Central nervous system lymphoma

Lymphoma can sometimes affect the central nervous system (the brain and spinal cord). This information explains more about this and how it may be treated:

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What is the central nervous system?

The central nervous system (CNS) is made up of the brain, the spinal cord and the nerves to the eyes (the ‘optic nerves’).

The brain is made up of:

- the cerebrum – controls our speech and understanding, our sensation and voluntary movement (movements we decide to make)
- the cerebellum – helps with movements and controls our balance
- the brainstem – controls the ‘core body functions’, such as our breathing, heart rate and blood pressure.

The spinal cord runs from the brain down the back within the bones of the spine. A series of nerves join directly onto the spinal cord. These carry information about sensation from around the body and transmit messages to control the muscles of the body.
A pair of nerves passes through each vertebra (spinal bone) and is named after that vertebra, so there are:

- cervical (neck) nerves, known as C1–C8
- thoracic (chest) nerves, known as T1–T12
- lumbar (lower back) nerves, known as L1–L5
- sacral (tail bone) nerves, known as S1–S5.

The spinal cord is not as long as the bony spine. It ends at the level of the L2 vertebra. Below this it becomes a tail of lumbar and sacral nerves called the ‘cauda equina’.

Other facts about the central nervous system

The **meninges** are the protective layers of tissue that cover the brain and spinal cord – this is what becomes inflamed in ‘meningitis’.

**Cerebrospinal fluid** (often shortened to **CSF**) is a clear fluid found in the space between the meninges and the brain and spinal cord. It is made in the **ventricles** of the brain (fluid-filled spaces – see image above) and flows around the outside of the brain and spinal cord.

The **blood–brain barrier** is the physical barrier that protects the CNS against infections. It also stops many drugs passing from the bloodstream through the CSF to the brain and spinal cord. It is why many of the usual chemotherapy drugs cannot be used to treat lymphoma in the CNS.
How does lymphoma affect the CNS?

A lymphoma that starts in the CNS is known as a ‘primary CNS lymphoma’ (sometimes called ‘PCNSL’). A ‘secondary lymphoma’ is a lymphoma that has spread from elsewhere in the body.

Lymphoma can:

- develop within the brain, either
  - as one or more lumps (masses) – these are usually seen in ‘primary CNS lymphoma’, or
  - spread within the meninges (known as ‘diffuse meningeal lymphoma’)
- involve the eye (known as ‘intraocular lymphoma’) either
  - on its own (‘primary intraocular lymphoma’), or
  - as part of a lymphoma affecting other parts of the CNS
- develop in the spinal cord (very uncommon) or press on the spinal cord from outside, causing ‘spinal cord compression’
- spread from a lymphoma elsewhere in the body (known as ‘secondary CNS lymphoma’, or sometimes ‘SCNSL’).

For each of the ways lymphoma can affect the CNS, we explain the likely symptoms and more about the treatments that you might be offered.

We have more detailed information about the types of treatment we mention, which you can read on our website at www.lymphomas.org.uk. You can also print this information at home or, if you prefer, our helpline can send you copies – email information@lymphomas.org.uk or ring 0808 808 5555.

Tests for CNS lymphoma

Several different tests can be used to diagnose and find out more about CNS lymphoma.

Don’t worry if you don’t have all of these tests. Your doctors will decide which tests you will need, how quickly and in which order, after you have told them about your symptoms and they have examined you to see how the lymphoma is affecting you.

**Blood tests:** These may include a test for HIV (human immunodeficiency virus). People with HIV are more likely to develop high-grade lymphoma, and particularly primary CNS lymphoma. If you did have HIV infection, this would need to be treated alongside your lymphoma, as the treatment would work better and be easier for you to cope with.

**Magnetic resonance imaging (MRI):** These scans are often the best way of looking at lymphoma in or near the CNS, including possible spinal cord compression.

**Computed tomography (CT) scan:** These scans are a good way of looking for lymphoma elsewhere in the body and may be used to look at the bones of the spine too.
Positron emission tomography (PET) scan: These scans are still being evaluated in CNS lymphoma but are very useful to look for lymphoma elsewhere in the body (they are sometimes performed instead of or combined with a CT scan).

Lumbar puncture (often called just an ‘LP’): This takes a sample of the CSF, which may contain lymphoma cells that can be looked at under a microscope and tested in the laboratory; your doctor might also inject a dose of chemotherapy (known as ‘intrathecal chemotherapy’) while the needle is in place. If you have secondary CNS lymphoma, this might become part of your regular treatment. Your doctor may want to wait to see the results of your scans before suggesting you have a lumbar puncture.

Biopsy: This is required if the lymphoma seems to be only in the brain (a primary CNS lymphoma) because it is vital to be certain of the diagnosis as other brain tumours are treated differently. A specialist neurosurgeon will take a brain biopsy. Specialist radiologists can also take biopsies from the spine. Before doing the test, they will talk to you about what is involved and any risks – these will depend on the type of biopsy and where it is being taken from.

Biopsies of lumps within the brain tissue are often done by ‘stereotactic biopsy’, which means CT scanning is used to help guide the biopsy needle to the right area. You will have a general anaesthetic if you need to have a brain biopsy or a biopsy from a lump in or near your spinal cord. If you have lymphoma in another part of the body, you may not need a biopsy of the brain or spine as it’s very likely to be the same lymphoma.

Bone marrow biopsy: A test to look for lymphoma cells in the bone marrow.

Specialist eye examination: This test is done in an ophthalmology department.

We have more information about tests for lymphoma, which you can read on our website at www.lymphomas.org.uk. You can also print this information at home or, if you prefer, our Freephone helpline can send you copies – email information@lymphomas.org.uk or ring 0808 808 5555.

Primary CNS lymphoma forming a lump in the brain

Primary CNS lymphoma most often grows as a lump (mass) within the brain. It is nearly always due to diffuse large B-cell lymphoma (DLBCL), a type of high-grade non-Hodgkin lymphoma.

Primary CNS lymphoma is an uncommon form of lymphoma. It occurs most often in people who are middle-aged or older. It is also slightly more common in people who have a weakened immune system, which might be caused by:

- HIV (human immunodeficiency virus) infection – this is seen much less commonly now that good antiviral treatments are available
- drugs that used to suppress the immune system following an organ transplant.
Lymphoma in or around the brain that is caused by a low-grade type of lymphoma is very uncommon. Some of these lymphomas, such as MALT lymphoma, can occur in younger people and more often in women. They usually respond very well to treatment, typically with radiotherapy, but sometimes surgery to remove the lump is all that is needed.

**Symptoms**

The symptoms will depend on where exactly the lymphoma is. About a third of people will have more than one lump of lymphoma in the brain. Symptoms can include:

- muscle weakness in a particular area, for instance in one limb
- loss of sensation in a particular area
- changes in vision or a partial loss of vision
- seizures (fits)
- headache
- nausea and vomiting
- problems with balance
- less definite symptoms that can come on gradually and may be difficult to pick up at first
  - vague confusion
  - a change in personality
  - increased irritability
  - poor attention (decreased ability to concentrate)
  - difficulty finding the right word even though this might be something quite simple (known as ‘expressive dysphasia’).

If lymphoma forms in certain areas of the brain, it may block the flow of CSF. This can lead to a build-up of CSF around the brain and an increase in its pressure, known as ‘intracranial hypertension’. The symptoms of intracranial hypertension include:

- a change in consciousness (becoming drowsy and unresponsive)
- headaches
- vomiting.

This complication of CNS disease is important because it needs to be treated urgently.

**Treatment**

**Steroids** are often the first treatment given for CNS lymphoma. They help to get rid of the swelling (oedema) in the tissues around the lymphoma. This often improves symptoms quite quickly. They can also shrink the lymphoma itself, at least for a short time, which may allow other treatments to be arranged.

Ideally, steroids are only given after any biopsies have been taken as the lymphoma can be harder to diagnose afterwards. Sometimes, they may though be started if the doctors think someone is very likely to have CNS lymphoma, especially if it is causing lots of problems.
Steroids can be given orally or intravenously (into a vein); often the drug dexamethasone is used.

Side effects of the steroids that can be a particular problem for people with CNS lymphoma include:

- difficulty sleeping because the steroids often have to be given throughout the day rather than just in the morning
- increased blood sugar levels because a high dose of steroids is often needed, especially at first
- changes in mood and behaviour – these may be confused with the symptoms of CNS lymphoma.

Chemotherapy is the main way of treating CNS lymphoma that is caused by high-grade lymphoma. The regimens used are based on drugs that are more likely to cross the blood–brain barrier, mainly high-dose methotrexate. CHOP chemotherapy (very often used to treat lymphoma outside the brain) does not work for CNS lymphoma as the blood–brain barrier stops the drugs reaching the lymphoma.

High-dose methotrexate is given by intravenous infusion (drip) over a few hours. It is often given as an inpatient treatment as you need to have lots of fluids before and afterwards. It is sometimes possible for the treatment to be given through a special pump, which allows people to spend some of their time at home (this is known as ambulatory chemotherapy). You will also need tests done on your blood and urine and to receive the drug folinic acid for a few days after your chemotherapy.

Often it will be combined with other chemotherapy drugs, such as high-dose cytarabine. A number of different regimens can be used – your doctor will be able to tell you exactly which drugs you will need and when. Some of the regimens have also included the antibody rituximab, although doctors are not yet sure how much this helps.

Side effects of this type of chemotherapy can include:

- nausea and vomiting
- low blood counts and risk of infection
- sore mouth
- fever
- unsteadiness when walking
- muscle aches
- rash
- bladder problems and the kidneys working less well.

Your hospital team should explain what you can expect, depending on the drugs involved.

New drugs continue to be tested in various regimens and clinical trials are ongoing.
Intrathecal chemotherapy is another possible way to get around the blood–brain barrier. The chemotherapy is given directly into the CSF, usually during a lumbar puncture. Only a limited number of drugs, including methotrexate, cytarabine and hydrocortisone (a steroid), can be safely given this way. Generally intrathecal chemotherapy is not given to people with primary CNS lymphoma, although it is often used to treat secondary CNS lymphoma.

Radiotherapy can be used to treat primary CNS lymphoma. It is usually targeted against all of the brain (known as ‘whole-brain radiotherapy’). For high-grade CNS lymphoma, it can work well in the short term but the lymphoma often relapses (comes back). It is therefore most often used after chemotherapy to try to ensure the lymphoma does not relapse. Sometimes radiotherapy is used on its own for people who are not fit enough to have chemotherapy.

If the CNS lymphoma is due to a low-grade lymphoma, however, radiotherapy may be the only treatment needed.

The side effects of whole-brain radiotherapy are more of a problem in older people, especially if it is given after high-dose methotrexate. They can include:

- many symptoms of the lymphoma seeming to get worse in the early stages of treatment
- fatigue – this might take some months to improve after treatment
- poor attention
- poor memory
- problems with language
- slowness of thinking, movement and/or speech
- difficulties solving problems, planning and making decisions (some of these problems can come on as late effects months or even years after the treatment).

Stem cell transplants are sometimes offered instead of radiotherapy after chemotherapy has controlled the lymphoma. Like whole-brain radiotherapy these may not be suitable for people who are older or less fit.

Intraocular lymphoma

Some cases of primary CNS lymphoma will involve only the eye (known as ‘intraocular lymphoma’). Around 1 in 10 people with primary CNS lymphoma have lymphoma that also involves the eye.

Lymphoma that involves the eye alone is known as ‘primary intraocular lymphoma’. It can also be called ‘primary vitreoretinal lymphoma’. In time, it may spread to involve other parts of the CNS.

Most people with intraocular lymphoma are over the age of 50.
Symptoms

When present, symptoms can include:

- blurred vision
- floaters (small dots or spots that seem to float quickly across your vision).

Surprisingly, only half of patients with eye involvement will notice a change in their vision.

Treatment

The possible treatments are similar to those that are used for other primary CNS lymphomas. Chemotherapy directly into the eye (‘intravitreal’ chemotherapy) can also be given. This is more often done if the lymphoma has relapsed or if doctors think the high doses of intravenous chemotherapy needed could be too much for someone.

Research suggests that the best treatment is probably chemotherapy that includes high-dose methotrexate (with or without other drugs) followed by radiotherapy. Radiotherapy is usually given to both eyes and the brain, even if there is only evidence of lymphoma in one eye, as otherwise relapse in the untreated eye or brain is likely.

Side effects of radiotherapy to the eyes can include:

- temporary loss of your eyelashes
- dry eyes
- cataracts (you might need to have cataract surgery later)
- glaucoma.

Diffuse meningeal lymphoma

Lymphoma can sometimes spread along the meninges that cover the brain, causing a form of meningitis. This usually happens when a lymphoma is already forming a lump within the brain or spine. It can also happen when there is no lump, but this is less common. It is more often seen when a lymphoma from outside the brain relapses, rather than when a primary CNS lymphoma is first diagnosed. Both diffuse large B-cell lymphoma and mantle cell lymphoma can affect the meninges if they relapse.

The lymphoma cells in this type of lymphoma can sometimes be found in a sample of CSF taken during a lumbar puncture.

Symptoms

Lymphoma growing in a diffuse (spread-out) pattern often causes more subtle symptoms than a larger lump of lymphoma in the brain would.
Treatment

Some doctors believe that intrathecal chemotherapy is important when treating this kind of CNS lymphoma, but this has not been proven. Others believe that high-dose intravenous methotrexate (with or without other chemotherapy drugs) is the best treatment in this kind of CNS lymphoma.

Intrathecal chemotherapy is chemotherapy injected directly into the CSF, usually during a lumbar puncture. Repeated doses of the drugs, which can include methotrexate, cytarabine and hydrocortisone (a steroid), need to be given. A slow-release form of intrathecal cytarabine (DepoCyt®), which can be given less often, is sometimes given instead.

Repeated lumbar punctures can be difficult, so some people have their intrathecal chemotherapy given through an Ommaya reservoir instead. This is made up of:

- a dome-shaped plastic device (the reservoir), which is placed under the scalp
- a small tube, which leads to the ventricles of the brain (spaces that contain CSF).

The doses of chemotherapy can be easily injected into the reservoir. This may be easier than having lots of lumbar punctures, but operations are needed both to put the device in and to remove it.

The side effects of intrathecal chemotherapy can include:

- headache
- nausea and vomiting
- fever
- low blood counts (some of the drug can be absorbed into the bloodstream and affect the bone marrow, although this is uncommon), which could increase the risk of infection.

Spinal cord compression

Spinal cord compression occurs when a lump of lymphoma presses on the spinal cord or the nerves that arise directly from it. Lymphoma that grows within the spine is very uncommon. More often the lymphoma is not actually within the CNS but is growing just outside the meninges.

Most types of lymphoma, including Hodgkin lymphoma and low-grade non-Hodgkin lymphoma, can cause spinal cord compression, but this only happens in a very few people.

Symptoms

Symptoms will depend on where the spine is being compressed, but can include:
- weakness and in some cases paralysis, most often affecting the legs but sometimes also the arms or trunk
- loss of sensation or a change in sensation, also most often affecting the legs but sometimes also the arms or trunk
- a change in bowel or bladder function
- a loss of sensation around the anus
- back pain – less common in lymphoma than in other cancers that cause damage to the bones of the spine too.

**Treatment**

It is important that spinal cord compression is recognised and that a scan and other tests if needed are done urgently. This will allow treatment to be started promptly and improve the chances of your nerves recovering.

The first treatment given is often a steroid such as dexamethasone. This helps to ease the pressure on the nerves quickly by getting rid of any swelling (oedema) around the lymphoma. It may also shrink the lymphoma itself in the short-term, allowing time for other treatments to be arranged.

Lymphoma within the spine is usually treated with chemotherapy regimens that include high-dose methotrexate or other drugs that are given to treat primary CNS lymphoma or other very fast-growing lymphomas. Radiotherapy might also be used.

Lymphoma that is outside the meninges but causing compression will respond to the treatments normally given for that type of lymphoma, such as R-CHOP. This may also be followed by radiotherapy to the area of spine that was affected.

Surgery is not used to cure lymphoma. It can, however, be used to help diagnose lymphoma and may sometimes be used to remove a slowly-growing lymphoma if it is compressing the spinal cord.

**Secondary CNS lymphoma**

A secondary lymphoma is one that has spread to the CNS from elsewhere in the body.

Certain people with high-grade lymphoma have a higher risk of this happening. Doctors may offer them extra treatment to try to prevent this (known as ‘CNS prophylaxis’). The regimens used to treat the lymphomas that grow fastest – lymphoblastic lymphoma and Burkitt lymphoma – usually include CNS prophylaxis with intrathecal and high-dose intravenous chemotherapy. Otherwise more than a quarter of people with these very fast-growing lymphomas would develop secondary CNS lymphoma.
Secondary CNS lymphoma may occur as diffuse meningeal lymphoma only, so might not cause any weakness or loss of sensation. If this happens, intrathecal chemotherapy could be enough to control the lymphoma. It means chemotherapy is given directly into the CSF, usually during a lumbar puncture.

Side effects of intrathecal chemotherapy can include:

- nausea and vomiting
- headache
- fever
- low blood counts (some of the drug can be absorbed into the bloodstream and affect the bone marrow, although this is uncommon), which increase the risk of infection.

Intrathecal chemotherapy can be given twice a week via lumbar punctures or into an Ommaya reservoir or every 2 weeks using a slow-release form of the drug cytarabine (DepoCyt®). Each method has different benefits and side effects – your doctor would talk to you about these.

Other people may have both lumps within the brain and meningeal lymphoma. It is also quite common for people to relapse elsewhere in the body at the same time as, or shortly after, developing secondary CNS lymphoma. Symptoms will depend on where the lymphoma is affecting, but often come on quickly when this happens.

Treatment ideally needs to be given to both the lymphoma in the brain and elsewhere in the body. In those who are fit enough, this is likely to involve high-dose salvage chemotherapy, including the drugs that cross the blood–brain barrier. For a few people further treatment with a stem cell transplant may be offered once the lymphoma has been controlled by chemotherapy.

Radiotherapy can be used to ease symptoms if chemotherapy is not used or has not worked well.

**Intravascular large B-cell lymphoma**

This is an uncommon type of high-grade B-cell lymphoma that usually affects many areas of the body. The lymphoma cells are typically seen in small blood vessels (capillaries). It can cause damage to various organs of the body – the CNS is affected in about a third of people with this type of lymphoma.

The typical symptoms of lymphoma such as weight loss, fevers and sweating are common.

This type of lymphoma usually occurs in older people. Many people are quite unwell by the time they are diagnosed.

Treatment with R-CHOP is usually given with intrathecal chemotherapy, but drugs that can cross the blood–brain barrier are often also needed.
What happens after treatment for CNS lymphoma?

Sometimes, the symptoms of CNS lymphoma will resolve quickly with treatment, even just with steroids. Other symptoms may, however, improve only very gradually after treatment. Some may never recover completely, especially if they were present for a long time before treatment, as nerve tissues grow very slowly.

If you have had muscle weakness, you will need physiotherapy to help you recover your strength. If your strength does not return quickly, physiotherapists and occupational therapists will offer help and advice to maximise what you can achieve. They will help you to set realistic goals and improve your quality of life. Their help might also stop your symptoms worsening or other problems developing in the longer term.

If you are having problems with your memory, find it difficult to think normally or need help dealing with the emotional aspects of your lymphoma, you may find support from a psychologist helpful.

Once you have finished your treatment and have left hospital, your doctors will continue to see you regularly in the outpatient clinic. They will want to know:

- how much your symptoms improve in the weeks and months after treatment
- whether all the side effects from your treatment have settled
- about your quality of life and whether anything can be done to improve this
- whether you develop any problems with ‘late effects’ of your treatment.

As well as being seen in the clinic, you may also have scans such as an MRI of the brain every few months after your treatment. Should your lymphoma start to relapse, this will help your doctors detect it as early as possible. It is though still important to tell the team if you notice anything that suggests your lymphoma could be relapsing. Call the hospital between appointments if you develop new symptoms or feel you are less well.

Your doctors and the other members of the hospital team will want to help you live the best life possible after your treatment. Talk to them about any problems you are having and ask about all the different kinds of support that can be offered.

What happens if CNS lymphoma relapses?

If your CNS lymphoma comes back (relapses), your doctors will talk to you about what further treatment you might have. This will depend on how fit you are at the time and what treatment you had before. It could include:
• salvage chemotherapy, possibly followed by a stem cell transplant
• newer drugs being tested in a clinical trial
• radiotherapy, if you didn’t have it before
• gentler treatments given with the aim of easing your symptoms while allowing you to spend as much time as possible at home with your family and friends.

Living with CNS lymphoma

Many people have never heard of lymphoma and this can make it hard to understand and explain to friends and family. In addition, illnesses that affect the brain and nerves can be difficult to live with. It is therefore very important that you find the right help if you have this type of lymphoma, or if you are caring for someone with this type of lymphoma.

If you would like to talk to someone about CNS lymphoma or its treatment, our helpline staff will be happy to talk (ring 0808 808 5555). They may also be able to put you in touch with a buddy, who has experience of this type of lymphoma.
We have more information about lymphomas and the treatments that are used, as well as about dealing with many of the symptoms and the possible side effects of treatment. You can read this on our website at www.lymphomas.org.uk. You can also print this information at home or, if you prefer, our helpline can send you copies – email information@lymphomas.org.uk or ring 0808 808 5555.

These organisations may also be able to offer support to people living with CNS lymphoma and their carers:

The Brain Tumour Charity
Tel: 0808 800 0004
www.thebraintumourcharity.org

Brainstrust
Tel: 01983 292 405
www.brainstrust.org.uk

Brain and Spine Foundation
Tel: 0808 808 1000
www.brainandspine.org.uk

Headway
Tel: 0115 924 0800
www.headway.org.uk

Royal National Institute for the Blind (RNIB)
Tel: 0303 123 9999
www.rnib.org.uk

Carers UK
Tel: 0808 808 7777
www.carersuk.org

Sources used

These are a few of the sources we used to prepare this information. The full list of sources is available on request. Please contact us by email (publications@lymphomas.org.uk) or by ringing 01296 619409 if you would like a copy.


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We continually strive to improve our resources for people affected by lymphoma and we would be interested in any feedback you might have about this information. Please visit www.lymphomas.org.uk/feedback or email publications@lymphomas.org.uk if you have any comments. Alternatively please phone our helpline on 0808 808 5555.

If you have found this information useful and would like to help make it available to other people coping with lymphoma, then please consider making a donation to support our work at www.lymphomas.org.uk/donate. We rely totally on voluntary donations. Thank you.

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