Non-Hodgkin Lymphoma Early Detection, Diagnosis, and Staging

Know the signs and symptoms of non-Hodgkin lymphoma. Find out how NHL is tested for, diagnosed, and staged.

Detection and Diagnosis

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

- Survival Rates and Factors That Affect Prognosis (Outlook) for Non-Hodgkin Lymphoma

Questions to Ask About Non-Hodgkin Lymphoma

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

- Questions to Ask About Non-Hodgkin Lymphoma

Can Non-Hodgkin Lymphoma Be Found Early?

At this time, there are no widely recommended screening tests for non-Hodgkin lymphoma (NHL). (Screening tests or exams are used to look for a disease in people who have no symptoms.) Still, in some cases, lymphoma can be found early.

The best way to find lymphoma early is to pay attention to possible signs and symptoms.

One of the most common symptoms is enlargement of one or more lymph nodes, causing a lump or bump under the skin that is usually not painful. This is most often on the side of the neck, in the armpit, or in the groin region.

Other symptoms can include fever, chills, night sweats, weight loss, feeling tired, and swelling in the abdomen. Most often, these symptoms are caused by something other than lymphoma, but it's important to have them checked by a doctor, especially if they don't go away or get worse.

Careful, regular medical checkups are important for people with known risk factors[1] for NHL (such as HIV infection, having an organ transplant or an autoimmune disease, or prior cancer treatment). These people do not often get lymphoma, but they and their doctors should be aware of possible symptoms and signs of lymphoma.

Hyperlinks

1. www.cancer.org/cancer/types/non-hodgkin-lymphoma/causes-risks-prevention/risk-factors.html

Signs and Symptoms of Non-Hodgkin Lymphoma

Sometimes NHL might not cause any symptoms until it grows quite large. Having one or more of the symptoms below doesn't mean you have lymphoma. In fact, many of the symptoms listed here are more likely to be caused by other conditions, such as an infection. Still, if you have any of these symptoms, have them checked by a doctor so that the cause can be found and treated, if needed.

Common signs and symptoms of lymphoma

Some common signs and symptoms of lymphoma include:

- Enlarged lymph nodes (sometimes felt as lumps under the skin, especially in the neck, underarm, or groin area)
- Fever and chills
- Weight loss
- Fatigue (feeling very tired)
- Swollen abdomen (belly)
- Feeling full after only a small amount of food
- Chest pain or pressure
- Shortness of breath or cough
- Severe or frequent infections
- Easy bruising or bleeding

Some people with non-Hodgkin lymphoma have what are known as

called **reactive nodes** or **hyperplastic nodes** and are often tender to the touch.

Symptoms from lymphoma in the abdomen

Lymphomas that start or grow in the abdomen (belly) can cause **swelling or pain in the abdomen**. This could be from lymph nodes or organs, such as the spleen or liver, getting bigger. It can also be caused by the buildup of large amounts of fluid.

An enlarged spleen might press on the stomach, which can cause a **loss of appetite** and **feeling full after only a small meal.**

Lymphomas in the stomach or intestines can cause **abdominal pain, nausea, or vomiting.**

Symptoms from lymphoma in the chest

When lymphoma starts in the thymus or lymph nodes in the chest, it may press on the nearby trachea (windpipe), which can cause **coughing, trouble breathing,** or a feeling of **chest pain or pressure.**

The superior vena cava (SVC) is the large vein that carries blood from the head and arms back to the heart. It passes near the thymus and lymph nodes inside the chest. Lymphomas in this area may push on the SVC, which can cause the blood to back up in the veins. This can lead to swelling (and sometimes a bluish-red color) in the head, arms, and upper chest. It can also cause trouble breathing and a change in

Lymphomas of the skin may be seen or felt. They often appear as **itchy, red, or purple lumps or bumps under the skin.** For more details, see Lymphoma of the Skin[1].

Tests for Non-Hodgkin Lymphoma

Medical history and physical exam

Most people with NHL see a doctor because they have felt a lump that hasn't gone away, they develop some of the other symptoms of NHL, or they just don't feel well and go in for a checkup.

Your doctor will want to get a complete medical history, including information about your symptoms, possible risk factors[2], and any other medical conditions you have.

Next, the doctor will examine you, paying special attention to the lymph nodes and other areas of your body that might be affected, including the spleen and liver. Because infections are the most common cause of enlarged lymph nodes, the doctor will look for an infection near the swollen lymph nodes.

The doctor also might order blood tests to look for signs of infection or other problems. Blood tests aren't used to diagnose lymphoma, though. If the doctor suspects that lymphoma might be causing your symptoms, they might recommend a biopsy of a swollen lymph node or other affected area.

Biopsy

For a biopsy, part or all of a lymph node (or tumor) is removed for testing in a lab.

A biopsy is the only way to confirm a person has NHL. But it's not always done right away because many symptoms of NHL can also be caused by other problems, like an infection, or by other kinds of cancer. Because enlarged lymph nodes are more often caused by infections than by lymphoma, doctors often prescribe antibiotics and wait a few weeks to see if the lymph nodes shrink. If the nodes stay the same or continue to grow, the doctor might then order a biopsy.

A biopsy might be needed right away if the size, texture, or location of a lymph node or the presence of other symptoms strongly suggests lymphoma.

Biopsies to diagnose non-Hodgkin lymphoma

There are several types of biopsies. Doctors choose which one to use based on each person's situation.

Excisional or incisional biopsy: This is the most common type of biopsy if lymphoma is suspected, because it almost always provides enough of a sample to diagnose the exact type of NHL.

In this procedure, a surgeon cuts through the skin to remove the lymph node.

- If the doctor removes the entire lymph node, it is called an **excisional biopsy**.
- If a small part of a larger tumor or node is removed, it is called an **incisional biopsy**.

If the enlarged node is just under the skin, this is a fairly simple operation that can often be done with local anesthesia (numbing medicine). But if the node is inside the chest or abdomen, you will also be sedated (given drugs to make you drowsy and relaxed) or you'll be given general anesthesia (drugs to put you into a deep sleep).

Needle biopsy: Needle biopsies are less invasive than excisional or incisional biopsies, but the drawback is that they might not remove enough of a sample to diagnose lymphoma (or to determine which type it is).

Most doctors don't use needle biopsies to diagnose lymphoma. But if they suspect that a lymph node is enlarged because of an infection or by the spread of cancer from another organ (such as the breast, lungs, or thyroid), a needle biopsy may be the first type of biopsy done. An excisional biopsy might still be needed even after a needle biopsy has been done, to diagnose and classify lymphoma.

There are 2 main types of needle biopsies:

- In a **fine needle aspiration (FNA) biopsy,** the doctor uses 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.
- For a **core needle biopsy,** the doctor uses a larger needle to remove a slightly larger piece of tissue.

To biopsy an enlarged node just under the skin, the doctor can often aim the needle while feeling the node. If the node or tumor is deep inside the body, the doctor can guide the needle using a computed tomography (CT) scan or ultrasound (see descriptions of imaging tests later in this section).

If lymphoma has already been diagnosed, needle biopsies are sometimes used to check abnormal areas in other parts of the body that might be from the lymphoma spreading or coming back after treatment.

Other types of biopsies

fluid is then taken out and checked in the lab for lymphoma cells.

Lab tests on biopsy samples

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

Flow cytometry and immunohistochemistry (IHC): For both flow cytometry and IHC, the biopsy samples are coated with antibodies (lab-made immune proteins) that will only stick to certain proteins on cells. The cells are then looked at in the lab (immunohistochemistry) or with a special machine (for flow cytometry), to see if the antibodies attached to them.

These tests can help determine whether 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 person has, based on if the lymphoma cells have certain proteins.

Chromosome tests: Normal human cells have 23 pairs of chromosomes (strands of DNA), each of which is a certain size and looks a certain way in the lab. But in some types of lymphoma, the cells have changes in their chromosomes, such as having too many, too few, or abnormal chromosomes. These changes can often help identify the type of lymphoma.

- **Cytogenetic testing (karyotyping):** In this lab test, the cells are checked for any abnormalities in the chromosomes. The cells need to be grown in the lab first, so the results can take a week or more.
- **Fluorescent in situ hybridization (FISH):** This test looks more closely at lymphoma cell DNA using special fluorescent dyes that only attach to specific genes or parts of chromosomes. FISH can find most chromosome changes that can be seen in standard cytogenetic tests, as well as some gene changes too small to be seen with cytogenetic testing. FISH is very accurate and can usually provide results within a couple of days.
- **Polymerase chain reaction (PCR):** PCR is a very sensitive DNA test that can find gene changes and certain chromosome changes too small to be seen with a microscope, even if there are very few lymphoma cells in a sample.

Other molecular/genetic tests: Other, newer types of lab tests might also be done on

the lymphoma cells to learn more about the gene and protein changes in the cells.

To learn more about these tests, see Biopsy and Cytology Tests[3].

Imaging tests

Imaging tests use x-rays, sound waves, magnetic fields, or radioactive particles to produce 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 enlarged lymph nodes in the chest in someone having chest pain or trouble breathing)
- To help determine the stage (extent) of the lymphoma
- To help show if treatment is working
- To look for possible signs of lymphoma coming back after treatment

Chest x-ray

A chest x-ray[4] might be done to look for enlarged lymph nodes in this area. This test isn't needed if a CT of the chest is done.

Computed tomography (CT) scan

A CT scan[5] combines many x-rays to make detailed, cross-sectional images of your body. This scan can help tell if any lymph nodes or organs in your body are enlarged. CT scans are useful for looking for lymphoma in the abdomen, pelvis, chest, head, and neck.

When looking for lymphoma in the body, CT scans are often combined with a PET scan (known as a PET/CT scan - see below).

CT-guided needle biopsy: A CT can also be used to guide a biopsy needle into a suspicious area. For this procedure, you lie on the CT scanning table while the doctor moves a biopsy needle through the skin and toward the area. CT scans are repeated until the needle is in the right place. A biopsy sample is then removed to be looked at in the lab.

Magnetic resonance imaging (MRI)

Like CT scans, MRIs[6] show detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays. This test is not used as often as CT scans for lymphoma, but if your doctor is concerned about spread to the spinal cord or brain, MRI can be very useful for looking at these areas.

Ultrasound

Ultrasound[7] uses sound waves and their echoes to create pictures of internal organs or masses. In the most common type of ultrasound, a small, microphone-like instrument called a *transducer* is placed on the skin (which is first lubricated with a gel). It gives off sound waves and picks up the echoes as they bounce off the organs. The echoes are converted by a computer into an image on a screen.

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

Positron emission tomography (PET) scan

For a PET scan[8], you are injected with a slightly radioactive form of sugar, which collects mainly in cancer cells. A special camera is then used to create a picture of areas of radioactivity in the body. The picture is not detailed like a CT scan or MRI, but it can provide helpful information about your whole body.

If you have lymphoma, a PET scan might be done to:

- See if an enlarged lymph node contains lymphoma.
- Find small areas that might be lymphoma, even if the area looks normal on a CT scan.
- Check if a lymphoma is responding to treatment. Some doctors will repeat the PET scan after 1 or 2 courses of chemotherapy. If it is working, the lymph nodes will no longer absorb the radioactive sugar.
- Help decide whether an enlarged lymph node still contains lymphoma or is just scar tissue after treatment.

PET/CT scan: Many centers have machines that can do both a PET scan and a CT 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 scan. PET/CT scans can often help pinpoint the areas of lymphoma better than a CT scan alone.

Bone scan

This test might be done if a person is having bone pain or has lab results that suggest the lymphoma may have reached the bones.

- Your heart function may be checked with an **echocardiogram** (an ultrasound of the heart) or a **MUGA scan.**
- Your lung function may be checked with **pulmonary function tests,** in which you breathe into a tube connected to a machine.

Hyperlinks

1. www.cancer.org/cancer/types/non-hodgkin-lymphoma/about/what-is-non-hodgkin-lymphoma.html
2. www.cancer.org/cancer/types/non-hodgkin-lymphoma/causes-risks-prevention/risk-factors.html
3. www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytology-tests.html
4. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/x-rays-and-other-radiographic-tests.html
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Non-Hodgkin Lymphoma Stages

After someone is diagnosed with non-Hodgkin lymphoma (NHL), doctors will try to figure out if it has spread, and if so, how far. This process is called **staging.** The stage describes how much cancer is in the body. It helps determine how serious the lymphoma is and how best to treat it.

How is the stage determined?

Tests used to gather information for staging can include:

- Physical exams

Physi2al exams

In general, the results of imaging tests such as PET or CT scans are the most important when determining the stage of the lymphoma.

Lugano classification

A staging system is a way for members of a cancer care team to sum up the extent of a cancer's spread. The current staging system for NHL in adults is known as the **Lugano classification**, which is a modified version of the older **Ann Arbor system**.

The stages are described by Roman numerals I through IV (1-4). Limited stage (I or II) lymphomas that affect an organ outside the lymph system (an extranodal organ) have an E added (for example, stage IIE).

Stage I

Either of the following means the disease is stage I:

- The lymphoma is in only 1 lymph node area or lymphoid organ such as the tonsils (I).
  The cancer is found only in 1 area of a single organ outside of the lymph system

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- The lymphoma is in lymph node areas on both sides of (above and below) the diaphragm.
- The lymphoma is in lymph nodes above the diaphragm, as well as in the spleen.

Stage IV

The lymphoma has spread widely into at least one organ outside the lymph system, such as the bone marrow, liver, or lung.

Bulky disease

This term is often used to describe large tumors in the chest. It is especially important

Survival Rates and Factors That Affect Prognosis (Outlook) for Non-Hodgkin Lymphoma

Survival rates can give you an idea of what percentage of people with the same type and stage of cancer are still alive a certain amount of time (usually 5 years) after they were diagnosed. Survival rates can't tell you how long you will live, but they may help give you a better understanding of how likely it is that your treatment will be successful.

Keep in mind that survival rates are estimates and are often based on previous outcomes of large numbers of people who had a specific cancer, but they can't predict what will happen in any particular person's case. These statistics can be confusing and may lead you to have more questions. Ask your doctor, who is familiar with your situation, how these numbers may apply to you.

What is a 5-year relative survival rate?

A **relative survival rate** compares people with the same type and stage of non-Hodgkin lymphoma (NHL) to people in the overall population. For example, if the **5-year relative survival rate** for a specific stage of NHL is 70%, it means that people who have that cancer are, on average, about 70% as likely as people who don't have that cancer to live for at least 5 years after being diagnosed.

Where do these numbers come from?

The American Cancer Society relies on information from the Surveillance, Epidemiology, and End Results (SEER) database, maintained by the National Cancer Institute (NCI), to provide survival statistics for different types of cancer.

The SEER database tracks 5-year relative survival rates for NHL in the United States, based on how far the cancer has spread. The SEER database, however, does not

group cancers by the Lugano classification (stage 1, stage 2, stage 3, etc.). Instead, it groups cancers into localized, regional, and distant stages:

- **Localized:** The cancer is limited to one lymph node area, one lymphoid organ, or one organ outside the lymph system.
- **Regional:** The cancer reaches from one lymph node area to a nearby organ, it's found in two or more lymph node areas on the same side of (above or below) the diaphragm, or it's considered bulky disease.
- **Distant:** The cancer has spread to distant parts of the body, such as the lungs, liver, or bone marrow, or to lymph node areas above and below the diaphragm.

5-year relative survival rates for NHL

The overall 5-year relative survival rate for people with NHL is 74%. But it's important to keep in mind that survival rates can vary widely for different types and stages of lymphoma.

Below are the 5-year relative survival rates for the two most common types of NHL in the United States – diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL) – based on people diagnosed between 2012 and 2018.

Diffuse large B-cell lymphoma

SEER stage	5-year relative survival rate
Localized	73%
Regional	74%
Distant	58%
All SEER stages combined	65%

Follicular lymphoma

SEER stage	5-year relative survival rate
Localized	97%
Regional	91%
Distant	87%

All SEER stages combined	90%

Understanding the numbers

These numbers apply only to the stage of the lymphoma when it is first diagnosed. They do not.95 Tm ( )Tat___lk.3| 1.n2g /G3 S 0 G 0.75 w 0 0 0 RG 71.63 72t y do61

- Performance status (PS) – how well a person can do normal daily activities
- The blood level of lactate dehydrogenase (LDH), which goes up with the amount of lymphoma in the body

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Good prognostic factors	Poor prognostic factors
Age 60 or below	Age above 60
Stage I or II	Stage III or IV
No lymphoma outside of lymph nodes, or	

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4 or fewer lymph node areas affected	More than 4 lymph node areas affected
Serum LDH is normal	Serum LDH is high

Patients are assigned a point for each poor prognostic factor. People without any poor prognostic factors would have a score of 0, while those with all poor prognostic factors would have a score of 5. The index then divides people with follicular lymphoma into 3 groups:

- **Low risk:** no or 1 poor prognostic factor(s)
- **Intermediate risk:** 2 poor prognostic factors
- **High risk:** 3 or more poor prognostic factors

For both the IPI and FLIPI, people in the low-risk group tend to have a better prognosis than those in the high-risk group.

Hyperlinks

1. www.cancer.org/cancer/types/non-hodgkin-lymphoma/about/what-is-non-hodgkin-lymphoma.html

References

Index. *Blood*. 2004;104:1258-1265.

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Questions to Ask About Non-Hodgkin Lymphoma

If you have non-Hodgkin lymphoma, it's important to have honest, open discussions with your cancer care team. Feel free to ask any question, no matter how small it might seem. Here are some questions you might want to ask.

When you're told you have non-Hodgkin lymphoma

- What type of non-Hodgkin lymphoma[1] do I have?
- Has my biopsy been reviewed by a pathologist who's an expert on lymphoma?
- Do I need any other tests before we can decide on treatment?
- Do I need to see any other types of doctors?
- What's the stage (extent) of the lymphoma? What does that mean in my case?
- Are there other factors that could affect my treatment options?
- If I'm concerned about the costs and insurance coverage for my diagnosis and treatment, who can help me?

When deciding on a treatment plan

- How much experience do you have treating this type of lymphoma?l

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 The Doctor-Patient Relationship[8].

Hyperlinks

1. www.cancer.org/cancer/types/non-hodgkin-lymphoma/about/what-is-non-hodgkin-lymphoma.html
2. www.cancer.org/cancer/types/non-hodgkin-lymphoma/treating.html
3. www.cancer.org/cancer/managing-cancer/finding-care/seeking-a-second-opinion.html