Diffuse large B-cell lymphoma

This page is about diffuse large B-cell lymphoma (DLBCL), the most common type of high-grade (fast-growing) non-Hodgkin lymphoma (NHL).

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What is diffuse large B-cell lymphoma (DLBCL)?

Lymphoma develops when lymphocytes (a type of white blood cell) start to divide in an uncontrolled way. There are lots of different types of
lymphoma. Diffuse large B-cell lymphoma (DLBCL) is the most common type of high-grade (fast-growing) non-Hodgkin lymphoma. There are several features that give DLBCL its name:

- it develops from abnormal B lymphocytes (B cells)
- the abnormal cells are larger than normal, healthy B cells
- the abnormal cells are spread diffusely (spaced out rather than grouped together) throughout the tumour and wipe out the normal structure of the lymph node (gland).

*Figure: Cells from a biopsy of DLBCL showing abnormal, large cells spread diffusely*

The vast majority of people have the most common type of DLBCL, which is described on this page. Some people have a rare type of DLBCL that has different features to the most common type. These differences can be seen under a microscope and in tests on the lymphoma cells. They can cause different symptoms, but they are all usually treated in the same way.

If you have been diagnosed with a rare type of DLBCL, you might want to read the sections at the end of this page with more information on the
features of these types and the symptoms they cause. If you have been diagnosed with DLBCL, and not one of the following rare types, you might want to skip these sections.

Rare types of DLBCL include:

- **T-cell/histiocyte-rich large B-cell lymphoma**
- **EBV-positive DLBCL of the elderly**
- **primary mediastinal (thymic) large B-cell lymphoma**
- **intravascular large B-cell lymphoma**
- **ALK-positive large B-cell lymphoma.**

Very rare types of large B-cell lymphoma can develop in people with severe immune system problems like human immunodeficiency virus (HIV), eg plasmablastic lymphoma.

If DLBCL starts in your central nervous system (CNS; brain, spinal cord and eyes), it is a primary CNS lymphoma.

Some types of DLBCL only affect the skin. We have separate information about skin lymphoma.

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**Who gets DLBCL and why?**

Around 4,800 people are diagnosed with DLBCL each year in the UK. It can occur at any age, including in children, but the risk of developing DLBCL increases with age. Most people diagnosed with DLBCL are 65 or over. DLBCL affects slightly more men than women.

In most cases, the **causes** of DLBCL are not known. Rarely, there is an association between DLBCL and **disorders of the immune system**. These include:

- autoimmune disorders like rheumatoid arthritis and systemic lupus erythematosus (DLBCL can develop as a result of chronic (long-term) inflammation)
- **HIV**
• **organ transplantation.**

However, most people with these disorders never develop lymphoma and most cases of DLBCL are not related to an underlying immune disorder.

Sometimes DLBCL develops in people who have had a low-grade (slow-growing) lymphoma in the past – their lymphoma transforms (changes) into a quicker growing DLBCL. If this is the case for you, you might also find our information on transformation helpful.

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**Symptoms**

Most people with DLBCL first notice painless lumps, often in their neck, armpit or groin. These are enlarged lymph nodes (swollen glands). They can grow quite quickly, over just a few weeks.

DLBCL can develop in lymph nodes deep inside your body where they can’t be felt from the outside. It is quite common for people with DLBCL to have lymphoma in extranodal sites (areas outside the lymph node). Large lumps can form – this is known as ‘bulky disease’.

DLBCL can be hard to diagnose as people have different **symptoms** depending what organs and tissues their lymphoma is affecting, for example:

- **DLBCL in your stomach or bowel** can cause abdominal (tummy) discomfort or pain, diarrhoea or bleeding
- **DLBCL in your chest** can cause a cough or breathlessness.

Some people with DLBCL experience fevers, night sweats and unexplained weight loss. These are known as ‘B symptoms’.

Fatigue and loss of appetite are also quite common, and some people experience severe itching.
Diagnosis and staging

DLBCL is usually diagnosed from a biopsy (sample of tissue taken to see if lymphoma cells are present).

Other tests might be done to give your doctor more information about the lymphoma. For example, there are several subtypes of DLBCL that can be detected:

- germinal centre B-cell-like or GCB subtype
- non-GCB types, usually activated B-cell-like (ABC subtype).

At the moment, most people with DLBCL have the same treatment. However, researchers are continuing to unpick the biology of lymphoma cells with the aim of identifying people who are more likely to respond to certain treatments. We have regular updates on clinical trials and advances in lymphoma research in our news section and in our magazine, Lymphoma matters.

Your doctor might use the term ‘double-hit lymphoma’ if your lymphoma cells have 2 major lymphoma-related changes in their genes. Double-hit DLBCL can need more intensive treatment.

You have other tests to:

- find out which parts of your body the lymphoma is growing in
- look at your general health, including how well organs like your heart and kidneys are working.

This is called ‘staging’. Stage 1 and 2 are ‘early-stage’ DLBCL. ‘Advanced-stage’ DLBCL is stage 3 and stage 4. Most people have advanced-stage DLBCL when they are diagnosed.

These tests usually include blood tests and scans like CT or PET/CT scans. You might also have bone marrow tests to see if you have lymphoma cells in your bone marrow.

Waiting for your test results is a worrying time, but it is very important that the diagnosis is correct so that you can have the best treatment.
Outlook

At any stage, DLBCL is usually treated with the aim of curing it. Your outlook depends on the stage of the lymphoma and your general health. Researchers are beginning to unpick the differences between distinct subtypes of DLBCL. This will help them to identify people who are most likely to benefit from certain treatments.

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

Your doctor might calculate a prognostic score using the International Prognostic Index (IPI), which takes several different risk factors into account. Your score on the IPI or your risk factors are used to plan your treatment.

High-grade lymphomas often respond well to treatment and many people go into remission (no evidence of lymphoma). In general, more people with early-stage DLBCL go into remission than people with advanced-stage DLBCL.

Survival statistics can be confusing as they don’t tell you what your individual outlook is – they only tell you how a group of people with the same diagnosis did over a period of time. Remember that treatments are improving all the time and survival statistics are usually measured over 5 or 10 years after treatment. Consider also that these statistics only tell you how people did in the past. Those people may have received treatment different to yours. Because of this variability, many people do not find survival statistics helpful.

If you want to know more about survival statistics for DLBCL, Cancer Research UK have some information that you might find useful.
Treatment

When your medical team plan how best to treat you, they consider several factors, including:

- the stage of the lymphoma
- information about the lymphoma from your biopsy and blood test results
- where in your body the lymphoma developed and what tissues and organs it is affecting
- your general health.

Some hospitals give scans part-way through treatment to see how you are responding.

If you are under 18, or are a parent or carer of someone under 18 who has DLBCL, our section on non-Hodgkin lymphoma in children has more information on treatment in this age group. Young people (up to 24) with DLBCL might also find our section on lymphoma in young people useful.

Your medical team should give you information about the possible side effects and late effects (side effects that develop long after treatment) of the treatment they recommend.

Treatment of early-stage DLBCL

Most people with early-stage DLBCL (stage 1 or stage 2) are treated with a short course of chemotherapy or chemo-immunotherapy (chemotherapy given with antibody therapy) followed by radiotherapy.

The most commonly used chemotherapy regimen (combination of drugs) is CHOP, which includes:

- 3 chemotherapy drugs: cyclophosphamide, hydroxydaunorubicin (doxorubicin) and vincristine (Oncovin®)
- prednisolone (a steroid).

Rituximab is usually added to the chemotherapy. Rituximab is an antibody therapy. This chemo-immunotherapy regimen is known as ‘R-CHOP’.

The drugs are given in cycles, with treatment given on certain days followed by a rest period for your body to recover before the next cycle. Each cycle
usually takes 3 weeks. Most people with early-stage DLBCL have 2–4 cycles of CHOP or R-CHOP. If you have very large lymph nodes (bulky disease), your doctor might recommend you have 4–6 cycles of chemotherapy before your radiotherapy.

You have most of the drugs given intravenously (into a vein). Prednisolone is given as tablets. Most people come into hospital to have their treatment and don’t need to stay overnight.

You may have radiotherapy to the area affected by lymphoma after your course of chemo-immunotherapy. Very occasionally, radiotherapy is used on its own if you are not well enough to have chemotherapy, eg if you have severe heart or lung disease.

If you have DLBCL in an area difficult to treat with radiotherapy, you might be treated with a longer course of chemotherapy.

**Treatment of advanced-stage DLBCL**

Advanced-stage DLBCL (stage 3 and 4) is usually treated with a longer course of R-CHOP. A total of 6–8 cycles of treatment are given.

If the lymphoma has features that suggest it will be difficult to treat, eg double-hit lymphoma, your doctor might suggest more intensive chemo-immunotherapy regimens, such as:

- R-CODOX-M / R-IVAC – which contains rituximab, cyclophosphamide, doxorubicin, vincristine, methotrexate, etoposide, ifosfamide and cytarabine.
- DA-EPOCH-R – which contains dose-adjusted etoposide, prednisolone, vincristine, cyclophosphamide and doxorubicin.

Some people are not well enough to have strong chemotherapy. Others have health problems, such as heart problems, that mean CHOP is not suitable for them. A different regimen is given in these cases, eg:

- R-miniCHOP – in which the dosage of each drug is reduced or some of the drugs might be left out
- R-GCVP – which uses gemcitabine in place of doxorubicin
- **R-CEOP** – which uses etoposide in place of doxorubicin.

Most people with advanced-stage DLBCL do not have radiotherapy as their lymphoma is widespread rather than localised to 1 or few areas. However, you might have radiotherapy if:

- you have localised lymphoma left after your chemotherapy
- you have bulky disease – the radiotherapy can help prevent the lymphoma relapsing (coming back) in these areas.

Your doctor might suggest a newer, targeted drug. These are usually only available through a clinical trial.

### CNS prophylaxis in DLBCL

Around 1 in 20 people have DLBCL that relapses in their central nervous system (CNS, which includes your brain and spinal cord) after going into remission. If this happens, the lymphoma is very difficult to treat.

If you are considered to be at high risk of the lymphoma relapsing in your CNS, you might be given preventative treatment – ‘CNS prophylaxis’. Most chemotherapy cannot reach your brain or spinal cord, so any lymphoma cells remaining there could grow and cause the lymphoma in your CNS.

In CNS prophylaxis, you are given drugs that reach the CNS. You might have intrathecal chemotherapy, where a drug like methotrexate is given by lumbar puncture directly into the fluid surrounding your spine. Some people have CNS prophylaxis intravenously. CNS prophylaxis might be given during your chemo-immunotherapy or after you have finished chemo-immunotherapy.

### Relapsed and refractory DLBCL

You are likely to have a scan at the end of treatment to see how well you have responded. Many people respond well to their first treatment for DLBCL and go into complete remission. However, some people need more treatment, for example:
- the lymphoma might be reduced but not completely cleared
- the lymphoma might be refractory to treatment (it did not get better).

Sometimes, the lymphoma relapses (comes back) after successful treatment. **Relapse** is most likely to happen within 2 years of the end of the first treatment. As time goes on, lymphoma is less likely to relapse.

Most people who have relapsed or refractory lymphoma are offered other treatments. This is sometimes known as ‘salvage’ treatment.

If you are well enough, your doctor might suggest you have high-dose chemo-immunotherapy. The aim of this type of treatment is to reduce the lymphoma and then increase your chance of remission using a **stem cell transplant**. A stem cell transplant works best if the lymphoma responds at least partially to the high-dose therapy.

Most people have a stem cell transplant using their own cells (autologous). In some cases, you might be given a donor stem cell transplant (allogeneic). For example, if you relapse after an autologous stem cell transplant or the doctors were unable to collect enough of your own stem cells.

There are several different chemo-immunotherapy regimens used for people who need more intensive (strong) treatment. Most people are given a platinum-based regimen, for example:

- R-GDP – rituximab with gemcitabine, dexamethasone and cisplatin
- R-DHAP – rituximab with dexamethasone, cytarabine and cisplatin
- R-ICE – rituximab with ifosfamide, carboplatin and etoposide.

If you are not well enough for a stem cell transplant, you might still be able to have chemo-immunotherapy.

There are also many targeted drugs in development for DLBCL. Your doctor might suggest you take part in a **clinical trial** to give you access to a newer drug.
Research and targeted treatments

Drugs being tested in DLBCL, but not yet approved in the UK include:

- drugs that block signals or the function of control proteins within the lymphoma cells, which, depending how they work, can be grouped as:
  - cell signal blockers, eg ibrutinib (Imbruvica®)
  - proteasome inhibitors, eg bortezomib (Velcade®)
- newer antibodies against CD20, the protein targeted also by rituximab, eg obinutuzumab (Gazyva®)
- antibody-drug conjugates, which join a strong anti-cancer drug to an antibody to deliver the drug directly to the cancer cells, eg brentuximab vedotin (Adcetris®), inotuzumab ozogamicin and polatuzumab vedotin
- immunomodulatory drugs, which affect the activity of your immune system, eg lenalidomide (Revlimid®)
- immune checkpoint inhibitors, which allow your immune system to recognise and kill the lymphoma cells, eg nivolumab and pembrolizumab
- newer chemotherapy drugs, eg pixantrone (Pixuviri®).

We have only included drugs in later phases of testing here. There are other drugs in early phase clinical trials and new drugs are being developed and tested all the time.

Another growing research area is CAR T-cell therapy. It involves engineering your own immune cells to recognise and attack your lymphoma cells. There is a lot of interest in this area, but trials are still in early phases.

Find out more about clinical trials and find a trial that might be suitable for you at Lymphoma TrialsLink.

Follow-up

You have a scan at the end of treatment to see how you have responded. This is usually a PET/CT scan. Sometimes it is hard to tell whether any lumps in your body after treatment are scar tissue or lymphoma. A PET/CT scan shows areas of active (growing) lymphoma.
You might need other tests after treatment finishes. Your doctor can use the results of the scan and other tests, if needed, to see if you are remission (no evidence of lymphoma) or if you need further treatment.

When you are in remission after treatment, you have regular follow-up appointments. These are to check that:

- you are recovering well from treatment
- you have no signs of relapse
- you are not developing any late effects (side effects that develop months or years after treatment).

At each appointment, your doctor examines you and asks if you have any concerns or symptoms. You might have blood tests. You are unlikely to have a scan unless you have troubling symptoms.

You are likely to be seen every 3 months at first. After a year, your appointments might be every 6 months. The risk of the DLBCL relapsing is highest in the first 2 years. As time goes on, relapse becomes less likely and you are seen less often. Hospitals differ in how long they normally follow-up for. The length of your follow-up also depends on your individual circumstances, eg what type of DLBCL you’ve had and what treatments you’ve had. People are usually followed up for 2–5 years after treatment for DLBCL.

**Life after lymphoma: Blair’s story**

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**Rare types of DLBCL**

There are a few rare types of DLBCL, including:

- **T-cell/histiocyte-rich large B-cell lymphoma**
- **EBV-positive DLBCL of the elderly**
- **Primary mediastinal large B-cell lymphoma (PMBL)**
- **Intravascular large B-cell lymphoma**
- **ALK-positive large B-cell lymphoma.**
These lymphomas cause different symptoms from the common type of DLBCL but the tests and treatments used are usually the same.

**If you do not have one of these rare types of DLBCL, you might want to skip this section.**

**T-cell/histiocyte-rich large B-cell lymphoma**

T-cell/histiocyte-rich large B-cell lymphoma mainly affects middle-aged men but it can affect men and women of any age.

In your biopsy, you have a small proportion of large B cells together with T cells and often histiocytes (another kind of immune cell). T-cell/histiocyte-rich large B-cell lymphoma can look like Hodgkin lymphoma under a microscope. It is important that is diagnosed accurately, so you can have the most effective treatment.

The most common symptoms are:

- swollen lymph nodes (glands)
- swelling of the liver or spleen, which can cause abdominal (tummy) swelling and discomfort
- feeling generally unwell, with B symptoms (fever, night sweats and unexplained weight loss).

**EBV-positive DLBCL of the elderly**

This type of lymphoma develops in people over 50, with an average age of early- to mid-70s. It is slightly more common in men.

It is thought this lymphoma develops when the Epstein–Barr virus (EBV) interferes with the body's immune system. This lymphoma is sometimes called 'age-related EBV-associated B-cell lymphoproliferative disorder'.

Many people in the world are infected by EBV and the infection does not usually cause any symptoms. It is not known why some people with EBV get lymphoma.
Your symptoms depend where the lymphoma is growing:

- Most people (7 in 10) have lymphoma in extranodal (outside the lymph nodes) sites, most commonly the skin, lung, tonsils or stomach.
- Some people (3 in 10) have this lymphoma only in the lymph nodes.

**Primary mediastinal (thymic) large B-cell lymphoma (PMBL)**

Primary mediastinal large B-cell lymphoma usually affects young adults. The average age of people who develop this lymphoma is 35. It is more common in women.

The lymphoma starts growing in the mediastinum, which is the area in the middle of the chest, behind the sternum (the breastbone). There is often a large lump of lymphoma (bulky disease). It can spread to lymph nodes.

PMBL can cause problems by pressing on the lungs, gullet or superior vena cava (the large vein that takes blood back from the body to the heart). It can also lead to collections of fluid around the heart (pericardial effusion) or the lung (pleural effusion). Possible early symptoms are:

- breathlessness
- cough
- difficulty swallowing
- swelling of the neck and face
- headaches
- dizziness.

Your doctor might recommend a more intensive chemotherapy regimen for this particular type of lymphoma, eg dose-adjusted EPOCH. Your doctor can give you more information about the risks and benefits of this approach.

**Intravascular large B-cell lymphoma**

This lymphoma occurs mainly in older adults – people in their mid-60s on average. A similar number of men and women are affected. The cancerous
lymphocytes are found within small blood vessels called ‘capillaries’.

Your symptoms depend on which capillaries are affected. Possible symptoms include:

- nervous system symptoms such as confusion, seizures, dizziness or weakness
- reddened patches or lumps in the skin
- B symptoms (fever, night sweats, unexplained weight loss).

If the lymphoma only affects your skin, you might be treated with radiotherapy alone.

**ALK-positive large B-cell lymphoma**

This very rare type of DLBCL affects people from all age groups. It occurs mainly in men. The lymphoma cells have a mutation that makes them express a protein called ‘anaplastic large-cell kinase (ALK)’ on their surface. They don’t usually have CD20 on their surface so rituximab does not work for this type of lymphoma.

Most people have enlarged lymph nodes (swollen glands) but the lymphoma can grow in the mediastinum (centre of the chest) or at extranodal sites (outside of the lymph nodes).

References

The full list of sources used in the preparation of this information is available on request. Please contact us by email on publications@lymphoma-action.org.uk or telephone on 01296 619409 if you would like a copy.


guidelines (Accessed May 2016).


Further reading

- Chemotherapy
- Glossary
- What is lymphoma?

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We would like to thank the Expert Reviewers and members of our Reader Panel who gave their time to review this information.
Tell us what you think and help us to improve our resources for people affected by lymphoma. If you have any feedback, please visit www.lymphoma-action.org.uk/feedback or email publications@lymphoma-action.org.uk.

All our information is available without charge. If you have found it useful and would like to make a donation to support our work you can do so on our website www.lymphoma-action.org.uk/donate. Our information could not be produced without support from people like you. Thank you.

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