Helpline (freephone) 0808 808 5555
information@lymphoma-action.org.uk
www.lymphoma-action.org.uk

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.

On this page

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

Lymphoma is a type of blood cancer that develops when white blood cells called **lymphocytes** grow out of control. Lymphocytes are part of your **immune system**. They travel around your body in your **lymphatic system**, helping you fight infections. There are two types of lymphocyte: **T lymphocytes (T cells)** and **B lymphocytes (B cells)**.

There are lots of different **types of lymphoma**. Diffuse large B-cell lymphoma (DLBCL) is the most common type of **non-Hodgkin lymphoma**. It is a **fast-growing (high-grade) lymphoma**.

It is called DLBCL because:

- it develops from abnormal B cells
- the abnormal cells are larger than normal, healthy B cells
- the abnormal cells are spread out (diffuse) rather than grouped together when they're examined under a microscope.

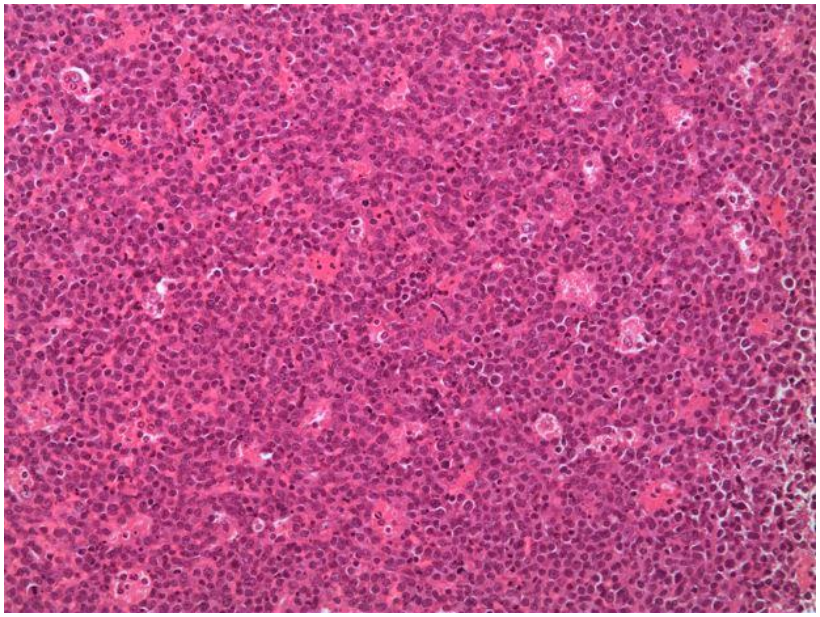

Figure: Cells from a biopsy of DLBCL showing abnormal, large B cells spread diffusely

Who gets DLBCL?

Around 5,500 people are diagnosed with DLBCL each year in the UK. It can develop at any age, including in children, but it is more common in older people. 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 **conditions affecting the immune system**. These include:

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

You may have a **slightly** increased risk of developing DLBCL if:

- you have a family member who has had lymphoma
- you have hepatitis C virus
- you were overweight as a young adult.

However, most people with these characteristics never develop lymphoma.

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

Symptoms of DLBCL

Most people with DLBCL first notice painless lumps, often in their neck, armpit or groin. These are **swollen (enlarged) lymph nodes**. They usually grow quite quickly, over just a few weeks. Sometimes, DLBCL can develop in lymph nodes deep inside your body where they can't be felt from the outside. The swollen nodes can form large lumps – known as 'bulky disease'. DLBCL can also develop outside lymph nodes, called 'extranodal' disease. This affects around 1 in 5 people with DLBCL.

The exact symptoms you experience depend on where in your body the DLBCL is. These are called **local symptoms**. They can be very variable depending on what organs or tissues are affected. For example:

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

Around 1 in 3 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 of DLBCL

The main way to diagnose DLBCL is to remove a swollen lymph node, or a sample of cells from it, and look at it under a microscope. This involves a small operation called a **biopsy**, which is usually done under a local anaesthetic. The sample is also tested for particular proteins that are found on

the surface of lymphoma cells. This can help your medical team decide on the most appropriate **treatment** for you.

You also have **blood tests** to look at your general health, check your **blood cell counts**, make sure your kidneys and liver are working well and rule out infections that could flare up when you have treatment.

You have other tests to find out which areas of your body are affected by lymphoma. This is called **staging**. Staging usually involves having a **PET scan** and a **CT scan**. Some people, particularly children, may have an **MRI scan**. You might have a sample of your bone marrow cells taken (a **bone marrow biopsy**), to check if you have lymphoma cells in your bone marrow. You might have a **lumbar puncture** to check if you have lymphoma cells in the fluid around your brain and spinal cord (cerebrospinal fluid or CSF).

You usually have your tests done as an outpatient. It takes a few weeks to get all the results. **Waiting for test results** can be a worrying time, but it is important for your doctor to gather all of this information in order to plan the best treatment for you.

Types of DLBCL

There is some complex information in this section. However, not all of it will apply to you. You may wish to read only information that is relevant to you, or you might prefer to skip this section completely. If you are not sure what type of lymphoma you have, ask your medical team.

Most people with DLBCL do not have a specific type. This is sometimes called ‘DLBCL not otherwise specified’ or ‘DLBCL NOS’. Even if you have DLBCL NOS, your biopsy sample might still be analysed to find the exact sort of B cell your lymphoma developed from. The main cell types are:

- germinal centre B cells (GCB)
- activated B cells (ABC).

At the moment, most people with DLBCL NOS have the same treatment. However, scientists are carrying out research to find out if different treatments are effective against types of DLBCL that developed from different cells. In the future, this might help doctors choose the most appropriate treatment for each individual person.

Rare types of DLBCL and other large B-cell lymphomas

Some people have a rare subtype of DLBCL or other large B-cell lymphoma. These subtypes are usually detected by looking at your biopsy sample under a microscope or using specialist laboratory tests. They can cause different symptoms from the most common type of DLBCL but they are usually treated in the same way.

Rare types of DLBCL and other large B-cell lymphomas include:

- primary mediastinal large B-cell lymphoma
- T-cell/histiocyte-rich large B-cell lymphoma
- EBV-positive DLBCL not otherwise specified
- ALK-positive large B-cell lymphoma
- intravascular large B-cell lymphoma.

If you have been diagnosed with a rare type of DLBCL, you might want to read the sections below with more information about the different subtypes and the symptoms they cause. We also have separate information pages on:

- **rare types of high-grade B-cell lymphoma that are difficult to classify**, including DLBCL that has two or three genetic mutations (**double-hit or triple-hit lymphoma**)
- DLBCL that starts in your central nervous system (primary **CNS lymphoma**)
- DLBCL that only affects your skin (a type of **B-cell skin lymphoma**)
- **DLBCL that develops in people who have HIV**.

If you have been diagnosed with DLBCL and not one of the specific rare subtypes, you might want to skip these sections.

Primary mediastinal large B-cell lymphoma (PMBL)

Primary mediastinal large B-cell lymphoma (PMBL) used to be classed as a subtype of DLBCL but it is now classed as a separate type of lymphoma. It typically affects people in their 20s and 30s. It is more common in women than men.

PMBL develops from B cells in the **thymus** (a small gland in your chest, behind your breastbone). It tends to grow as a large lump inside the chest where you can't see it or feel it. It can spread to lymph nodes but it doesn't usually spread to other parts of the body.

PMBL can cause symptoms by pressing on the lungs, gullet or the large vein that carries blood from the body to the heart (the superior vena cava or SVC). It can also cause fluid to build up around the heart (pericardial effusion) or the lungs (pleural effusion). Symptoms might include:

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

Treatment for PMBL is similar to treatment for DLBCL with the usual addition of radiotherapy. However, your medical team might suggest stronger treatment (such as **DA-EPOCH** plus **rituximab**) even if your lymphoma is at early-stage. You might be asked if you'd like to take part in a **clinical trial**.

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

T-cell/histiocyte-rich large B-cell lymphoma gets its name from the cells pathologists can see when they look at a biopsy sample under a microscope. It can develop at any age but it most commonly affects middle-aged men.

The most common symptoms are:

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

Under a microscope, T-cell/histiocyte-rich large B-cell lymphoma can look like **Hodgkin lymphoma**. It is important that it's diagnosed accurately, so you can have the most effective treatment.

EBV-positive DLBCL not otherwise specified

This subtype of DLBCL typically develops in people over 50, although it can affect younger people. It is linked to a virus called Epstein–Barr virus (EBV), which infects B cells. Most people have been infected with EBV but it doesn't usually cause any symptoms. Only a very small number of people who have had EBV go on to develop lymphoma. Scientists don't know why this is.

Symptoms of EBV-positive DLBCL depend on where the lymphoma is growing:

- Most people (7 in 10) have lymphoma growing outside their lymph nodes (extranodal lymphoma), most commonly in the skin, lungs, tonsils or stomach. The **symptoms** you have depend on where in your body the lymphoma
  is growing.
- Some people (3 in 10) have lymphoma only in their lymph nodes.

Treatment for EBV-positive DLBCL is the same as for DLBCL NOS.

ALK-positive large B-cell lymphoma

This is a very rare subtype of DLBCL that can affect people of any age. It is more common in men than women. The lymphoma cells have a mutation that means they make a protein called ‘anaplastic large-cell kinase’ (ALK). Unlike other types of DLBCL, they don’t usually make a protein called CD20, so **rituximab** does not work for this type of lymphoma.

Most people with this subtype of lymphoma have enlarged lymph nodes but the lymphoma can also grow in the chest or other parts of the body.

Treatment for ALK-positive large B-cell lymphoma is the same as for DLBCL NOS but rituximab is not usually used.

Intravascular large B-cell lymphoma

This lymphoma mainly affects older adults. The abnormal lymphocytes are found within small blood vessels called ‘capillaries’.

This subtype of lymphoma doesn’t usually cause enlarged lymph nodes. The exact symptoms depend on which capillaries are affected, but might 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)
- enlarged liver or spleen.

Treatment for intravascular large B-cell lymphoma is the same as for DLBCL NOS.

Outlook for DLBCL

At any stage, DLBCL is usually treated with the aim of curing it. It often responds well to treatment and many people go into **complete remission** (no evidence
of lymphoma).

Your specific outlook depends on the **stage** of your lymphoma, the exact type of DLBCL you have, your general health and many other individual factors. Your medical team is best placed to advise you on your outlook based on your individual circumstances. They can use the results of your tests and other individual factors (for example, your age and how fit you are) to calculate a score that helps predict how likely you are to respond to a particular treatment.

Survival statistics can be confusing as they don't tell you what your **individual** outlook is – they only tell you how a group of people with the same diagnosis did over a period of time. Remember that treatments are improving all the time and survival statistics are usually measured over 5 or 10 years after treatment. This means that statistics only tell you how people did in the past. Those people may not have received the same treatment as you. 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 of DLBCL

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

The treatment your medical team recommends for you depends on the stage of your lymphoma and the signs and symptoms you have. **Stage 1** or **stage 2** DLBCL is known as 'early-stage' lymphoma. **Stage 3** or **stage 4** DLBCL is known as 'advanced-stage' lymphoma. Most people have advanced-stage DLBCL when they are diagnosed.

When choosing your treatment, your team also takes into account your age, your general health and fitness, your feelings about treatment and factors that may be important to you in the future, such as having a family.

Your doctor also considers any potential **side effects**, long-term or **late effects** (health problems that develop months or years after treatment) of the treatment. Your medical team should explain the possible side effects and late effects of your planned treatment.

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**), sometimes followed by **radiotherapy**.

The most commonly used **chemotherapy regimen** (combination of drugs) is **CHOP**: **c**yclophosphamide, **h**ydroxydaunorubicin (doxorubicin), vincristine (also known as **O**ncovin®) and **p**rednisolone. This is usually given with an antibody therapy called **rituximab**. The combination is known as 'R-CHOP'.

You have most of the drugs through a drip into a vein (intravenously). Prednisolone is given as tablets. Most people have the treatment in hospital as an outpatient and go home the same day. 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 is usually 3 weeks.

Most people with early-stage DLBCL have three to four cycles of R-CHOP. If you have PMBL, very large lymph nodes (bulky disease), or if your lymphoma affects areas that are not suitable for radiotherapy, your doctor might recommend six cycles
of chemotherapy.

After your course of chemo-immunotherapy, you might have radiotherapy to the area affected by lymphoma, particularly if you have areas of bulky disease. Your specialist should talk to you about the possible risks and benefits of radiotherapy in your individual situation.

Treatment of advanced-stage DLBCL

Advanced-stage DLBCL (stage 3 and 4) is also usually treated with chemo-immunotherapy, but you are likely to have more cycles of treatment. The most common regimen is 6 to 8 cycles of R-CHOP.

If you are not well enough to have strong **chemotherapy**, or you have other health conditions that mean R-CHOP is not suitable for you, you might have a gentler regimen such as:

- R-miniCHOP – in which the dose of each drug might be reduced or some of the drugs might be left out
- R-CEOP – which uses etoposide instead of doxorubicin.

If your medical team thinks you are at high risk of your lymphoma coming back, or if you have a particularly aggressive subtype, they might recommend a more intensive treatment, such as:

- **DA-EPOCH-R: d**ose-**a**djusted **e**toposide, **p**rednisolone, vincristine (**O**ncovin®), **c**yclophosphamide and doxorubicin (or **h**ydroxydaunorubicin) plus **r**ituximab
- **R-CHEOP: r**ituximab plus **c**yclophosmamide, doxorubicin (or **h**ydroxydaunorubicin), **e**toposide, vincristine (**O**ncovin®) and **p**rednisolone
- **R-CODOX-M/R-IVAC**: **r**ituximab plus **c**yclophosphamide, vincristine (**O**ncovin®), **dox**orubicin and **m**ethotrexate / **r**ituximab plus **i**fosfamide, etoposide (**V**P-16) and cytarabine (**A**ra-**C**).

Most people with advanced-stage DLBCL do not have **radiotherapy**. However, you might have radiotherapy if:

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

CNS prophylaxis in DLBCL

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

If your doctor thinks you have a high risk of DLBCL affecting your CNS, you might be given treatment to try and prevent this. This is called ‘CNS prophylaxis’. **Most people do not need CNS prophylaxis.** If you have been told you might benefit from it, you may want to look at our separate **information on CNS prophylaxis**.

Follow-up of DLBCL

You have a **scan** when you finish your treatment to see how you have responded. This is usually a PET/CT scan. You might also have other tests. Your doctor can use the results of the scan and other tests, if needed, to see if

you are in **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 the lymphoma coming back (relapsing)
- 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 usually seen every 3 months at first. If you are well, your appointments gradually become less frequent.

Most people are followed-up for 2 to 3 years after treatment for DLBCL. Some hospitals offer follow-up for 5 years or longer. You might have regular follow-up appointments, or you might be given guidance on **booking your own appointments** as-and-when you need them.

After your follow-up period ends, your GP usually becomes your main point of contact if you have any concerns or notice anything unusual. Your GP should have a record of your diagnosis and all the treatment you've had.

Relapsed and refractory DLBCL

Many people respond well to their first treatment for DLBCL and go into **complete remission**. However, some people need more treatment. This might be the case if:

- the lymphoma is reduced but not completely cleared (partial response)
- the lymphoma did not respond to treatment (refractory lymphoma).

You might also need more treatment if your lymphoma comes back (**relapses**) after successful initial treatment. Relapse is most likely to happen within 2 years of the end of your first treatment. As time goes on, lymphoma is less likely to relapse.

Most people who have relapsed or refractory lymphoma are offered more chemo-immunotherapy. This is sometimes known as 'salvage' treatment. The most commonly used regimens include:

- **R-GDP** – **r**ituximab with **g**emcitabine, **d**examethasone and cisplatin (also known as **P**latinol®)
- **R-DHAP** – **r**ituximab with **d**examethasone, **h**igh-dose cytarabine (also known **A**ra-C) and cisplatin (also known as **P**latinol®)
- **R-ICE** – **r**ituximab with **i**fosfamide, **c**arboplatin and **e**toposide.

The aim of salvage treatment is to reduce the lymphoma as much as possible. You might also have radiotherapy if you have lymphoma that is causing local symptoms. If you are fit enough, you then have a **stem cell transplant** to increase your chance of having a long-lasting remission. A stem cell transplant works best if the lymphoma responds at least partially to salvage therapy.

Most people have a stem cell transplant using their own stem cells (**autologous stem cell transplant**) but some people might need a stem cell transplant using donor stem cells (**allogeneic stem cell transplant**). This might be the case if doctors are unable to collect enough of your own stem cells, or if your lymphoma relapses after an autologous stem cell transplant.

If you are not well enough for a stem cell transplant, you might be offered treatment with polatuzumab vedotin. This is a type of treatment called an **antibody–drug conjugate**: an antibody joined to a strong anti-cancer drug. The antibody sticks to protein called CD79b on the surface of B cells. This carries the drug directly to the B cells and kills them. You have it in combination with bendamustine (a **chemotherapy** drug) and rituximab.

You might be given another, different chemo-immunotherapy regimen. 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.

If you have DLBCL that comes back after two or more courses of treatment, you might have treatment with a chemotherapy drug called **pixantrone**, although this is rarely used. Some people might be eligible to have **CAR T-cell therapy**. This involves genetically modifying your own T cells so they can recognise and kill lymphoma cells. CAR T-cell therapy is a very intensive treatment that can cause serious side effects. You have to be fit enough to have it. It is only given in hospitals with the facilities and staff to treat these side effects effectively.

Research and targeted treatments

Treatment for DLBCL is usually successful but doctors continue to research treatments that are effective with as few **side effects** and **late effects** as possible. Current research is focusing particularly on targeted drugs, including:

- **antibody-drug conjugates**
- **cell signal blockers**
- **newer antibodies against CD20**
- **checkpoint inhibitors**.

Research is also studying if there are any particular groups of people with DLBCL who will benefit from particular treatments, based on the biochemical or genetic profile of the lymphoma cells.

Your doctor may ask if you would like to take part in a clinical trial. Clinical trials allow new treatments to be evaluated and compared with more established treatments. Studying treatments is the only way that new and, hopefully, better treatments can become available.

Find out more about clinical trials or find a trial that might be suitable for you on **Lymphoma TrialsLink**.

We have separate information about the topics in **bold font**. Please get in touch if you'd like to request copies or if you would like further information about any aspect of lymphoma. Phone 0808 808 5555 or email **information@lymphoma-action.org.uk**.

References

The full list of references for this page is available on our website. Alternatively, email **publications@lymphoma-action.org.uk** or call 01296 619409 if you would like a copy.

Acknowledgements

- With thanks to Dr Robert Marcus, Consultant Haematologist, London, for reviewing this information. Dr Marcus has received lecture fees from Roche and Gilead.
- The image of DLBCL cells was kindly provided by Dr Daniel Hodson, MRC Clinician Scientist Fellow, University of Cambridge, and Dr Hesham Eldaly, Consultant Histopathologist, Addenbrooke's Hospital, Cambridge.
- We would like to thank the members of our Reader Panel who gave their time to review this information.

Content last reviewed: July 2019
Updated: August 2020
Next planned review: July 2022
LYMweb0018DLBCL2019v4

Health & care information you can trust
The Information Standard Certified Member

Tell us what you think and help us to improve our resources for people affected by lymphoma. If you have any feedback, please visit **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 **lymphoma-action.org.uk/Donate**. Our information could not be produced without support from people like you. Thank you.

Disclaimer

We make every effort to make sure that the information we provide is accurate at time of publication, but medical research is constantly changing. Our information is not a substitute for individual medical advice from a trained clinician. If you are concerned about your health, consult your doctor.

Lymphoma Action cannot accept liability for any loss or damage resulting from any inaccuracy in this information or third party information we refer to, including that on third party websites.

Neither the Information Standard scheme operator nor the scheme owner shall have any responsibility whatsoever for costs, losses or direct or indirect

damages or costs arising from inaccuracy of information or omissions in the information published on the website on behalf of Lymphoma Action.