

# Treating Non-Hodgkin Lymphoma in Children

If your child or teen has been diagnosed with non-Hodgkin lymphoma (NHL), the treatment team will discuss the options with you. It's important to weigh the benefits of each treatment option against the possible risks and side effects.

#### How is non-Hodgkin lymphoma treated?

The types of treatment used for childhood NHL can include:

- Chemotherapy for Non-Hodgkin Lymphoma in Children
- Drugs Other Than Chemo for Non-Hodgkin Lymphoma in Children
- High-Dose Chemotherapy and Stem Cell Transplant for Non-Hodgkin Lymphoma in Children
- Radiation Therapy for Non-Hodgkin Lymphoma in Children
- Surgery for Non-Hodgkin Lymphoma in Children

#### **Common treatment approaches**

Chemotherapy (sometimes along with other drugs) is the main treatment for children and teens with NHL, because it can reach all parts of the body and kill lymphoma cells wherever they may be. Even if the lymphoma appears to be limited to a single lymph node based on exams and tests, the lymphoma cells have often spread to other parts of the body by the time it is diagnosed.

Other types of treatment, such as surgery, might also be used in some situations. Sometimes high-dose chemotherapy followed by a stem cell transplant might be needed if the lymphoma comes back after treatment. Treatment of Non-Hodgkin Lymphoma in Children, by Type and Stage

Today, most children and teens with cancer are treated at specialized children's cancer centers. These centers offer the most up-to-date-treatment by conducting clinical trials (studies of promising new therapies). Children's cancer centers often conduct many clinical trials at any one time, and in fact most children treated at these centers take part in a clinical trial as part of their treatment.

Clinical trials are one way to get state-of-the art cancer treatment. Sometimes they may be the only way to get access to newer treatments (although there is no guarantee that newer treatments will be better). They are also the best way for doctors to learn better methods to treat these cancers. Still, they might not be right for everyone.

If you would like to learn more about clinical trials that might be right for your child, start by asking the treatment team if your clinic or hospital conducts clinical trials.

<u>Clinical Trials</u>

#### Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your child's tumor or relieve symptoms. These methods can include

#### • When Your Child Has Cancer

#### Help getting through cancer treatment

Your child's cancer care team will be your first source of information and support, but

# Chemo drugs used to treat non-Hodgkin lymphoma in children

Children and teens with NHL get a combination of several chemo drugs over a period of time. The number of drugs, their doses, and the length of treatment depend on the <u>type</u><sup>1</sup> and <u>stage</u><sup>2</sup> of the lymphoma. Some of the chemo drugs commonly used to treat childhood lymphoma include:

- Cyclophosphamide
- Vincristine
- Doxorubicin (Adriamycin)
- Prednisone
- Dexamethasone
- Cytarabine, also known as ara-C
- Methotrexate
- L-asparaginase, PEG-L-asparaginase (pegaspargase)
- Etoposide
- 6-mercaptopurine
- Ifosfamide

# How is chemo given?

Doctors give chemo in cycles, in which a period of treatment is followed by a rest period to allow the body time to recover. Each chemo cycle generally lasts for several weeks.

Chemo drugs are usually given into a vein (IV) or taken by mouth. If there's a chance the lymphoma may have reached the brain or spinal cord, chemo may also be given into the cerebrospinal fluid (known as **intrathecal chemo**).

Most chemo treatments are given in an outpatient setting (in the doctor's office or clinic or hospital outpatient department), but some – especially at the start of treatment – may need to be given while the child stays in the hospital.

Often before chemo is about to start, surgery is done to insert a small plastic tube, called a <u>central venous catheter (CVC) or venous access device (VAD)<sup>3</sup></u>, into a large blood vessel. The end of the tube stays just under the skin or sticks out in the chest area or upper arm. The CVC is left in place during treatment (often for many months) to give IV drugs such as chemo and to take blood samples. This lowers the number of needle sticks needed during treatment.

# Possible risks and side effects of chemo

Chemo drugs can cause side effects. These depend on the type and dose of drugs given and how long treatment lasts.

Common chemo side effects can include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea or constipation
- Increased chance of infections (due to low white blood cell counts)
- Easy bruising or bleeding (due to low blood platelet counts)
- Fatigue (due to low red blood cell counts)

These side effects usually go away after treatment is finished. If serious side effects occur, the dose of chemo may need to be reduced or treatment may need to be delayed.

There are often ways to lessen these side effects. For example:

- Drugs can be given to help prevent or reduce **nausea and vomiting**.
- **Infections** can be very serious in children getting chemo. Drugs known as growth factors can be given to keep the blood cell counts higher.

**Tumor lysis syndrome** is a possible side effect of chemo in children who have large numbers of lymphoma cells in the body before treatment. It occurs most often with the first cycle of chemo. Killing the lymphoma cells releases their contents into the bloodstream. This can overwhelm the kidneys, which can't get rid of all of these substances at once. Excessive amounts of certain minerals may also lead to heart and nervous system problems. The risk of tumor lysis syndrome happening can be lowered by making sure the child gets lots of fluids during treatment and by giving drugs such as bicarbonate, allopurinol, and rasburicase, which help the body get rid of these substances.

#### Side effects of certain chemo drugs

Some possible side effects occur only with certain drugs. For example:

**Cyclophosphamide** and **ifosfamide** can damage the bladder, which can cause blood in the urine. The risk of this can be lowered by giving the drugs with plenty of fluids and with a drug called **mesna**, which helps protect the bladder. These drugs can also damage the ovaries or testicles, which could affect fertility (the ability to have children).

- 4. <u>www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/peripheral-neuropathy.html</u>
- 5. <u>www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/after-treatment/long-term-effects.html</u>
- 6. <u>www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy.html</u>
- 7. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

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Last Revised: August 10, 2021

# **Drugs Other Than Chemo for Non-**

# Hodgkin Lymphoma in Children

In recent years, drugs have been developed that target specific parts of cancer cells. These drugs work differently from standard chemotherapy (chemo) drugs, and they often have different side effects. Some of these drugs might be useful in certain cases of childhood non-Hodgkin lymphoma (NHL), either by themselves or with chemo.

## **Monoclonal antibodies**

Antibodies are proteins normally made by the body's immune system to help fight infections. Lab-made versions, called monoclonal antibodies, can be designed to attack a specific target, such as a protein on the surface of lymphoma cells.

Several monoclonal antibodies are now used to treat lymphoma in adults. Some of these are now being studied or used in children as well.

#### Rituximab

This antibody attaches to the CD20 protein on the surface of some types of lymphoma cells, which causes the cells to die. Rituximab is often used with chemotherapy as part of the treatment for Burkitt lymphoma, Burkitt-like lymphoma, and diffuse large B-cell lymphoma.

Treatment is typically given as an intravenous (IV) infusion in the doctor's office, clinic, or hospital.

Rituxan was the original brand name for rituximab, but several versions like it (called biosimilars) are now available as well, including Ruxience, Truxima, and Riabni.

Common **side effects** of rituximab are usually mild but can include chills, fever, nausea, rashes, fatigue, and headaches during or after the infusion. Side effects are less likely with later doses. Rituximab can also increase a person's risk of some types of Sev28wbsm 0 01 cific takes the second secon

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Mosse YP, Lim MS, Voss SD, et al. Safety and activity of crizotinib for paediatric patients with refractory solid tumours or anaplastic large-cell lymphoma: A Children's Oncology Group phase 1 consortium study. *Lancet Oncol.* 2013;14:472480.

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Last Revised: December 6, 2021

# High-Dose Chemotherapy and Stem Cell Transplant for Non-Hodgkin Lymphoma

# in Children

High-dose chemotherapy and stem cell transplant (SCT) is not used as the first treatment for non-Hodgkin lymphoma (NHL) in children, but a transplant may be an option if the first treatment does not work or if the lymphoma comes back after treatment.

The doses of chemotherapy (chemo) drugs normally are limited by the side effects these drugs can cause. Higher doses can't be used, even if they might kill more cancer cells, because they would severely damage the bone marrow, where new blood cells are made.

A stem cell transplant (also known as a bone marrow transplant) lets doctors give higher doses of chemotherapy (sometimes along with radiation therapy). After getting high-dose chemo, the child gets a transplant of blood-forming stem cells to restore the bone marrow.

# **Types of transplants**

The main types of stem cell transplants<sup>1</sup> are based on the source of the stem cells.

matched donor.

A stem cell transplant is a <u>complex treatment</u><sup>3</sup>

Children. In: Blaney SM, Adamson PC, Helman LJ, eds. *Pizzo and Poplack's Principles and Practice of Pediatric Oncology*. 8th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2021.

- Sometimes it is used along with chemo. This might be done if the lymphoma has reached the brain or spinal cord.
- It may be used as a form of urgent treatment in children with symptoms caused by large tumors in the chest.
- It may be used as part of treatment for children who are getting high-dose chemo and a stem cell transplant.
- It can be used to relieve symptoms from lymphoma, such as pain from a tumor that's pressing on nerves.

## How is radiation therapy given?

Radiation focused on a cancer from a machine outside the body is called **external beam radiation**. This is the type of radiation therapy most often used to treat childhood NHL.

Before the radiation treatment starts, the team will take careful measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation. This planning session, called **simulation**, often includes getting <u>imaging tests</u><sup>1</sup> such as CT or MRI scans.

The treatment itself is much like getting an x-ray, but the radiation is stronger. It is painless, but some younger children might need to be sedated to help make sure they don't move during the treatment. Each treatment lasts only a few minutes, although the setup time – getting your child into place for treatment – usually takes longer. The number of treatments will depend on the reason they're being given.

### Possible riskn.

serious, and some may not occur until many years later.

- Radiation therapy to the chest may damage the lungs or heart, which could raise the risk of lung or heart problems later in life. In the long term, radiation to the chest may also increase the risk of lung cancer (especially in people who smoke) and of breast cancer.
- Radiation therapy to the brain might cause headaches and problems such as memory loss, personality changes, and trouble learning at school.
- **Radiation to the abdomen** in girls can damage the ovaries. This might lead to abnormal menstrual cycles or problems getting pregnant or having children later on.
- Radiation to other parts of the body may slow a child's growth or increase the risks for certain other cancers, such as those of muscle or bone (called sarcomas) or of the digestive tract.

Because of these possible long-term effects, doctors try to avoid using radiation therapy in children or limit the doses used whenever possible. For more on possible long-term effects, see Late and Long-term Effects of Treatment for Non-Hodgkin Lymphoma in Children<sup>2</sup>.

## More information about radiation therapy

To learn more about how radiation is used to treat cancer, see <u>Radiation Therapy</u><sup>3</sup>.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u><sup>4</sup>.

## **Hyperlinks**

- 1. <u>www.cancer.org/treatment/understanding-your-diagnosis/tests/imaging-radiology-</u> tests-for-cancer.html
- 2. <u>www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/after-treatment/long-term-effects.html</u>
- 3. <u>www.cancer.org/treatment/treatments-and-side-effects/treatment-</u> <u>types/radiation.html</u>
- 4. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

#### References

- To get <u>biopsy</u><sup>1</sup> samples for lab tests to determine the exact <u>type of NHL</u><sup>2</sup> a child has, if non-surgical procedures (needle biopsy, bone marrow biopsy, etc.) can't get enough tissue for testing.
- To insert a small plastic tube, called a <u>central venous catheter</u><sup>3</sup> (CVC) or venous access device (VAD), into a large blood vessel near the heart. The end of the tube stays just under the skin or sticks out in the chest area or upper arm. This is left in place during treatment to give intravenous (IV) drugs such as chemo and to take blood samples. This lowers the number of needle sticks needed during treatment.
- To relieve some emergency situations, such as if a lymphoma has blocked a child's intestines.

# Possible risks and side effects of surgery

Possible complications of surgery depend on the location and extent of the operation and the child's health beforehand. Serious complications, although rare, can include problems with anesthesia, bleeding, blood clots, wound infections, and pneumonia. Most children will have some pain for a while after the operation, although this can usually0 0/1selis,62745 dur1 g 0 0 0 rS661oluring treatment.

and can cause problems with the kidneys and other organs. Doctors try to prevent this by making sure the child gets lots of fluids before and during treatment, and by giving certain drugs to help the body get rid of these substances.

Even children and teens with early-stage (stage I or II) lymphomas are assumed to have more widespread disease than can be detected with exams or imaging tests. Because of this, local treatments such as surgery or radiation therapy alone are very unlikely to cure them. Therefore, chemotherapy is an important part of treatment for all childhood NHLs.

Treatment of lymphoblastic lymphoma (LBL)

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**Chemotherapy** (chemo), often along with the **monoclonal antibody** rituximab, is the main form of treatment for these lymphomas. This combination is sometimes called **chemoimmunotherapy**.

**Stages I and II:** While chemo (often along with rituximab) is the main treatment of these lymphomas, surgery may be done before chemo if the tumor is in only one area, such as a large abdominal (belly) tumor.

Several different chemo drugs are used. The length of treatment ranges from about 9 weeks to 6 months. Most pediatric oncologists feel that the 9-week treatment is adequate if all of the tumor is removed with surgery first.

Chemotherapy into the spinal fluid is needed only if the lymphoma is growing around the head or neck.

**Stages III and IV:** Children with more advanced lymphomas are generally treated with rituximab plus more intensive chemotherapy. Because these lymphomas tend to grow quickly, the chemo cycles are short, with little rest between courses of treatment.

For example, a treatment plan known as the French LMB protocol regimen alternates between different combinations of drugs every 3 to 4 weeks for a total of about 6 to 8 months. Other similar treatment regimens are the German BFM protocol and the St. Jude Total B regimen.

Chemotherapy must also be given into the spinal fluid.

# Treatment of anaplastic large cell lymphoma (ALCL)

Chemotherapy (chemo) is the main form of treatment for childhood ALCL. Studies are being done to determine if adding another drug to chemo, such as crizotinib (Xalkori) or brentuximab vedotin (Adcetris), might make treatment more effective.

**Stages I and II:** Treatment for these lymphomas usually consists of chemo with 4 or more drugs given for about 3 to 6 months. The usual chemo regimen contains a 4-drug combination of cyclophosphamide, vincristine, prednisone, and either doxorubicin or methotrexate. (These are known as the CHOP or COMP regimens.)

Chemo is given into the spinal fluid only if the lymphoma is near the head or neck.

**Stages III and IV:** ALCL doesn't often reach the bone marrow or spinal fluid, but if it does, it requires more intensive treatment. Chemo typically includes several drugs given

over 9 to 12 months.

Intrathecal chemotherapy is given into the spinal fluid as well.

# Treatment of recurrent lymphoma

Generally, if the lymphoma comes back (recurs) after the first treatment, it is harder to

Wilkins; 2021.

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Last Revised: August 10, 2021

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