Post-transplant lymphoproliferative disorder (PTLD)

This page is about post-transplant lymphoproliferative disorder (PTLD), which is lymphoma that can develop in people who have had a transplant.

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What is PTLD?

Post-transplant lymphoproliferative disorders (PTLD) are lymphomas that occur after a transplant.

PTLD is a proliferation (rapid increase) of lymphoid (immune) cells. It can develop in people who are taking immunosuppressive drugs to prevent rejection of an organ or an allogeneic (donor) bone marrow or stem cell transplant. PTLD is an increase of cells that sometimes goes away if immunosuppression (lowered immune system) improves. It can also be an
aggressive (fast-growing) type of lymphoma. PTLD is classified into 4 main types:

- **Early lesions**, which normally go away if immunosuppressive drugs are reduced.

- **Polymorphic PTLD (P-PTLD)**, which contains a mixture of different types of lymphoid cells.

- **Monomorphic PTLD (M-PTLD)**, which contains 1 type of cell and is the most common type of PTLD. It is usually a non-Hodgkin B-cell lymphoma but can be another type. **Diffuse large B-cell lymphoma (DLBCL)** is the most common form of M-PTLD, but sometimes **Burkitt lymphoma** and other, rarer lymphomas can occur.

- **Classical Hodgkin lymphoma-type**, which is rare.

Your risk of developing PTLD is greatest during the first few months after a transplant, when you are on the highest level of immunosuppressive drugs. Note that it can develop later, even several years after your transplant.

Very few people develop PTLD after a transplant. If it does occur, it can be a very serious complication. If you do develop PTLD, your prognosis (outlook) depends on what type of PTLD you have and how well it responds to treatment. Talk to your doctor about your individual risks and outlook.

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**Why do some people develop PTLD after a transplant?**

Several factors are at play in the development of lymphoma, but in many cases the **cause** is unknown. Scientists are investigating how all the factors work together. The aim is to identify people at greatest risk of developing lymphoma and work out the best treatments.

Many post-transplant lymphomas are related to infection with a virus called the Epstein–Barr virus (EBV). EBV is a very common virus, affecting about 9 in 10 adults and can cause glandular fever. The **immune system** keeps EBV under control instead of destroying it. It causes no long-term problems for the vast majority of people with a healthy immune system.
Infections that are normally kept under control by the immune system can be re-activated if the immune system is suppressed (lowered). If you have not previously had EBV, a transplant may introduce EBV-infected cells from your donor. EBV infects B cells and many B-cell lymphomas in people with immune problems are associated with EBV.

A proportion of post-transplant lymphomas are EBV-negative (not related to EBV). They tend to occur months or years after transplant, when the risk of lymphoma is generally lower than it is in the early months after transplant. The causes of these lymphomas are not clear.

### How common is PTLD?

The risk of PTLD developing after transplant depends on the type of transplant you have.

The number of adults who develop PTLD after a transplant is:

- around 1 in 200 people who have had a donor bone marrow or stem cell transplant
- between 1–3 in 100 people who have had a kidney or a liver transplant
- between 1–6 in 100 people who have had a heart or a heart-lung transplant
- between 4–10 in 100 people who have had a lung transplant
- around 1 in 5 people who have had a small bowel transplant.

The risks of developing PTLD are often reported to be higher in children. This may be because children are unlikely to have had EBV, and their immune systems will not have developed immunity to it. The transplanted organ or bone marrow may contain EBV-infected cells as EBV infection is extremely common. Exposure to EBV can’t be avoided and there is no effective vaccine against it.
 Symptoms

The most common symptom of PTLD is a painless lump, usually in the neck, armpit or groin. This is a swollen lymph node (gland) where abnormal lymphocytes (white blood cells that fight infection) collect. However, abnormal lymphocytes can also collect in areas deep within the body, in which case the lump can’t be felt from the outside.

Diagnosis of PTLD can be difficult. You might have more general symptoms, such as fever and night sweats, or feel generally unwell. In people who have had a transplant, these general symptoms might be mistaken for other infections, symptoms of transplant rejection or a reaction to medication.

An early diagnosis gives the best chance of successful treatment. If you have had a transplant, look out for any changes in your health. Contact your medical team if you are worried about your health.

A biopsy is required to diagnose PTLD. Other tests including scans, and possibly a bone marrow biopsy, are also done to give doctors the information they need to decide on the best treatment.

 Treatment

If you develop PTLD, your transplant doctors should work closely with your lymphoma doctors to ensure that you are getting the best advice and treatment. You should be looked after very closely by both teams.

If you are on immunosuppressive drugs, the first step is to reduce them, if possible. This has to be done carefully to avoid rejection of the transplant. It may be done gradually over several weeks or months depending on how aggressive your PTLD is.

Your transplant is then monitored carefully. How much your immunosuppression drugs can be reduced depends on several factors. These might include how many abnormal cells are in your body, the type of transplant you have had and your general health.

If you have early lesions or P-PTLD, reducing immunosuppression may restore your immune system enough to destroy the abnormal cells completely. You might only need your immunosuppressive drugs to be
reduced slightly. If the disease is more extensive, a bigger reduction of immunosuppression is needed and some drugs may be stopped completely.

Sometimes your immunosuppression can’t be reduced or reducing it is not enough. In such cases, other treatments might be needed.

**Other treatments for PTLD**

If your PTLD does not resolve with reduced immunosuppression, or your lymphoma is aggressive, you need other treatments. Your specialists will then work together to decide on the best treatment for you. Treatment depends on what type of PTLD you have and how widespread it is. Other risk factors, like your age and general health, are also considered. Some drugs may not be suitable for you as they can cause too much damage to the transplanted organ. Available treatments include:

- The antibody drug **rituximab** is part of standard treatment of B-cell non-Hodgkin lymphoma. It can be effective as a single agent in treatment of PTLD, especially after your immunosuppressive drugs have been reduced. Rituximab alone may be sufficient to treat your PTLD. It may also be given if you are not well enough to have chemotherapy.

- A **chemotherapy regimen** (combination of drugs) may be needed if reduction in immunosuppression and inclusion of rituximab are not sufficient. People with aggressive or widespread disease might need chemotherapy as their first treatment. The CHOP chemotherapy regimen is often used, but different options might be recommended. Chemotherapy is often given together with rituximab. This is known as a ‘chemo-immunotherapy’ regimen.

- **Radiotherapy** might be used for localised (only in one place) disease. It may also be used if the abnormal cells are in your central nervous system (brain, spinal cord and optic [eye] nerves). Sometimes radiotherapy is given to control symptoms (for example pain or breathlessness) by reducing the size of the lymphoma. Radiotherapy given with the aim of easing symptoms is called ‘palliative’ radiotherapy.

- Surgery may be used if the abnormal cells are in one place and can be removed.

- Other treatments might be offered, for example as part of a **clinical trial** (a scientific study that tests medical treatments). This could be a clinical
trial that includes only people with PTLD or people with the type of lymphoma you have.

Some types of treatment that target EBV can be used and are under investigation for treatment of PTLD. These are called ‘cellular’ therapies. For example, cytotoxic (kills cells) T-cells from a donor (someone else) might be given to kill the EBV-infected cells.

What are the risks if you have had a transplant and developed lymphoma?

If you have had an organ transplant and developed PTLD, you need to be monitored very carefully by your medical team to support you through your treatment for lymphoma. However, there are some known risks you need to be aware of if you have both conditions.

Increased risk of infection

Treatment for lymphoma can reduce your white blood cell counts, leaving you more vulnerable to infections. You may develop neutropenia (low levels of neutrophils, a type of white blood cells), which is very common in people being treated for lymphoma. If your immune system is already affected by immunosuppressive drugs, you have an even higher risk of serious infections if you become neutropenic.

Note: you can get infections even if you do not have neutropenia.

Call your medical team immediately if you have any symptoms of infection, including, but not limited to:

- fever (temperature above 38°C)
- shivering, with or without a fever
- chills and sweating
- feeling generally unwell, confused or disoriented
- earache, cough, sore throat or mouth
- redness and swelling around skin sores, injuries to intravenous lines
- diarrhoea
- a burning or stinging sensation when passing urine
- unusual vaginal discharge or itching
- unusual stiffness of the neck and discomfort around bright lights.

If you have PTLD, you may be given **growth factors** called G-CSF to help restore your white blood cell counts after chemotherapy. You may also be given other drugs, such as antibiotics, to prevent infections.

**Risk of transplant rejection**

Although you are monitored carefully, there is still a risk that your transplanted organ will be rejected if your immunosuppressive therapy is reduced.

If you need another transplant, the risk of PTLD coming back when you are on full immunosuppressive therapy again is low. If possible, for example you had a kidney transplant, it is often recommended that your re-transplant is delayed (often for more than a year) after treatment for PTLD. This is to make sure that the PTLD is under control before your next surgery.

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**References**

These are some of the sources we used to prepare this information. The full list of sources is available on request. Please contact us by email at publications@lymphoma-action.org.uk or phone on 01296 619409 if you would like a copy.


Further reading

- What is lymphoma?
- Chemotherapy
- Rituximab
- Diffuse large B-cell lymphoma
- Burkitt lymphoma
- Classical Hodgkin lymphoma
- Glossary

Acknowledgements

- 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.

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