

Non-Hodgkin Lymphoma in Children Early Detection, Diagnosis, and Staging

Detection and Diagnosis

Finding lymphoma early often allows for more treatment options. Some early lymphomas may have signs and symptoms that can be noticed, but that is not always the case.

- Can Non-Hodgkin Lymphoma in Children Be Found Early?
- Signs and Symptoms of Non-Hodgkin Lymphoma in Children
- Tests for Non-Hodgkin Lymphoma in Children

Stages for Non-Hodgkin Lymphoma in Children

After a lymphoma diagnosis, staging provides important information about the extent of cancer in the body and anticipated response to treatment.

• Stages of Non-Hodgkin Lymphoma in Children

Outlook (Prognosis)

Doctors often use survival rates as a standard way of discussing someone's outlook (prognosis). Some people want to know about survival statistics, while others might not find the numbers helpful, or might even not want to know them.

Survival Rates for Childhood Non-Hodgkin Lymphoma

Questions to Ask About Non-Hodgkin Lymphoma in Children

Here are some questions you can ask the cancer care team to help you better understand your child's diagnosis and treatment options.

• Questions to Ask Your Child's Health Care Team About Non-Hodgkin Lymphoma

Can Non-Hodgkin Lymphoma in Children Be Found Early?

Non-Hodgkin lymphoma (NHL) is uncommon in children and teens, and there are no widely recommended screening tests for this cancer. (Screening is testing for cancer in people who don't have any symptoms.) Still, sometimes NHL can be found early.

The best way to find lymphoma early is to be aware of its possible signs and symptoms and to take your child to the doctor if something concerns you.

Careful, regular medical checkups are important for children, especially those with known <u>risk factors¹</u> for NHL, such as:

- Certain inherited immune deficiencies
- Prior cancer treatment or organ transplant
- HIV infection²

Most children and teens with these conditions do not develop NHL, but it's important for parents and doctors to know the possible symptoms and signs of lymphoma.

Hyperlinks

- 1. <u>www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/causes-risks-prevention/risk-factors.html</u>
- 2. <u>www.cancer.org/cancer/cancer-causes/infectious-agents/infections-that-can-lead-to-cancer/viruses.html</u>

References

Gross TG, Kamdar KY, Bollard CM. Chapter 19: Malignant Non-Hodgkin Lymphomas in 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.

National Cancer Institute Physician Data Query (PDQ). Childhood Non-Hodgkin Lymphoma Treatment. 2021. Accessed at https://www.cancer.gov/types/lymphoma/patient/child-nhl-treatment-pdq on June 10, 2021.

Sandlund JT, Onciu M. Chapter 94: Childhood Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa: Elsevier; 2020.

Termuhlen AM, Gross TG. Overview of non-Hodgkin lymphoma in children and adolescents. UpToDate. 2021. Accessed at https://www.uptodate.com/contents/overview-of-non-hodgkin-lymphoma-in-children-and-adolescents on June 10, 2021.

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Signs and Symptoms of Non-Hodgkin Lymphoma in Children

Childhood non-Hodgkin lymphoma (NHL) can cause many different signs and symptoms, depending on the <u>type of NHL</u>¹ and where it is in the body. Common symptoms include:

- Enlarged lymph nodes (seen or felt as lumps under the skin)
- Abdominal (belly) swelling or pain
- Feeling full after eating only a small amount of food
- · Shortness of breath, wheezing, or cough
- Fever
- Weight loss

- Night sweats
- Fatigue (feeling very tired)

Enlarged lymph nodes

Non-Hodgkin lymphoma may grow in lymph nodes under the skin (on the sides of the neck, in the underarm area, above the collar bone, or in the groin area). The enlarged nodes are often seen or felt as **lumps under the skin** and are not usually painful. They are often first noticed by the child, parent, or a health care provider.

Enlarged lymph nodes in children are more often caused by infections than by NHL. Lymph nodes that grow in reaction to infection are called **reactive nodes** or **hyperplastic nodes** and are often tender to the touch.

Lymphoma in the abdomen (belly)

Lymphoma growing inside the abdomen can cause **swelling or pain in the abdomen**. There may also be a buildup of fluid that causes even more swelling.

Lymphoma can sometimes enlarge the spleen, which might then press on the stomach. This can cause a **loss of appetite** and **feeling of fullness after only a small meal**.

When lymphoma causes swelling in or near the stomach or intestines, bowel movements may be blocked, which may lead to **belly pain**, **nausea**, **and vomiting**.

Lymphoma might also block urine from leaving the kidneys. This can lead to **low urine output**.

Lymphoma in the chest

When lymphoma starts in the thymus (a small organ in the middle of the chest) or lymph nodes in the chest, it can press on the nearby trachea (windpipe). This can lead to **coughing, wheezing, shortness of breath, and trouble breathing**.

The superior vena cava (SVC) is a large vein that carries blood from the head and arms back to the heart. It passes next to the thymus and lymph nodes inside the chest. Lymphomas in this area may press on the SVC, which can make the blood back up in the veins. This is can lead to swelling in the face, neck, arms, and upper chest (sometimes with a bluish-red skin color). It can also cause trouble breathing, as well as headaches, dizziness, and a change in consciousness if it affects the brain. This

condition, known as **SVC syndrome**, can be life-threatening, so it needs to be treated right away.

Lymphoma in the brain and spinal cord

Some types of lymphoma can spread to the area around the brain and spinal cord. This can cause problems such as **headache**, **nausea**, **vision changes**, **facial numbness**, **and trouble talking**.

Lymphoma in the skin

Some lymphomas can affect the skin itself. They can cause **itchy**, **red or purple lumps or nodules under the skin**.

General lymphoma symptoms (B symptoms)

Along with causing symptoms in the part of the body where it starts, NHL can also cause general symptoms such as:

- Fever and chills
- Sweating (particularly at night)
- Unexplained weight loss

When talking about lymphoma, doctors sometimes call these **B symptoms**. B symptoms are often found in more rapidly growing lymphomas.

Sometimes lymphoma can spread to the bone marrow and crowd out the normal, healthy cells that make new blood cells. This can cause **low blood cell counts** and can lead to problems like:

- Severe or frequent infections (from low white blood cell counts)
- Easy bruising or bleeding (from low blood platelet counts)
- Fatigue and pale skin (from low red blood cell counts)

Many of the signs and symptoms above are more likely to be caused by something other than a lymphoma, such as an infection. Still, if your child or teen has any of these symptoms, check with the doctor so that the cause can be found and treated, if needed.

Hyperlinks

1. <u>www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/about/types-non-hodgkin-children.html</u>

References

Gross TG, Kamdar KY, Bollard CM. Chapter 19: Malignant Non-Hodgkin Lymphomas in 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.

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Sandlund JT, Onciu M. Chapter 94: Childhood Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa: Elsevier; 2020.

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Tests for Non-Hodgkin Lymphoma in Children

Non-Hodgkin lymphoma (NHL) is usually found when a child or teen is brought to a doctor because of signs or symptoms he or she is having. This might lead the doctor to suspect lymphoma, but tests will be needed to confirm it.

The exams and tests below might be done to diagnose lymphoma, to find out what type it is, and to learn how advanced it is.

Medical history and physical exam

The doctor will ask about any symptoms, including how long they have been present, and might also ask about possible <u>risk factors</u>¹, such as immune system problems.

The physical exam will probably focus on any enlarged lymph nodes or other areas of concern. For example, the abdomen (belly) may be felt to see if the spleen or liver is enlarged.

The most common cause of enlarged lymph nodes in children is an infection, so this is often what doctors think of first. Because of this, the diagnosis of NHL in a child can sometimes be delayed. Children with swollen lymph nodes might be watched closely for a time or given a course of antibiotics first to see if the nodes will shrink. If they don't, more tests will be done, such as a biopsy to remove part or all of a swollen node (see next section). But if the lymph nodes seem to be growing quickly or the child's health seems to be getting worse, a biopsy may be needed right away.

Biopsy

Lymphoma can't be diagnosed in a child based only on symptoms or a physical exam. Most of the symptoms NHL can cause are more often caused by other problems, like infections. They may also be caused by other kinds of cancers. And if a child does have NHL, it's important to know which type it is², because some types are treated differently.

The only way to be sure of the diagnosis is to remove some or all of an abnormal lymph node (or tumor) to look at it with a microscope and do other lab tests. This is called a biopsy.

Types of biopsies used to diagnose non-Hodgkin lymphoma

There are different <u>types of biopsies</u>³. Doctors choose which one to use based on the situation. The goal is to get a sample large enough to make an accurate diagnosis as quickly as possible, with as few side effects as possible.

Surgical (open) biopsy: In this procedure, either an entire lymph node (an **excisional biopsy**) or a small part of a large tumor (an **incisional biopsy**) is removed through a cut in the skin.

If it can be done, this type of biopsy is usually preferred when lymphoma is suspected, as it almost always provides enough of a sample to diagnose the exact type of NHL.

If the area to be biopsied is a lymph node near the skin surface, this might be done with either local anesthesia (numbing medicine at the biopsy site) and sedation, or with general anesthesia (where the child is in a deep sleep). If the node (or tumor) is inside the chest or abdomen, general anesthesia typically is needed.

Needle biopsy: These biopsies use hollow needles to remove small pieces of tissue. There are 2 main types:

- In a **fine needle aspiration (FNA) biopsy**, the doctoruses a very thin, hollow needle attached to a syringe to withdraw (aspirate) a small amount of tissue from an enlarged lymph node or a tumor mass.
- For a **core needle biopsy**, the doctor uses a larger needle to remove a slightly larger piece of tissue.

If an enlarged lymph node is just below the skin, the doctor can aim the needle while feeling the node. If the enlarged node or tumor is deep in the body (such as in the chest or abdomen), the doctor can guide the needle while watching it on an imaging test such as a CT scan or ultrasound (described later in this section).

The main advantage of a needle biopsy is that it does not require surgery. This can be especially important for children with tumors in the chest, because general anesthesia (where the child is in a deep sleep) can sometimes be dangerous for these children. A needle biopsy can also be useful when the lymphoma is in a place other than the lymph nodes, such as the bones.

In children, needle biopsies can often be done using local anesthesia to numb the area, along with sedation to make the child sleepy. General anesthesia is needed less often.

The main drawback of needle biopsies (especially FNA) is that sometimes the needle might not remove enough to make a definite diagnosis. Most doctors don't use needle biopsies if they strongly suspect lymphoma (unless other types of biopsies can't be done for some reason). But if the doctor suspects that lymph node swelling is caused by an infection (even after antibiotics), a needle biopsy may be the first type of biopsy done. Even after a needle biopsy has been done, a surgical biopsy might still be needed to diagnose and classify the lymphoma.

After lymphoma has been diagnosed, needle biopsies are sometimes used to check areas in other parts of the body where lymphoma might be spreading or coming back

after treatment.

Other types of biopsies

Other types of biopsies are not normally used to diagnose lymphoma, but they might be done if a lymphoma has already been diagnosed to help show how far it has spread.

Bone marrow aspiration and biopsy

These tests can show if a lymphoma has reached the bone marrow. The 2 tests are usually done at the same time. Biopsy samples are usually taken from the back of the pelvic (hip) bones, although sometimes they may be taken from the front of the hip bones or from other bones.

For a **bone marrow aspiration**, the skin over the hip and the surface of the bone is numbed with local anesthetic. In most cases, children will be given other medicines to make them drowsy or asleep during the biopsy. A thin, hollow needle is then inserted into the bone, and a syringe is used to suck out a small amount of liquid bone marrow.

A **bone marrow biopsy** is usually done just after the aspiration. A small piece of bone and some marrow is removed with a slightly larger needle that is put into the bone. After the biopsy is done, pressure will be put on the site to help stop any bleeding.

Lumbar puncture (spinal tap)

This test is used to look for lymphoma cells in the cerebrospinal fluid (CSF), which is the fluid that surrounds the brain and spinal cord.

For this test, an area in the lower part of the back near the spine is numbed. Usually the child also is given medicine to make him or her sleep during the procedure. A small, hollow needle is then placed between the bones of the spine to withdraw some of the fluid.

If a child has already been diagnosed with lymphoma, a lumbar puncture can also be used to put <u>chemotherapy</u>⁴ drugs into the CSF to try to prevent or treat the spread of lymphoma to the spinal cord and brain.

Pleural or peritoneal fluid sampling

Lymphoma that has spread to the thin membranes that line the inside of the chest and abdomen can cause fluid to build up. Pleural fluid (inside the chest) or peritoneal fluid

(inside the belly) can be removed by putting a hollow needle through the skin into the chest or abdomen.

- When this procedure is used to remove fluid from the chest, it's called a **thoracentesis**.
- When it's used to collect fluid from inside the belly, it's known as a paracentesis.

Before the procedure, the doctor uses a local anesthetic to numb the skin and may give the child other medicines so they are drowsy or asleep during the procedure. The fluid is then drawn out and checked for lymphoma cells.

Lab tests on biopsy samples

All biopsy samples and fluids are looked at by a pathologist (a doctor specially trained in using lab tests to identify cancer cells). The doctor uses a microscope to look at the size and shape of the cells and how they are arranged. This can show if a child has lymphoma, and sometimes what type of lymphoma it is. But usually other types of lab tests will be needed as well.

Flow cytometry and immunohistochemistry

For flow cytometry and immunohistochemistry tests, samples of cells are treated with antibodies (proteins that stick only to certain other proteins on cells). For immunohistochemistry, the cells are then looked at with a microscope to see if the antibodies stuck to them (meaning they have these proteins), while flow cytometry uses a special machine to look at them.

These tests can help determine if a lymph node is swollen because of lymphoma, some other cancer, or a non-cancerous disease. The tests can also be used for **immunophenotyping** (determining which type of lymphoma a child has, based on certain proteins in or on the cells). Different types of lymphocytes (the cells from which lymphomas start) have different proteins on their surface, which relate to the type of lymphocyte and how mature it is.

Chromosome tests

These tests evaluate the chromosomes (long strands of DNA) in the lymphoma cells. In some types of lymphoma, the cells have chromosome changes such as having too many, too few, or other abnormalities. These changes can often help identify the type of lymphoma.

- **Cytogenetics:** In this test, the cells are looked at under a microscope to see if the chromosomes have any abnormalities. A drawback of this test is that it usually takes about 2 to 3 weeks because the lymphoma cells must grow in lab dishes before their chromosomes are ready to be seen with a microscope.
- Fluorescent in situ hybridization (FISH): This test looks more closely at lymphoma cell DNA using fluorescent dyes that only attach to specific gene or chromosome changes. FISH can find most chromosome changes (such as translocations) that can be seen under a microscope on standard cytogenetic tests, as well as some changes too small to be seen with usual cytogenetic testing. FISH is very accurate and results are usually ready within a couple of days.
- **Polymerase chain reaction (PCR):** This is a very sensitive DNA test that can also find some chromosome changes too small to be seen with a microscope, even if there are very few lymphoma cells in a sample.

For more information, see <u>Testing Biopsy and Cytology Specimens for Cancer</u>⁵.

Blood tests

Blood tests measure the amounts of certain types of cells and chemicals in the blood. They are not used to diagnose lymphoma, but they might be one of the first types of tests done in children with symptoms to help determine what is going on. If a child has been diagnosed with lymphoma, these tests can also sometimes help show how advanced the lymphoma is.

- A complete blood count (CBC) measures the levels of different cells in the blood, such as the red blood cells, white blood cells, and platelets. In children already known to have lymphoma, low blood cell counts might mean that the lymphoma is growing in the bone marrow and damaging new blood cell production. In children getting chemotherapy, this test can also be used to see if treatment is affecting the bone marrow.
- Blood levels of **lactate dehydrogenase (LDH)** may be checked. LDH is often abnormally high in patients with fast-growing lymphomas.
- Blood chemistry tests can help detect liver or kidney problems caused by the spread of lymphoma cells or certain chemotherapy drugs. These tests can also help determine if treatment is needed to correct low or high blood levels of certain minerals.
- Tests may also be done to make sure the **blood is clotting properly**.
- For some types of lymphoma, other blood tests might be done to see if the child

has been infected with certain viruses, such as the **Epstein-Barr virus (EBV)**, **hepatitis B virus (HBV)**, or **human immunodeficiency virus (HIV)**. Infections with some of these viruses can affect the way your child will be treated.

Imaging tests

Imaging tests use x-rays, sound waves, magnetic fields, or radioactive substances to create pictures of the inside of the body. These tests might be done for a number of reasons, including:

- To look for possible causes of certain symptoms (such as trouble breathing)
- To help determine the stage (extent) of the lymphoma, once it has been diagnosed
- To help show if treatment is working
- To look for possible signs of lymphoma coming back after treatment

A child with a known or suspected lymphoma might need one or more of these tests.

Chest x-ray

A chest x-ray⁶ may be done to look for enlarged lymph nodes inside the chest. But this test isn't likely to be needed if a CT scan of the chest is done.

Computed tomography (CT or CAT) scan

A <u>CT scan</u>⁷ combines many x-rays to make detailed, cross-sectional images of the body. CT scans are often used to look for enlarged lymph nodes or other masses in the neck, chest, abdomen, and pelvis.

During the test, your child will need to lie still on a table that slides in and out of the ringshaped scanner. Some younger children may be given medicine to help keep them calm or even asleep during the test to help make sure the pictures come out well.

CT-guided needle biopsy: A CT scan can also be used to guide a biopsy needle precisely into a suspected tumor or enlarged lymph node. For this procedure, the child remains asleep on the CT scanning table, while the doctor advances a biopsy needle through the skin and toward the area. CT scans are repeated until the needle is in the right place. The biopsy sample is then removed and looked at in the lab.

Ultrasound (sonogram)

<u>Ultrasound</u>⁸ uses sound waves and their echoes to create pictures of internal organs or masses.

Ultrasound can be used to look at lymph nodes near the surface of the body or to look inside the abdomen (belly) for enlarged lymph nodes or organs such as the liver or spleen. It can also show if the kidneys have become swollen if the outflow of urine has been blocked by enlarged lymph nodes.

Ultrasound-guided needle biopsy: Ultrasound is also sometimes used to help guide a biopsy needle into an enlarged lymph node.

Magnetic resonance imaging (MRI) scan

An <u>MRI</u>⁹, like a CT scan, shows detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets to make pictures, instead of x-rays.

This test is not used as often as CT scans for lymphoma, but MRI is very useful for looking at the brain and spinal cord if a child has symptoms that might be caused by problems in the nervous system.

MRIs take longer than CT scans, often up to an hour. Your child may have to lie inside a narrow tube, which can be distressing, so sedation is sometimes needed. Newer, more open MRI machines may be another option, although your child will still have to lie still.

Positron emission tomography (PET) scan

For a <u>PET scan</u>¹⁰, a slightly radioactive sugar is injected into the blood. (The amount of radioactivity used is very low and will pass out of the body within a day or so.) Because lymphoma cells grow quickly, they absorb more of the sugar. After about an hour, your child will be moved onto a table in the PET scanner. He or she will lie on the table for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body. Younger children may be given medicine to help keep them calm or even asleep during the test.

The picture from a PET scan is not detailed like a CT or MRI scan, but it provides helpful information about the whole body.

PET scans can be used for many reasons in a child with lymphoma:

- They can help tell if an enlarged lymph node contains lymphoma
- They can help spot small areas in the body that might be lymphoma, even if the area looks normal on a CT scan
- They can help tell if a lymphoma is responding to <u>treatment</u>¹¹. Some doctors will repeat the PET scan after 1 or 2 courses of <u>chemotherapy</u>¹². If the chemo is working, the lymphoma will no longer show up as well on the scan.
- They can be used after treatment to help decide if an enlarged lymph node still contains lymphoma or is just scar tissue

PET/CT or PET/MRI scan: Some newer machines can do a PET as well as a CT or MRI scan at the same time. This lets the doctor compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT or MRI scan.

Bone scan

A <u>bone scan</u>¹³ is not usually needed unless a child has bone pain or has lab test results that suggest the lymphoma might have reached the bones.

For this test, a radioactive substance called **technetium** is injected into the blood. (The amount of radioactivity used is very low and will pass out of the body within a day or so. Technetium travels to damaged areas of the bone over a couple of hours. Your child then lies on a table while a special camera detects the radioactivity and creates a picture of the skeleton. Younger children may be given medicine to help keep them calm or even asleep during the test.

A bone scan can detect bone damage from lymphoma. But it may also show other things that are not cancer, so other tests might be needed to be sure.

Hyperlinks

- 1. <u>www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/causes-risks-prevention/risk-factors.html</u>
- 2. <u>www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/about/types-non-hodgkin-children.html</u>
- 3. <u>www.cancer.org/treatment/understanding-your-diagnosis/tests/testing-biopsy-and-</u> cytology-specimens-for-cancer/biopsy-types.html
- 4. <u>www.cancer.org/cancer/childhood-non-hodgkin-</u> lymphoma/treating/chemotherapy.html
- 5. www.cancer.org/treatment/understanding-your-diagnosis/tests/testing-biopsy-and-

cytology-specimens-for-cancer.html

- 6. <u>www.cancer.org/treatment/understanding-your-diagnosis/tests/x-rays-and-other-radiographic-tests.html</u>
- 7. <u>www.cancer.org/treatment/understanding-your-diagnosis/tests/ct-scan-for-</u> <u>cancer.html</u>
- 8. <u>www.cancer.org/treatment/understanding-your-diagnosis/tests/ultrasound-for-</u> <u>cancer.html</u>
- 9. www.cancer.org/treatment/understanding-your-diagnosis/tests/mri-for-cancer.html
- 10. <u>www.cancer.org/treatment/understanding-your-diagnosis/tests/nuclear-medicine-</u> <u>scans-for-cancer.html</u>
- 11. <u>www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/treating.html</u>
- 12. <u>www.cancer.org/cancer/childhood-non-hodgkin-</u> lymphoma/treating/chemotherapy.html
- 13. <u>www.cancer.org/treatment/understanding-your-diagnosis/tests/nuclear-medicine-</u> scans-for-cancer.html

References

Gross TG, Kamdar KY, Bollard CM. Chapter 19: Malignant Non-Hodgkin Lymphomas in 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.

Link MP, Jaffe ES, Leonard JP. Pediatric Hodgkin and non-Hodgkin lymphomas. In: *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017:959-965.

National Cancer Institute Physician Data Query (PDQ). Childhood Non-Hodgkin Lymphoma Treatment. 2021. Accessed at https://www.cancer.gov/types/lymphoma/patient/child-nhl-treatment-pdq on June 10, 2021.

Sandlund JT, Onciu M. Chapter 94: Childhood Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa: Elsevier; 2020.

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Stages of Non-Hodgkin Lymphoma in Children

What is the stage of a lymphoma?

A lymphoma's stage tells you how much and where the cancer is in the body when it is first diagnosed. Along with the <u>type of non-Hodgkin lymphoma (NHL)¹</u>, the stage is important in determining the treatment options and prognosis (outlook) for a child or teen with NHL.

The stage is based on the results of physical exams, biopsies, and imaging tests (CT scan, PET scan, etc.), which are described in Tests for Non-Hodgkin Lymphoma in Children.

A staging system describes how far a cancer has spread in a standard way. The system most often used to describe the spread of NHL in children is the **International Pediatric Non-Hodgkin Lymphoma Staging System (IPNHLSS)**, which is a modified version of the older St. Jude staging system. This system is different from the one used for lymphomas in adults.

International Pediatric Non-Hodgkin Lymphoma Staging System (IPNHLSS)

The IPNHLSS divides childhood NHL into 4 stages:

- Stage I and II lymphomas are usually considered **limited-stage** disease and are treated the same way.
- Stage III and IV lymphomas are usually thought of as **advanced-stage** disease and are also treated alike.

Stage I

The lymphoma is in only one place, either as a single tumor **not** in lymph nodes, **or** in lymph nodes in one part of the body (the neck, groin, underarm, etc.). The lymphoma is not in the chest or abdomen (belly).

Stage II

Stage II lymphomas are not in the chest, and one of the following applies:

- The lymphoma is a single tumor and is also in nearby lymph nodes in only one part of the body (the neck, groin, underarm, etc.).
- The lymphoma is in more than one set of lymph nodes, all of which are either above or below the diaphragm (the thin breathing muscle that separates the chest and abdomen). For example, this might mean nodes in the underarm and neck area are affected but not the combination of underarm and groin nodes.
- The lymphoma started in the digestive tract (usually at the end of the small intestine) and can be removed by surgery. It might or might not have reached nearby lymph nodes.

Stage III

For stage III lymphomas, one of the following applies:

- The lymphoma started in the chest (usually in the thymus, the lymph nodes in the center of the chest, or the lining of the lung).
- The lymphoma started in the abdomen and has spread too widely within the abdomen to be removed completely by surgery.
- The lymphoma is next to the spine (and may be elsewhere as well).
- The lymphoma is more than one tumor outside of the lymph nodes, which might be above or below the diaphragm (the thin breathing muscle that separates the chest and abdomen). This might include tumors in the bones or skin.
- The lymphoma is in more than one set of lymph nodes above and below the diaphragm. For example, the lymphoma is in both underarm and groin lymph nodes.
- The lymphoma is a single tumor in a bone, and it is in a nearby area as well (either in or outside the lymph nodes).

Stage IV

The lymphoma is in the central nervous system (brain or spinal cord) and/or the bone marrow when it is first found. (If more than 25% of the bone marrow is made up of cancer cells, called blasts, the cancer is classified as <u>acute lymphoblastic leukemia</u>² [ALL] instead of lymphoma.)

Lymphoma staging can be confusing. If you are unsure about what it means for your child, ask your child's doctor to explain it to you.

Other prognostic factors

Along with the stage of the lymphoma (and the type of lymphoma), some other factors can also affect a child's outlook (prognosis). These include:

- The child's age (younger children tend to do better.)
- The blood LDH level (children with lower LDH levels tend to do better.)
- Where the lymphoma is in the body
- How well the lymphoma responds to initial treatment

If you have questions about what these prognostic factors might mean for your child, ask your child's doctor to explain them to you.

Hyperlinks

- 1. <u>www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/about/types-non-hodgkin-children.html</u>
- 2. www.cancer.org/cancer/leukemia-in-children.html

References

Gross TG, Kamdar KY, Bollard CM. Chapter 19: Malignant Non-Hodgkin Lymphomas in 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.

Link MP, Jaffe ES, Leonard JP. Pediatric Hodgkin and non-Hodgkin lymphomas. In: *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017:959-965.

Rosolen A, Perkins SL, Pinkerton CR, et al. Revised International Pediatric Non-Hodgkin Lymphoma Staging System. *J Clin Oncol.* 2015;33(18):2112-2118. Sandlund JT, Onciu M. Chapter 94: Childhood Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa: Elsevier; 2020.

Termuhlen AM, Gross TG. Overview of non-Hodgkin lymphoma in children and adolescents. UpToDate. 2021. Accessed at https://www.uptodate.com/contents/overview-of-non-hodgkin-lymphoma-in-children-and-adolescents on June 10, 2021.

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Survival Rates for Childhood Non-Hodgkin Lymphoma

Survival rates are one way to get an idea of the outlook for children and teens with a certain type and stage of cancer. They can't tell exactly what will happen with any person, but they may help give you a better understanding about how likely it is that treatment will be successful.

What is a survival rate?

Statistics on the outlook (prognosis) for a certain type and stage of cancer are often given as survival rates. For example, the **5-year survival rate** is the percentage of people who live at least 5 years after being diagnosed with cancer. A 5-year survival rate of 80% means that an estimated 80 out of 100 people who have that cancer are still alive 5 years after being diagnosed. Of course, many of these people live much longer than 5 years.

Many cancer doctors prefer not to use the word "cure" when discussing cancer treatment and prognosis (outlook), because it can be hard to know for sure that all of the cancer is gone after treatment. But when it comes to children and teens with non-Hodgkin lymphoma (NHL), those who are still alive and free of lymphoma after 5 years are very likely to have been cured, as it's rare for these cancers to return after this much time.

Survival rates don't tell the whole story

Survival rates are often based on previous outcomes of large numbers of children who had the disease, but they can't predict for sure what will happen in any particular child's case. There are some limitations to keep in mind:

- The outlook for children and teens with NHL varies by the <u>type</u>¹ and <u>stage</u> (extent) of the lymphoma. But other factors can also affect a child's outlook, such as the location and size of the tumor(s), and how well the lymphoma responds to <u>treatment</u>². The outlook for each child is unique based on their circumstances.
- The numbers below are among the most current available. But to get these survival rates, doctors have to look at children who were treated at least several years ago. As treatments are improving over time, children who are now being diagnosed with NHL may have a better outlook than these statistics show.

Your child's doctor can tell you how these numbers might apply to your child's particular situation.

Survival rates for childhood non-Hodgkin lymphoma

Advances in treatment have increased the overall survival rates for children and teens with NHL dramatically in recent decades.

The ranges of numbers given below are based on the results of several studies that have used different treatment regimens or included slightly different groups of patients.

Lymphoblastic lymphoma

With intensive treatment, the long-term survival rate for children and teens with limited stage (stage I or II) lymphoblastic lymphoma is higher than 90%.

The long-term survival rate for more advanced (stage III or IV) lymphoblastic lymphomas is generally higher than 80%.

Burkitt and Burkitt-like lymphoma

Treatment of limited stage (stage I and II) Burkitt lymphomas is usually very successful, with a long-term survival rate of over 90%.

The long-term survival rate for children and teens with more advanced (stage III or IV) Burkitt lymphoma ranges from about 80% to 90%.

Diffuse large B-cell lymphoma

The long-term survival rate is over 90% for limited stage (stage I and II) diffuse large B-cell lymphoma (DLBCL).

The long-term survival rate for children and teens with advanced (stage III or IV) DLBCL ranges from about 80% to 90%.

Anaplastic large cell lymphoma

The long-term survival rate for limited stage anaplastic large cell lymphoma (ALCL) is about 90%.

ALCL is more likely to be advanced at the time it is diagnosed, for which the long-term survival rate is in the range of 60% to 75%.

Remember, all of these survival rates are only estimates – they can't predict what will happen with any child. We understand that these statistics can be confusing and may lead you to have more questions. Talk to your child's doctor if you'd like to get a better understanding of what these numbers mean.

Hyperlinks

- 1. <u>www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/about/types-non-hodgkin-children.html</u>
- 2. www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/treating.html

References

Gross TG, Kamdar KY, Bollard CM. Chapter 19: Malignant Non-Hodgkin Lymphomas in 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.

National Cancer Institute Physician Data Query (PDQ). Childhood Non-Hodgkin Lymphoma Treatment. 2021. Accessed at

https://www.cancer.gov/types/lymphoma/hp/child-nhl-treatment-pdq on June 10, 2021.

Smith MA, Seibel NL, Altekruse SF, et al. Outcomes for children and adolescents with cancer: Challenges for the twenty-first century. *J Clin Oncol*. 2010:28:2625–2634.

Termuhlen AM, Gross TG. Overview of non-Hodgkin lymphoma in children and adolescents. UpToDate. 2021. Accessed at https://www.uptodate.com/contents/overview-of-non-hodgkin-lymphoma-in-children-and-adolescents on June 10, 2021.

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Questions to Ask Your Child's Health Care Team About Non-Hodgkin Lymphoma

It is important to have open, honest discussions with your child's cancer care team. Ask any question, no matter how minor it might seem. For instance, consider asking these questions:

When you're told your child has non-Hodgkin lymphoma

- What type of non-Hodgkin lymphoma¹ does my child have?
- What is the stage (extent) of the lymphoma, and what does that mean?
- What tests need to be done before we can decide on treatment?
- Do we need to see any other types of doctors?

When deciding on a treatment plan

- How much experience do you have treating this type of lymphoma?
- What are our <u>treatment options</u>²?
- What treatment do you recommend and why?

- Should we get a <u>second opinion</u>³ before starting treatment? If so, can you suggest a doctor or cancer center?
- How soon do we need to start treatment?
- What should we do to be ready for treatment⁴?
- Who else will be on the treatment team, and what do they do?
- How long will treatment last? What will it be like? Where will it be done?
- How much of the treatment will need to be done in the hospital?
- How will treatment affect our daily lives?
- What are the risks and side effects of treatment?
- Which side effects start shortly after treatment and <u>which ones might develop later</u> <u>on</u>⁵?
- Will treatment affect my child's ability to learn, grow, and develop?
- What are the chances of curing the lymphoma?
- What will our options be if the treatment doesn't work or if the lymphoma comes back?

You should also talk with your child's doctor before treatment to find out about the <u>possible long-term side effects</u>⁶. For example, you might want to ask about how treatment could affect your child's fertility later on. Here are some questions you might want to ask about the risks of infertility with treatment:

- Will this treatment affect my child's <u>ability to have children</u>⁷ someday?
- Can anything be done to prevent or lower the risk of infertility? Would this interfere with my child's cancer treatment?
- Should we talk to a fertility specialist?
- Once my child finishes treatment, how will we know if they might have fertility problems?

During treatment

Once treatment begins, you'll need to know what to expect and what to look for. Not all of these questions may apply, but getting answers to the ones that do could be helpful.

- How will we know if the treatment is working?
- Is there anything we can do to help manage side effects⁸?
- What symptoms or side effects should we tell you about right away?
- How can we reach you or someone on your team on nights, weekends, or

holidays?

• Are there any limits on what my child can do during treatment?

After treatment

- What type of <u>follow-up</u>⁹ will my child need after treatment?
- Are there any limits on what they can do after treatment?
- What symptoms should we watch for?
- How will we know if the lymphoma has come back? What will our options be if that happens?
- Do you know of any local or online support groups where we can talk to other families who are coping with childhood lymphoma?

Along with these examples, be sure to ask any other questions you might have. For instance, you might want more information about recovery times so that you can plan work and school schedules. Or you might want to know more about <u>clinical trials</u>¹⁰.

Keep in mind that doctors aren't the only ones who can give you information. Other health care professionals, such as nurses and social workers, can answer some of your questions. To find out more about communicating with your health care team, see <u>The</u> <u>Doctor-Patient Relationship</u>¹¹.

Hyperlinks

- 1. <u>www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/about/types-non-hodgkin-children.html</u>
- 2. www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/treating/by-stage.html
- 3. <u>www.cancer.org/treatment/finding-and-paying-for-treatment/choosing-your-</u> <u>treatment-team/seeking-a-second-opinion.html</u>
- 4. <u>www.cancer.org/treatment/treatments-and-side-effects/planning-managing.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/children-and-cancer/when-your-child-has-cancer/late-effects-of-cancer-treatment.html</u>
- 7. <u>www.cancer.org/treatment/treatments-and-side-effects/physical-side-</u> <u>effects/fertility-and-sexual-side-effects/preserving-fertility-in-children-and-teens-</u> <u>with-cancer.html</u>

- 8. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html
- 9. www.cancer.org/cancer/childhood-non-hodgkin-lymphoma/after-treatment/followup.html
- 10. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
- 11. <u>www.cancer.org/treatment/finding-and-paying-for-treatment/choosing-your-</u> <u>treatment-team/the-doctor-patient-relationship.html</u>

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