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Post-transplant lymphoproliferative disorder (PTLD)

This page is about post-transplant lymphoproliferative disorders (PTLD). PTLDs are lymphomas that can develop in people who are having treatment to suppress their immune system after a transplant.

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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**.

What is post-transplant lymphoproliferative disorder (PTLD)?

Post-transplant lymphoproliferative disorder (PTLD) is the name for types of **lymphoma** that sometimes develop in people who have had a transplant. It can affect people who are taking medicines to suppress their immune system:

- after an organ transplant to prevent rejection
- after an **allogeneic (donor) stem cell transplant** to prevent **graft-versus-host disease**.

PTLD is rare. Most people who have had transplants do not develop PTLD.

There are four main types of PTLD, ranging from pre-cancerous conditions to faster-growing lymphomas:

1. In **early PTLD**, lymphocytes and other **immune cells** divide excessively and can build up in **lymph nodes**. These cells are not strictly cancerous, but they might change into cancerous cells if they are not treated. Early PTLD often gets better by reducing or stopping the drugs that suppress the immune system. There are three types of early PTLD:
    - plasmacytic hyperplasia
    - infectious mononucleosis-like PTLD
    - florid follicular hyperplasia.
2. In **polymorphic PTLD**, a mixture of abnormal lymphocytes develop. Some of these cells might be cancerous. They can build up in lymph nodes or other parts of your body (extra-nodal sites).
3. **Monomorphic PTLD** is the most common type. In monomorphic PTLD, the abnormal cells are cancerous. They are all the same type of cell – usually **B cells**, but sometimes other immune cells. There are different types of monomorphic PTLD, depending on the type of lymphoma the cells look like under a microscope. The most common type is **diffuse large B-cell lymphoma (DLBCL)**, but sometimes **Burkitt lymphoma** and other, rarer lymphomas such as **T-cell lymphomas** can develop.
4. **Classical Hodgkin lymphoma** PTLD is rare. Under a microscope, cells called Reed-Sternberg cells are present. These are characteristic of Hodgkin lymphoma. Classical Hodgkin lymphoma PTLD can develop as a late complication of transplantation.

What causes PTLD?

Many cases of PTLD are related to infection with a virus called Epstein–Barr virus (EBV). This is sometimes called 'EBV-positive PTLD'.

EBV is a very common virus: about 9 in 10 adults have been infected with it. EBV infects **B lymphocytes**. It may not cause any symptoms at all and most people don't know they've had it. Sometimes, it can cause glandular fever. After you've been exposed to it, EBV stays in your body but it is normally kept under control by your immune system. If EBV isn't kept under control, it might cause some of your lymphocytes to change into cancerous cells.

When you have a transplant, you receive medicines to lower your immune system. This helps prevent rejection after a solid organ transplant, or **graft-versus-host disease** after an **allogeneic (donor) stem cell transplant**.

- If you've had EBV in the past, it might flare up when your immune system is lowered after your transplant.
- If you have not had EBV before, a transplant might introduce EBV-infected cells from your donor. Your doctors try to avoid this but because there are lots of factors to consider when matching a recipient and a donor, it is not always possible.

Some cases of PTLD are not related to EBV (EBV-negative PTLD). They tend to occur months or years after transplant, when the risk of lymphoma is usually lower than it is in the early months after transplant. The causes of these lymphomas are not clear. EBV-negative PTLD is more common in people who have had solid organ transplants than stem cell transplants.

Who might get PTLD?

PTLD is rare. Most people who have transplants do not develop PTLD.

If you've had a solid organ transplant, your risk of developing PTLD largely depends on the intensity and duration of the medicines you've had to suppress your immune system.

Your risk of developing PTLD after a solid organ transplant also depends partly on the type of transplant you've had and whether or not you've had EBV infection in the past. You are more likely to develop PTLD if you have not had EBV, because the donor tissue could introduce it into your body for the first time.

The risk of developing PTLD is higher for people who've had a gut transplant or a transplant involving multiple organs than other solid organ transplants. Scientists think this is because these transplants contain more lymphatic tissue than other organs.

The risk of getting PTLD after a donor stem cell transplant depends mainly on how well matched you and your donor are and what **conditioning treatment** you had before your transplant. Most cases occur within the first 6 months after transplant.

People who have a stem cell transplant from a partially-matched donor or using stem cells from umbilical cord blood have a higher risk of developing PTLD than people who have a stem cell transplant from a well-matched donor.

The risk of developing PTLD is higher in children than adults. This is because children are less likely than adults to have had EBV, which may be introduced in the donor tissue.

Your chances of developing PTLD are highest during the first few months after a transplant, when you are on a stronger dose of immunosuppressive medicine. However, it can sometimes develop later, even several years after your transplant. If you've had a solid organ transplant, there can be a 'second peak' of developing PTLD ten years or more after your transplant.

Your transplant team will talk to you about your individual risk and any signs or symptoms you should look out for. Ask them if you have any questions about PTLD.

Symptoms of PTLD

People with PTLD often have very general **symptoms**, such as:

- **fever**
- **fatigue**
- unexpected **weight loss** over a few weeks
- drenching **night sweats**
- **swollen lymph nodes**.

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.

Some people develop a painless lump or lumps, usually in the neck, armpit or groin. These are **swollen lymph nodes** (glands). You might have swollen lymph nodes deep within the body, where you can't feel them from the outside. PTLD can also develop in other parts of your body. In this case, the symptoms depend on where it is growing.

If you have had a transplant, look out for any changes in your health. Contact your medical team if you have any concerns.

Diagnosis and staging of PTLD

Diagnosing PTLD early gives the best chance of successful treatment.

If you've had a stem cell transplant, you might have regular blood tests to check the level of EBV in your blood. A high level of EBV might mean you are at risk of PTLD. If this is the case, your medical team might recommend having treatment to prevent PTLD developing. This usually involves starting treatment with rituximab or T-cell therapy. An alternative option might involve reducing the dose of your immunosuppressive treatment.

PTLD is diagnosed by taking a **biopsy** from an affected part of the body. You will also need other tests, including **blood tests**, a body scan **(usually a PET/CT scan)**, and possibly a **bone marrow biopsy**. These help your medical team work out exactly which parts of your body are affected (**staging**). These tests make sure your medical team has all the information they need to decide on the best treatment for you.

Outlook for PTLD

Most cases of PTLD can be treated successfully, especially if they are diagnosed early. People who have had a stem cell transplant and are at risk of developing PTLD are usually monitored closely to make sure it is picked up early.

Treatment options for PTLD have improved dramatically in the last few decades. Be wary of looking at websites or research papers that have out-of-date information about the outlook for people with PTLD. These might not reflect current treatment pathways.

Treatment for PTLD

If you develop PTLD, your transplant team will work closely with your **lymphoma team** to decide on the best treatment for you. The treatment you need depends on what type of PTLD you have and how widespread it is. Your medical team will also consider other factors, including your age, general fitness and any other illnesses you have.

The most common treatments for PTLD are:

- **a reduction in the dose of your immunosuppressive drugs**
- **rituximab**
- **chemotherapy**
- **surgery or radiotherapy**
- **T-cell therapy.**

Reduction in the dose of your immunosuppressive drugs

The first step in treating PTLD is to reduce your immunosuppressive treatment to the lowest possible dose. This has to be done carefully to prevent your immune system rejecting your transplant. Depending on how aggressive your PTLD is, your dose of immunosuppressants might be reduced gradually over several weeks or months.

You are monitored closely to make sure you're not rejecting your transplant and to find out if your PTLD is responding to the reduction in immunosuppressive treatment.

In some cases of early PTLD, reducing your immunosuppressive drugs might be the only treatment you need. However, most people with early PTLD will need additional treatment (for example, rituximab) whilst reducing your immunosuppressive drugs.

Rituximab

Most people will have rituximab, which is an **antibody therapy** that helps your immune system recognise and destroy **B cells**. You might have treatment with rituximab if:

- you have early PTLD that doesn't completely respond to a reduction in your dose of immunosuppressive drugs
- you have a more aggressive form of PTLD.

Rituximab only works against types of PTLD that have developed from B cells.

Depending on the type of PTLD you have and how well you respond to treatment, you might have rituximab on its own or it might be combined with chemotherapy.

Chemotherapy

You might need **chemotherapy** if:

- you have not responded completely to a reduction in immunosuppressive treatment and rituximab therapy
- you have a specific type of PTLD such as **T-cell lymphoma**, **Burkitt lymphoma** or **Hodgkin lymphoma**, where rituximab isn't effective or isn't an option
- you have PTLD affecting your central nervous system (**CNS lymphoma**).

The **chemotherapy regimen** (combination of drugs) you need depends on the type of PTLD you have. If you have a B-cell lymphoma, it is often given together with rituximab. This is called 'chemo-immunotherapy'.

Surgery or radiotherapy

Surgery or **radiotherapy** are not usually used to treat PTLD. Occasionally:

- You might have radiotherapy, or surgery to remove affected lymph nodes, if you have PTLD that is only affecting one part of your body.
- You might have radiotherapy as well as chemotherapy if you have classical Hodgkin lymphoma PTLD.
- Rarely, you might have radiotherapy as well as chemotherapy if you have **T-cell lymphoma** PTLD, or if you're unable to have intensive chemotherapy.
- You might have radiotherapy as a temporary or palliative treatment to control symptoms (for example pain or breathlessness) by reducing the size of the lymphoma.

EBV-specific T-cell therapy

EBV-specific T-cell therapy aims to target and kill cells that are infected with EBV. It involves having treatment with specific **T cells** that recognise EBV. These EBV-specific T cells kill the PTLD. The T cells are usually collected from a matched donor. You have them through a drip into your vein, similar to a **blood transfusion**.

EBV-specific T-cell therapy might be used to treat people who have EBV-positive PTLD in their brain or spinal cord, or for people who have not responded to other treatment options.

Risks associated with PTLD

If you have PTLD, you are monitored very carefully by your medical team to support you through your treatment for lymphoma. However, there are some risks you need to be aware of if you have lymphoma and you have also had a transplant. Ask your medical team if you're not sure what to look out for or if you have any questions about PTLD.

Increased risk of infection

Treatment for lymphoma will reduce your white blood cell counts, leaving you more vulnerable to infections. If your immune system is already affected by immunosuppressive drugs, you have an even higher risk of serious infections.

If you receive chemotherapy for PTLD, you will usually be given a **growth factor** called G-CSF to help your white blood cell count recover in between cycles of chemotherapy. You will usually be given other drugs, such as antibiotics, antivirals and antifungal medicines, to prevent infections.

Contact your medical team immediately if you have any signs of infection.

Risk of transplant rejection

If your immunosuppressive therapy needs to be reduced to treat PTLD, there is a risk that your body might reject your transplant. You are monitored carefully to try to prevent this. However, if it happens, you might need another transplant.

If possible, your team will try to wait at least 1 year after your treatment for PTLD before you have another transplant. This reduces the risk of PTLD coming back. If you need another transplant, scientists don't know the risk of developing PTLD again.

Follow-up of PTLD

If you have PTLD, you are monitored very carefully by your medical team to support you through and after your treatment for lymphoma to see how well it has worked. This is usually done using a PET-CT scan. Your doctor may also want to monitor levels of EBV in your blood if your PTLD is EBV positive.

If you are not in complete remission after receiving rituximab for PTLD after a solid organ transplant, your medical team are likely to recommend immuno-chemotherapy, such as R-CHOP. This is followed by another PET-CT scan.

If you are not in complete remission after receiving rituximab for PTLD after a stem cell transplant, your medial team are likely to recommend a treatment called EBV-specific T cell therapy.

However, there are some risks you need to be aware of if you have lymphoma and you have also had a transplant. Ask your medical team if you're not sure what to look out for or if you have any questions about PTLD.

Relapsed or refractory PTLD

Sometimes, PTLD does not respond (refractory), or comes back (relapses), after treatment. If this is the case, your medical team might ask you if you'd like to take part in a **clinical trial** to help find out what the best treatment is for relapsed or refractory PTLD.

If you don't want to take part in a clinical trial, or if there isn't one that is suitable for you, your medical team will discuss other treatment options with you. This depends on the type of PTLD you have. It might include high-dose chemotherapy followed by a **stem cell transplant**. EBV-specific T cell therapy or **targeted treatments** might be an option for some people.

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References

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