

# The lymphatic system and the immune system

Lymphoma is a cancer that usually grows in the body's lymphatic system. The lymphatic system has a number of functions, but one of its most important roles is in our fight against infection – as part of our immune system. In this article we are aiming to:

- explain what the lymphatic system does in the body
- describe what the lymphatic system is – what cells, tissues, vessels and organs it is made up of
- outline what is meant by the 'immune system'
- explain how the lymphatic and immune systems are affected by lymphoma and by lymphoma treatments.

## What does the lymphatic system do?

The lymphatic system has three main functions:

- It returns excess fluid that has accumulated in the tissues to the bloodstream.
- It absorbs fats and fatty acids from the bowel and transports them into the bloodstream.
- It participates in our defence against infection.

### Clearance of fluids from the tissues

The cells of the body are supplied with oxygen and nutrients from the bloodstream via the tiniest of blood vessels, which are called capillaries. Because our capillaries contain more water than the tissues around them and because the blood circulates under enough pressure to keep it moving, water leaks out into the spaces around the capillaries and accumulates around the cells. This is called 'interstitial fluid'.

Interstitial fluid is necessary in small quantities because it contains the oxygen and nutrients our cells need, but too much interstitial fluid can cause problems such as swelling in the tissues (this is called 'oedema').

The process of recycling excess fluid and returning it to the bloodstream is an important role of the lymphatic system. The lymphatic system takes the excess fluid from around the cells, filters it and returns it to the bloodstream. It has been estimated that the average adult lymphatic system moves around 4 litres of fluid in this way every day.

### Fat absorption

The blood supply to our bowel absorbs most of the nutrients from our food, but most fats and fatty acids are actually absorbed into the lymphatic system first, before being transported into the blood.

The lining of our bowel consists of tiny, finger-shaped structures that project out into the bowel. Each one is called a villus. In the middle of each villus is a tiny lymph vessel or 'lacteal'. The fats are absorbed through the wall of the villus and enter the lacteal, where they form part of a fluid called 'chyle'. Lymphatic vessels then transport the fats into the bloodstream.

## Defence against infection

The lymphatic system is part of our immune system, which is our defence against infection. This is a very important function of the lymphatic system.

The lymph nodes (often referred to as our 'glands') are where the immune response starts off. Invading organisms such as bacteria are broken down by special cells called **dendritic cells**. The dendritic cells take information about the invading organism to lymph nodes. Immune cells called **lymphocytes** are alerted to this information, and they multiply in the lymph node so that their numbers are sufficient to fight the invasion. They move from the lymph node into the blood and are taken to where they are needed.

This process will usually happen in the area where infection has got into the body – an infection will therefore cause swelling in the lymph nodes that drain fluid from that part of the body. When you have a throat infection, for example, the lymph nodes in the neck sometimes swell up.

Other parts of the lymphatic system all have their own individual jobs to do. We will describe the structures that make up the lymphatic system, such as the lymph nodes, in the next section and we will go into more detail about how immunity works on pages 5–8.

## What makes up the lymphatic system?

The lymphatic system is a network running throughout your body, consisting of fluid called lymph, tubes or vessels that transport the lymph, and other organs that contain lymphatic (or 'lymphoid') tissue. **Lymph** is a transparent, straw-coloured fluid. It contains water, cells, proteins and other substances – it is made up of whatever needs to be drained or moved from one place to another.

Lymph is contained in, and moves around in, lymphatic vessels. The **lymphatic vessels** are numerous and can be found everywhere in our bodies except for the bone marrow, the outer layer of the skin and the central nervous system (the brain and spinal cord). They begin as fine tubes called 'lymph capillaries', so small that they are only visible with a microscope. The lymph capillaries surround the cells in our body tissues and also surround our smallest blood vessels (the 'blood capillaries').

Lymph capillaries merge to form larger lymph vessels, which in turn merge to form trunks. The lymphatic trunks drain large areas. Lymphatic trunks then merge to form the **lymphatic ducts**. We have two lymphatic ducts – one that drains the upper right quarter of the body and one that drains everywhere else. The lymphatic ducts drain the lymph into large veins near the heart.

The purpose of all these vessels is to move the lymph away from the tissues and back to the blood circulation. There is no pumping system – the movement of the fluid relies on physical activity – the movements of breathing and of our muscles as we move about. The vessels also contain valves at regular intervals, which prevent the fluid from going backwards.

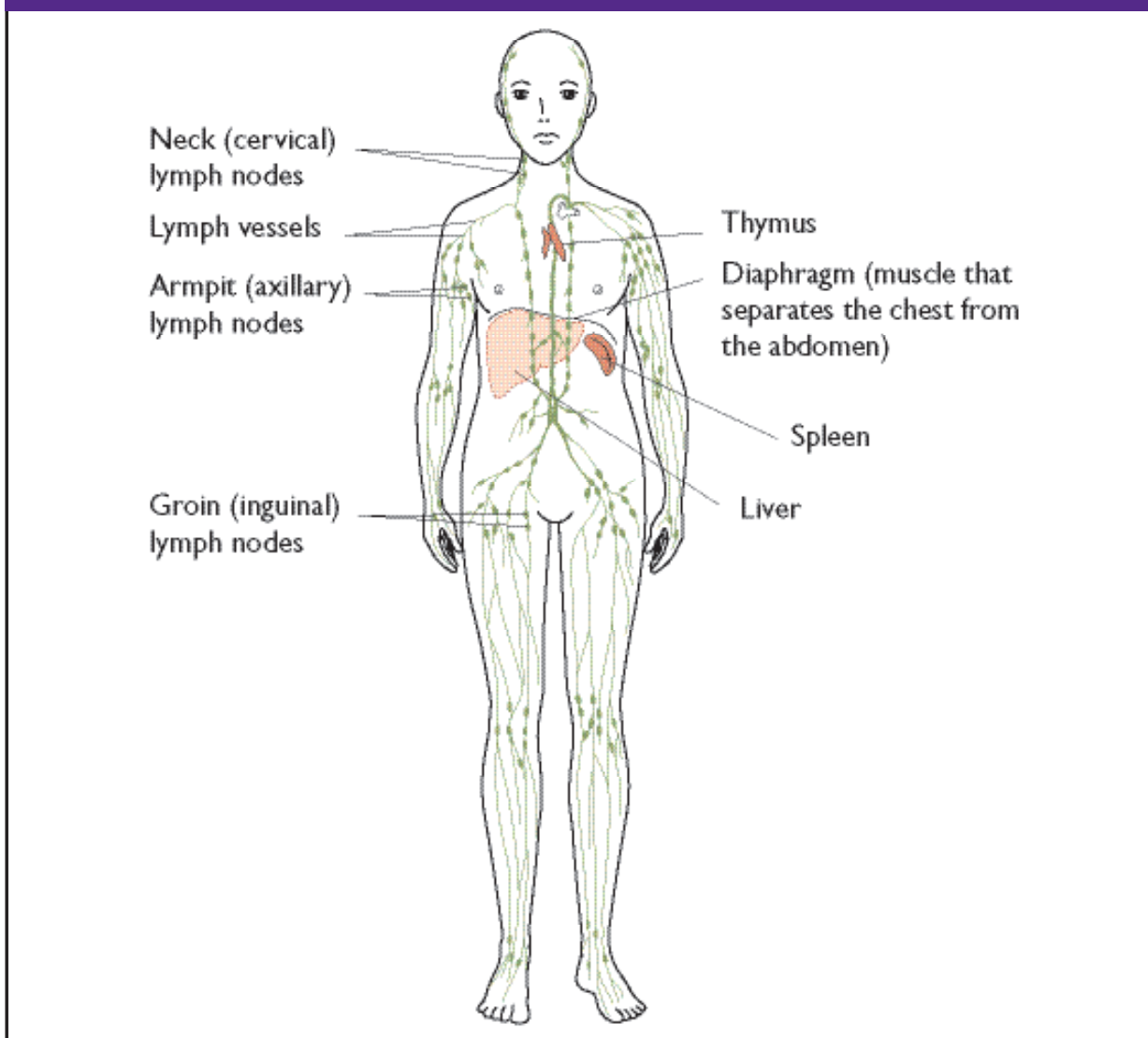
Apart from the lymphatic vessels, the lymphatic system is made up of primary and secondary lymphoid tissues. The immune cells are manufactured in the **primary lymphoid tissues**, which are the:

- bone marrow
- thymus.

The other parts of the lymphatic system – where the immune cells mature, where they meet foreign invaders like infectious organisms, and where the immune response is triggered – are known as **secondary lymphoid tissues** and they include the:

- lymph nodes
- spleen
- tonsils and adenoids
- patches of lymphoid tissue in the gut wall (called Peyer's patches).

### The lymphatic system



## Lymph nodes

At various intervals the lymphatic vessels pass through lymph nodes. The lymph nodes filter the lymph before it re-enters the blood. They are the places where infectious organisms and other foreign invaders meet the immune cells (the lymphocytes). Lymph nodes are found throughout the body. The only place where they are not found is in the brain and spinal cord.

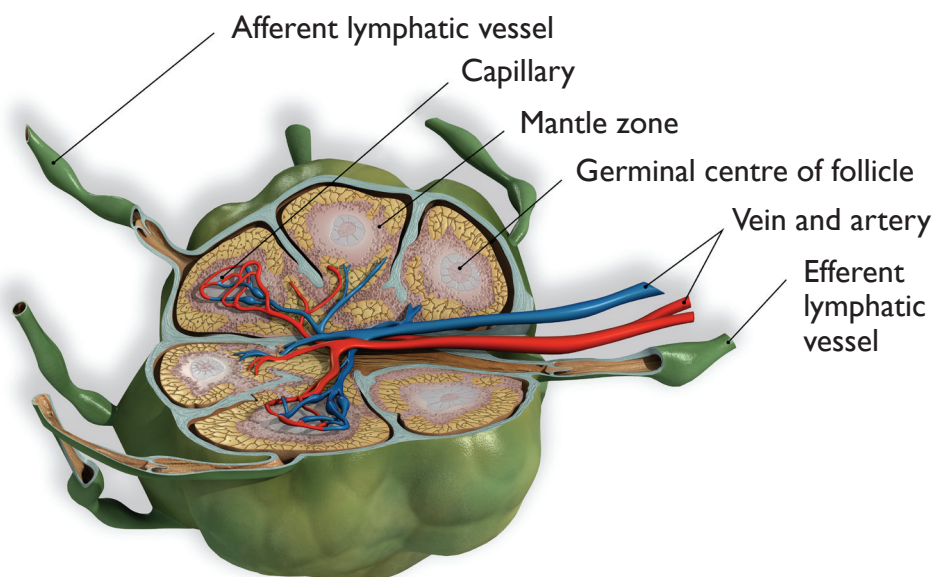
There are three large clusters of lymph nodes on each side of the body – in the armpit (axillary nodes), the neck (cervical nodes) and the groin (inguinal nodes). There are also groups of lymph nodes deeper within the body. You might have heard, for example, of lymph nodes in the area around the heart and between the lungs (mediastinal nodes) or in the abdomen.

Lymph nodes are pinkish or putty-coloured, bean-shaped, and about 1–2.5 cm in length. They are composed of masses of cells in a capsule (an outer covering) of fibrous tissue. The node is divided into sections. The outer area of the node is called the **cortex**. In the cortex there are discrete round areas known as the **follicles**. Each follicle has a central part – the germinal centre – where the immune cells (B lymphocytes or B cells, see page 6) reside and multiply in response to a stimulus such as infection. This germinal centre is surrounded by a **mantle layer** (sometimes called the 'mantle zone'), a layer of resting B cells. The names of these regions are sometimes used to name the particular lymphoma that can start to grow there – such as follicular lymphoma or mantle cell lymphoma. The inner area of the node is the **paracortex**, which is where dendritic cells and T lymphocytes (T cells) are found. T cells are described in more detail on page 7.

Lymph nodes also contain small blood vessels (arteries and veins). This is to ensure that the lymphocytes produced in response to an infection can quickly enter the blood and be taken to where they are needed.

The traffic through the lymph node is one-way – the lymph comes in through 'afferent' lymphatic vessels on the convex side of the bean shape and goes out through 'efferent' vessels on the concave side. There are more afferent than efferent vessels. This means that pressure is maintained in the node to help the process of filtering the lymph.

**A lymph node**



(Science Photo Library / C0081105.2011622)

## Spleen

The spleen is a sponge-like organ that is located in the upper left-hand side of your abdomen, behind your stomach and just underneath your diaphragm (the muscle and fibrous layer that separates the chest from the abdomen). It is the largest of the lymphatic organs of the body and is similar in structure to a lymph node except that it is much bigger. The spleen is also highly vascular, which means it is full of blood vessels.

The spleen consists of two types of tissue – the white pulp and the red pulp. The white pulp is made up mainly of lymphocytes, which are a type of white blood cell. The red pulp is made up of blood-filled passageways called 'venous sinuses' and cords of blood cells.

The lymph node acts as a filter for the lymph and the spleen does the same for the blood. The blood enters the spleen through the splenic artery, moves through the venous sinuses to be filtered, and leaves through the splenic vein. Lymphocytes in the spleen fight infections in the blood and cells in the spleen called 'macrophages' dispose of debris.

The spleen also removes old and damaged red blood cells from the circulation. Another important function of the spleen is to act as a reservoir for platelets, which are tiny cell fragments that normally help with the clotting of our blood when we cut ourselves. In the event of severe bleeding, the spleen can release these platelets into the bloodstream to help clot the blood and stop the bleeding.

## Tonsils and adenoids

The tonsils are three clusters of lymphatic tissue that are found in the pharynx, which is the area where the nasal passages, throat and mouth meet. These clusters are called the 'pharyngeal tonsils'. One cluster is found near the opening of the nasal cavity (sometimes called the adenoids); another cluster is near the opening of the mouth cavity (the palatine tonsils); and the third group is at the back of the tongue (the lingual tonsils). Most potential infections will enter our bodies through the mouth and nose – these are the body cavities that are most exposed to the outside world. The tonsils provide extra defence against infections at this 'front line' against invading organisms.

## Thymus

The thymus is a primary lymphoid organ. It is located in your chest between your aorta (the main artery coming from your heart) and your breastbone. Young lymphocytes called T cells that are still too immature to function as part of the immune system are transported in the circulation from the bone marrow (the other primary lymphoid organ) to the thymus. There they mature into 'immunocompetent' T cells that are capable of working in our defence against infection (they get their name from the 't' of 'thymus'). These more mature T cells move from the thymus into the circulation for transport to other parts of the body.

## What is the immune system?

Our bodies fight a daily battle against foreign organisms and abnormal cells. The lymphatic system plays an important part in this. Our immune system is a sophisticated combination of physical barriers, immune cells and chemicals that act as weapons in this battle.

## Physical barriers to infection

The first phase of our immune system consists of physical barriers designed to stop infection getting into the body in the first place, and these are the:

- skin
- mucosa (sometimes called mucous membranes)
- secretions from the mucosa.

Our **skin** is an important physical barrier against infection, providing a thick layer of defence. People with damaged skin – following burns to a large area, for example – are very prone to infection.

The **mucosa** is the moist tissue that lines the surfaces of the eye, the nasal and respiratory passages, the mouth and digestive system (the bowel), and the genital and urinary tracts. It traps foreign organisms in a number of ways. Tears, saliva and other fluids wash away organisms from the mucosa before they can get a foothold. These fluids are kept moving. In the eyes this happens when we blink. In the urinary tract, flowing urine washes organisms away. In the respiratory tract, little hairs called ‘cilia’ are constantly moving, beating foreign particles out of the lungs into the back of the throat.

The **secretions** on these surfaces are also designed to fight infections. Sticky mucus traps organisms and prevents them from reaching the mucosa underneath it. The secretions are acidic and contain chemicals and compounds called ‘enzymes’ that damage foreign organisms. They also contain antibodies and a group of proteins called complement, which are discussed in more detail on page 7.

## Cells of the immune system

If an organism gets past the skin or the mucosa, immune cells called **macrophages** are the next line of defence. These are found throughout the body tissues, but are more numerous in areas at high risk of infection. They recognise foreign organisms and ‘eat’ or engulf them (‘phage’ comes from the Greek word for ‘eat’). Macrophages are only capable of dealing with small numbers of invading cells, however, and they usually have to call for back-up by sending out chemical messengers. Their main reinforcements are complement and antibodies.

**Neutrophils** are small, short-lived immune cells that are manufactured in the bone marrow and enter the tissues from the blood. They gather in large numbers at sites of infection. They recognise foreign organisms in much the same way as macrophages, then swallow the invaders and kill them. They are particularly important in fighting bacterial infections. Neutrophils cause the surrounding area to become inflamed. Inflammation increases the strength of the local immune reaction to destroy the invading cells. Neutrophils also send out signals to attract other immune cells.

**B lymphocytes** or B cells are immune cells that are found in lymph nodes. They get their name from the ‘b’ of ‘bone marrow’, where they are made. These cells respond to infections by producing specialised proteins called **antibodies**, which act against the organism in various ways. Antibodies recognise and stick to foreign materials like infectious organisms.

During its development, each B cell learns to make one type of antibody, which recognises a single foreign protein (known as the ‘antigen’). The B cell carries copies of that antibody on its surface.



If the B cell comes into contact with the antigen it is primed for, it divides to make daughter cells, which divide again and again and produce more of the same antibody. The cells take time to multiply, so it can take several days for antibody production to reach its peak. After the infection is over, most of the B cells die, but some live on as memory B cells. If the B cell meets the same organism again, the production of the antibody is much quicker this time because of this memory, and the body's immune response to a repeat infection is therefore quicker.

**How do antibodies work?** The antibodies made by the B cells go into the bloodstream and they are also found in the secretions on mucosal surfaces. They fight invading organisms in several ways. First, when antibodies attach themselves to proteins on bacteria and viruses, they stop the invader from doing what it is supposed to do, for instance sticking to and infecting other cells. Also, macrophages and neutrophils recognise antibodies attached to foreign organisms, and use this as a signal to eat them. Antibodies attached to the organism also activate the chemicals of complement.

**Complement** is a concoction of about 40 proteins that are made in the liver and are then found in body fluids. Complement is released when an antibody attaches to a foreign invader. When complement comes into contact with organisms it is activated and changes form. The complement can then cause the organism or foreign cell to die. If this doesn't happen, the altered complement on the surface of the organism or foreign cell acts as a signal to macrophages that the organism should be eaten.

**T lymphocytes** (T cells) are sophisticated immune cells that start their life in the bone marrow. They mature in the thymus (see page 5), then move from the thymus to the lymph nodes, where they will encounter foreign particles and organisms. Each T cell has a protein on its surface (a surface receptor protein) that, like an antibody, recognises a specific foreign protein. If the T cell comes into contact with a protein that it has been programmed to recognise, it grows and divides into mature T cells, which go on to take on a variety of different tasks in the immune response:

- Some T cells develop into 'cytotoxic' T cells which kill invading organisms directly. This is very important in the fight against organisms that grow inside our own cells (like viruses and tuberculosis bacteria). Cytotoxic T cells also identify and kill any of our own cells that might be turning cancerous. Something goes wrong with this process when people develop cancer.
- Some T cells develop into 'helper' T cells – their job is to boost the production of antibodies from the B cells and they also activate macrophages and neutrophils.
- Some mature T cells remain as 'memory' T cells so that the immune response to that organism is quicker the next time.

Other cells of the immune system that you might hear mentioned are dendritic cells, histiocytes and natural killer or NK cells. **Dendritic cells** are increasingly being recognised as pivotal in the immune system. They are involved in the activation of B cells and T cells and are important in the memory function of the immune system – how it remembers the foreign substances it has reacted against before. They were recently described as being like the 'conductor of the immune system orchestra'.

**Histiocytes** are immune cells found in the tissues. Their job is to alert the B cells and T cells to the presence of foreign materials; they also get rid of waste-products in the tissues. **NK cells** are similar to T cells but can kill cells that have been infected by viruses and tumour cells without having to go through the stage of maturing in the thymus, as T cells have to do.

## How does lymphoma affect the immune system?

When a lymphoma develops, cancerous lymphoma cells are produced instead of some of your normal immune cells, and this can mean that:

- the part of the lymphatic system that is affected can't do its usual job properly
- enlarged lymph nodes can press on surrounding areas and damage healthy tissues
- lymphoma cells can use up lots of your body's energy and resources, eventually placing a strain on other tissues.

Because lymphoma is a disease of immune cells, it can interfere with the working of the immune system. The effects your lymphoma has on your body will depend on which type of immune cell has become cancerous and on what part of your body is involved. For example, in people with Hodgkin lymphoma the T cells don't seem to work properly. This slightly increases the risk of getting infections such as cold sores, shingles and tuberculosis. Some people with non-Hodgkin lymphoma will have problems with their B cells and the production of antibodies. This can increase the risk of infections like pneumonia and meningitis.

All the blood cells circulating in the bloodstream and the immune cells are made in the bone marrow and lymphoma can involve the bone marrow. If there is lymphoma in the bone marrow, this can lead to a reduction in the production of blood cells. If a lot of the bone marrow is involved it can result in a serious shortage of neutrophils. This increases the risk of infection, particularly from bacteria. In addition, if the bone marrow is severely affected, this can lead to a lack of red blood cells (causing anaemia) and to a reduction in the number of platelets (increasing the tendency to bruising and bleeding).

If you have lymphoma in the spleen, it can make the spleen do too much of its usual job. The enlarged spleen will remove healthy red blood cells from the circulation as well as the damaged ones. This can lead to anaemia, a common symptom of lymphoma in the spleen.

## How does treatment for lymphoma affect the immune system?

Having treatment for lymphoma has a significant impact on the immune system in several different ways:

- **Chemotherapy** causes damage to the rapidly dividing cells of the bone marrow. This leads to a reduction in the production of blood cells. Neutrophils are especially important in fighting bacterial infections like pneumonia, septicaemia (blood poisoning), meningitis and urinary infections. Neutrophil numbers commonly fall 1–2 weeks after chemotherapy treatments. A low neutrophil count – **neutropenia** – will therefore mean you are at increased risk of infection. The longer the neutrophil count remains low, the higher the risk.



Supportive treatment with therapy called a 'growth factor' can be used to stimulate neutrophil development and speed up neutrophil recovery after chemotherapy. It is extremely important that you seek medical help immediately if you develop a high temperature or any other symptoms or signs of infection while you are having chemotherapy. You might need to be in hospital for intravenous antibiotics.

- **Steroids** are an important part of the treatment of lymphoma and they can have quite marked effects on your immunity. The most important effect is an increase in the risk of infections with the viruses that cause cold sores and chickenpox (which can reactivate as shingles) and of fungal infections like thrush. When big doses of steroids are given for a long time this increases the risk of more serious infections, such as a kind of pneumonia called *Pneumocystis pneumonia* or PCP, and you might be given special antibiotics to prevent this.
- **Drips and central lines** can also pose a problem because they breach the skin barrier and can allow infectious agents to enter your bloodstream. They must therefore be carefully checked and cleaned.
- **Dry mucous membranes** – chemotherapy agents and radiotherapy to the head and neck can reduce the production of saliva and other mucosal secretions. This means that you can experience dryness in the eyes, mouth and nose, which makes the physical barriers to infection less effective. If the treatment also causes mouth ulcers, this provides an easy way for bacteria to enter the body and further increases the risk of infection.
- **Splenectomy** – a few people with lymphoma will have their spleen removed, either as part of their lymphoma treatment or occasionally during the diagnosis stage. This operation is called a splenectomy. Having no spleen can lead to an increased risk of infection by some bacteria and so people having this operation are given vaccinations against pneumococcus, meningococcus and *Haemophilus* bacteria beforehand and might be offered low-dose penicillin afterwards.

These effects of lymphoma treatments on the body's immunity are especially pronounced after bone marrow and stem cell transplants because of the higher doses of chemotherapy that are used. Immediately after a transplant, people have very little immunity and are at high risk of all kinds of infection. It can take more than a year for antibody levels to recover after a transplant. Because of the destruction of memory cells, some people might need to have their childhood vaccinations repeated, especially after an allogeneic transplant.

## The immune system after recovery from lymphoma

After you have had treatment for lymphoma, minor changes in the immune system might be detectable forever. There is no evidence that this is associated with an increased risk of infection, however. The only people known to have a long-term increased risk of infection after treatment for lymphoma are people who have had a splenectomy – this is why they receive special vaccinations and might be prescribed long-term antibiotics.

If you are not on any immediate treatment for your lymphoma (often called 'watch and wait') or if your treatment has finished and you are in remission, you will still get infections occasionally like everybody else, and your body will still fight them. This means that your glands can become swollen when you have infections like a sore throat or a skin infection, just as they would have

done before you developed lymphoma. If they don't go down again when the infection gets better or if you are at all concerned, you should speak to your GP or ask to see your medical team at the hospital.

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## More information

The Lymphoma Association has a wide range of booklets and information sheets on all aspects of lymphoma and the treatments that are available. We also have information sheets on splenectomy and on shingles. Visit our website at [www.lymphomas.org.uk](http://www.lymphomas.org.uk) or telephone our freephone helpline (0808 808 5555) if you would like to receive any of this information or if you would like to talk to someone about your lymphoma.

## Feedback

We continually strive to improve our information resources for people affected by lymphoma and we would be interested in any feedback you might have on this article. Please visit [www.lymphomas.org.uk/feedback](http://www.lymphomas.org.uk/feedback) or email [publications@lymphomas.org.uk](mailto:publications@lymphomas.org.uk) if you have any comments you would like to make. Alternatively please phone our helpline on 0800 808 5555.

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