Introduction

Double Hit (DHL) and Triple Hit Lymphoma (THL) are both genetic mutations (or changes) found in some people with non-Hodgkin's lymphoma (NHL). They are considered high-grade B-cell lymphomas. Both DHL and THL are rare, but THL is the rarest.

If you’ve been diagnosed with a double or triple hit lymphoma, you have a type of fast-growing blood cancer. Fast growing cancers are called “aggressive”.

Who gets DHL and THL?

Some people with Diffuse Large B-cell Lymphoma (DLBCL) or Burkitt’s lymphoma may have DHL or THL mutations. These lymphomas affect your white blood cells called B-cell lymphocytes (B-cells). B-cells are made in your bone marrow (the spongy middle part of your bones), before moving into your lymphatic system. They usually live in your lymph nodes and your spleen, but some can also be found in your thymus, blood and other parts of your body.

What do B-cells do?

B-cells are an important part of your immune system and fight infection and
diseases to keep you healthy. They remember infections you had in the past, so if you get the same infection again, your immune system can fight it more effectively.

If you have an infection, some of your B-cells move out of your spleen and lymph nodes, to the area where your infection is. This means B-cells can be found in any part of your body. When these cells don’t grow or work properly, you can be diagnosed with lymphoma. You will have cancerous B-cells called lymphoma cells.

**Signs and Symptoms**

Because these subtypes are fast-growing blood cancers, you may notice a lump that comes up quickly - usually in your neck, armpit or groin. It may or may not be painful, depending on where it is, and if it’s putting pressure on any other parts of your body, like nerves or organs.

Other symptoms you may have are:
- feeling unusually tired (fatigued).
- feeling out of breath.
- bruising or bleeding more easily than usual.
- infections that don’t go away, or keep coming back (recurrent).
- B-symptoms.

**Diagnosis and Staging**

If your doctor suspects you may have lymphoma you will need a biopsy. A biopsy is a procedure to remove part, or all of an affected lymph node or a sample of your bone marrow. The biopsy is then checked by scientists to see if there are changes that help the doctor diagnose lymphoma. When you have a biopsy, you may have a local or general anaesthetic. This will depend on what part of your body the biopsy is taken from.

If you have lymphoma, your doctor will organise more tests to check if it has spread to other parts of your body. These tests are called “staging”. Your DHL or THL stage will depend on where your lymphoma cells are, and how many areas of your body it is in. You might have Stage 1, 2, 3 or 4.

**Staging tests**

Staging tests may include:
- Positron Emission Tomography (PET) scan
- Computed Tomography (CT) scan
- Bone Marrow Biopsy
- Lumbar Puncture

You can find more information on staging tests at our website. Just look down the left-hand side to find the test you want more information on: [https://www.lymphoma.org.au/lymphoma/tests-diagnosis-and-staging/](https://www.lymphoma.org.au/lymphoma/tests-diagnosis-and-staging/)
Stage I (1) and II (2) lymphoma are considered early-stage lymphomas, meaning that only one or two areas either above OR below your diaphragm have lymphoma. Stage III (3) lymphoma is considered an advanced stage and means that you have lymphoma on both sides of your diaphragm.

Stage IV (4) lymphoma is the most advanced stage, and means you have lymphoma on both sides of your diaphragm, and in one of your organs such as your liver, lungs, brain, bones or bone marrow.

Cytogenetic tests

Cytogenetics are tests on your blood and biopsies that look for changes in your chromosomes or genes. We usually have 23 pairs of chromosomes, and they are numbered according to their size.

On your chromosomes are many genes that tell the proteins and cells in your body how to look or act. If there is a change (variation) in these chromosomes or genes, your proteins and cells may not work properly.

When you have DHL or THL, you have a rearrangement of your genes. This means that some of your genes have rearranged themselves and are no longer in the right place. This rearrangement means your genes are now unable to give proper instructions to your B-cells on how, and when to grow. If you have DHL, you have rearrangements in a gene called MYC and, either your BCL2 or your BCL6 gene. Only one of your BCL genes is rearranged in double hit, but you have two total rearrangements with MYC and BCL. If you have THL, you will have rearrangements in all three genes.

Ask your doctor to explain your individual changes

<table>
<thead>
<tr>
<th>Rearrangements in Double hit and Triple hit lymphoma</th>
<th>MYC</th>
<th>BCL2</th>
<th>BCL6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double hit</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Double hit</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Triple hit</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

DHL and THL are not the same as Double Expressor Lymphoma (DEL). If you have DEL, you have a different type of genetic change resulting in too many of the genes, though they remain in the correct place.
Before you start treatment

Before you start treatment you will also need to have some baseline tests done. These can include blood tests to check how well your liver and kidneys are working, scans on your heart, or lung function tests. These are to make sure that you are well enough to have treatment without it causing you to become too unwell. Throughout your treatment you will have regular blood tests which will be compared to these baseline tests. You may also have further lung tests and heart scans to make sure that the treatment has not caused any damage to your organs.

Fertility – some cancer treatments can make it harder to fall pregnant, or to get somebody pregnant. If you (or your child) are planning to have children later in life, talk to your doctor about how to preserve your fertility.

Questions for your doctor before you start treatment

Starting treatment can feel overwhelming, and even knowing what questions to ask can be difficult. To help get you started, we have put together some questions you may like to consider asking. Click here to download our Questions to ask your Doctor* factsheet or scan the QR code at the end of this document.

Treatment

If you have DHL or THL, you will start treatment soon after you are diagnosed. This treatment will be a combination of different medicines. They may include chemotherapies, and a monoclonal antibody. You may also be offered radiation treatment, but this will depend on where your lymphoma is.

Chemotherapy (chemo): These medicines might be a tablet or given as a drip (infusion) in a cancer clinic or hospital. If you have lymphoma in your central nervous system (CNS) which includes your brain and spinal cord or, if your doctor thinks the lymphoma may spread there, you will also have chemo as an injection into your back. The doctor then delivers chemo into your cerebral spinal fluid (CSF) that surrounds your brain and spine. This is called intrathecal (IT) chemo. Chemo kills fast growing cells, so it can also affect some of your good cells that grow fast. This can cause unwanted side-effects from chemo. These can include hair loss, a sore mouth, nausea and vomiting, diarrhea or constipation.

Monoclonal Antibody (MAB): Given as an infusion in a cancer clinic or hospital. MABs attach to lymphoma cells and attract other disease fighting white blood cells and proteins to the cancer. This helps your own immune system to fight the lymphoma. It is easy to tell which medicines are monoclonal antibodies because their
Double Hit Lymphoma (DHL) & Triple Hit Lymphoma (THL)

generic name always ends with “mab”, such as rituximab.

**Radiation / Radiotherapy**: Radiation therapy is a cancer treatment that uses high doses of radiation, to kill cancer cells and shrink tumours. Before having radiation, you will have a planning session. This session is important for the radiation therapists to plan how to target the radiation to the lymphoma, and avoid nearby healthy tissue. Radiation therapy is usually given over 3-5 weeks. During this time, you will need to go to the radiation centre everyday (Monday-Friday) for treatment.

If you need help with a place to stay during treatment, please talk to your doctor or nurse about what help is available to you. You can also contact the Cancer Council or Leukemia Foundation in your state and see if they can help with somewhere to stay.

**High dose chemotherapy followed by a stem-cell transplant** – to learn more about stem cell transplants please see more information [here](#), or scan the QR code

- transplants in lymphoma
- allogeneic stem cell transplants
- autologous stem cell transplants.

**Chimeric antigen receptor therapy (CAR T-cell therapy)** – For information on CAR T-cell therapy [here](#).

**Clinical trial** – These may include targeted therapies and other treatments. Ask your doctor if you are eligible for any clinical trials.

**Treatment**

The first time you start treatment for lymphoma it’s called first-line treatment. Sometimes lymphoma may not go away with first-line treatment. If this happens, it is called “refractory” disease. For some people, the lymphoma may go away for a while, and then come back. This is a “relapse”. If you have refractory or relapsed lymphoma you will be offered a different type of treatment. This next treatment will be second-line treatment.

**First-line treatment**

You will need to start soon after diagnosis. Some of the more common first-line treatments for lymphomas with DHL and THL mutations may include one of the following protocols:

- **DA-EPOCH-R** - combination of chemotherapy and a monoclonal antibody.
- **R- Hyper CVAD** - combination of chemotherapy and a monoclonal antibody.
- **R- CODOX-M** – combination of chemotherapy and a monoclonal antibody.
- **Radiotherapy** – if you have early stage disease you may have radiation treatment.
- **Intrathecal chemo** – Your doctor will
consider this if you have lymphoma in your CNS, or are at risk of having it spread there.

- **Autologous stem cell transplant** - this may be offered if you are in remission after your first-line treatment. The aim is to strengthen (or consolidate) the response you had to initial chemotherapy. This increases your chances of being cured from your lymphoma. That is, making the lymphoma go away forever.

- **You may also be able to join a clinical trial.**

For more information on treatment protocols please see [here](#).

**Second and subsequent lines of treatment**

If your doctor thinks you have relapsed, or that you have refractory disease, you will need another biopsy. This will be similar to what you had before you started treatment the first time.

If you have relapsed or refractory disease you may be offered one of the below treatment types:

- **Salvage chemotherapy with ICE-R** – a combination of different chemotherapies and a monoclonal antibody
- **Autologous stem cell transplant (AuSCT)**
- **Chimeric antigen receptor (CAR) T-cell Therapy** (as a third or fourth-line of treatment)
- **Combination of other chemotherapy**
- **Clinical trial participation.**

More information on treatment options can be found on our website [here](#).

**Clinical Trials**

Clinical trials are important to find new medicines, or combinations of medicines, to improve treatment for people with DHL or THL in the future. They may also offer you a chance to try a new medicine, or treatment before it would otherwise be available. If you are interested in participating in a clinical trial, ask your doctor what clinical trials you are eligible for. You can also read our ‘Understanding Clinical Trials’ fact sheet for websites to find a clinical trial.

**Follow up after treatment ends**

Finishing treatment can be a time of mixed emotions. You may feel relieved and excited, or you may feel worried and scared. You may even alternate between all of these emotions. This is very normal. However, you will not be alone. You will continue to see your specialist team on a regular basis, and be checked for any signs and symptoms of your lymphoma relapsing, and your doctor will also want to make sure you’re not having any side effects from your treatment. Your doctor will let you know how often they want to see you, however the longer time you are
in remission the less often they will need to see you.

If you have any concerns or worries please contact your healthcare team or contact our lymphoma care nurses on 1800 953 081. You can also email us on nurse@lymphoma.org.au.

**Summary**

- Double hit and triple hit lymphoma refers to the type of genetic mutation you have.
- These mutations can occur in some people with aggressive B-cell lymphomas, including Diffuse Large B-Cell Lymphoma and Burkitt Lymphoma.
- Talk to your doctor about your individual mutations, and how these may affect your treatment.
- Talk to your doctor about preserving your fertility before you start treatment.
- If you have a double or triple hit lymphoma you will need to start treatment very soon after diagnosis.
- Contact your doctor if you get B-symptoms or if you have any other concerns.

**Resources and support**

**Lymphoma Australia** offers a wide range of resources and support for people living with lymphoma or CLL, and their carers. How to access our resources:

- **Visit** our website [www.lymphoma.org.au](http://www.lymphoma.org.au) for more information.
- **Phone** our Lymphoma Care Nurse Hotline on 1800 953 081.
- **Email** our Lymphoma Care Nurses nurse@lymphoma.org.au
- **Booklet:** Understanding Non-Hodgkin Lymphoma (NHL)
- **Downloadable information:** Visit our [website](http://www.lymphoma.org.au), or give us a call if you would like some more information on a variety topics related to lymphoma
- **Join** our Facebook page [Lymphoma Down Under](http://www.facebook.com) (make sure you complete all the membership questions when you join).

**Cancer Council** offers a range of services, including free counselling, to support people affected by cancer, including patients, families and friends. Services may be different depending on where you live. You can contact them at [www.cancer.org.au](http://www.cancer.org.au) or by phone on 13 11 20.

**Medicare Australia:** Check with your GP if you are eligible for a Mental Health Treatment Plan (MHTP). This plan is funded by Medicare and can provide you with up to 10 sessions with a registered psychologist. More information can be found [here](http://www.medicare.gov.au).

**WeCan** is an Australian supportive care website to help find the information, resources and support services you may need following a diagnosis of cancer. You can visit their website at [www.wecan.org.au](http://www.wecan.org.au).
Canteen provides support for young people aged 12–25 years who have cancer, or, who have a parent with cancer. Find out more at their website here www.canteen.org.au.


Useful links

- Questionst to ask your doctor
- Burkitt Lymphoma Website
- Definitions
- DLBCL Website

Disclaimer: Lymphoma Australia has taken every precaution to make sure the information in this document is accurate and up-to-date. However, this information is intended for educational purposes only and does not substitute for medical advice. If you have any concerns about your health or wellbeing, please contact your treating team.