

Low-grade non-Hodgkin lymphoma

Follicular lymphoma

Chronic lymphocytic leukaemia

Small lymphocytic lymphoma

Mantle cell lymphoma

Marginal zone lymphomas

Cutaneous (skin) lymphoma

Lymphoplasmacytic lymphoma

Waldenström's macroglobulinaemia



About this book

Low-grade non-Hodgkin lymphomas (NHLs) are a slow-growing type of lymphoma.

This booklet tells you what low-grade NHL is, and how it is diagnosed and treated. It offers tips on coping well and there is space for you to make notes.

The booklet is divided into parts. You can dip in and out of it and read only the sections relevant to you at any given time.

Important and summary points are set to the section colour font.



Lists practical tips.



Space for questions and notes.



Signposts to other resources you might find relevant.

This booklet uses some scientific words. Words that are in **orange bold** are explained in the Glossary on pages 137–139.

The information in this booklet can be made available in large print.



Your lymphoma type and stage

Your treatment

Health professional	Name and contact details
GP	
Consultant haematologist/ oncologist	
Key worker	
Clinical nurse specialist	

Acknowledgements

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Overview

Lymphoma is a cancer of the lymphatic system. The cancerous cells are **lymphocytes** – a type of **white blood cell** that fights infection. Lymphoma can develop when lymphocytes do not die, divide or grow properly. There are lots of different types of lymphoma. Low-grade non-Hodgkin lymphomas (NHLs) are slow-growing types that usually develop from abnormal B lymphocytes (B cells).

Lymphoma can develop anywhere in your body, so there are many different possible symptoms. It is most common to have swollen **lymph nodes** (glands) with no or few other symptoms. Some people have no symptoms when they are diagnosed.

How is it diagnosed?

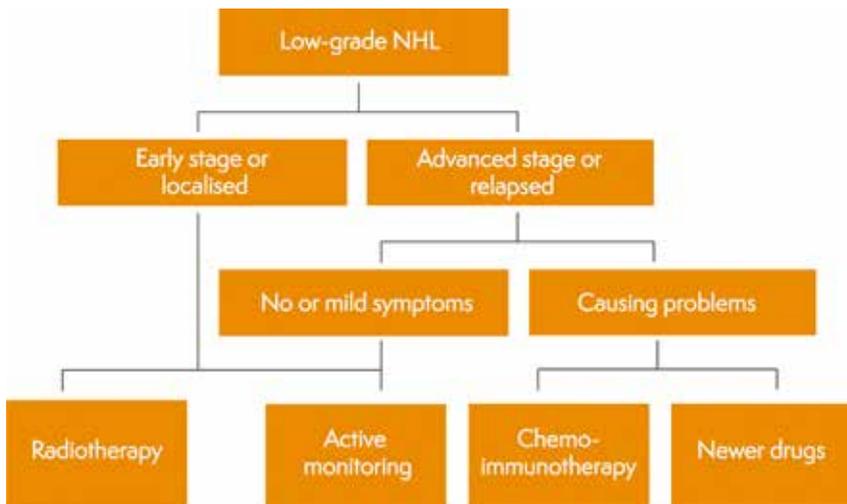
Low-grade NHL can be difficult to diagnose as the symptoms develop slowly and are similar to other conditions. Most people have a **biopsy** as part of diagnosis. You have other tests, too. Blood tests and scans can tell more about how your body is affected by lymphoma and about your general health. Some people have tests to look for lymphoma in certain parts of the body, for example, a **bone marrow** biopsy.

How is it treated?

If your lymphoma is early-stage (localised), radiotherapy to the affected area can sometimes cure the lymphoma. Most

people have advanced-stage (widespread) lymphoma, which is difficult to cure. Treatment aims to control the lymphoma and you might have several courses of treatment over the years. People with low-grade NHL often live with their lymphoma for many years and can have a normal life expectancy. Many people spend much of this time off treatment or on very gentle treatments. Some people never need treatment.

If you do not need to start treatment straightaway, you might have regular check-ups – active monitoring (or ‘watch and wait’). Some people have a short course of an **antibody** treatment (usually rituximab), then go onto active monitoring. If your lymphoma is causing problems, treatment is started, usually chemo-immunotherapy (chemotherapy with antibody therapy) but many newer drugs are becoming available.





I felt numb but not surprised when I was diagnosed. No amount of preparation for the news actually helped. I knew there were many questions I needed to ask, and yet, in that instant, I could not think of a single one.

Julian, diagnosed with nodal marginal zone lymphoma at 66

What is lymphoma?

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What is the lymphatic system?

The lymphatic system is part of your immune system – your body's natural defence against infection. A network of tubes called lymph vessels and **lymph nodes** (glands) runs throughout your body. The lymphatic system also includes organs that are part of your **immune system**, such as the **spleen** and **thymus**.

White blood cells called **lymphocytes** help your body fight infection. They collect in your lymph nodes. Some groups of lymph nodes are easy to feel, particularly in your neck, under your arms and in your groin. Others are deeper inside your body and can only be seen on scans.

What is lymphoma?

Lymphoma can happen when lymphocytes start to grow in an abnormal, uncontrolled way.

Lymphoma is not just one disease. There are many different types of lymphoma, but they all start with a cancerous lymphocyte.

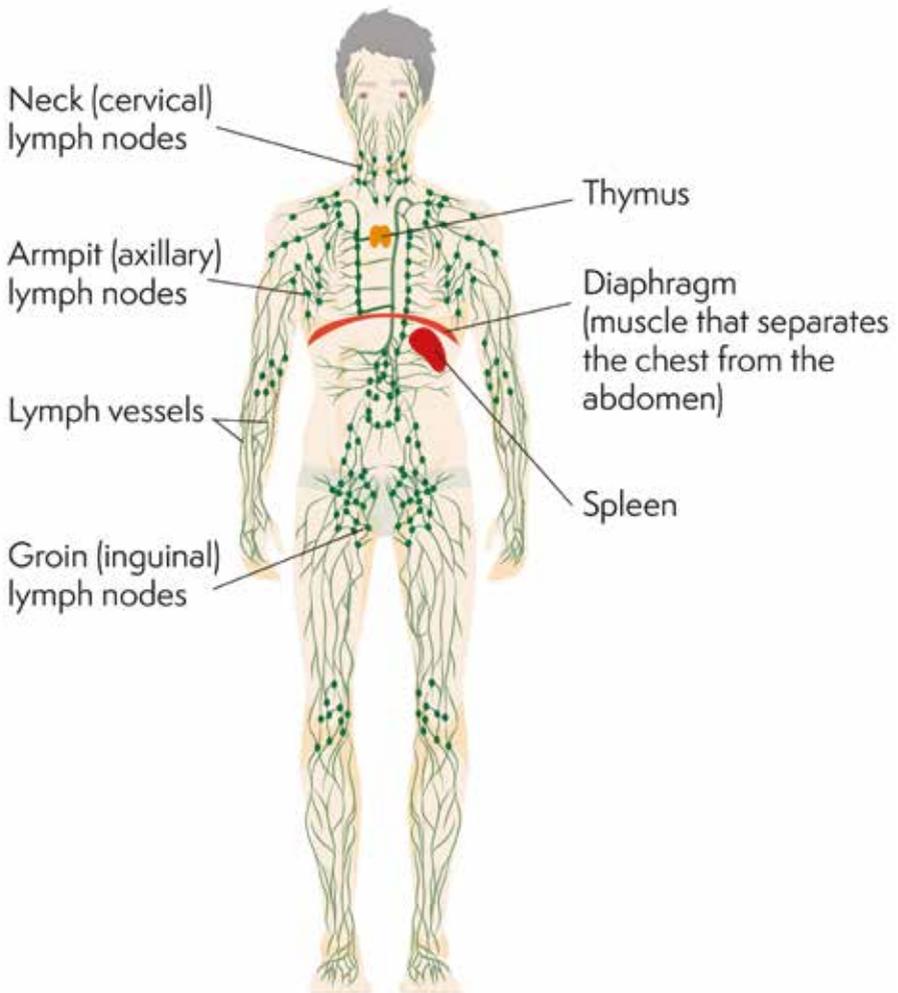


Figure: The lymphatic system

How do lymphomas develop?

Lymphocytes are always dividing to make new cells. When you are fighting an infection, your body makes many new lymphocytes very quickly. Many types of lymphocytes are produced, but only those that help to fight the infection are useful to the immune system. Any lymphocytes that do not target that infection usually die and only the useful lymphocytes survive. This process is carefully controlled by your body. Lymphoma can develop when this carefully controlled system breaks down.

Genetic changes in cells can mean they no longer respond properly to signals in the body. The cells might divide when they don't need to or might not die when they should. This breakdown in control lets abnormal lymphocytes build up and they can form a lump. This lump is lymphoma.

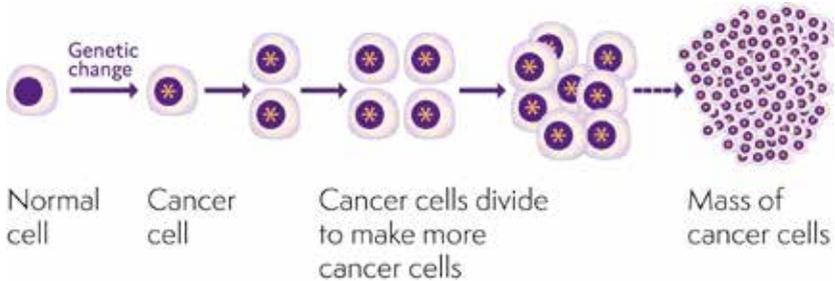


Figure: How cancer develops

Lymphoma most commonly develops in the lymph nodes.

Abnormal lymphocytes may also collect in other parts of the body, such as the spleen, liver and bone marrow. Lymphoma that grows outside the lymphatic system is called '**extranodal**'.

What types of lymphoma are there?

There are more than 60 different types of lymphoma.

The simplest distinction is between Hodgkin lymphomas and non-Hodgkin lymphomas (NHL), depending on the types of cell they contain. NHL can be further grouped as:

- B-cell lymphomas (which develop from B cells) or T-cell lymphomas (which develop from T cells).
- High-grade (fast-growing or aggressive) or low-grade (slow-growing or indolent) lymphomas.

There are lots of types of lymphoma within each group.

Each type of lymphoma behaves differently and may need specific treatment. It is important that you know what type of lymphoma you have so you can find information that is relevant to you. Ask your medical team to write your type of lymphoma in the section at the front of this booklet.

There is more about the different types on pages 120–136.

What is 'B-cell' or 'T-cell' non-Hodgkin lymphoma?

B cells and T cells are the main types of lymphocyte.

Both types of lymphocyte are made in the **bone marrow**. B cells also mature in the bone marrow, but T cells mature in the thymus (a gland in your chest). Both types then live mainly in your lymph nodes and other lymphatic tissues, ready to fight infection.

B cells and T cells have different roles in the immune system:

- B cells respond to infections by producing **antibodies** that attach themselves to substances not normally found in the body, for example bacteria, and attract other parts of the immune system to destroy the 'invader'.
- T cells can become several different types of T cell. They can attack 'invaders' like viruses and cancer directly.

There is another type of lymphocyte called a natural killer (NK) cell. These are like T cells, except they do not develop in the thymus. They kill cells that have been infected by a virus or are turning into cancer.

Most low-grade NHLs diagnosed in the UK are B-cell lymphomas. T-cell lymphomas are usually high-grade or fast growing.

What does 'low-grade' mean?

'Low-grade' means the cancer cells are dividing slowly, so low-grade lymphomas are slow-growing or 'indolent'.

Some people have low-grade NHL for years before it is diagnosed.

I was only diagnosed with lymphoma because of a diagnosis of something else. I had a CT scan, which revealed large lymph nodes all over the body.

Michael, diagnosed with small lymphocytic lymphoma (SLL) at 62



What causes lymphoma?

In most cases, lymphoma has no known cause.

Scientists do know that:

- You are unlikely to have done anything to cause the lymphoma.
- You did not catch your lymphoma from anyone and you can't pass it on to someone else.

Anyone can develop lymphoma, but the risk is higher for people whose immune system does not work well (known as 'immunodeficiency'). For example, lymphoma is more common in people who have HIV or people who have had an organ transplant.

Some types of lymphoma (pages 120–136) are linked with certain infections or autoimmune conditions (where your immune system attacks your own body).

What are the symptoms of lymphoma?

Lymphoma can be difficult to diagnose as many of the symptoms of lymphoma are seen in other, less serious conditions.

People with the same type of lymphoma can have different symptoms to each other. Some people with low-grade NHL have no symptoms when they are first diagnosed. The lymphoma might be picked up by chance on a test for something else.



I felt absolutely fine – I had no suspicion at all that anything was wrong with me. I went for a routine mammogram where they noticed enlarged lymph nodes under my armpits.

Pat, diagnosed with follicular lymphoma at 56

People with low-grade NHL often have mild symptoms.

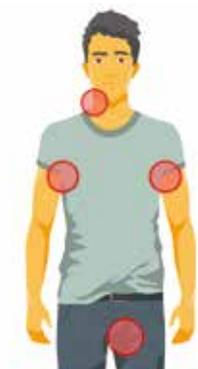
Some symptoms are common to many types of cancer, for example fatigue (extreme tiredness). Cancer cells take up energy and nutrients that healthy cells need, so people often feel very tired.

I told my GP about the lump in my neck and that I had been feeling tired and when she prodded my abdomen it felt really tender. Up until this point it had not occurred to me – or I did not want it to occur to me – that there was something wrong.

Debbie, diagnosed with follicular lymphoma at 45

Lymph nodes swell when lymphocytes collect to fight an infection, but this swelling, which can be painful, usually goes down in a couple of weeks.

The most common symptom of lymphoma is a painless lump that does not go away.



Swollen lymph nodes – often in the neck, armpit or groin. Not all lymphomas have obvious lumps. Sometimes lumps are deep inside where you can't feel them.

Other common symptoms include:



Fatigue (extreme tiredness)



Unexplained weight loss
(without dieting)



Drenching sweats
(especially at night)



Itching (with or without
a rash)

Some people get fevers. Fevers often occur together with night sweats and weight loss. They can occur separately. These three symptoms are known as 'B symptoms'. Some people have repeated or persistent infections (infections they can't shake off).

If lymphoma develops outside of the lymph nodes, for example in the stomach, lungs, skin or brain, you might not have a lump that you can feel. You might have other symptoms. The symptoms you are likely to get depend on where the lymphoma is. For example, lymphoma can cause:

- abdominal (tummy) pain or back pain
- diarrhoea or change in bowel habit
- jaundice (yellowing of the skin and whites of the eyes)
- a persistent cough or breathlessness.

You might have different symptoms or a combination of symptoms.

There is no single symptom that is unique to lymphoma – most people have a mixture of symptoms.

My memory started to go. I was getting increasingly sleepy in the afternoons and very, very out of breath. It took about 6 months to get a diagnosis.

Roger, diagnosed with Waldenström's macroglobulinaemia at 54





After my diagnosis, I started doing all those things you never get around to, and accomplished far more than I would have done otherwise. Maybe it was being busy that helped me come to terms with the lymphoma, but all I could do was deal with it in the best way for me. I felt I was on borrowed time. That was 14 years ago.

Pat, diagnosed with follicular lymphoma at 56

Tests, scans and staging

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This section describes the most common tests for lymphoma. You may not have them all – your doctor decides what tests you need. You may have some of these tests after you are diagnosed to find out more about the lymphoma and how it is affecting you. You also have tests and scans during your treatment and afterwards. You can come back to this section whenever it is relevant to you.

Being diagnosed

Getting a diagnosis means finding out what is wrong. You need tests at a hospital to confirm you have lymphoma. This should usually include a biopsy of an abnormal lump. For some types of lymphoma, abnormal cells are taken from other places, like your bone marrow. You are likely to have other tests, too.



Following a bone marrow biopsy I was diagnosed with follicular lymphoma – I had never even heard these words before! For me the really frightening thing was the word ‘cancer’.

Malcolm, diagnosed with follicular lymphoma at 60

It can take a couple of weeks to get the results of all the tests. This can be a worrying time, but it is important that your doctors find out as much as possible about your lymphoma so they can give you the best treatment.

They want to find out:

- what type of lymphoma you have (see pages 120–136)
- the stage of your lymphoma (how much of your body is affected – see page 32)
- how the lymphoma is affecting you and make sure you are fit enough for the treatment they recommend.

Blood tests

You have blood tests as part of your diagnosis, at regular intervals during treatment or monitoring and during your follow-up. Blood tests help doctors check your general health and assess how your lymphoma is affecting you. They can help doctors decide when you need treatment, what treatment you are fit enough to have and whether you have any health conditions that mean you might need additional treatments to support your body.

During treatment, blood tests also help to find out how well your body is tolerating the treatment. These tests can help doctors decide when it is safe for you to have the next dose of treatment and if you need any treatment for side effects (unwanted effects of your lymphoma treatment). A blood test alone very rarely tells you if lymphoma is present.

Biopsy

In this test, a doctor removes a sample of the abnormal

tissue (for example, a lymph node) for examination under a microscope and other tests. For most people, a biopsy is the only way to tell whether or not a lump is lymphoma.

What happens?

Most biopsies are done as outpatient procedures under local or general anaesthetic, so you can go home the same day. You might have to stay in hospital overnight.

The type of biopsy that you are offered depends on what is standard practice at your hospital and where the abnormal tissue is. You might have:

- an **excision biopsy**, where the surgeon removes a whole lymph node
- a **core biopsy**, where a radiologist removes a small sample of the lymph node using scans to guide them.

If the affected lymph nodes are deep inside your body, the surgeon or radiologist may remove all or part of a node using laparoscopic surgery (keyhole surgery) or by endoscopy (thin tube with a camera passed through the mouth).

The biopsy is examined under a microscope by a pathologist (a doctor who studies diseased tissues under a microscope). They do tests on the cells to find out exactly what type of lymphoma you have. These tests give more information about the cells, for instance, about changes to their DNA or to the proteins on their surface. The results usually take around a

week to come back, but can take longer if the lymphoma is rare or difficult to diagnose. Occasionally, a second biopsy is needed to give enough information to make a diagnosis.

X-rays and scans

There are lots of lymph nodes deep inside your body and there are parts of your body that can't be seen from the outside. X-rays and scans (see pages 26–29) are used by doctors to assess what parts of your body are affected by lymphoma. There are different types of scans that build up images in different ways, for example:

- X-rays and **CT** or **CAT scans** use X-rays
- an **MRI** uses magnetic waves
- a **PET** uses radioactive sugar to identify active cells, such as cancer cells, and is usually combined with a CT scan as a single scan
- an **ultrasound** uses sound waves.

Some scans are better than others at assessing different parts of your body. Don't worry if you have a different type of scan to someone else – your doctor decides which type of scan is best for your circumstances. You may need more than one type.

X-rays and scans don't hurt and are usually done on an outpatient basis, so you can go home after your test.

X-rays

X-rays are used to look at various parts of your body. For example, you may have a chest X-ray to see if there are any enlarged lymph nodes in your chest. You don't feel anything during the test, and it should only take a few minutes.

CT or CAT scans

Computed tomography (CT) or **computed axial tomography (CAT) scans** use a series of X-rays to form pictures of your body in cross-section (image 'slices' through your body).

Most people have a special liquid dye (a contrast agent) that makes organs easier to see. You have it before the scan either as a drink or an injection into a vein. The dye might make you feel hot all over your body, but this usually only lasts a few minutes. Tell the staff if you feel this way.

To have the scan, you lie on a padded table that moves your body through a camera that is shaped like a ring doughnut. The space is quite open so you shouldn't feel 'hemmed in' or claustrophobic. The scan can take 5–45 minutes depending what area is scanned, but preparation can take longer if you are having the special dye. You need to lie still and you might be asked to hold your breath for up to 20 seconds at a time.

PET scans

Positron-emission tomography (PET) scans help doctors tell the difference between scar tissue and growing lymphoma.

They use a radioactive form of sugar to look at how active the cells are. More active cells, like cancer cells, take up more sugar than normal cells. The radioactivity in the cancer cells is then detected with a special camera.

A PET scan is normally combined with a CT scan in a single scan. The PET scan looks at activity of the cells; the CT scan gives a more detailed picture of structures inside your body.

When you arrive at the clinic, you have the radioactive sugar as an injection into a vein. You then have to rest for an hour or more while the cells take up the sugar. The scan is similar to a CT but you have to be in hospital for around 2–3 hours in total to have the radioactive sugar.



Stock photo. Posed by model

Figure: A PET scan

You may have a PET/CT scan as part of diagnosis and to check how well your treatment has worked. Some people have PET/CT scans during treatment to find out how well the treatment is working. Doctors continue to learn how best to use these scans, but they are increasingly important in assessing lymphoma.

MRI scans

Magnetic resonance imaging (MRI) scans are particularly good for looking at soft tissues, such as the brain.



© The Royal Marsden NHS Foundation Trust

Figure: An MRI scan

To have the scan, you lie on a padded table that moves you into a cylinder (tube). The cylinder uses a strong magnet. Tell the staff if you have any metal implants, such as a pacemaker or an artificial joint. You should also mention any recent operations, including your biopsy, as surgeons sometimes use metal staples instead of stitches to close the wound.

The scan normally takes 30–60 minutes. The scanner can be very noisy and, as you are in a small space, you may feel 'hemmed in' or claustrophobic. Let the staff know if you are worried about this or anything else relating to having an MRI.



Tips about scans

- Read and follow any instructions carefully, for example you might be asked not to eat or exercise before your scan.
- Tell your medical team about any other conditions you have – you might not be able to have contrast dye with some medical conditions. If you have diabetes, your doctor needs to take special care with a PET scan.
- Ask what you should wear and if you need to remove any jewellery.
- Ask if you can listen to music during the scan.
- Talk to the staff in the department if you are worried about anything regarding your X-ray or scan.

Bone marrow biopsy

If your doctor thinks lymphoma might be in your bone marrow, you might have a bone marrow biopsy.

What happens?

In a bone marrow biopsy, a sample of bone marrow, usually from your hip, is removed and looked at under a microscope.

Bone marrow tests are usually done as an outpatient.

You have the area numbed with a local anaesthetic. Then the doctor passes the biopsy needle through the skin and into the bone. Two types of bone marrow sample are usually taken:

- **bone marrow aspirate**, which is a little of the liquid found in the bone marrow space
- **bone marrow trephine**, which is a small sample of harder bone marrow tissue.

The procedure can be uncomfortable. You may need painkillers before and after your bone marrow test. If you are very anxious, it may be possible for you to have a mild sedative beforehand or gas and air (oxygen and nitrous oxide) during the procedure. Sedatives aren't recommended for everyone so ask about this when you're told you need the test.

Questions about tests and scans

- What tests do I need and why?
- Are the tests painful?
- Do I need an anaesthetic or sedation for any of these tests?
- Where or when will I have the tests?
- Is there anything I need to be careful of after the test?
- Can I drive? Can I go back to work straightaway?
- How long before I get the results?
- Will someone explain the test results to me?



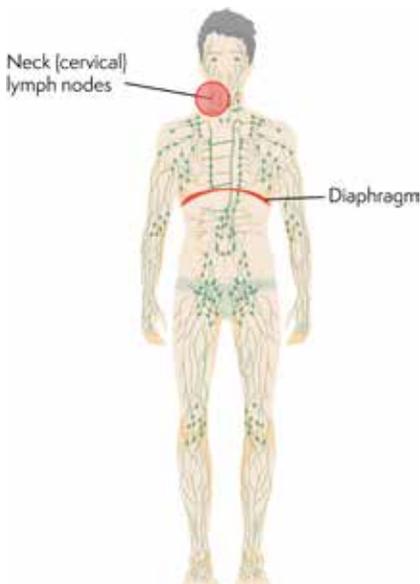
Notes

What does 'stage' mean?

Once all the test results are ready, your doctor can tell where the lymphoma is in your body. This is the 'stage' of your lymphoma. It is important in planning your treatment. For most types of NHL, the different stages are:

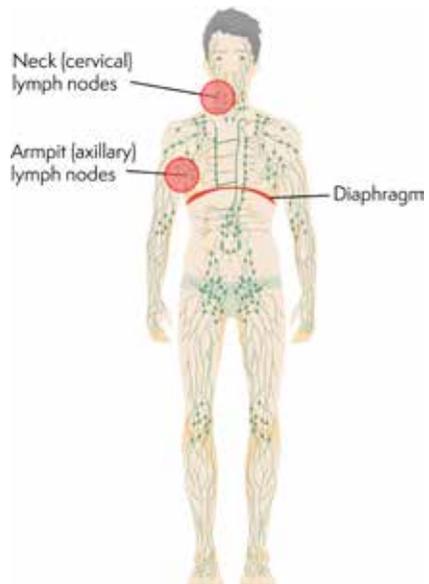
Stage 1

One group of lymph nodes affected either above or below the diaphragm*



Stage 2

Two or more groups of lymph nodes affected either above or below the diaphragm*

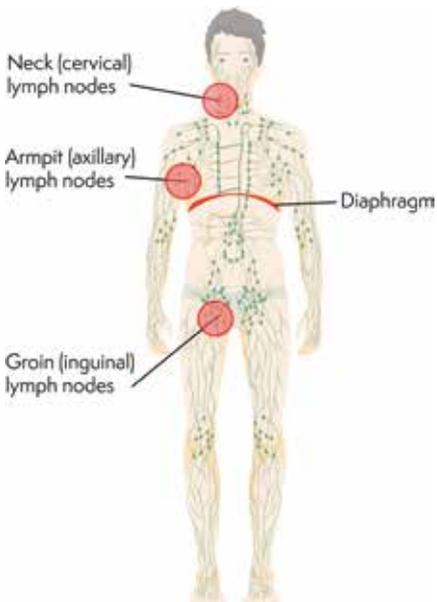


You may see stages of lymphoma written down as Roman numerals: I, II, III, IV.

* the diaphragm illustrated on pages 32 and 33 is the muscle that separates the chest from the abdomen

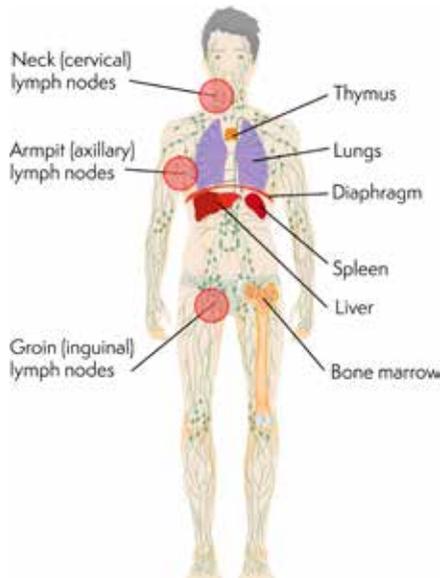
Stage 3

Lymph nodes affected on both sides of the diaphragm*



Stage 4

Lymphoma is found in organs outside the lymphatic system or in the bone marrow



Letters might be added to the stage:

A	You don't have any B symptoms (fevers, night sweats and weight loss)
B	You have one or more of the B symptoms (weight loss, night sweats or fevers)
E	You have extranodal lymphoma – lymphoma outside your lymphatic system but localised (stage 1E or 2E)
X	You have bulky disease – you have very enlarged lymph nodes in one or more areas. These areas may need extra treatment.

Some types of lymphoma, for example chronic lymphocytic leukaemia (CLL), are staged differently. In general, a higher stage number means the lymphoma is more widespread.

Ask your medical team to write your type and stage of lymphoma at the front of this booklet so you can find it easily.

Grading of follicular lymphoma

People with follicular lymphoma might be given a numbered grade as well as a stage: grade 1, 2, 3A and 3B. The grade relates to the number of large follicular cells that can be seen under a microscope, where grade 1 is the lowest and grade 3B is the highest. Grade 3B follicular lymphoma usually behaves

and is treated like a high-grade NHL, for example diffuse large B-cell lymphoma.

What do 'early-stage' and 'advanced-stage' mean?

Early-stage lymphoma is localised lymphoma. Stage 1 and some stage 2 lymphomas are early-stage.

Advanced-stage lymphoma is more widespread lymphoma. Stage 3 and 4 lymphomas are advanced-stage. Some stage 2 lymphomas are grouped as advanced-stage, for example those with large lumps or that are causing symptoms.

The lymphatic system covers the whole body so it is common for lymphoma to be found in several places.

Most people with low-grade NHL have advanced-stage lymphoma when it is diagnosed. There are good treatments for lymphoma at all stages.



Although a long time ago, I can still clearly recall the shock of being told I had an incurable and rare type of lymphoma.

Ashley, diagnosed with mycosis fungoides (cutaneous T-cell (skin) lymphoma) more than 45 years ago at 17

How is low-grade NHL treated?

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Planning treatment

Once your doctors have the results of all the tests, they have the information they need to decide if you need treatment straightaway and, if so, what treatment would be best for you. They base their recommendations on several factors, including:

- the type of lymphoma you have
- the stage of your lymphoma
- what problems, if any, the lymphoma is causing.

Other important points that your doctors take into account include:

- your thoughts on treatment and what is important to you
- your general health and how fit you are
- any other medical conditions that are affecting you
- the size of any lumps of lymphoma and where they are
- your blood test results.

Some people with low-grade NHL do not need to start treatment straightaway. This does not mean you are not suitable for treatment, just that there is no advantage in treating the lymphoma until it is causing problems. Some people are monitored (pages 58–61) and never need treatment.

Completing the tests and planning your monitoring or treatment can take a few weeks. This might seem like a long time, but the information being collected is very important. Your doctor needs to know as much as possible about you and your illness. It is natural to feel worried when you are waiting to find out more or waiting to start treatment. You may find it helpful to talk about it to someone, for example a specialist nurse, your GP or a Lymphoma Action buddy.

People with the same type of lymphoma often have different treatments. Don't be worried if the people you talk to at the hospital are having treatments different from yours. Your treatment is tailored to you.

Who is involved in my care?

You have a lead consultant responsible for your care – this is likely to be a haematologist (a doctor who specialises in treating blood problems) or an oncologist (a doctor who specialises in treating cancer). You see other doctors who work with your consultant as well.

Your case is likely to be discussed in a multidisciplinary team (MDT) meeting, where several specialists discuss the best treatment for you based on your test results and individual circumstances.

Your hospital might have a clinical nurse specialist (CNS) or other specialist cancer nurse who is experienced in working with people with lymphoma.

You will see a range of different health professionals specialised in different areas. Use the table at the front of the booklet to keep track of them.

Where will I be treated?

You may have your treatment at a local hospital or at a larger hospital with a cancer centre. Sometimes people have their treatment shared between places ('shared care' arrangement).

Your GP, or the doctor who diagnoses your lymphoma, should send you to the nearest hospital with a lymphoma specialist.

Children and young people with lymphoma are usually treated by specialists at a children and young people's cancer centre known as a Principal Treatment Centre (PTC). Young people's care may also be shared with a local designated teenage and young adult hospital, with guidance from the PTC.



We have a booklet specially designed for young people with lymphoma. We also have specific information for under-25s on our website. Find out more at www.lymphoma-action.org.uk or call our Information and Support Team on 0808 808 5555.

Most people with low-grade NHL have most or all of their treatment as an outpatient, meaning you are unlikely to have to stay in hospital overnight.

You may have to stay in hospital for some of your treatment or if you have problems, for example, infections. It can help to find out what facilities are available and to ask what you can bring with you to make your stay more comfortable.

Ask all the questions you have about your hospital and how your care is going to be arranged.

Aims of treatment

The aim of your treatment depends on several factors, including what type of lymphoma you have, what stage it is at and your general health and fitness.

Your doctor is likely to talk about 'remission' rather than 'cure':

- remission is when the lymphoma has been controlled by the treatment
- cure is when the treatment gets rid of the lymphoma so it won't come back.

If you are in remission and your lymphoma never **relapses** (comes back), you are 'cured'. However, low-grade NHL is difficult to get rid of permanently. The majority of cancer

treatments are most effective at killing fast growing cells. As low-grade lymphoma cells grow slowly, they are less susceptible to treatment and some lymphoma cells may remain after treatment. These cells can build up and cause a relapse.

As relapse is likely, doctors aim to put low-grade NHL into remission for as long as possible, rather than cure it.

You can have different degrees of response to treatment, for example:

- A **complete response** means there is no sign of lymphoma on scans or in the blood or bone marrow after treatment.
- A **partial response** means the lymphoma has shrunk by at least half.

Early-stage low-grade NHL

Early-stage low-grade NHL is localised to just one or a few groups of lymph nodes close together or in one part of the body. Treatment can sometimes be localised just to this area. Some people with early-stage low-grade NHL are treated with the aim of curing the lymphoma. The longer you stay in remission after treatment for early-stage low-grade NHL, the more likely it is that you are cured.

Advanced-stage low-grade NHL

Most people with low-grade NHL have advanced-stage lymphoma when they are diagnosed. 'Advanced' doesn't mean

'untreatable' – just that the lymphoma is affecting several groups of lymph nodes or several areas of the body.

Most people with advanced-stage low-grade NHL live for many years with their lymphoma, and may need treatment from time-to-time.

Advanced-stage low-grade NHL usually behaves like a chronic (long-term) illness. Treatment usually puts the lymphoma into remission for a time. When it relapses, it needs another course of treatment. This is sometimes known as a 'relapsing and remitting' course of disease. Treatment options for low-grade NHL are increasing and the lymphoma can usually be kept under control for many years even if it needs several courses of treatment.

Treatment usually aims to keep the lymphoma under control for as long as possible with as few side effects as possible.



A diagnosis isn't necessarily as bad as it may seem at first and often it can be dealt with. It is now 27 years since I was first diagnosed and I have had eight courses of treatment. There were times when I would sit and think about the lymphoma but on the whole I just make every day count. I always had a zest for life and still have today.

Carole, diagnosed with follicular lymphoma at 37

Questions to ask about hospital and your medical team

- Does the hospital have a lymphoma clinical nurse specialist or other specialist cancer nurse?
- Does my doctor meet regularly with other lymphoma specialists?
- What other experts are there to help if I need them? For example, can I meet with a dietitian or a counsellor if I need to?
- Does the hospital take part in clinical trials?
- How can I access a clinical trial that might help me?
- What facilities and support are available at the hospital and in the local community?



Notes

What is the usual treatment for low-grade NHL?

Treatment for low-grade NHL is planned individually so you might have different treatment to someone else with the same type of lymphoma.

There are lots of possible treatments for low-grade NHL and the treatment recommended for you depends on lots of factors, including:

- What stage your lymphoma is and how the lymphoma is affecting you.
- What type of lymphoma you have: some treatments work better for some types of lymphoma than for others.
- Whether this is your first treatment or your lymphoma has relapsed: some treatments are recommended for first-line treatment, others only for **relapsed** or **refractory** lymphoma. See page 101 for more about considerations when you relapse.
- Side effects and safety: some treatments are more likely to cause side effects than others or can't be given if you have certain medical conditions. Your doctor has to weigh up the risks and benefits of any treatment they recommend.
- How quickly you need treatment: some treatments work more quickly than others. You might need quick treatment if your lymphoma is causing serious problems.
- Convenience and your preferences: some treatments need more regular hospital visits than others, and you might need to stay in hospital for some types of treatment.

This section gives an overview of the likely treatments for different situations. There is more about each type of treatment on pages 57–93. Treatment for relapsed low-grade NHL is described on pages 102–103.

Treatment for early-stage low-grade NHL

If the lymphoma is localised (in one area or in areas close together) and is not too large, you are likely to be treated with radiotherapy to the affected area. You are then followed-up closely to check for relapse. If your lymphoma does relapse, the treatments described for advanced-stage low-grade NHL are likely to be used.

If you can't have radiotherapy, for example because the affected areas are too far apart or too large, your treatment is likely to depend on how the lymphoma is affecting you:

- If you are well, you might have active monitoring ('watch and wait') until you need treatment.
- If the lymphoma is causing problems for you, you are likely to be treated as for advanced-stage low grade NHL.



My scan showed that the disease was confined to my neck, armpit and just above my collar bone. I was stage 2A with no symptoms and I was in good general health so my medical team recommended radiotherapy.

Julian, diagnosed with nodal marginal zone lymphoma at 66

Treatment for advanced-stage low-grade NHL

If you have advanced-stage low-grade NHL, but the lymphoma is not causing problems, you might have:

- active monitoring until you need treatment (see pages 58–61)
- a short course of an **antibody** treatment (for example rituximab), which can help to delay the time until you need more treatment.

If only one area of lymphoma is causing problems, you might have radiotherapy to that area. This can shrink the lymphoma in that area and reduce symptoms. You then have a period of active monitoring.

When you need more treatment, for example because of troublesome symptoms, most people with low-grade NHL have chemo-immunotherapy (chemotherapy with antibody treatment).

People with some types of lymphoma then have maintenance treatment. For maintenance treatment, you are given antibody treatment every 2–3 months, usually for up to 2 years.

Maintenance treatment helps to keep the lymphoma under control and reduce the risk of relapse.

Some types of low-grade NHL are linked to infections and treating the infection can clear the lymphoma. Others are restricted only to the skin and might respond to topical treatment (treatment applied to the skin). Read more about your type of lymphoma on pages 120–136.

Lymphoma treatments with other conditions

Many people diagnosed with low-grade NHL are over 60. Other health problems become more common as people get older so some treatments may not be suitable.

Your doctors want to give you the most effective treatment for your lymphoma but they have to balance this against the risk of you developing serious side effects.

For example, some chemotherapy drugs can affect your heart so doctors may avoid those drugs if you have heart problems.

Your doctor may arrange for you to have organ function tests to make sure your heart, lungs and kidneys are working well,

for example an echocardiogram (a heart scan) or spirometry (a lung test).

Some people are not able to have as much treatment as those who are in better health. If you are over 60, your **bone marrow** may also take longer to recover after each cycle of chemotherapy. You might need lower doses or longer gaps between treatments. Some people have other treatments, such as growth factors (for example G-CSF), which boost blood counts and reduce the risk of side effects.

Some of the chemotherapy regimens offered for low-grade NHL are considered gentle forms of treatment and cause fewer side effects than more intensive regimens. Some of the newer targeted drugs may offer alternatives to standard chemotherapy. Some clinical trials look at the best ways to use these drugs. Ask your doctor if there is a suitable clinical trial for you.

You are advised not to get pregnant if you are having, or will soon start treatment for lymphoma. If you're already pregnant when you are diagnosed, your medical team will take this into account when planning your treatment. Ask your medical team to guide you.

www.lymphoma-action.org.uk/Pregnancy for more information on pregnancy and lymphoma.



Research and clinical trials

Your doctor may ask if you would like to take part in a clinical trial. Clinical trials are research studies involving human volunteers. Some trials are designed to test new treatments that haven't yet been tried in low-grade NHL. Others aim to improve treatments currently in use. They may test whether the lymphoma could be treated with newer targeted drugs instead of chemotherapy, for example. Taking part in a clinical trial is voluntary – you do not have to take part. If you do decide to take part in a clinical trial, you can change your mind at any time.



Find out more about clinical trials in our dedicated section at www.lymphoma-action.org.uk/TrialsLink. You can search for a trial that might be suitable for you, or download or request our *Clinical Trials* booklet.

What is transformation?

Usually, low-grade NHL is made up mainly of small, slow-growing lymphoma cells. Sometimes, the proportion of larger, faster-growing lymphoma cells increases. This is called transformation. Transformed lymphoma behaves like a high-grade lymphoma, such as diffuse large B-cell lymphoma (DLBCL).

Transformation can happen with many types of low-grade NHL but is most common in follicular lymphoma. Follicular lymphoma transforms in about 2–3 in every 100 people each year.

During any period of active monitoring or follow-up after treatment, your medical team are looking for signs of transformation. These might include:

- a change in your symptoms, for example, rapidly growing **lymph nodes** or organs (for example **spleen**), or development of **B symptoms**
- an increase in certain chemicals measured in blood tests, for example lactate dehydrogenase (LDH) or calcium.

If your doctor thinks your lymphoma might have transformed, they will do a **biopsy** to look for large, fast-growing cells in the abnormal tissue (for example, in the rapidly growing lymph node). They might do other tests too.

If your lymphoma does transform, it will need to be treated like a high-grade lymphoma. The most common treatment is chemo-immunotherapy, which might be followed with a **stem cell transplant** if you are fit enough. Even if the high-grade lymphoma is cleared by treatment, you might still have low-grade lymphoma cells remaining. These remaining cells can cause a relapse of low-grade lymphoma in the future.

Will my doctor help me make decisions about treatment?

You and your doctor can decide together what treatment is best for you.

Some types of lymphoma have a standard treatment that has been shown to give the best outcomes. If you are fit enough, your doctor is likely to recommend you go ahead with that treatment.

If you have other health conditions, or are generally less fit, your doctor might recommend a gentler treatment or adapt the treatment to make it safer for you. Such treatments may be associated with fewer or less severe side effects, and might be less likely to give you a long-lasting remission.

You might be offered a choice of treatments.

It can be difficult to weigh up the benefits and risks of the possible treatments, but it is important that whatever decision you make is the right one for you. Your doctor can help you weigh up the options and you can talk to other people, too. Consider your clinical nurse specialist, if you have one, your family and friends or your GP. Ask as many questions as you need to help you understand your options and to make a decision.

Questions about treatment

- What treatment am I having?
- What does the treatment involve?
- How long will it take for the treatment to work?
- How effective is this treatment? Will it cure the lymphoma?
- Would it be helpful to get a second opinion or be treated in another centre (especially for rarer lymphomas)?
- I have another illness – how will this affect my treatment?
- When will my treatment start?
- Where will I have my treatment? Do I need to come into hospital?
- How long will each treatment session last for?
- How many weeks or months will I be having treatment for?
- What happens if I decide I don't want any treatment?



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I was hoping the scan would show that the chemotherapy was working and there was some reduction in the lymphoma. I was told the scan was back to normal, which was flabbergasting.

Michael, diagnosed with small lymphocytic lymphoma (SLL) at 62

Treatments for low-grade NHL

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This section describes the types of treatment used for low-grade NHL, including active monitoring before or between treatments. Read only the sections that describe the types of treatment you are having. It can be confusing to read about types of treatment you are not likely to have. Ask your medical team for advice.

Active monitoring or ‘watch and wait’

Some people newly diagnosed with low-grade NHL do not start treatment straightaway. Instead, they have active monitoring, which is sometimes called ‘watch and wait’. You might also hear it called ‘active surveillance’. Other people have a period of active monitoring after treatment that reduces, but does not completely get rid of, the lymphoma.

“

I know much more now (in my second period of ‘watch and wait’) so I can put it into perspective and I realise that rushing into treatment that is not essential is not a good idea.

Maureen, diagnosed with follicular lymphoma at 69

Research suggests that for some types of low-grade NHL there is no benefit in treating the lymphoma before it is causing problems. Treatment is just as effective if it is only started when needed.

There are also several advantages to delaying treatment:

- you avoid the side effects of treatment
- you can reserve effective treatments for when they are really needed
- your lymphoma might remain stable for years or might never need treatment.

Not having treatment doesn't mean nothing is being done. Your medical team see you regularly to check for signs that you need to start treatment. You are likely to have appointments every few months. They will ask about any symptoms and how you are feeling and are likely to do blood tests. Your doctor might do other tests, for example scans, if needed. You should get in touch with your medical team if you have any problems between appointments. They can reassure you or see you sooner if necessary. You might need to start treatment if:

- your symptoms become too troublesome or you develop **B symptoms**
- your affected **lymph nodes** are growing quickly or in new places
- your blood test or other test results suggest your lymphoma is affecting your organs or **bone marrow**.

Other problems, such as a virus, can cause symptoms. It is also common for affected lymph nodes to grow slightly and shrink back again without treatment. Your doctor might want to keep a closer eye on you for a time to see if the symptoms settle down again.

As low-grade NHL grows slowly, there is rarely an urgent need for treatment to start.

Your medical team can give you more information about what to look out for and when to call them.

Some people find it difficult to have lymphoma and not have active treatment. It isn't because there is no suitable treatment for you but treatment is being reserved until the lymphoma is causing significant problems and your doctor thinks you need to start treatment.



Pages 107–119 have a brief overview about life with lymphoma. Our *Living with lymphoma* booklet can give you more practical advice on coping with your feelings. It also offers tips on changes you might want to consider to look after your general health and fitness while on active monitoring.

Questions to ask about active monitoring or 'watch and wait'

- Why don't I need treatment straightaway?
- Are there any risks in delaying treatment?
- How long might I be on active monitoring?
- How will you know when I need treatment?
- Is there anything I should look out for between appointments?
- Who should I contact if I have any concerns?
- Can I work, carry on with my hobbies and go on holiday while on active monitoring?
- What support is on offer at the hospital or from local groups?



Notes

Chemotherapy

Chemotherapy is treatment with drugs that kill cells. Chemotherapy drugs normally work best on cells that are dividing quickly – like cancer cells, but also blood cells and cells that line the gut. Each drug targets cells in a different way, so giving several drugs increases the chances of killing more cells. Chemotherapy regimens (combinations of drugs) are often known by the initials of the names of drugs they include – each letter stands for the name of a drug such as CVP (see page 66).

To kill as many cells as possible, chemotherapy is usually given in cycles.

A cycle is a block of chemotherapy that is followed by a rest period that allows the healthy cells to recover.

You have several treatment cycles, each of which takes a few weeks. With each treatment cycle, more cells are destroyed and the lymphoma gradually shrinks. The whole treatment course usually takes several months. The exact timetable for your treatment depends on the particular chemotherapy drugs you are having.

How is chemotherapy given?

Most people with low-grade NHL have chemotherapy as an outpatient; they go to the hospital on treatment days and go home afterwards. Some people stay in hospital for their

chemotherapy if they have a regimen that takes longer to give or that is more likely to cause severe side effects. Whatever type of treatment you are having, you may need to stay in hospital if you have severe side effects, for example, very low **blood counts** or an infection (see pages 67–73 for more on side effects).

Your medical team should give you specific information about your treatment plan and what to expect.

Intravenous chemotherapy

Many chemotherapy drugs are given **intravenously**.



A bolus or 'push' dose is where a drug is given by injection into your vein. This can take a few minutes.



Some intravenous drugs have to be given through a drip (**infusion**), which can take several hours.

Some people have a central line fitted, for example a Hickman® line or a peripherally inserted central catheter (PICC line). This is a tube that stays in place for the whole of your treatment so you don't need to have a needle every time you need treatment or a blood test. You might have a central line or peripheral line if you need intensive treatment or have problems having repeated needles into your veins.

The line is inserted either through a vein in your arm or directly into your chest during a small operation.

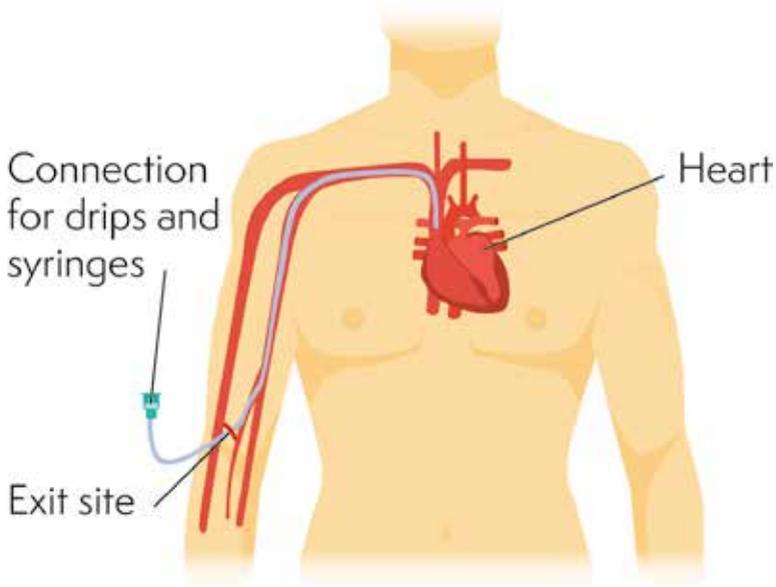


Figure: PICC line (inserted into arm)

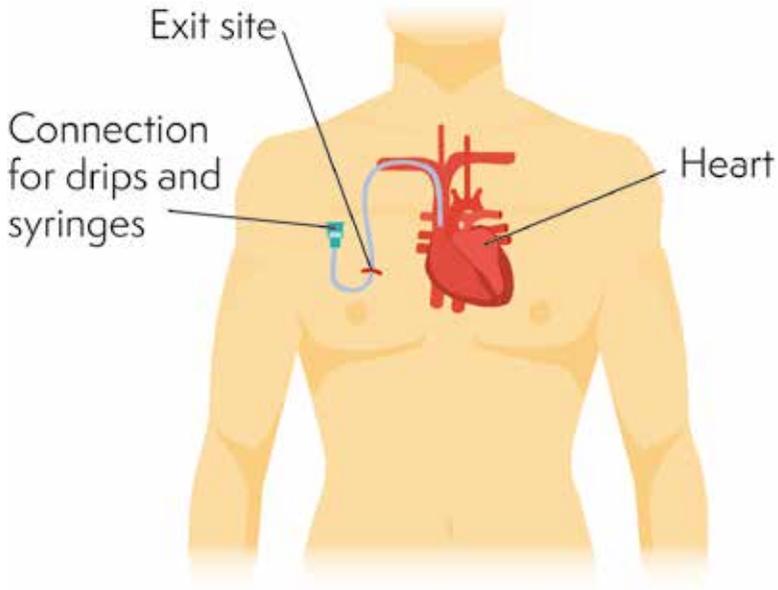


Figure: Central line (inserted into chest)

Your nurse should show you how to look after your line to help prevent infection and tell you what to do if you have any problems with it.

Some chemotherapy drugs can sting as they go into the vein. Tell your nurse if you have any discomfort as things can be done to relieve it.

Oral chemotherapy

Some chemotherapy for low-grade NHL is given as chemotherapy tablets or capsules that you take orally (by mouth), for example, chlorambucil. You are given instructions on what to take and when, and how to handle and store the drugs.

Oral chemotherapy drugs are often gentler than intravenous regimens.

CVP chemotherapy

The most common chemotherapy regimen for low-grade NHL is CVP:

- cyclophosphamide
- vincristine
- prednisolone.

It is usually given together with the antibody treatment rituximab, and is then known as R-CVP. There is more about rituximab on page 77.

CVP is usually given in cycles of 3 weeks for 6–8 cycles. Most people have this treatment in a day unit as an outpatient. You have two drugs intravenously on the first day of each cycle. You also take tablets for the first 5 days of each cycle – you can take these at home. The remainder of the cycle is a rest period for your body to recover before the next cycle begins.

You are likely to be given other drugs to help prevent side effects (supportive care – see pages 92–93).

Other chemotherapy regimens

Some types of low-grade NHL are treated with other chemotherapy regimens, for example:

- chlorambucil or bendamustine on their own or with rituximab
- CHOP, which includes the same drugs as CVP plus doxorubicin. It is usually given with rituximab; it is then called R-CHOP
- fludarabine, which is often given with cyclophosphamide and rituximab, as a regimen called 'FCR'.

There are many other different regimens and we don't list them all in this booklet, but pages 120–136 explain some of the differences in treatment for each type of low-grade NHL. Ask your team if you are unsure about anything to do with your treatment.

Side effects of chemotherapy

Chemotherapy works by killing any dividing cells. It kills lymphoma cells as well as healthy cells, particularly cells that divide rapidly, for example, blood cells or the cells that line the gut.

The damage to healthy cells causes many of the side effects (unwanted effects on your body) of chemotherapy.

Some side effects are common with many different chemotherapy drugs. Other side effects are associated only with certain drugs. The hospital should give you information about your drugs and what to expect. It is impossible to say before you start treatment which side effects you will get.

Each person gets slightly different side effects, even if they are having the same treatment as someone else.

“

During treatment I felt like a real fighter. I felt I could deal with most things and had a strange confidence that I would get over it. But it helped me to think that it was actually the chemotherapy that was making me feel so ill and not the lymphoma itself. It helped me to think that once the treatment finished, things would start to improve.

Pat, diagnosed with follicular lymphoma at 56

Effects on the blood

Some of the most common and serious side effects are effects on the blood. Most chemotherapy regimens cause temporary damage to the bone marrow. Your **bone marrow** makes blood cells. The different types of blood cells do different jobs in your body. The table on the next page explains what they are and what low levels (a shortage) might mean.

	White cells	Red cells	Platelets
			
Medical name	Neutrophils and lymphocytes	Erythrocytes	Platelets
What do they do?	Fight infection	Carry oxygen	Stop bleeding
What's the shortage called?	Neutropenia and lymphopenia	Anaemia	Thrombocytopenia
What are the symptoms?	Infections	Pale skin, feeling tired, breathless, cold, dizzy	Bruising easily, bleeding longer or without warning (for example nosebleeds)
What happens if you have a shortage?	<ul style="list-style-type: none"> • Delay treatment • Antibiotics if you have an infection • Growth factors (G-CSF) if needed 	<ul style="list-style-type: none"> • Red blood cell transfusion if needed 	<ul style="list-style-type: none"> • Delay treatment • Platelet transfusion if needed

Other common side effects

Some side effects are common with many different chemotherapy drugs:

- nausea (feeling sick) and vomiting
- change in taste, heartburn, indigestion and problems eating, which can cause weight loss
- bowel problems, like diarrhoea and constipation
- weight gain (often due to steroids like prednisolone)
- hair loss
- fatigue (extreme tiredness)
- cancer-related cognitive impairment ('chemo brain'; problems thinking and concentrating)
- changes in mood
- sore mouth due to mucositis (damage to cells lining your mouth)
- peripheral neuropathy (nerve damage), which can cause tingling or numbness in your hands and feet
- temporary or permanent stop of periods in women.



Visit www.lymphoma-action.org.uk/SideEffects for more information and advice on coping with side effects.



Tips for dealing with side effects

- Tell your medical team if you feel unwell in any way or if you have a fever (temperature above 38°C). Infections can be life-threatening and need prompt treatment.
- Ask your medical team for advice if you are experiencing side effects. They often can give you medicines that can help or they can give advice to manage side effects better.
- Tell your medical team if any medicines you are given don't work – there are often alternatives.

Late effects of chemotherapy

Late effects are health problems that might only develop months or years after treatment. Talk to your medical team about the risks associated with your treatment. It is important to be aware of what late effects can happen so you can look out for symptoms. Checking for late effects is an important part of your follow-up (see page 96 for more on follow-up). As late effects can develop many years after treatment, make sure you talk to your GP about what to look out for too.

If you are worried about any symptoms you are having, talk to your medical team.

Possible long-term and late effects of chemotherapy include the following, but some people develop other problems.

Effects on fertility: fertility problems are more likely with certain drugs, together with other factors like your age. Some women also have a premature (early) menopause after chemotherapy and may need hormone replacement therapy (HRT). Your specialist should discuss potential changes to your fertility and any options with you before treatment starts.

Heart problems: certain drugs like doxorubicin can cause heart problems years later. You might need tests to see how well your heart is working before treatment and may need to avoid certain drugs if you already have heart problems. Your medical team can advise you of steps you can take to reduce the impact of possible heart problems in the future.

Blood disorders: some chemotherapy treatments slightly increase your risk of developing another cancer or some blood disorders in the future, such as myelodysplastic syndrome (MDS) and leukaemia. Even increased, this risk is still small.

Questions to ask about side effects

- What side effects am I likely to get?
- How long after treatment do side effects usually start?
- How long do side effects last for?
- How long will it take to recover from my chemotherapy?
- What late effects are associated with my treatment?
- Is there anything I should look out for or any screening programmes I should be aware of?
- Who should I contact if I am worried about symptoms after treatment?
- How can I reduce my risk of late effects?



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Antibody therapy

Antibodies are made by the body's **immune system** and are an important part of its defence against infection. They stick to proteins called 'antigens' on the surface of cells that don't belong in your body, for example, bacteria or viruses. They also attract other cells of the immune system that help to destroy the infection.

Lymphoma cells have proteins on their surface, too, and these can be used as a target for man-made antibodies. These are monoclonal antibodies; this means they are all exactly the same and stick to the same antigen.

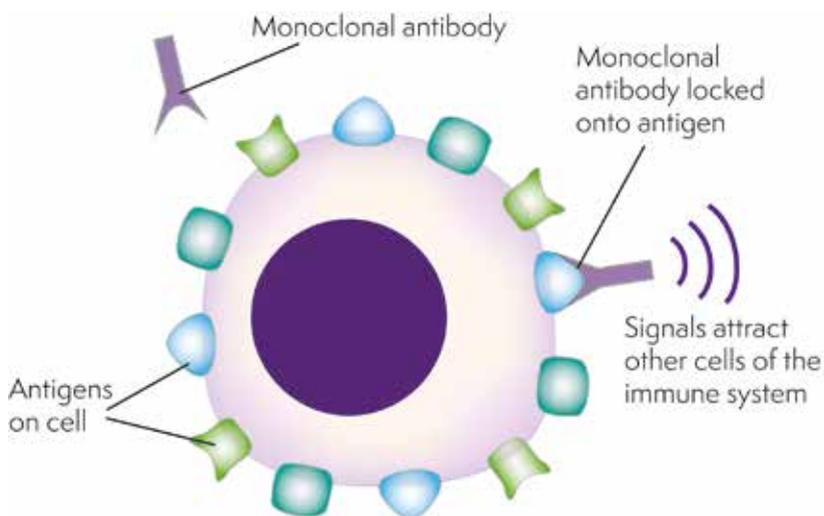


Figure: Monoclonal antibodies binding to antigens on a cancer cell

Antibody therapy (sometimes called 'immunotherapy') aims to target cancer cells more directly than chemotherapy or radiotherapy. This reduces the effects on normal cells that cause many of the side effects of less targeted treatments.

The antibody most often used for low-grade lymphoma is called rituximab. Biosimilar versions of rituximab are becoming available. These are drugs that are highly similar and shown to be equally effective. Rituximab targets an antigen called CD20 found on B cells. Newer antibodies that target CD20 are also beginning to be used for low-grade lymphomas or are in clinical trials, for example, obinutuzumab and ofatumumab.

How is antibody therapy given?

Most antibody therapy is given intravenously.

Rituximab

Rituximab for low-grade NHL is usually given at the start of each cycle of chemotherapy. Some people have a short course of rituximab on its own. You have it as an outpatient and don't normally have to stay in hospital. It can be given as:

- an intravenous drip
- a subcutaneous (under the skin) injection into your abdomen (tummy).

The first intravenous infusion is given slowly over a few hours to help prevent side effects. If you don't have a bad reaction, subsequent doses may be given more quickly (over about

an hour). The subcutaneous injection is quicker (around 5 minutes), but is not available in all centres and is not suitable for everyone.

You can only have the subcutaneous injection if you have already had a full dose of rituximab intravenously and you didn't have a bad reaction.

Obinutuzumab

Obinutuzumab is given with other treatments for follicular lymphoma or chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL). It is given by intravenous infusion. The first dose may be given very slowly and split over 2 days. It can also be given as maintenance treatment for follicular lymphoma.

Ofatumumab

Ofatumumab can be used with other drugs for some people with CLL/SLL and is being tested in clinical trials for other types of lymphoma. It is given by intravenous infusion and slowly to begin with – the infusion rate is increased gradually if you tolerate the drug well.

Side effects of antibody therapy

Most side effects of antibody therapy occur while the drip is being given (known as 'infusion-related' side effects) rather than later on. They are more common with the first infusion and include shivers, fevers and other flu-like symptoms.

When given subcutaneously, the skin where the injection was given can become red, swollen and painful. You are given other drugs such as paracetamol and antihistamines to reduce the chances of infusion-related side effects.

Rarely, antibody therapy may cause a more serious allergic reaction, causing symptoms like fever, chills, swelling and difficulty breathing. If this happens, you may need to stay in hospital for a while to recover. You may be able to have the infusion more slowly in future or you may be given supportive treatments to reduce the reaction. Rarely, your doctor may decide to avoid this treatment.

Antibody therapies can also cause other side effects, like low **blood counts** (see page 69) and low levels of your normal antibodies, which can increase the risk of infection. Your medical team should give you information on the side effects of any treatment they recommend.

Other targeted therapies

Targeted therapies are sometimes also called 'biological' therapies. The changes that make lymphoma cells cancerous often affect normal biological pathways, allowing the cancer cells to grow and divide. Targeted therapy can disrupt this process, stopping the abnormal cells growing or causing them to die.

The main kind of targeted therapy used in low-grade NHL is antibody therapy. Many other targeted therapies are being tested in clinical trials. A few are now being used to treat low-grade NHL, as described briefly in the sections below. Not all of these are funded on the NHS throughout the UK. Clinical trials continue to find out how best these and other new treatments can be used in people with lymphoma.



Find out which targeted treatments are funded for your type of lymphoma at www.lymphoma-action.org.uk/Newer-Drugs. Visit www.lymphoma-action.org.uk/TrialsLink to find clinical trials that might be suitable for you.

Most of these newer drugs are taken orally as capsules or tablets. You often take them long-term, until they stop helping you or cause troublesome side effects.

Cell signal blockers: ibrutinib and idelalisib

Ibrutinib and idelalisib target two different pathways that both help B cells stay alive and divide. Blocking these pathways can make lymphoma cells die. Both drugs are taken as tablets once a day until the lymphoma stops responding or you develop troublesome side effects.

Proteasome inhibitors: bortezomib

Many proteins help to control what happens in lymphoma cells and how the cells divide. Proteasomes break down the proteins that are involved in this process.

Bortezomib is a proteasome inhibitor, which blocks the work of proteasomes and upsets the balance of proteins within the cells. This seems to be particularly harmful to lymphoma cells and causes them to die. It is given intravenously or subcutaneously (by injection just under the skin).

Immunomodulators: lenalidomide

Lenalidomide affects the activity of the immune system in several different ways, both in helping the immune system to attack the lymphoma cells and in preventing the lymphoma from growing.

It is taken as tablets once a day for the first 21 days of each 28 day cycle. The cycles continue until the lymphoma stops responding or you develop troublesome side effects.

Programmed cell death inducers: venetoclax

Lymphoma cells have developed ways to survive when they would normally have undergone programmed cell death, the process where the body gets rid of cells that are no longer needed. Venetoclax is a programmed cell death inducer that blocks a protein that helps lymphoma cells survive. It is taken as tablets and the dose is slowly increased over the first few weeks of treatment. You then continue to take it until the lymphoma stops responding or you develop troublesome side effects.

Radioimmunotherapy: Zevalin®

Zevalin is an antibody to CD20 joined to a radioactive particle, yttrium-90. It is used to deliver a small dose of radiation

directly to the lymphoma cells. It is only available at certain hospitals as it requires specialist facilities.

Zevalin is given as a single dose intravenously over 10 minutes. A low dose of rituximab is given 7–9 days before Zevalin. A second dose of rituximab is given just before Zevalin.

Radiotherapy

Radiotherapy uses high-energy X-rays to kill lymphoma cells by stopping them dividing. Lymphoma cells are very sensitive to radiotherapy, but the treatment is usually only given to small areas. In low-grade NHL, radiotherapy is used for:

- localised (early-stage) lymphoma
- small areas that are causing problems in more widespread lymphoma.

How is radiotherapy given?

Radiotherapy is usually given daily, Monday to Friday, and treatment is spread over a few weeks. You can go home after each session. Radiotherapy is only available at specialist centres, so you may need to travel for your treatment. Your care there is overseen by a clinical oncologist (radiotherapist – a doctor who specialises in treating people with radiotherapy). They see you to discuss your treatment before it begins and you can ask any questions you have.



Figure: A radiotherapy machine

You might need to make several visits to the radiotherapy department to plan your treatment before it starts. This usually includes a CT scan to map the area to be treated. This is a planning scan.

Each treatment takes 5–20 minutes and is painless. Most of this time is spent making sure you are in the correct position. It is very important that precisely the same area is treated each time.

“

Having radiotherapy was very straightforward. I hardly knew anything was happening apart from the machine arching around and some buzzing. The overriding requirement is not to move. I found that the best way to cope was to think about totally different things.

Julian, diagnosed with nodal marginal zone lymphoma at 66

Radiotherapy for lymphoma does not make you radioactive. There is no risk to those around you.

Side effects of radiotherapy

Although radiotherapy itself is painless, it can have uncomfortable side effects. Side effects of radiotherapy depend on which part of your body is being treated and the amount of radiotherapy you are having. Your team give you information about what to expect and how to take care of yourself.

You may have no side effects to start with – they tend to become gradually more obvious towards the end of the course and in the week or two after you have finished radiotherapy. Most radiotherapy side effects are short-term, but some can be long-term or permanent.

You are usually seen weekly in a review clinic in the radiotherapy department to see how you are getting on. It is important to let your team know about any side effects you have. Tell them if any of your side effects change during the course of your treatment. There are usually things that can be done or medicines that can be prescribed to help with side effects.

Many people have fatigue (feel very tired) after radiotherapy. It can take months after treatment for fatigue to go away completely.

In the area being treated, you might have sore skin and hair loss, but these are temporary.

Other side effects can happen if you have radiotherapy in certain areas.

- **Sore mouth and difficulty swallowing** – this can happen if you have radiotherapy to your head, neck or upper chest.
- **Nausea (feeling sick)**, can happen if you have radiotherapy to your abdomen (tummy).
- **Effects on the blood**, usually if there are large bones in the treatment area. A low **white blood cell** count (**neutropenia**) can increase your risk of infection. A shortage of red blood cells (**anaemia**) can increase fatigue and make you feel short of breath. Radiotherapy rarely causes a **shortage of platelets (thrombocytopenia)**.

Late effects of radiotherapy

Radiotherapy can also cause **late effects**, which are side effects that develop months or years after treatment. The effects you are at risk of depend on what area of your body was treated and how much radiotherapy was given.

It is important to know that much of what is known about the risks of late effects of radiotherapy comes from older studies. Modern treatments have reduced the risk of some of these complications.

Ask your medical team what to look out for. It is important to be aware of what late effects can happen so you can look out for symptoms. You can reduce your risk of problems such as heart disease and stroke by keeping a healthy lifestyle.

Checking for late effects is an important part of your follow-up (see page 96 for more on follow-up). Problems can develop many years after treatment so make sure you talk to your GP about your risk of late effects too.

Possible long-term and late effects of radiotherapy include the following problems.

Increase in risk of heart disease and stroke: radiotherapy in the area of the heart can increase your risk of heart disease. Radiotherapy to the chest or neck might also cause hardening of your arteries. This can affect the blood supply to your brain or heart, increasing your risk of stroke or heart attack.

Lung problems: scarring of lung tissue, or fibrosis, can be a side effect of radiotherapy to the chest. Once it develops, it is usually permanent. It can be mild and not cause any symptoms. Some people can become short of breath and unable to do as much exercise as they used to. Smoking or other lung diseases increase the risk of scarring.

Reduced thyroid function: radiotherapy to the neck or upper chest area can affect your thyroid gland, which may then make less of the hormone thyroxine. This is called 'hypothyroidism' and may slow your metabolism making you feel cold and tired, and causing you to gain weight easily. This is not an immediate effect but can happen years after radiotherapy. It is usually picked up early by regular thyroid function blood tests. Hypothyroidism is usually easily treated with thyroxine tablets.

Second cancers: although it is used to treat cancer, radiotherapy can damage normal cells and increase the risk of developing another cancer many years later. The risk of second cancers has reduced with the use of better scans and modern techniques that target radiotherapy more accurately. What second cancers you are at risk of depends on which part of your body was treated with radiotherapy. For example, radiotherapy to breast tissue in young women increases the risk of breast cancer. Women who have had radiotherapy may be offered breast screening at an earlier age than usual.

Your specialist should tell you what late effects you are at risk of and give you advice on how to reduce your risk. Make sure your GP or anyone else treating you knows about your lymphoma and the treatment you have had.

Contact your GP or medical team if you have concerns about your health at any time after your treatment.

Stem cell transplant

For most types of lymphoma, higher doses of treatment and a **stem cell transplant** are only given if initial treatments haven't worked or your lymphoma has come back. For low-grade NHL you are only likely to have a stem cell transplant if your lymphoma relapses quickly, or is expected to, and you are fit enough to withstand the treatment.

High doses of treatment can work well to treat **relapsed** or **refractory** lymphoma. However, they also cause damage to your **bone marrow** to the extent that it might not be able to recover by itself. Stem cells are special cells from the bone marrow that are continually making normal blood cells. If your bone marrow is damaged, you might not have enough stem cells to make the normal blood cells you need.

A stem cell transplant allows you to have high-dose treatment by giving you healthy blood stem cells after treatment.

Stem cells are usually collected before high-dose chemotherapy (and sometimes radiotherapy). Most people with lymphoma have an **autologous** stem cell transplant. This means that their own stem cells are collected before high-dose therapy then given back to them after high-dose therapy.

Stem cell transplants take several weeks to complete and your recovery may take many months. They carry risks as well as benefits, particularly if you are having an allogeneic stem cell transplant. They are not suitable for everyone. If your doctors are thinking about this form of treatment for you, they will talk to you in detail about it.

What happens during an autologous stem cell transplant?

If you are having an autologous stem cell transplant, you have treatments to increase your number of stem cells and move them from your bone marrow into your bloodstream. They are then collected and frozen. When you have enough frozen stem cells and are ready for your transplant, you are admitted to hospital and have high doses of chemotherapy drugs for a few days.

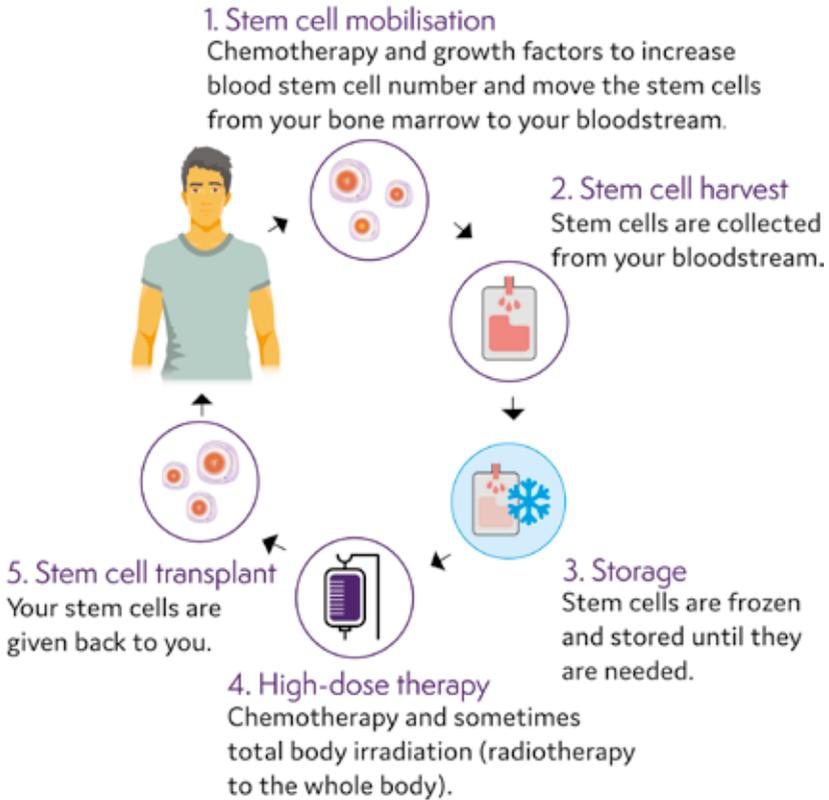


Figure: The autologous stem cell transplant process

After high-dose therapy, you are given the stem cells back, just like a blood transfusion. You are closely monitored while the stem cells settle in your bone marrow where they start to grow and make new blood cells for your body. This helps your bone marrow to recover from the side effects of high dose treatment.

What is an allogeneic stem cell transplant?

Some people have a stem cell transplant using cells from a donor (another person). These are called '**allogeneic**' stem cell transplants. Allogeneic stem cell transplants are less commonly used for low-grade NHL than autologous stem cell transplants. They have a higher risk of complications and you need to be fit enough to have one safely. The donor stem cells produce a new **immune system** that can recognise and kill the lymphoma cells, reducing the risk of relapse. However, the donor cells can also attack your normal tissues.

Allogeneic stem cell transplants can offer a higher chance of cure than other treatments for some people with lymphoma that is difficult to treat.

Visit www.lymphoma-action.org.uk/SCT for more information about both autologous and allogeneic stem cell transplants or call our Information and Support Team on 0808 808 5555.



Maintenance treatment

Many people with low-grade NHL have maintenance treatment after a course of treatment.

The aim of maintenance treatment is to make your remission last as long as possible by 'mopping up' any lymphoma cells left after treatment that can't be detected on scans but could lead to **relapse**.

The antibody treatment rituximab is usually used for maintenance, but another antibody might be used. The treatment is given once every 2–3 months, usually for up to 2 years, although some people might have maintenance for longer.

Most people tolerate maintenance treatment well, without significant side effects, but it isn't suitable for everyone. It is only used for certain types of lymphoma (see pages 120–136). You and your doctor can decide together whether maintenance treatment is appropriate for you.

Supportive care

You have supportive care alongside your treatment for lymphoma to manage side effects and reduce symptoms, for example, painkillers and antiemetics (anti-sickness drugs). The type of supportive care you need depends how you are affected by your lymphoma and its treatment, for example:

- **Steroids** treat your lymphoma but can also control sickness and help you feel better.
- **Growth factors** boost your blood cell counts and reduce your risk of infection. The most common growth factor given is G-CSF (see page 69), which boosts infection-fighting white blood cells called neutrophils.
- **A blood transfusion** may be given if you develop anaemia (a shortage of red blood cells).
- **A platelet transfusion** may be given if you develop **thrombocytopenia** (a shortage of **platelets**), especially if your platelet levels are very low or you are having problems with bleeding, for example nosebleeds.
- **Prophylactic medication** may be given to prevent certain unusual or serious infections that you are at higher risk of developing while your immune system is low due to the lymphoma or its treatment.

Prophylactic medications (given to prevent disease) commonly include antibiotics (for example, co-trimoxazole prevents *Pneumocystis jirovecii*, which causes a type of pneumonia), anti-viral drugs (for example aciclovir) and anti-fungal drugs (for example fluconazole or itraconazole). You take each of these drugs as tablets. Your doctor will tell you if you need them and for how long you should continue to take them.



I have had eight different types of chemotherapy during my life with lymphoma. I feel very lucky that each time my lymphoma has relapsed new treatments were offered and that 27 years later I am able to tell my story.

Carole, diagnosed with follicular lymphoma at 37

What happens after treatment?

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When your course of treatment has finished, you are likely to have a scan to check that your treatment has been successful.

Follow-up

When you are in remission after treatment, you see your specialist or another member of the medical team regularly in the clinic. These follow-up appointments are important in supporting your recovery. They have several aims:

- to monitor how well you are recovering from your treatment
- to help you manage side effects and to look out for **late effects**
- to check there are no signs of lymphoma **relapsing**
- to give you a chance to raise concerns and ask questions.

At each appointment, you have a brief physical examination and may have blood tests. Unless there is a particular reason to do them, you are unlikely to have routine X-rays or scans. Doctors prefer to keep their patients' exposure to radiation to a minimum.

If you are well, your treatment is unlikely to change because of a scan result so follow-up scans are usually unnecessary.

Most relapses are only treated when the lymphoma is causing problems. See page 101 for more about relapse.

People with low-grade NHL usually have follow-up appointments every 3–6 months, but this varies according to your individual circumstances. If you stay well, your appointments may become less frequent. Some people go onto a self-management scheme.

Self-management schemes

If you have been in remission for a while and are considered to be at low risk of relapse, your doctor might suggest you go onto a self-management scheme, sometimes called 'patient triggered follow-up'. This is not available at all hospitals, but, increasingly, people with low-grade NHL are being given guidance to be able to manage their own follow-up.

Self-management is an option because most relapses are picked up by people with lymphoma themselves when they develop symptoms.

You know your own body best and are most likely to know when there is a problem that needs checking out.

If self-management is available and considered appropriate for you, you are given guidance on how to look after yourself and what to look out for, often as part of a workshop. There are often regular sessions you can attend to learn more about managing your lymphoma. You might be asked to have regular blood tests at your GP surgery. You can then contact your

medical team if you feel you need to be checked up. They will be able to reassure you or arrange an appointment for you.

This approach avoids the need for travel and lengthy waits at hospital appointments and gives you more control over your situation.

What should I do if I am worried?

If you are worried about your health at any time, you don't have to wait for your next appointment. Contact your GP or medical team to discuss your concerns. If necessary, they can arrange an early clinic appointment for you. Keep the contact details of your medical team, even after you have finished treatment.

You might worry when your follow-up appointments are coming up. They are a reminder of your illness when you are trying to get on with your life. But remember, these appointments are an important part of your care. They can reassure you that all is well or catch any problems early. Your appointments also give you a chance to talk about anything that might be on your mind. It can help to write down what's bothering you when you think of it and take a list of questions with you to the appointment.



I have been in remission for 11 years now, and check-ups are only annually. However, I still don't feel that I can relax 100% health-wise. I am aware that lymphoma can appear almost anywhere in the body, which makes any strange, unexplained pain or symptom potentially worrying. However, the anxiety has greatly decreased as the years go by.

Caroline, diagnosed with follicular lymphoma at 40



Questions to ask when treatment finishes

- Will I be on any treatment at all after the main course of treatment has finished?
- How often will I be seen in the clinic?
- What will happen at my follow-up appointments?
- Will I have any regular tests?
- Is there anything I should look out for?
- How will I know if the lymphoma has come back?
- Why won't I have regular scans?
- Who do I contact if I am worried about anything between appointments?



Notes

What is 'refractory' lymphoma?

Most types of low-grade NHL respond well to treatment but, for a small number of people, the lymphoma does not respond. Lymphoma that does not go into remission after treatment is known as '**refractory**' lymphoma. It is usually treated in the same way as relapsed low-grade NHL (see below).

What is relapse?

Some people with early-stage low-grade NHL can be cured by their first course of treatment. However, low-grade NHL usually comes back or progresses (gets worse) at some time and needs more treatment. This is a **relapse**.

Treatment is continually improving for low-grade NHL and remissions are becoming longer.

The time between treatment courses varies considerably from person to person but many people stay in remission for years after their first treatment. It is likely that the gap between treatments will shorten each time.

When the lymphoma relapses, it might come back where it was before or it might affect another part of your body. For this reason, you might have the same symptoms as you had when you were first diagnosed, but you might have different symptoms. Your medical team should tell you what

symptoms to look out for and who to contact if you are concerned that your lymphoma might have relapsed.

What happens if my doctor suspects a relapse?

Your doctor will arrange tests for you if they suspect a relapse. You are likely to have the same tests you had when you were first diagnosed, such as a **biopsy** and scans. Your doctor needs to know how the lymphoma is affecting you so they can recommend a treatment plan. It is also important to check that the lymphoma is still low-grade and has not transformed (changed) into a faster growing type of lymphoma. Transformed lymphoma needs different treatment (see page 50).

Treatment for relapsed low-grade NHL

Relapse of low-grade NHL can be frightening and upsetting, but it is important to remember that it can be treated. Your doctor takes many factors into account when recommending your next treatment, including:

- the type of lymphoma you have and how it is affecting you
- what treatment you had before and how your lymphoma responded to it
- how well you coped with your previous treatment
- how quickly your lymphoma came back
- how fit you are at the time of your relapse.

If you have had a long remission and your lymphoma is not very widespread, you might even have a period of active monitoring ('watch and wait') before treatment is needed. When you do have treatment, you might have gentler treatments. This could be the same treatment as you had before or your doctor might suggest a different treatment.

If your lymphoma came back quickly or you have already relapsed more than once, your doctor might suggest a more intensive treatment than you'd had previously. If you are fit enough and respond to chemotherapy, your treatment might include a **stem cell transplant** (see page 88) to give you a better chance of a long-lasting remission.

Newer drugs are becoming increasingly important in the treatment of relapsed low-grade NHL. Newer drugs are often available first to people who have relapsed or refractory lymphoma and can offer alternatives to intensive chemotherapy and stem cell transplants. Some are already in routine use. Your doctor might suggest a clinical trial testing newer drugs or new approaches with the aim of improving the treatment of relapsed low-grade NHL.

Visit www.lymphoma-action.org.uk/TrialsLink to find out more about clinical trials and to find a trial suitable for you.



Coping with the fear of relapse

It is natural to feel worried about your lymphoma relapsing. While in remission, you might find that you are more sensitive to aches, pains and other bodily sensations than you used to be.



Five years after my treatment, I was put on maintenance rituximab and have needed no other treatment since then. I have check-ups every 4 months and feel I am doing wonderfully well. But I am realistic and know it may come back, and know to look out for lumps, tiredness, sweats and stomach problems. The best piece of advice I was given was 'listen to your body'.

Pat diagnosed with follicular lymphoma at 56

This fear can be particularly strong in types of cancer that are likely to relapse, like low-grade NHL. It might help to remember that these types of lymphoma usually grow very slowly and behave like a chronic condition rather than like more aggressive forms of cancer.

As part of your follow-up, your medical team will be checking for signs of relapse. There is rarely an urgent need for treatment even if relapse is suspected.

Everyone copes with the fear of relapse in their own way. It can help to talk over your fears with your medical team,

with your friends and family and with other people affected by lymphoma. Talking through your concerns could help you process your thoughts and lower your anxiety. You may like to get in touch with a member of our Information and Support Team, who are there to talk about any aspect of lymphoma and might be able to put you in touch with someone else in a similar situation through our Buddy scheme or a support group.

**Call our Information and Support Team on
0808 808 5555 or email us at
information@lymphoma-action.org.uk.**



Tips for coping with the fear of relapse



- Learn more about your lymphoma and the possible treatments – this helps some people to feel more in control.
- Talk to other people affected by lymphoma – join a support group, talk to others on our online forum, or request a buddy.
- Consider talking through your fears with a professional, for example, a counsellor.
- Keep busy – many people living with lymphoma have a full and active life.



I get on with life as normal. But, having follicular lymphoma, I do think about whether it will return, but then I jog myself back into the here and now and enjoy each day as it comes.

Malcolm, diagnosed with follicular lymphoma at 60

Life with low-grade NHL

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Most people live for many years with low-grade NHL and many can have a normal life expectancy. You are likely to have long periods where you are not having treatment and feel well. Some people never need treatment for their lymphoma. It is important that you do not put your life on hold. Be reassured that low-grade NHL usually grows slowly and you are monitored closely.



This section gives a brief overview of things you might need to consider when getting on with your life after being diagnosed with low-grade NHL. Our booklet *Living with lymphoma* gives more information on these topics, www.lymphoma-action.org.uk/Living-With-Lymphoma

Feelings

It is hard to predict exactly how you will feel after your diagnosis and how your lymphoma and its treatment will affect your day-to-day life. Emotional struggles can be very difficult if you are not having treatment straightaway because your doctor has recommended active monitoring ('watch and wait').

It is hard to predict how you will feel when you have treatment. Your initial symptoms might improve, but you might develop side effects, particularly as the treatment goes on. Some people have few side effects from their treatment

and are able to carry on almost as usual. Others need to make changes, at least for a while. If you are having radiotherapy, side effects may be worse when you are near the end of your treatment course and for a short time afterwards.

Many people have strong and difficult feelings at different stages: when they are diagnosed, during treatment and afterwards.



Support groups make you realise there is life after lymphoma. Many people struggling cannot see beyond the immediate future. At a support group, there are people going through problems and those who have been through a similar experience to you and have come out the other side.

Michael, diagnosed with small lymphocytic lymphoma (SLL) at 62

You might have mixed feelings when you finish treatment. This can come as a surprise, if you're expecting to feel happy and relieved.

Occasionally, people can feel more anxious and down once their treatment has finished, even if they are in remission. Many people with low-grade NHL worry about **relapse**.

It can help to talk about your feelings, especially during times when you are finding it harder to cope.

“

I went to see a counsellor at the hospital and had some quite deep conversations. I didn't feel that it had helped at the time, but on reflection it may have started something inside me.

Malcolm, diagnosed with follicular lymphoma at 60

Your nurse specialist is often a good person to talk to; they know the kind of feelings people often have. They can also give you advice on what to be careful of and tips on how to carry on with your life during active monitoring or treatment and afterwards.

“

I contacted Lymphoma Action and found them enormously helpful and calming. I was able to talk about things that I didn't want to talk to my doctor about. I was put in contact with a buddy, which was both helpful and reassuring. I am now a buddy for the charity myself, which is particularly important to me, as I want to be able to give others hope and support, just as my buddy did.

Caroline, diagnosed with follicular lymphoma at 40



Share your concerns about lymphoma with our Information and Support team: call 0808 808 5555 or email at information@lymphoma-action.org.uk.

Helping yourself

Many people find that having a serious illness makes them reassess their lifestyle. There are many things you can do to help yourself to cope with treatment and to help yourself recover afterwards. Keeping healthy can also ensure that you are in the best shape for any future treatment.



Once I had picked myself up off the floor, I started to think about what I could do to help myself. At the time I was a fairly typical teenager and suddenly I had to think more carefully about myself and since then, have always been careful about my weight, made sure I eat healthily, take regular exercise and avoid too much stress.

Ashley, diagnosed with mycosis fungoides (cutaneous T-cell (skin) lymphoma) more than 45 years ago at 17



Tips for looking after yourself

- Drink plenty of liquids, especially if you are having chemotherapy.
- Eat a healthy diet with plenty of fruit and vegetables and keep your body at a healthy weight; if you are having problems eating or are losing weight because of your treatment, ask your medical team for advice.
- Stop smoking; lung infections are more common with chemotherapy and with smoking. Your risk of developing long-term treatment side effects is also higher if you smoke.
- Protect your skin from the sun.
- Keep active – getting up and walking is a great start to exercising and you can build up slowly. Exercise can help to reduce fatigue and make you feel better in general. Ask your specialist nurse if there are any post treatment exercise programmes you can join.



I found myself trying various things to assist my recovery such as relaxation and meditation, green tea and cutting out caffeine, various vitamin supplements and eating organic. I don't know whether these things helped, but it made me feel like I was doing something proactive.

Caroline, diagnosed with follicular lymphoma at 40

Working and studying

Your employer must, by law, make any reasonable adjustments to allow you to continue working. Most people need time off from work or study during their treatment. Some people need to reduce their hours or change the kind of work they do after being diagnosed with low-grade NHL.



Tips for work and study

- Let your employer, school or institution know about your illness and treatment so they can support you.
- Consider how much work you are able to cope with; you may be able to reduce your hours.
- Find out whether you might be entitled to any benefits, for example at GOV.UK: www.gov.uk/browse/benefits.

Sex and contraception

Lots of people are less interested in sex than usual during treatment, but interest usually returns when you are feeling well. If you have any concerns, talk to your medical team.

There is no reason you shouldn't have sex during treatment if you feel like it, but there are some specific precautions you should take.



Tips for safe sex

- Use condoms for 5 days after each chemotherapy treatment and avoid oral sex and open-mouthed kissing during this time. Ask your medical team for advice about sex while you are on other types of treatment.
- Use effective contraceptives as treatment could damage sperm or eggs and could harm a developing baby.
- Ask your medical team for advice on contraception – oral contraceptive tablets may be metabolised (removed from your body) more quickly when you're having treatment.

Everybody's circumstances are different and advice varies, but if you are having chemotherapy doctors often recommend that:

- Women with lymphoma don't become pregnant during their treatment and for up to 2 years afterwards.
- Men with lymphoma prevent making their partner pregnant during their own chemotherapy and for at least 3 months afterwards.

There might be different timelines for certain drugs or for newer drugs. Discuss these issues with your medical team so they can give the best advice for you.

Hobbies and socialising

It is important that you allow yourself time to do the things you enjoy whether you are on active monitoring, being treated, or in a period of remission. When you feel well enough continue as much as possible with your hobbies and social life. This can help to make you feel more 'normal'.



Tips about hobbies and socialising

- You might need to avoid crowds at certain times because of the risk of infection. Your medical team should give you advice about this.
- Check with your medical team if any of your hobbies are adventurous, very active, or dangerous.

Holidays and travel

Holidays and travel can be difficult during treatment, for example when your blood counts are low. Lymphoma affects your immune system and many of the treatments for lymphoma, including **maintenance** treatment, can also make you more prone to getting infections. You could be exposed to new infections in different parts of the world. These could be difficult for your body to fight. It is important that you know what to consider when making travel plans.



Tips for travel

- Discuss your plans well in advance with your medical team, so that they can offer you advice.
- Find out what vaccinations you need and if it is safe for you to have them.
- Travel insurance can be difficult to find and expensive so factor this into your plans.



My view is that specific cover for a medical condition is essential. I needed medical attention on the second day of our trip to Portugal.

Michael, diagnosed with small lymphocytic lymphoma (SLL) at 62

When someone close to you has lymphoma

When someone you care about has lymphoma, it can be a difficult time for you, too. You may feel helpless watching the person go through all the tests and treatments. You may feel you don't know what to do or how to help.

There are many things you can do – you can find some suggestions below. Don't forget to take care of yourself, too. If you become rundown or ill, you will not be able to support someone else.

You probably have many of the same feelings as your loved one. You need time to deal with them, too. Talk to someone – friends, family, or a specialist – if you are finding it difficult to cope.

People sometimes worry that they don't know what to say to the person affected by an illness or that they might say the wrong thing. Just being ready to listen is often a huge help. Let the person with lymphoma know that you love them and care for them in whatever way you can.



Tips for how you might help friends or loved ones with lymphoma

- Provide transport to hospital.
- Go to hospital appointments with them to help remember what is being said.
- Keep them company if they don't want to be alone. For some people, having someone there is reassuring even if they don't want to talk.
- Help with shopping or preparing meals.
- Take care of other family members.
- Encourage them to spend time seeing other people or doing things they enjoy when they are able to.
- Organise fun things to do when they feel up to it.



My husband was my emotional support. When I cried, he cried; when I was angry, he was angry. He took advantage of the counselling offered at the hospital about caring for someone with a chronic disease, which he found really valuable. My son was unbelievably practical and between them I felt I had the perfect balance.

Debbie, diagnosed with follicular lymphoma at 45

Precautions after treatment for lymphoma

You need to take certain precautions after some treatments for lymphoma. Your medical team should explain what you need to be aware of and should give you information that you can show anyone treating you in the future. For example:

- If you need an operation, the anaesthetist needs to know what treatment you have had.
- If you've had your spleen removed or radiotherapy to your spleen, you need to take low-dose protective antibiotics and you might need extra vaccinations.
- You might need irradiated blood if you need a blood transfusion after certain treatments. Irradiated blood is blood treated with X-rays to kill any donor white cells that might attack your own cells.
- Some people treated with steroids do not make enough natural steroids after treatment. Should this be the case, you might need steroid replacements if you have an accident.



Tips for future health care

- Tell anyone treating you about your lymphoma and the treatment you've had.
- Carry any warning cards you are given.
- Ask for information about your treatment.

Types of low-grade NHL

This part of the booklet looks in more detail at the most common types of low-grade NHL.

We would suggest that, at least at first, you read only the section on your own type of low-grade NHL.

If you are not sure exactly what kind of lymphoma you have, check with your doctor. It may be confusing or distressing to read about illnesses that are not relevant to you. You can ask your doctor to write your type in the front of this booklet.

We have not been able to give details of every type of low-grade NHL. If you have been told you have a type of lymphoma that you do not see listed in this booklet, you may wish to check with your doctor. We may have listed your lymphoma under another name. If not, your doctor might be able to tell you if we included a lymphoma similar to yours.

Visit our website www.lymphoma-action.org.uk for more information on types of low-grade non-Hodgkin lymphoma.

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Follicular lymphoma

Follicular lymphoma is the most common single type of low-grade NHL. It grows very slowly and most people (4 in 5) are at an advanced-stage when they are diagnosed.

Who gets it?

Follicular lymphoma is uncommon under the age of 50, but can affect people of any age.

What are the symptoms?

You may have few symptoms or none at all. Most people have one or more painless enlarged **lymph nodes**, often in the neck, armpit or groin. You may have some of the other common symptoms of lymphoma, for example, weight loss, fevers, night sweats, fatigue, itching or being more prone to infection. If the lymphoma affects your **bone marrow** or **spleen**, you might have low **blood counts**.

How is it treated?

Early-stage follicular lymphoma might be treated with radiotherapy with the aim of curing the lymphoma. If radiotherapy isn't possible, you may have active monitoring ('watch and wait') until the lymphoma worsens and you need treatment. Some people have the same treatment as advanced-stage disease.

Advanced-stage lymphoma that isn't causing troublesome symptoms might have active monitoring ('watch and wait') or a short course of rituximab (**antibody** therapy) followed by active monitoring. Some people never need treatment.

If you need treatment, you are likely to have chemotherapy with antibody therapy. The regimen chosen will be based on your individual circumstances. This is likely to be followed by **maintenance** treatment with an antibody treatment for up to two years.

At **relapse**, you might have the same chemotherapy with antibody therapy again, a different regimen (combination of drugs) or one of several other options, for example, active monitoring, radiotherapy to troublesome areas, or newer drugs. If you need more intensive treatment, your doctor might suggest high-dose chemotherapy and a **stem cell transplant**.

If you have grade 3B follicular lymphoma, which is a faster growing type, you are likely to have the same treatment used for high-grade NHL, for example, R-CHOP (rituximab antibody therapy with CHOP chemotherapy).

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

CLL and SLL are different forms of the same disease. In CLL, most of the lymphoma cells are in the **bone marrow**. In SLL, they are mainly in the **lymph nodes** and **spleen**. CLL is diagnosed and staged differently to other types of low-grade NHL.



**Our website has more detailed information about CLL.
Find out more at www.lymphoma-action.org.uk/CLL**

Who gets it?

CLL/SLL can occur at any age but is uncommon in young people and more common over the age of 60. It affects more men than women.

What are the symptoms?

Most people (more than 3 in 4) have no symptoms to start with and the lymphoma is often discovered by chance on a blood test. Symptoms develop over months or years as the abnormal lymphocytes build up in the bone marrow, blood, spleen, liver and lymph nodes. You might develop enlarged lymph nodes, often in several places; flu-like symptoms, fatigue, weight loss and night sweats, low blood counts and frequent or persistent (long-lasting) infections.

Sometimes CLL/SLL causes the immune system to attack your blood cells – this is called autoimmunity and can affect your **red blood cells** (autoimmune haemolytic anaemia or AIHA) or your **platelets** (immune thrombocytopenic purpura or ITP).

How is it treated?

Most people with CLL/SLL don't need treatment straightaway if the lymphoma is not causing any problems. These people have active monitoring ('watch and wait'), sometimes for many years. Some people never need any treatment.

When you need treatment, most people have a combination of rituximab **antibody** therapy with chemotherapy. The most common chemotherapy drugs are a combination of fludarabine with cyclophosphamide or just bendamustine. If you need a gentler treatment, chlorambucil chemotherapy tablets might be recommended.

CLL/SLL with certain genetic changes (17p or TP53 changes) can be more difficult to treat, but there are several newer drugs that can be very effective for these people. Newer drugs might also be used for people who **relapse**.

Mantle cell lymphoma

Mantle cell lymphoma usually grows quickly, but the cells can resemble a low-grade lymphoma. In most cases it is treated like a high-grade lymphoma but in some cases it can grow slowly.



Management of high-grade mantle cell lymphoma is described in our booklet *High-grade non-Hodgkin lymphoma* and on our website at www.lymphoma-action.org.uk/MCL

Who gets it?

Mantle cell lymphoma is significantly more common in men than women and occurs most often in people in their 60s.

What are the symptoms?

Mantle cell lymphoma usually causes swollen **lymph nodes** but may also be found in the **bone marrow**, bloodstream, bowel, **spleen**, tonsils or rarely in the central nervous system (brain and spinal cord).

How is it treated?

Early-stage disease might be treated with radiotherapy with the intention of curing the lymphoma. If you are not suitable for radiotherapy, a period of active monitoring ('watch and wait') might be suggested.

If you need treatment, most people are treated with chemotherapy together with rituximab (chemo-immunotherapy). If you respond to chemo-immunotherapy and are fit enough, your doctor might suggest a **stem cell transplant** to make your remission last longer. After chemotherapy or a stem cell transplant, you may have **maintenance** rituximab.

Newer drugs are increasingly used, particularly for **relapsed** disease.

Marginal zone lymphomas

Marginal zone lymphomas (MZL) develop from B cells that are normally found in the marginal zone, which is at the edge of areas of lymphoid tissue where B cells are found (lymphoid tissue is part of the **immune system**, for example **lymph nodes** or **spleen**).

There are several types of MZL. Two of these are **extranodal** and affect mucosa-associated lymphoid tissue (MALT), which is soft, moist, tissue that lines many parts of your body and helps protect your body from infections and toxins, or occurs as a natural response to infection or inflammation. MALT tissue is found in your mouth, gut, breathing passages and other internal organs. If lymphoma develops in MALT tissue in your stomach, it is called gastric MALT lymphoma (see page 129). If it develops in other MALT tissue, it is called non-gastric MALT lymphoma (see page 130).

MZL can also develop in the **spleen** – splenic marginal zone lymphoma (see page 131) and in the **lymph nodes** – nodal marginal zone lymphoma (see page 132).

Gastric MALT lymphoma

Gastric MALT lymphoma develops in the stomach. It is normally diagnosed when people have an endoscopy to investigate symptoms like persistent indigestion.

Who gets it?

Gastric MALT lymphoma is strongly linked to *Helicobacter pylori* (a type of bacteria) infection. This infection doesn't usually cause serious problems but is also linked to stomach ulcers and indigestion.

What are the symptoms?

Most people have persistent indigestion, which is usually the only symptom. Some people have abdominal (tummy) pain, nausea and vomiting and weight loss. Rarely, bleeding or a mass in the stomach occurs.

How is it treated?

Clearing the *H. pylori* infection with antibiotics and acid reducing medication also clears the lymphoma in most people. It can take months and several courses of treatment to clear the infection. If there is still lymphoma remaining, you might need chemotherapy (usually CVP or chlorambucil) with **antibody** therapy.

If the lymphoma **relapses**, the same treatments are usually successful again. Radiotherapy can also be very effective.

Non-gastric MALT lymphoma

Non-gastric MALT can develop in areas where MALT tissue has formed in response to inflammation. It is sometimes called '**extranodal** MALT lymphoma'.

Who gets it?

Most people with these conditions do not develop lymphoma but MALT tissue can form in response to:

- a chronic (long-lasting) infection, for example, *Campylobacter jejuni*, a cause of food poisoning, or *Borrelia burgdorferi*, which causes Lyme disease
- an autoimmune condition (a condition in which the immune system reacts against your own tissue), for example Hashimoto's thyroiditis or Sjögren's syndrome.

What are the symptoms?

Most people have no symptoms. Lymphoma might be found through a test for something else. If you do have symptoms, these depend on where the lymphoma is growing. It most commonly affects the salivary glands, thyroid, lungs, skin, bowel or tissues around the eye.

How is it treated?

If your lymphoma is linked to an infection, antibiotics might clear the infection and the lymphoma. Radiotherapy or active monitoring are used for early-stage lymphoma. Widespread MALT lymphoma or MALT lymphoma that does not clear after antibiotics usually needs chemotherapy with rituximab.

Splenic marginal zone lymphoma

Splenic marginal zone lymphoma (MZL) is a rare type of low-grade NHL that develops in the **spleen**.

Who gets it?

Splenic MZL can affect people of any age but is most common in people in their 60s. It is linked to certain infections and autoimmune conditions like Sjögren's syndrome or systemic lupus erythematosus (SLE) but the cause is usually unknown.

What are the symptoms?

Splenic MZL causes enlargement of your spleen, which might feel like a lump at the top left of your abdomen (tummy). Some people have low **blood counts**, for example **anaemia** (low red blood cells), which can cause tiredness and shortness of breath and **thrombocytopenia** (low platelets), which can cause you to bruise or bleed more easily than usual.

How is it treated?

If you have few or no symptoms, you are likely to have active monitoring ('watch and wait'). Sometimes, the lymphoma is linked to hepatitis C virus infection and clearing the infection can clear the lymphoma. If you need treatment, you may have a splenectomy (your spleen is removed), **antibody** therapy alone or with chemotherapy, or radiotherapy. The same treatments are used for **relapsed** splenic MZL but newer drugs might be offered, usually as part of a clinical trial.

Nodal marginal zone lymphoma

Nodal marginal zone lymphoma (MZL) develops in **lymph nodes**.

Who gets it?

Nodal MZL can occur at any age but is most common in people in their 60s. It is sometimes linked with hepatitis C virus infection.

What are the symptoms?

Most people have one or more areas of painless swollen lymph nodes, usually in the neck or groin. This is usually the only symptom, but some people also feel very tired and a few have **B symptoms**.

How is it treated?

If you have few or no symptoms, you are likely to have active monitoring. If the lymphoma is linked to hepatitis C virus infection, clearing the infection might clear the lymphoma. If you need treatment, you might have radiotherapy if the lymphoma is localised (in one or few areas). Most people who need treatment have chemotherapy with **antibody** therapy. The same treatments are used for **relapsed** nodal MZL, but newer drugs might be offered, usually as part of a clinical trial.

Waldenström's macroglobulinaemia (lymphoplasmacytic lymphoma)

In lymphoplasmacytic lymphoma (LPL), the abnormal cells are B cells that are in the process of turning into plasma cells. Almost all cases of LPL are a type called 'Waldenström's macroglobulinaemia' (WM).

Who gets it?

Most people who develop WM are over 65. It is slightly more common in men than in women. WM and similar diseases sometimes cluster in families, but the risk of a family member developing WM is still low.

What are the symptoms?

Symptoms develop very slowly over time.

The abnormal cells collect in the blood and **bone marrow** and can cause low **blood counts**. WM also causes abnormal amounts of immunoglobulin (a type of **antibody**) to collect, which can cause hyperviscosity (thickening of the blood). This can cause nosebleeds, vision changes, dizziness or headaches, drowsiness, poor concentration, confusion and shortness of breath.

Less commonly, swollen **lymph nodes** and **B symptoms** can occur.

How is it treated?

Most people have active monitoring ('watch and wait') to start with and do not need treatment for years, sometimes never.

When you need treatment, this is likely to be chemotherapy together with **antibody** therapy. You might need treatment to remove immunoglobulins from your blood if they are causing significant problems.

If WM **relapses**, you may have another period of active monitoring before treatment. You might then have the same treatment as before, a different regimen (combination of drugs) or a newer drug, possibly as part of a clinical trial.

Cutaneous (skin) lymphoma

Cutaneous (skin) lymphomas start in the skin. They are difficult to diagnose as they resemble other more common skin conditions. Cutaneous lymphomas differ from other types of low-grade NHL because treatments are often topical (applied to the skin) rather than systemic (affect the whole body). There are lots of different types of cutaneous lymphoma. Most develop from T cells but some develop from B cells. They are typically chronic (long-term) conditions and are not usually life-threatening.

Who gets it?

Most cutaneous lymphomas affect people over 50 but they can occur at any age. They are more common in men.

What are the symptoms?

T-cell cutaneous lymphomas can start as flat, dry red patches on the skin. They might be itchy. The patches can be harder and thicker – these are called plaques. Papules (small raised areas like a rash) and nodules or tumours (larger swellings) can develop. Some people have erythroderma – large areas of red, thick, swollen and sore skin. B-cell cutaneous lymphomas often start as papules and tumours. Swollen **lymph nodes** can develop.



Patches of dry red skin



Plaques – thickened



Patches with papules



Tumour or nodule

Figure: Photos showing patches, plaques, papules and a tumour

How is it treated?

Topical treatments are often used for early-stage disease, for example steroid and chemotherapy creams, ointments and gels; light treatment and radiotherapy. If the lymphoma is advanced or doesn't respond to topical treatments, you might have systemic steroids, chemotherapy, **antibody** treatment or newer drugs. Some more aggressive types of skin lymphoma need more intensive treatment and can be life-threatening.

Glossary

Allogeneic using someone else's tissue

Anaemia shortage of red blood cells or haemoglobin in the blood

Anaesthetic drugs given to make a part of the body numb (a local anaesthetic) or put the whole body to sleep (a general anaesthetic)

Antibody an immune system protein that sticks to disease causing cells or organisms, such as bacteria, leading to their death

Autologous using a person's own tissue

B symptoms three particularly significant symptoms of lymphoma – fevers, night sweats and unexplained weight loss

Biopsy a test that takes some cells to be looked at under a microscope

Blood count a blood test that counts the cells in your blood, including the red blood cells, the different kinds of white blood cells, and platelets

Bone marrow spongy material at the centre of larger bones, which produces our blood cells

Bulky disease very enlarged lymph nodes

Central nervous system (CNS) the brain and spinal cord

Erythrocytes red blood cells, which carry oxygen around the body

Extranodal lymphoma outside of the lymphatic system

HIV human immunodeficiency virus, a virus that causes weakness in part of the immune system leading to AIDS (acquired immune deficiency syndrome)

Immune system the parts of the body that fight off and prevent infection

Infusion treatment given intravenously through a pump or drip

Intravenous into a vein

Late effects side effects that can persist or develop months or years after treatment has finished

Lymphocyte specialised white blood cells that help fight infection; including B lymphocytes (B cells) and T lymphocytes (T cells)

Lymphopenia shortage of lymphocytes

Lymph node gland that acts like a filter in the lymphatic system; involved in fighting infection

Maintenance treatment to keep lymphoma in remission after successful treatment

Neutropenia shortage of neutrophils in the blood, which makes you more prone to infection

Neutrophil a type of white blood cell that is important in fighting infections caused by bacteria or fungi

Platelets tiny fragments of cells in your blood that help form blood clots and stop bleeding

Red blood cell a cell that contains haemoglobin, which allows it to carry oxygen around the body

Refractory lymphoma that hasn't responded well to treatment

Relapse lymphoma that comes back after treatment

Spleen an organ of the immune system involved in fighting infection and filtering the blood

Stem cell transplant the process of giving back previously harvested stem cells (an autologous stem cell transplant) or of giving donated stem cells (an allogeneic stem cell transplant)

Subcutaneous underneath the skin

Thrombocytopenia shortage of platelets in the blood

Thymus a gland in your chest where T cells mature

White blood cell a cell found in the blood and in many other tissues that helps our bodies to fight infections; there are several different kinds including lymphocytes and neutrophils

Information and support

If you'd like to talk to someone about anything to do with lymphoma (including how you feel) get in touch.



Call our Freephone helpline Monday to Friday on 0808 808 5555. You can also use Live Chat on our website



Come to one of our support groups. Find one near you at www.lymphoma-action.org.uk/SupportGroups



Join our online forum to chat with others who are affected by lymphoma



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Visit www.lymphoma-action.org.uk/TrialsLink to find clinical trials that might be suitable for you.

On our website, you'll find a list of other organisations you may find helpful. There are many other organisations offering specialised help.

How you can help us

We continually strive to improve our resources for people affected by lymphoma and are interested in any feedback you might have about this booklet. Please visit our website at www.lymphoma-action.org.uk/Book-Feedback or email us at publications@lymphoma-action.org.uk with any comments. You can also call our helpline on 0808 808 5555.

We produce other publications that give information about lymphoma and what to expect from treatment. Visit our website at www.lymphoma-action.org.uk or call our Information and Support Team on 0808 808 5555 for more information.



References

The full list of references is available on request. Please email publications@lymphoma-action.org.uk or call 01296 619409 if you would like a copy.

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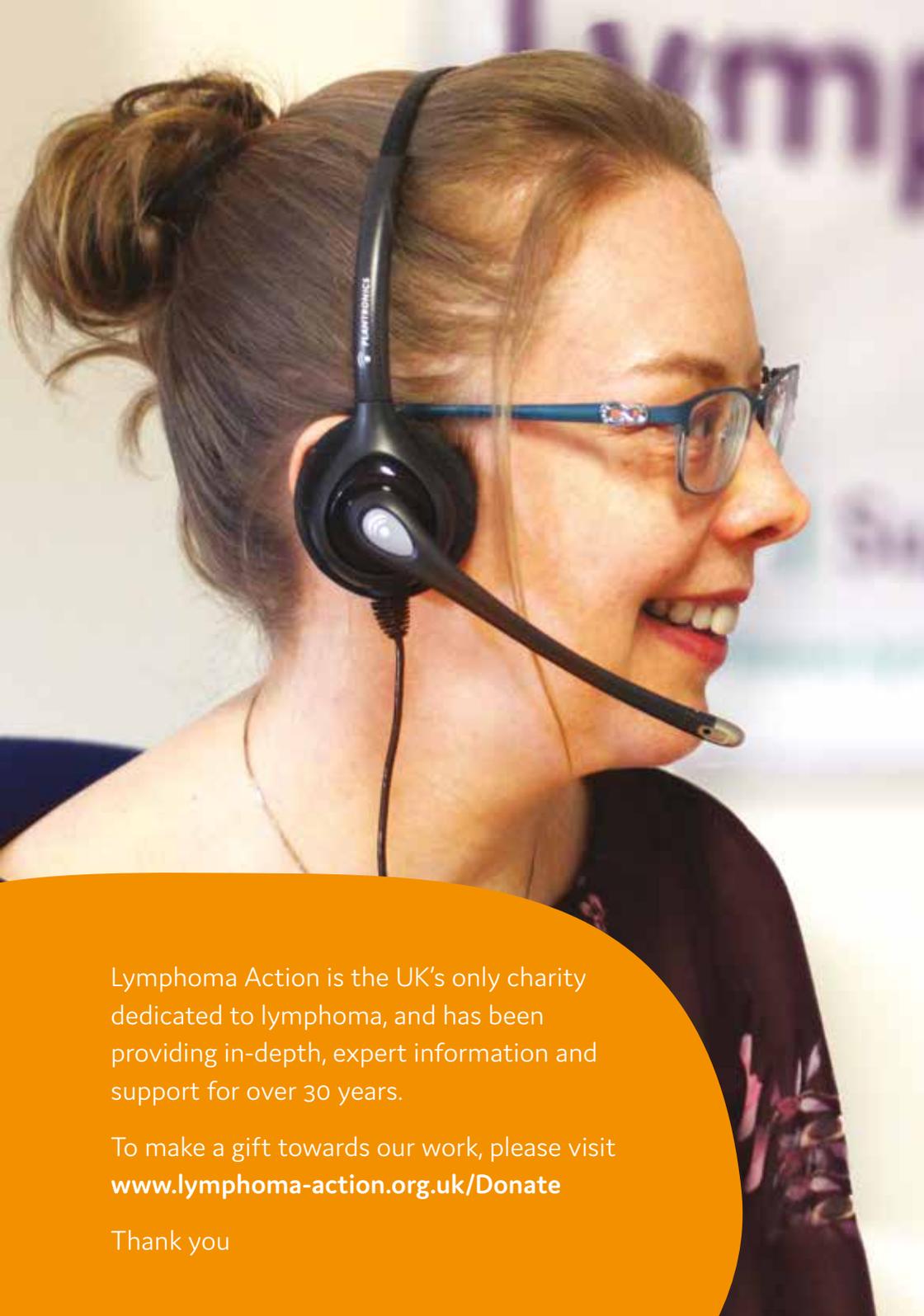
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Lymphoma Action is the UK's only charity dedicated to lymphoma, and has been providing in-depth, expert information and support for over 30 years.

To make a gift towards our work, please visit www.lymphoma-action.org.uk/Donate

Thank you

This booklet will help you understand more about low-grade non-Hodgkin lymphoma (NHL). It describes what low-grade NHL is, how it typically affects people, how it is treated and what to expect during and after treatment.

Lymphoma Action has been providing information and support to people affected by lymphoma for over 30 years. We're here for you.



Freephone helpline **0808 808 5555**



information@lymphoma-action.org.uk



www.lymphoma-action.org.uk

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Lymphoma Action
3 Cromwell Court
New Street, Aylesbury
Bucks HP20 2PB
General enquiries 01296 619400

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