your blood rise rapidly
- your lymph nodes, spleen or liver become very enlarged
- you develop low blood counts due to the abnormal lymphocytes collecting in your bone marrow
- you have autoimmune anaemia or thrombocytopenia that is not responding to treatment.

There are different treatment options for CLL so your medical team consider several factors when they plan your treatment, including:

- the stage of the CLL and whether it has high-risk genetic mutations
- how the CLL is affecting you
- your general health
- your preferences.

What is the usual first treatment for CLL?

Most people have **chemotherapy** as a first treatment for CLL, usually with **antibody treatment** (for example **rituximab**) – this combination is sometimes called 'chemo-immunotherapy'. If you are fit enough, the most common **regimen** (combination of drugs) is FCR (fludarabine, cyclophosphamide and rituximab).

If FCR is not suitable for you, other options include:

- bendamustine chemotherapy, with or without rituximab
- chlorambucil chemotherapy tablets with one of the newer antibody treatments, **obinutuzumab** or **ofatumumab**.

These regimens both include intravenous treatments (given into a vein). For FCR and chlorambucil-based treatments, you also take some of the drugs orally, as tablets.

Note: after you have had treatment with fludarabine or bendamustine you must be given specially prepared 'irradiated blood' if you need to have **blood transfusions** in future. This is so that you don't develop a rare but serious complication of blood transfusion called 'transfusion-associated graft-versus-host disease'.

If your doctor thinks your CLL will respond to gentler treatment or you cannot have stronger treatment, they might recommend chlorambucil chemotherapy tablets alone.

Your doctor might suggest a different chemotherapy regimen or a **targeted drug**, possibly as part of a clinical trial. Find out more about clinical trials and search for a trial that might be suitable for you at [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 for humanity by taking part.

Michael, diagnosed with CLL at 63

If your CLL has features that mean it is unlikely to respond well to chemotherapy, for example high-risk genetic mutations, newer drugs can be very effective.

You also have treatments that help to control symptoms or side effects. These might include:

- antibiotics, antifungal and antiviral drugs to prevent or treat infections
- **growth factor (G-CSF) injections** to boost blood counts and help fight infection
- **immunoglobulin replacement therapy**, where donor antibodies are given to help fight infection if your own antibody levels are low
- **red blood cell transfusions and/or platelet transfusions** to boost blood counts
- drug treatments for autoimmune low blood counts – **steroids** are usually given initially, but there are other treatment options.

Note: antibodies are naturally produced by your body to fight infection so the antibodies in immunoglobulin replacement therapy are not the same as man-made antibody treatments for CLL like rituximab.

Other treatments that are occasionally used for CLL include:

- **Radiotherapy**, which might be used for early-stage SLL, where it can sometimes cure the lymphoma. Radiotherapy is not often used for CLL but might rarely be used to reduce large lymph nodes if other treatments are not suitable or did not work.
- A **splenectomy** (surgery to remove the spleen) or splenic radiotherapy (radiotherapy to the spleen) might be used rarely if autoimmune complications of CLL are severe and do not respond to other treatments. This treatment doesn't usually treat the CLL itself.
- **Steroids**, which are often used to treat side effects but can also help to control the CLL.

Rarely, if you respond well to your first treatment, your doctor might suggest an **allogeneic stem cell transplant**, which could offer a longer-lasting remission. This is an intensive form of treatment and is only suitable for people who are fit enough.

All treatment has a risk of **side effects** (unwanted effects). Your medical team can give you more information about the typical side effects of the treatment they recommend for you.

Follow-up

Most people go back onto **active monitoring** after treatment if the CLL is under control.

Relapsed and refractory CLL

Remissions (time when the CLL is under control) are increasing in length with new and more effective treatments for CLL. However, CLL usually flares up again after a period of remission. Most people need several courses of treatment during their illness.

If your lymphoma doesn't respond well to your first treatment, it is called 'refractory' and you might need a different or stronger treatment.

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

- what treatment you had before
- how long your remission was after your previous treatment
- how your previous treatment affected you.

You might have the same treatment that you had previously if you coped well with it and had a good response to it. Your doctor might suggest a different treatment, particularly if your CLL **relapsed** quickly after your last treatment. For example, you might have a different chemo-immunotherapy regimen.

Newer targeted treatments might be available for relapsed or refractory CLL.

Research and targeted treatments

Newer targeted treatments are often available first for people with relapsed and refractory lymphoma. For CLL, targeted treatments are also beginning to be used as a first treatment, particularly for people with high-risk genetic mutations.

There are several targeted treatments already approved for CLL and many clinical trials testing new treatments for this type of lymphoma. Our newer drugs page has the latest information on drugs available for CLL and other types of lymphoma. You can also search our clinical trials information service, **Lymphoma TrialsLink**, to find clinical trials currently open in the UK for people with CLL.

At the time of writing, the following targeted treatments are approved for some people with CLL and might be available on the NHS in some parts of the UK although the funding available varies. Your medical team can give you more information about treatments that might be suitable for you.

Ibrutinib

Ibrutinib is a cell signal blocker. It blocks signals that B cells send to help them stay alive and divide.

- It is given on its own as a first-line treatment for people with high-risk genetic mutations.
- For relapsed or refractory CLL, it is usually given on its own, but within clinical trials it is being combined with other drugs including **rituximab** and **venetoclax**.

Idelalisib

Idelalisib is also a cell signal blocker. It is approved for:

- first-line treatment of people with high-risk genetic mutations
- in combination with **antibody treatment** for people with relapsed or refractory CLL.

Obinutuzumab

Obinutuzumab is a newer antibody that attaches to the same target as rituximab does, a protein called 'CD20'. It is approved for use with chlorambucil as a first treatment for people who can't have fludarabine.

Ofatumumab

Ofatumumab is also a newer antibody to CD20. It is approved:

- with chlorambucil or bendamustine chemotherapy as a first treatment for people who can't have fludarabine
- for people with CLL who have had other treatments.

Venetoclax

Venetoclax blocks proteins that help lymphoma cells survive. This can make the lymphoma cells die.

- It can be given with rituximab for people with CLL that has not responded (refractory) or has come back (relapsed) after previous treatment.
- It can be given on its own for people with high-risk genetic mutations who cannot have a cell signal blocker or have not responded to a cell signal blocker, or to people who have not responded to previous therapy with a cell signal blocker and chemo-immunotherapy.

Transformation

Rarely, CLL **transforms** (changes) into a more aggressive type of lymphoma, usually **diffuse large B-cell lymphoma** (DLBCL). This is known as 'Richter syndrome'. Evidence suggests up to 1 in every 100 people with CLL develop Richter syndrome each year.

As part of your **follow-up**, your medical team check for signs of transformation. These include:

- fast growing lymph nodes or masses in your body
- a change in your symptoms, for example **B symptoms** (weight loss, night sweats, fevers)
- an increase in certain chemicals measured in **blood tests**, for example lactate dehydrogenase (LDH) or calcium.

Tests such as a **biopsy** and a **PET** or **CT scan** might be done if your doctor suspects your CLL has transformed.

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 **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 are given treatment to control your symptoms.

Living with CLL

Most people live with CLL for many years. For some people, having CLL does not affect their life expectancy, but it can affect their quality of life. Issues such as chronic fatigue and recurrent infections are more common in people with CLL than in the general population.

It is important that you discuss these issues with your medical team. Although **fatigue** can be very challenging, there are things you can do to help manage it. Seek medical advice promptly if you have any **symptoms of infection** as it is important that you get early treatment with antibiotics and anti-viral drugs.

Some people have **immunoglobulin replacement therapy**, where you have infusions (drips) that include donor antibodies to reduce the number of infections you have. People with CLL and **MBL** should have **vaccinations** against influenza (flu) and pneumonia. You should not have live vaccines, such as the shingles/zoster vaccine as this can cause problems for people with a weakened immune system.

We have more information covering many aspects of **living with a chronic condition** like CLL.

We also offer a range of **support services** to help you live your life with CLL. We also have a Live your Life programme of free support, events and activities for people with a lymphoma diagnosis and their family, carers or friends.

HealthTalk have a range of videos of people talking about their experiences of CLL that you might find useful.

Our **list of organisations** that offer support and information for people with lymphoma might also be useful. The following organisations offer support and information that is particularly relevant for people with CLL:

- **The CLL Support Association**
- **Leukaemia CARE.**

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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