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About Non-Hodgkin Lymphoma

Overview and Types

If you have been diagnosed with non-Hodgkin lymphoma or are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

- [What Is Non-Hodgkin Lymphoma?](#)
- [Types of B-cell Lymphoma](#)
- [Types of T-cell Lymphoma](#)

Research and Statistics

See the latest estimates for new cases of non-Hodgkin lymphoma and deaths in the US and what research is currently being done.

- [Key Statistics for Non-Hodgkin Lymphoma](#)
- [What's New in Non-Hodgkin Lymphoma Research and Treatment?](#)

What Is Non-Hodgkin Lymphoma?

Cancer starts when cells begin to grow out of control. Cells in nearly any part of the body can become cancer, and can spread to other areas. To learn more about how cancers start and spread, see [What Is Cancer?](#)¹

Non-Hodgkin lymphoma (also known as non-Hodgkin's lymphoma, NHL, or sometimes

just lymphoma) is a cancer that starts in white blood cells called *lymphocytes*, which are part of the body's immune system.

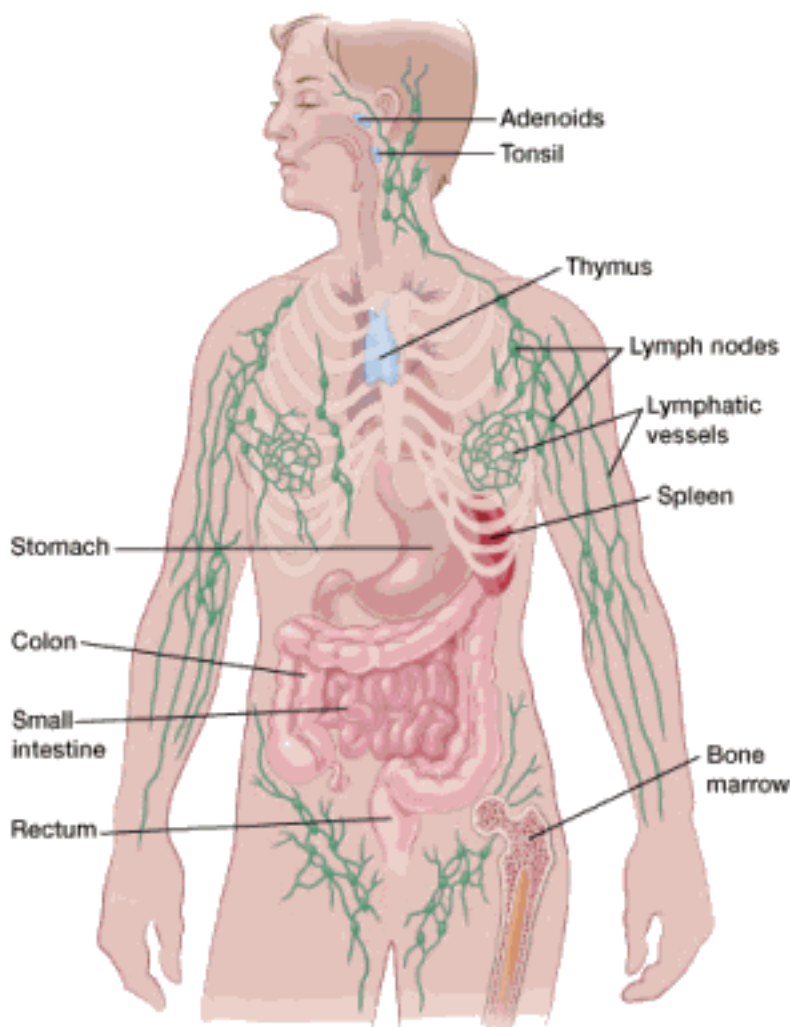
- NHL is a term that's used for many different types of lymphoma that all share some of the same characteristics. There is another main type of lymphoma, called Hodgkin lymphoma, which is treated differently. See [Hodgkin Lymphoma](#)².
- NHL most often affects adults, but children can get it too. See [Non-Hodgkin Lymphoma in Children](#)³.
- NHL usually starts in lymph nodes or other lymph tissue, but it can sometimes affect the skin. See [Lymphoma of the Skin](#)⁴.

Where lymphoma starts

Lymphoma affects the body's lymph system (also known as the *lymphatic system*). The lymph system is part of the immune system, which helps fight infections and some other diseases. It also helps fluids move through the body.

Lymphomas can start anywhere in the body where lymph tissue is found. The major sites of lymph tissue are:

- **Lymph nodes:** Lymph nodes are bean-sized collections of lymphocytes and other immune system cells throughout the body, including inside the chest, abdomen, and pelvis. They are connected by a system of lymphatic vessels.
- **Spleen:** The spleen is an organ under the lower ribs on the left side of the body. The spleen makes lymphocytes and other immune system cells. It also stores healthy blood cells and filters out damaged blood cells, bacteria, and cell waste.
- **Bone marrow:** The bone marrow is the spongy tissue inside certain bones. This is where new blood cells (including some lymphocytes) are made.
- **Thymus:** The thymus is a small organ behind the upper part of the breastbone and in front of the heart. It's important in the development of T lymphocytes.
- **Adenoids and tonsils:** These are collections of lymph tissue in the back of the throat. They help make antibodies against germs that are breathed in or swallowed.
- **Digestive tract:** The stomach, intestines, and many other organs also have lymph tissue.



Types of non-Hodgkin lymphoma

Treatment for NHL depends on which type it is, so it's important for doctors to find out the exact type of lymphoma you have. The type of lymphoma depends on what type of lymphocyte is affected (B cells or T cells), how mature the cells are when they become cancerous, and other factors.

B-cell vs T-cell lymphomas

The lymph system is made up mainly of lymphocytes, a type of white blood cell that helps the body fight infections. There are 2 main types of lymphocytes:

- **B lymphocytes (B cells):** B cells normally help protect the body against germs

(bacteria or viruses) by making proteins called antibodies. The antibodies attach to the germs, marking them for destruction by other parts of the immune system.

- **T lymphocytes (T cells):** There are several types of T cells. Some T cells destroy germs or abnormal cells in the body. Other T cells help boost or slow the activity of other immune system cells.

Lymphoma can start in either type of lymphocytes, but B-cell lymphomas are most common.

Indolent vs. aggressive lymphomas

Types of NHL can also be grouped based on how fast they grow and spread:

- **Indolent lymphomas** grow and spread slowly. Some indolent lymphomas might not need to be treated right away, but can be watched closely instead. The most common type of indolent lymphoma in the United States is follicular lymphoma.
- **Aggressive lymphomas** grow and spread quickly, and usually need to be treated right away. The most common type of aggressive lymphoma in the United States is diffuse large B cell lymphoma (DLBCL).
- Some types of lymphoma, like mantle cell lymphoma, don't fit neatly into either of these categories.

Regardless of how quickly they grow, all non-Hodgkin lymphomas can spread to other parts of the lymph system if not treated. Eventually, they can also spread to other parts of the body, such as the liver, brain, or bone marrow.

Classifying types of NHL

There are many different types of non-Hodgkin lymphoma (NHL), so classifying it can be quite confusing (even for doctors). Several different systems have been used, but the most recent system is the **World Health Organization (WHO) classification**. The WHO system groups lymphomas based on:

- The type of lymphocyte the lymphoma starts in
- How the lymphoma looks under a microscope
- The chromosome features of the lymphoma cells
- The presence of certain proteins on the surface of the cancer cells

Hyperlinks

1. www.cancer.org/cancer/cancer-basics/what-is-cancer.html
2. www.cancer.org/cancer/hodgkin-lymphoma.html
3. www.cancer.org/cancer/childhood-non-hodgkin-lymphoma.html
4. www.cancer.org/cancer/skin-lymphoma.html

References

Freedman AS, Jacobson CA, Mauch P, Aster JC. Chapter 103: Non-Hodgkin's lymphoma. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015.

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Last Medical Review: August 1, 2018 Last Revised: August 1, 2018

Key Statistics for Non-Hodgkin Lymphoma

Non-Hodgkin lymphoma (NHL) is one of the most common cancers in the United States, accounting for about 4% of all cancers. The American Cancer Society's most recent estimates for non-Hodgkin's lymphoma are for 2019

- About 74,200 people (41,090 males and 33,110 females) will be diagnosed with NHL. This includes both adults and children.
- About 19,970 people will die from this cancer (11,510 males and 8,460 females).

Overall, the chance that a man will develop NHL in his lifetime is about 1 in 42; for a woman, the risk is about 1 in 54. But each person's risk can be affected by a number of [risk factors](#)¹.

NHL can occur at any age. In fact, it is one of the more common cancers among [children](#)², [teens](#)³, and [young adults](#)⁴. Still, the risk of developing NHL increases throughout life, and more than half of patients are 65 or older at the time of diagnosis. The aging of the American population is likely to lead to an increase in NHL cases during the coming years.

Visit the [American Cancer Society's Cancer Statistics Center](#)⁵ for more key statistics.

Hyperlinks

1. www.cancer.org/cancer/non-hodgkin-lymphoma/causes-risks-prevention/risk-factors.html
2. www.cancer.org/cancer/cancer-in-children.html
3. www.cancer.org/cancer/cancer-in-adolescents.html
4. www.cancer.org/cancer/cancer-in-young-adults.html
5. <https://cancerstatisticscenter.cancer.org/>

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Last Medical Review: August 1, 2018 Last Revised: January 8, 2019

What's New in Non-Hodgkin Lymphoma Research and Treatment?

Research into the causes, prevention, and treatment of non-Hodgkin lymphoma (NHL) is being done in many medical centers throughout the world.

Genetics

Scientists are making a lot of progress in understanding how changes in the DNA inside normal lymphocytes can cause them to develop into lymphoma cells. Once this is understood, drugs may be developed that block these processes.

Progress in understanding DNA changes in lymphoma cells has already led to improved and highly sensitive tests for detecting this disease. Some of these tests are already in use, and others are being developed. They may be used to:

- Detect lymphoma cells in a biopsy sample
- Determine what type of lymphoma a person has
- Help determine if a lymphoma is likely to grow and spread, even within a certain subtype of lymphoma
- Help figure out if a certain treatment is likely to be helpful
- Help determine if a lymphoma has been destroyed by treatment or if a relapse is likely

For example, in recent years, genetic tests have shown that there are different subtypes of diffuse large B-cell lymphoma (DLBCL), even though they look the same under the microscope. These subtypes seem to have different outcomes (prognoses) and responses to treatment. The hope is that such tests can be used to help guide treatment decisions.

Treatment

Much of the research being done on NHL is focused on looking at new and better ways to treat this disease.

Chemotherapy

Many new chemotherapy drugs are being studied in [clinical trials](#)¹. In recent years, these studies have led to the approval of drugs such as bendamustine (Treanda) and pralatrexate (Folotyn) for use against certain types of lymphoma. Other studies are looking at new ways to combine drugs using different doses or different sequences of drugs.

Stem cell transplants

Researchers continue to improve [stem cell transplant](#)² methods, including new ways to collect the stem cells before the transplant.

Autologous transplants (which use the patient's own stem cells rather than cells from a donor) have the risk of reintroducing lymphoma cells back into the patient after treatment. Researchers are testing new and improved ways to separate out the last traces of lymphoma cells from the stem cells before they are returned to the patient. Some of the new monoclonal antibodies developed for treating lymphoma may help remove these remaining cells.

Researchers are also studying the effectiveness of non-myeloablative (reduced-intensity) stem cell transplants in people with lymphoma. This approach may allow more people to benefit from stem cell transplants, especially those who are older or in poor health.

Targeted therapies

As researchers have learned more about lymphoma cells, they have developed newer drugs that target specific parts of these cells. These targeted drugs are different from standard chemotherapy drugs, which work by attacking rapidly growing cells. Targeted drugs may work in some cases where chemotherapy doesn't, and they often have different side effects.

Some targeted drugs, such as ibrutinib (Imbruvica), acalabrutinib (Calquence), and idelalisib (Zydelig), are already being used to treat some types of NHL, and are being studied for use against other types.

Some other targeted drugs that have shown promise against lymphoma in early studies include:

- **Phosphatidylinositol 3 kinase (PI3K) inhibitors**, such as duvelisib, tenalisib, and buparlisib
- **BCL-2 inhibitors**, such as venetoclax (Venclexta)
- **Janus kinase (JAK) inhibitors**, such as ruxolitinib
- **Tyrosine kinase inhibitors**, such as crizotinib, for lymphomas that express the ALK protein.

These and many other targeted drugs are now being studied in [clinical trials](#)³.

Immunotherapy

Doctors have known for some time that people's immune systems may help fight their cancer. Scientists are now trying to develop ways to encourage this immune reaction. Some types of immunotherapy are already being used to treat lymphoma, as discussed in [Immunotherapy for Non-Hodgkin Lymphoma](#)⁴.

Monoclonal antibodies: Lymphoma cells have certain proteins on their surface. Monoclonal antibodies can be made to target these proteins and destroy the lymphoma cells while causing little damage to normal body tissues. This treatment strategy has already proven effective. Several such drugs, including rituximab (Rituxan), are already used to treat lymphoma.

Some newer antibodies are attached to substances that can poison cancer cells, and are known as *antibody-drug conjugates* (ADCs) or immunotoxins. They act as homing devices to deliver the toxins directly to the cancer cells. For example:

- **Brentuximab vedotin (Adcetris)** is made up of an antibody to CD30 that is attached to a cell poison. It has been shown to help treat patients with anaplastic large cell lymphoma (ALCL), and is now being studied for use against other types of lymphoma.
- **Moxetumomab pasudotox** targets the CD22 antigen on certain lymphoma cells, bringing along a toxin known as PE38. It's being used in clinical trials to treat hairy cell leukemia (HCL).

Other ADCs are now being studied as well, including polatuzumab vedotin.

Immune checkpoint inhibitors: Immune system cells normally have substances that act as checkpoints to keep them from attacking other healthy cells. Cancer cells sometimes take advantage of these checkpoints to avoid being attacked by the immune system. Some newer drugs, such as pembrolizumab (Keytruda) and nivolumab (Opdivo), work by blocking these checkpoints, which can boost the immune response against cancer cells. These drugs have shown promise in treating several types of cancer, and are now being studied for use against some types of lymphoma.

Chimeric antigen receptor (CAR) T-cell therapy: In this treatment, immune cells called T cells are removed from the patient's blood and altered in the lab to have specific receptors (called *chimeric antigen receptors*, or CARs) on their surface. These receptors can attach to proteins on the surface of lymphoma cells. The T cells are then multiplied in the lab and given back into the patient's blood, where they can seek out the lymphoma cells and launch a precise immune attack against them.

This technique has shown encouraging results in early clinical trials against some hard-to-treat lymphomas. Doctors are still improving how they make the T cells and are learning the best ways to use them. There are two FDA approved CAR T-cell therapies for certain kinds of advanced or recurrent large B-cell lymphoma. CAR T-cell therapy for other types of non-Hodgkin lymphoma is only available in clinical trials at this time.

Lymphoma vaccines: Unlike vaccines against infections like measles or mumps, these vaccines are designed to help treat, not prevent, lymphomas. The goal is to create an immune reaction against lymphoma cells in patients who have very early disease or in patients whose disease is in remission. One possible advantage of these types of treatments is that they seem to have very limited side effects. So far, there have been a few successes with this approach, and it's a major area of research in lymphoma treatment. At this time, lymphoma vaccines are only available in [clinical trials](#)⁵.

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
2. www.cancer.org/cancer/non-hodgkin-lymphoma/treating/bone-marrow-stem-cell.html
3. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
4. www.cancer.org/cancer/non-hodgkin-lymphoma/treating/immunotherapy.html
5. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html

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Last Medical Review: August 1, 2018 Last Revised: August 1, 2018

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