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

Learn about the signs and symptoms of non-Hodgkin lymphoma (NHL) in children and teens. Find out how NHL is tested for, diagnosed, and staged.

#### **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.

## Can Non-Hodgkin Lymphoma in Children Be Found Early?

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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><sup>1</sup> 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 a0 goytlls, if iyourchill or pten fhs aS1 of the e

#### **Hyperlinks**

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

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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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### Tests for Non-Hodgkin Lymphoma in Children

#### Types of biopsies used to diagnose non-Hodgkin lymphoma

There are different <u>types of biopsies</u><sup>3</sup>. 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.

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

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.

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- 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  $\underline{x\text{-ray}}^6$  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><sup>7</sup> 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><sup>8</sup> 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 MRI<sup>9</sup>, 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

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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><sup>11</sup>. Some doctors will repeat the PET scan after 1 or 2 courses of <u>chemotherapy</u><sup>12</sup>. 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><sup>13</sup> 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**

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### Stages of Non-Hodgkin Lymphoma in Children

- What is the stage of a lymphoma?
- International Pediatric Non-Hodgkin Lymphoma Staging System (IPNHLSS)
- Other prognostic factors

#### 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)</u><sup>1</sup>, 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:

- Tisheallympathtonenaerins la Bis Trigile tourin or Cahel esnall storying the earliery Cyron photo Cate & Greenouthy one part of the body (the neck, groin, under arm, 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 buat the5 T5oois (I)Tj 1u7Tj 0 g ET q BT 1 0 0 1 87.7 unde2 Tf 0 0

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

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### Survival Rates for Childhood Non-Hodgkin Lymphoma

What is a survival rate?

- Survival rates don't tell the whole story
- 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

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

- When you're told your child has non-Hodgkin lymphoma
- When deciding on a treatment plan
- During treatment
- After treatment

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 lymphoma<sup>1</sup> 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 treatment options<sup>2</sup>?
- What treatment do you recommend and why?
- Should we get a <u>second opinion</u><sup>3</sup> 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 <u>ready for treatment</u><sup>4</sup>?
- 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 which ones might develop later on<sup>5</sup>?
- 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><sup>6</sup>. 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><sup>7</sup> 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?

- 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><sup>10</sup>.

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><sup>11</sup>.

#### **Hyperlinks**

www.cancer.org/cancer/types/childhood-non-hodgkin-lymphoma/about/types-non-hodgkin-children.html
 www.cancer.org/cancer/types/childhood-non-hodgkin-lymphoma/treating/by-

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