



[cancer.org](https://www.cancer.org) | 1.800.227.2345

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.

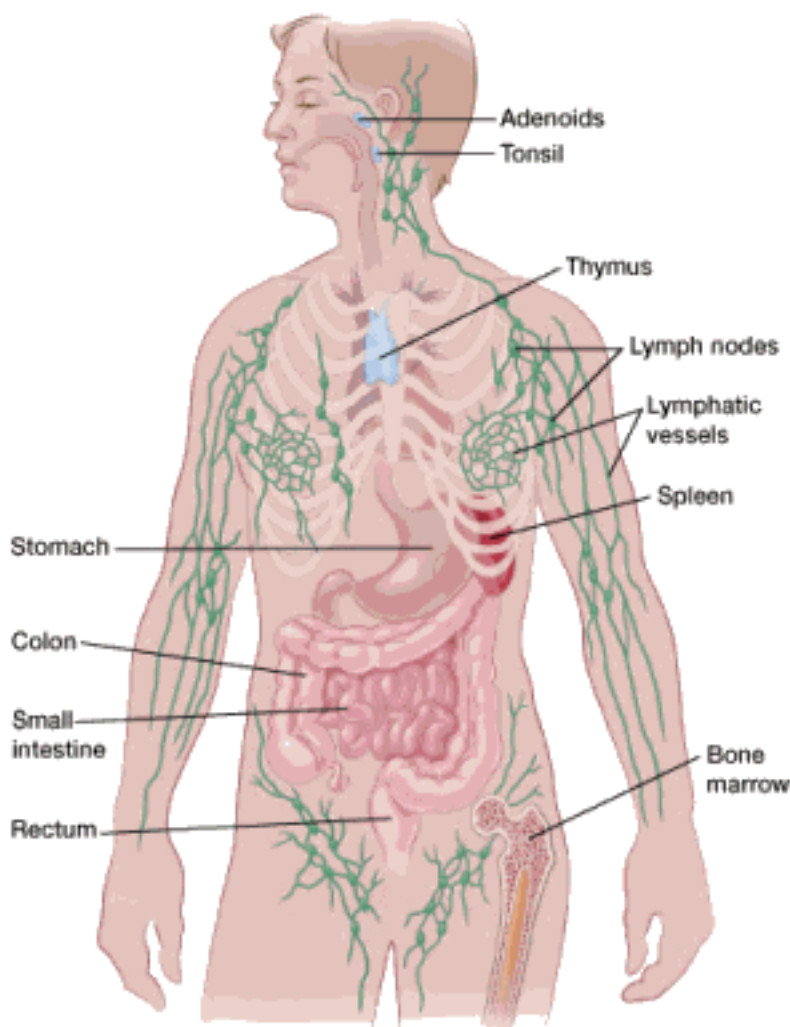
- NHL is a term that's used for many different types of lymphoma that all share some of the same characteristics. There is another main type of lymphoma, called Hodgkin lymphoma, which is treated differently. See [Hodgkin Lymphoma](#)².
- NHL most often affects adults, but children can get it too. See [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.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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/>

References

American Cancer Society. *Cancer Facts & Figures 2019*. Atlanta, Ga: American Cancer Society; 2019.

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.

Noone AM, Howlander N, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2015, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2015/, based on November 2017 SEER data submission, posted to the SEER web site, April 2018.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

References

Abramson JS. Updated safety and long term clinical outcomes in TRANSCEND NHL 001, pivotal trial of lisocabtagene maraleucel (JCAR017) in R/R aggressive NHL. In: *J Clin Oncol* 36, 2018; Abstract 7505.

Barta SK. Phase II study of the PD1-inhibitor pembrolizumab for the treatment of relapsed or refractory mature t-cell lymphoma. In: *J Clin Oncol* 36, 2018; Abstract 7568.

Batlevi CL. Phase I/II clinical trial of ibrutinib and buparlisib in relapsed/refractory diffuse large B-cell lymphoma, mantle cell lymphoma, and follicular lymphoma. In: *J Clin Oncol* 36, 2018; Abstract 7520.

Dyer Martin JS. Acalabrutinib monotherapy in patients (pts) with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL). In: *J Clin Oncol* 36, 2018; Abstract 7547.

FDA approves axicabtagene ciloleucel for large B-cell lymphoma. (2017, October 17). Retrieved from <https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm581296.htm>.

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.

Kreitman RJ. Moxetumomab pasudotox in heavily pretreated patients with relapsed/refractory hairy cell leukemia: Results of a pivotal international study. In: *J Clin Oncol* 36, 2018; Abstract 7004.

Kreitman RJ, Stetler-Stevenson M, Margulies I, et al. Phase II trial of recombinant immunotoxin RFB4(dsFv)-PE38 (BL22) in patients with hairy cell leukemia. *J Clin Oncol*. 2009;27:2983-2990.

Liu Y. Durable clinical responses observed from non-Hodgkin lymphoma patients treated with autologous CAR-T cells targeting CD19. In: *J Clin Oncol* 36, 2018; Abstract 3045.

Oki Y. Tenisib, a dual PI3K / inhibitor: Safety and efficacy results from an on-going phase I/Ib study in relapsed/refractory T-cell lymphoma. In: *J Clin Oncol* 36, 2018; Abstract 7510.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical*

Oncology. 5th ed. Philadelphia, Pa: Elsevier; 2014.

Sehn LH. Randomized phase 2 trial of polatuzumab vedotin (pola) with bendamustine and rituximab (BR) in relapsed/refractory (r/r) FL and DLBCL. In: *J Clin Oncol* 36, 2018; Abstract 7507.

Wang ML, Rule S, Martin P, et al. Targeting BTK with ibrutinib in relapsed or refractory mantle-cell lymphoma. *N Engl J Med*. 2013;369:507-516.

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

Written by

The American Cancer Society medical and editorial content team
(www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

American Cancer Society medical information is copyrighted material. For reprint requests, please see our Content Usage Policy (www.cancer.org/about-us/policies/content-usage.html).

cancer.org | 1.800.227.2345



[cancer.org](https://www.cancer.org) | 1.800.227.2345

Non-Hodgkin Lymphoma Causes, Risk Factors, and Prevention

Risk Factors

A risk factor is anything that affects your chance of getting a disease such as cancer. Learn more about the risk factors for non-Hodgkin lymphoma.

- [Non-Hodgkin Lymphoma Risk Factors](#)
- [What Causes Non-Hodgkin Lymphoma?](#)

Prevention

There is no way to completely prevent cancer. But there are things you can do that might lower your risk. Learn more.

- [Can Non-Hodgkin Lymphoma Be Prevented?](#)

Non-Hodgkin Lymphoma Risk Factors

A risk factor is anything that changes your chance of getting a disease like cancer. Different cancers have different risk factors. Some risk factors, like smoking, can be changed. Others, like a person's age or family history, can't.

But having a risk factor, or even many risk factors, does not mean that you will get the

disease. And many people who get the disease may have few or no known risk factors.

Researchers have found several factors that can affect a person's chance of getting non-Hodgkin lymphoma (NHL). There are many types of lymphoma, and some of these factors have been linked only to certain types.

Age

Getting older is a strong risk factor for lymphoma overall, with most cases occurring in people in their 60s or older . But some types of lymphoma are more common in younger people.

Gender

Overall, the risk of NHL is higher in men than in women , but there are certain types of NHL that are more common in women. The reasons for this are not known.

Race, ethnicity, and geography

In the United States, whites are more likely than African Americans and Asian Americans to develop NHL.

Worldwide, NHL is more common in developed countries, with the United States and Europe having some of the highest rates. Some types of lymphoma are linked to certain infections (described further on) that are more common in some parts of the world.

Family History

Having a first degree relative (parent, child, sibling) with NHL increases your risk of developing NHL.

Exposure to certain chemicals and drugs

Some studies have suggested that chemicals such as benzene and certain herbicides and insecticides (weed- and insect-killing substances) may be linked to an increased risk of NHL. Research to clarify these possible links is still in progress.

Some chemotherapy drugs used to treat other cancers may increase the risk of developing NHL many years later. For example, patients who have been treated for

Hodgkin lymphoma have an increased risk of later developing NHL. But it's not totally clear if this is related to the disease itself or if it is an effect of the treatment.

Some studies have suggested that certain drugs used to treat rheumatoid arthritis (RA), such as methotrexate and the tumor necrosis factor (TNF) inhibitors, might increase the risk of NHL. But other studies have not found an increased risk. Determining if these drugs increase risk is complicated by the fact that people with RA, which is an autoimmune disease, already have a higher risk of NHL (see below).

Radiation exposure

Studies of survivors of atomic bombs and nuclear reactor accidents have shown they have an increased risk of developing several types of cancer, including NHL, [leukemia](#)¹, and [thyroid cancer](#)².

Patients treated with radiation therapy for some other cancers, such as [Hodgkin lymphoma](#)³, have a slightly increased risk of developing NHL later in life. This risk is greater for patients treated with both radiation therapy and chemotherapy.

Having a weakened immune system

People with weakened immune systems have an increased risk for NHL. For example:

- People who receive organ transplants are treated with drugs that suppress their immune system to prevent it from attacking the new organ. These people have a higher risk of developing NHL.
- The [human immunodeficiency virus \(HIV\)](#)⁴ can weaken the immune system, and people infected with HIV are at increased risk of NHL.
- In some genetic (inherited) syndromes, such as ataxia-telangiectasia (AT) and Wiskott-Aldrich syndrome, children are born with a deficient immune system. Along with an increased risk of serious infections, these children also have a higher risk of developing NHL.

Autoimmune diseases

Some autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus (SLE or lupus), Sjogren (Sjögren) disease, celiac disease (gluten-sensitive enteropathy), and others have been linked with an increased risk of NHL.

In autoimmune diseases, the immune system mistakenly sees the body's own tissues as foreign and attacks them, as it would a germ. Lymphocytes (the cells from which lymphomas start) are part of the body's immune system. The overactive immune system in autoimmune diseases may make lymphocytes grow and divide more often than normal. This might increase the risk of them developing into lymphoma cells.

Certain infections

Some types of infections may raise the risk of NHL in different ways.

Infections that directly transform lymphocytes

Some viruses can directly affect the DNA of lymphocytes, helping to transform them into cancer cells:

- Infection with human T-cell lymphotropic virus (HTLV-1) increases a person's risk of certain types of T-cell lymphoma. This virus is most common in some parts of Japan and in the Caribbean region, but it's found throughout the world. In the United States, it causes less than 1% of lymphomas. HTLV-1 spreads through sex and contaminated blood and can be passed to children through breast milk from an infected mother.
- Infection with the Epstein-Barr virus (EBV) is an important risk factor for Burkitt lymphoma in some parts of Africa. In developed countries such as the United States, EBV is more often linked with lymphomas in people also infected with HIV, the virus that causes AIDS. EBV has also been linked with some less common types of lymphoma.
- Human herpes virus 8 (HHV-8) can also infect lymphocytes, leading to a rare type of lymphoma called primary effusion lymphoma. This lymphoma is most often seen in patients who are infected with HIV. HHV-8 infection is also linked to another cancer, [Kaposi sarcoma](#)⁵. For this reason, another name for this virus is *Kaposi sarcoma-associated herpes virus* (KSHV).

Infections that weaken the immune system

Infection with human immunodeficiency virus (HIV), also known as the AIDS virus, can weaken the immune system. HIV infection is a risk factor for developing certain types of NHL, such as primary CNS lymphoma, Burkitt lymphoma, and diffuse large B-cell lymphoma.

Infections that cause chronic immune stimulation

Some long-term infections may increase a person's risk of lymphoma by forcing their immune system to be constantly active. As more lymphocytes are made to fight the infection, there is a greater chance for mutations in key genes to occur, which might eventually lead to lymphoma. Some of the lymphomas linked with these infections actually get better when the infection is treated.

- *Helicobacter pylori*, a type of bacteria known to cause stomach ulcers, has also been linked to mucosa-associated lymphoid tissue (MALT) lymphoma of the stomach.
- *Chlamydia psittaci* (formerly known as *Chlamydia psittaci*) is a type of bacteria that can cause a lung infection called *psittacosis*. It has been linked to MALT lymphoma in the tissues around the eye (called *ocular adnexal marginal zone lymphoma*).
- Infection with the bacterium *Campylobacter jejuni* has been linked to a type of MALT lymphoma called *immunoproliferative small intestinal disease*. This type of lymphoma, which is also sometimes called *Mediterranean abdominal lymphoma*, typically occurs in young adults in eastern Mediterranean countries.
- Long-term infection with the hepatitis C virus (HCV) seems to be a risk factor for certain types of lymphoma, such as splenic marginal zone lymphoma .

Body weight and diet

Some studies have suggested that [being overweight or obese](#)⁶ may increase your risk of NHL. Other studies have suggested that a diet high in fat and meats may raise your risk. More research is needed to confirm these findings. In any event, [staying at a healthy weight and eating a healthy diet](#)⁷ have many known health benefits outside of the possible effect on lymphoma risk.

Breast implants

Although it is rare, some women with breast implants develop a type of anaplastic large cell lymphoma (ALCL) in their breast. This seems to be more likely with implants that have textured (rough) surfaces (as opposed to smooth surfaces).

Hyperlinks

1. www.cancer.org/cancer/leukemia.html
2. www.cancer.org/cancer/thyroid-cancer.html
3. www.cancer.org/cancer/hodgkin-lymphoma.html
4. www.cancer.org/cancer/cancer-causes/infectious-agents/hiv-infection-aids.html
5. www.cancer.org/cancer/kaposi-sarcoma.html
6. www.cancer.org/cancer/cancer-causes/diet-physical-activity/body-weight-and-cancer-risk.html
7. www.cancer.org/healthy/eat-healthy-get-active.html

References

Cerhan JR, Krickler A, Paltiel O, et al. Medical History, Lifestyle, Family History, and Occupational Risk Factors for Diffuse Large B-Cell Lymphoma: The InterLymph Non-Hodgkin Lymphoma Subtypes Project. *Journal of the National Cancer Institute Monographs*. 2014;2014(48):15-25. doi:10.1093/jncimonographs/lgu010.

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.

Hartge P, Smith MT. Environmental and behavioral factors and the risk of non-Hodgkin lymphoma. *Cancer Epidemiol Biomarkers Prev*. 2007;16:367-368.

Kushi LH, Doyle C, McCullough M, et al. American Cancer Society guidelines on nutrition and physical activity for cancer prevention: Reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin*. 2012;62:30-67.

National Cancer Institute. Physician Data Query (PDQ). Adult Non-Hodgkin Lymphoma Treatment. 2018. Accessed at www.cancer.gov/types/lymphoma/hp/adult-nhl-treatment-pdq on May 1, 2018.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

Slager SL, Benavente Y, Blair A, et al. Medical History, Lifestyle, Family History, and Occupational Risk Factors for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: The InterLymph Non-Hodgkin Lymphoma Subtypes Project. *Journal of the National Cancer Institute Monographs*. 2014;2014(48):41-51.

doi:10.1093/jncimonographs/lgu001.

Smedby KE, et al. Autoimmune disorders and risk of non-Hodgkin lymphoma subtypes: a pooled analysis within the InterLymph Consortium. *Blood* 111.8 (2008): 4029-4038.

Smedby KE, Sampson JN, Turner JJ, et al. Medical History, Lifestyle, Family History, and Occupational Risk Factors for Mantle Cell Lymphoma: The InterLymph Non-Hodgkin Lymphoma Subtypes Project. *Journal of the National Cancer Institute Monographs*. 2014;2014(48):76-86. doi:10.1093/jncimonographs/lgu007.

US Food and Drug Administration. Breast Implants: Update - Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL). 2017. Accessed at www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm547622.html on April 30, 2018.

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

What Causes Non-Hodgkin Lymphoma?

Researchers have found that non-Hodgkin lymphoma (NHL) is linked with a number of [risk factors](#), but the cause of most lymphomas is not known. This is complicated by the fact that lymphomas are actually a diverse group of cancers.

Changes in genes

Scientists have made a lot of progress in understanding how certain changes in DNA can cause normal lymphocytes to become lymphoma cells. DNA is the chemical in our cells that makes up our genes, which control how our cells function. We look like our parents because they are the source of our DNA. But DNA affects more than just how we look.

Some genes control when cells grow, divide, and die:

- Genes that help cells grow, divide, and stay alive are called *oncogenes*.
- Genes that help keep cell division under control or make cells die at the right time are called *tumor suppressor genes*.

Cancers can be caused by DNA mutations (changes) that turn on oncogenes or turn off tumor suppressor genes.

Some people inherit DNA mutations from a parent that increase their risk for some types of cancer. Having a family history of lymphoma (Hodgkin Lymphoma, Non Hodgkin Lymphoma, CLL) does seem to increase your [risk of lymphoma](#).

Gene changes related to NHL are usually acquired during life, rather than being inherited. Acquired gene changes can result from exposure to radiation, cancer-causing chemicals, or infections, but often these changes occur for no apparent reason. They seem to happen more often as we age, which might help explain why most lymphomas are seen in older people.

Some of the gene changes that lead to certain types of lymphoma are now known. For example, in follicular lymphoma, the cells often have an exchange of DNA (known as a *translocation*) between chromosomes 14 and 18, which turns on the BCL-2 oncogene. (Chromosomes are long strands of DNA in each cell.) This oncogene stops the cell from dying at the right time, which can lead to lymphoma.

Scientists are learning much about the exact gene changes involved in the different types of NHL. This information is being used to develop more accurate tests to detect and classify certain types of lymphoma. Hopefully, these discoveries can be used to develop new treatments as well.

While researchers are beginning to understand some of the gene changes that can lead to NHL, they still do not know why many of these gene changes develop, especially in people with no apparent risk factors.

Changes in the immune system

Lymphocytes (the cells from which lymphomas start) are immune system cells, so it's not surprising that changes in the immune system seem to play an important role in many cases of lymphoma:

- People with **immune deficiencies** (due to inherited conditions, treatment with certain drugs, organ transplants, or HIV infection) have a much higher chance of developing lymphoma than people without a weakened immune system.
- People with certain **autoimmune diseases** (where the immune system constantly attacks a certain part of the body) have an increased risk of lymphoma.
- People with certain **chronic infections** are also at increased risk, probably

because the immune system is constantly making new lymphocytes to fight the infection, which increases the chances for mistakes in their DNA.

References

Cerhan JR, Krickler A, Paltiel O, et al. Medical History, Lifestyle, Family History, and Occupational Risk Factors for Diffuse Large B-Cell Lymphoma: The InterLymph Non-Hodgkin Lymphoma Subtypes Project. *Journal of the National Cancer Institute Monographs*. 2014;2014(48):15-25. doi:10.1093/jncimonographs/lgu010.

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.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

Slager SL, Benavente Y, Blair A, et al. Medical History, Lifestyle, Family History, and Occupational Risk Factors for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: The InterLymph Non-Hodgkin Lymphoma Subtypes Project. *Journal of the National Cancer Institute Monographs*. 2014;2014(48):41-51. doi:10.1093/jncimonographs/lgu001.

Smedby KE, Sampson JN, Turner JJ, et al. Medical History, Lifestyle, Family History, and Occupational Risk Factors for Mantle Cell Lymphoma: The InterLymph Non-Hodgkin Lymphoma Subtypes Project. *Journal of the National Cancer Institute Monographs*. 2014;2014(48):76-86. doi:10.1093/jncimonographs/lgu007.

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

Can Non-Hodgkin Lymphoma Be

Prevented?

There is no sure way to prevent non-Hodgkin lymphoma (NHL). Most people with NHL have no [risk factors](#) that can be changed, so there is no way to protect against these lymphomas. But there are some things you can do that might lower your risk for NHL, such as limiting your risk of certain infections and doing what you can to maintain a healthy immune system.

Infection with HIV, the virus that causes AIDS, is known to increase the risk NHL, so one way to limit your risk is to avoid known risk factors for HIV, such as intravenous drug use or unprotected sex with many partners. You can read more about HIV infection in [HIV Infection, AIDS, and Cancer](#).¹

Preventing the spread of the human T-cell lymphotropic virus (HTLV-1) could have a great impact on non-Hodgkin lymphoma in areas of the world where this virus is common, such as Japan and the Caribbean region. The virus is rare in the United States but seems to be increasing in some areas. The same strategies used to prevent HIV spread could also help control HTLV-1.

Helicobacter pylori (*H.pylori*) infection has been linked to some lymphomas of the stomach. Treating *H. pylori* infections with antibiotics and antacids may lower this risk, but the benefit of this strategy has not been proven yet. Most people with *H. pylori* infection have no symptoms, and some have only mild heartburn. More research is needed to find the best way to detect and treat this infection in people without symptoms.

Some lymphomas are [caused by treatment of other cancers](#)² with radiation and chemotherapy or by the use of immune-suppressing drugs to avoid rejection of transplanted organs. Doctors are trying to find better ways to treat cancer and organ transplant patients without increasing the risk of lymphoma as much. But for now, the benefits of these treatments still usually outweigh the small risk of developing lymphoma many years later.

Some studies have suggested that [being overweight or obese](#)³ may increase your risk of non-Hodgkin lymphoma. Other studies have suggested that a diet high in fat and meats may raise your risk. [Staying at a healthy weight and eating a healthy diet](#)⁴ may help protect against lymphoma, but more research is needed to confirm this.

Hyperlinks

1. <https://www.cancer.org/cancer/cancer-causes/infectious-agents/hiv-infection-aids.html>
2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/second-cancers-in-adults.html
3. www.cancer.org/cancer/cancer-causes/diet-physical-activity/body-weight-and-cancer-risk.html
4. www.cancer.org/healthy/eat-healthy-get-active.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.

Kushi LH, Doyle C, McCullough M, et al. American Cancer Society guidelines on nutrition and physical activity for cancer prevention: Reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin*. 2012;62:30-67.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

Written by

The American Cancer Society medical and editorial content team
(www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

American Cancer Society medical information is copyrighted material. For reprint requests, please see our Content Usage Policy (www.cancer.org/about-us/policies/content-usage.html).

cancer.org | 1.800.227.2345



[cancer.org](https://www.cancer.org) | 1.800.227.2345

Non-Hodgkin Lymphoma Early Detection, Diagnosis, and Staging

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.

- [Can Non-Hodgkin Lymphoma Be Found Early?](#)
- [Signs and Symptoms of Non-Hodgkin Lymphoma](#)
- [Tests for Non-Hodgkin Lymphoma](#)

Stages of Non-Hodgkin Lymphoma

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

- [Non-Hodgkin Lymphoma Stages](#)

Outlook (Prognosis)

Doctors often use survival rates as a standard way of discussing a person's outlook (prognosis). These numbers can't tell you how long you will live, but they might help you better understand your prognosis. Some people want to know the survival statistics for people in similar situations, while others might not find the numbers helpful, or might even not want to know them.

- [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?

Screening tests or exams are used to look for a disease in people who have no symptoms. At this time, there are no widely recommended screening tests for non-Hodgkin lymphoma (NHL). This is because no screening test has been shown to lower the risk of dying from this cancer. 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 which is usually not painful. This is most often on the side of the neck, in the armpit, or in the groin.

Other symptoms can include fever, chills, night sweats, weight loss, feeling tired, and swelling in the abdomen. More 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 check-ups are important for people with known [risk factors](#)¹ for NHL (such as HIV infections, organ transplants, 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/non-hodgkin-lymphoma/causes-risks-prevention/risk-factors.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.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

Signs and Symptoms of Non-Hodgkin Lymphoma

Non-Hodgkin lymphoma (NHL) can cause many different signs and symptoms, depending on the type of lymphoma and where it is in the body. Sometimes it might not cause any symptoms until it grows quite large.

Having one or more symptoms doesn't mean you definitely 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.

Some common signs and symptoms include:

- Enlarged lymph nodes
- 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 *B symptoms*:

- Fever (which can come and go over several days or weeks) without an infection
- Drenching night sweats
- Weight loss without trying (at least 10% of body weight over 6 months)

Swollen lymph nodes

Non-Hodgkin lymphoma can cause lymph nodes to become enlarged. Enlarged lymph nodes close to the surface of the body (such as on the sides of the neck, in the groin or underarm areas, or above the collar bone), may be seen or felt as **lumps under the skin**. These are usually not painful.

Although enlarged lymph nodes are a common symptom of lymphoma, they are much more often caused by infections. Lymph nodes that grow in reaction to infection are 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 enlarging, but it can also be caused by the build-up 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 consciousness if it affects the brain. This is called **SVC syndrome**. It can be life-threatening and must be treated right away.

Symptoms from lymphoma affecting the brain

Lymphomas of the brain, called primary brain lymphomas, can cause **headache, trouble thinking, weakness in parts of the body, personality changes**, and sometimes **seizures**.

Other types of lymphoma can spread to the area around the brain and spinal cord. This can cause problems such as **double vision, facial numbness, and trouble speaking**.

Symptoms from lymphoma in the skin

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

Hyperlinks

1. 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.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

Tests for Non-Hodgkin Lymphoma

Most people with non-Hodgkin lymphoma (NHL) see their 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 check-up.

If you have signs or symptoms that suggest you might have lymphoma, exams and tests will be done to find out for sure and, if so, to determine the exact [type of lymphoma](#)¹.

Medical history and physical exam

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

Next, the doctor will examine you, paying special attention to the lymph nodes and other areas of the 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, he or she might recommend a biopsy of a swollen lymph node or other affected area.

Biopsy

For a biopsy, a small piece of a lymph node or, more often, an entire lymph node 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. For example, enlarged lymph nodes are more often caused by infections than by lymphoma. Because of this, 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 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 preferred and 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 be sedated (given drugs to make you drowsy and relaxed) or 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 do not use needle biopsies to diagnose lymphoma. But if the doctor suspects that your 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 mass.
- 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 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

These procedures are not normally done to diagnose lymphoma, but they might be used to help determine the stage (extent) of a lymphoma that has already been diagnosed.

Bone marrow aspiration and biopsy: These procedures are often done after lymphoma has been diagnosed to help determine if it has reached the bone marrow. The 2 tests are often done at the same time. The samples are usually taken from the back of the pelvic (hip) bone, although in some cases they may be taken from other bones.

For a **bone marrow aspiration**, you lie on a table (either on your side or on your belly). After cleaning the skin over the hip, the doctor numbs the area and the surface of the bone with local anesthetic, which can cause a brief stinging or burning sensation. 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. Even with the anesthetic, most people still have some brief pain when the marrow is removed.

A **bone marrow biopsy** is usually done just after the aspiration. A small piece of bone and marrow is removed with a slightly larger needle that is pushed into the bone. The biopsy can also cause some brief pain.

Lumbar puncture (spinal tap): This test looks for lymphoma cells in the cerebrospinal fluid (CSF), which is the liquid that bathes the brain and spinal cord. Most people with lymphoma will not need this test. But doctors may order it for certain types of lymphoma or if a person has symptoms that suggest the lymphoma may have reached the brain.

For this test, you may lie on your side or sit up. The doctor first numbs an area in the lower part of your back over the spine. A small, hollow needle is then placed between

the bones of the spine to withdraw some of the fluid.

Pleural or peritoneal fluid sampling: Lymphoma that has spread to the chest or abdomen can cause fluid to build up. Pleural fluid (inside the chest) or peritoneal fluid (inside the abdomen) can be removed by placing a hollow needle through the skin into the chest or abdomen.

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

The doctor uses a local anesthetic to numb the skin before inserting the needle. The 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 may show not only if the person has a lymphoma, but also what type of lymphoma it is. But usually other types of lab tests are needed as well.

Flow cytometry and immunohistochemistry: For both flow cytometry and immunohistochemistry, the biopsy samples are treated with antibodies that 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 certain proteins in or on the cells. Different types of lymphocytes have different proteins on their surface, which correspond to the type of lymphocyte and how mature it is.

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.

- **Cytogenetics:** In this lab test, the cells are checked for any abnormalities in the chromosomes.

- **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 very few lymphoma cells are present in a sample.

For more information, see [Testing Biopsy and Cytology Specimens for Cancer](#)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

The [chest might be x-rayed](#)⁴ to look for enlarged lymph nodes in this area.

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.

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) scan

Like CT scans, [MRI scans](#)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 is 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 computer 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 because 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 or MRI scan, 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 the chemotherapy 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: Some machines 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 is usually done if a person is having bone pain or has lab results that suggest the lymphoma may have reached the bones.

For bone scans, a radioactive substance called *technetium* is injected into a vein. It travels to damaged areas of bone, and a special camera can then detect the radioactivity. Lymphoma often causes bone damage, which may be seen on a bone scan. But bone scans can't show the difference between cancers and non-cancerous problems, such as arthritis and fractures, so further tests might be needed.

Other tests

Blood tests

[Blood tests](#)⁹ are not used to diagnose lymphoma, but they can sometimes help determine how advanced the lymphoma is.

- A **complete blood count (CBC)** measures the levels of different cells in the blood. For a person already known to have lymphoma, low blood cell counts might mean that the lymphoma is growing in the bone marrow and affecting new blood cell formation.
- **Blood chemistry tests** are often done to look at how well the kidney and liver function are working.
- If lymphoma has been diagnosed, the **lactate dehydrogenase (LDH)** level may be checked. LDH levels are often increased in patients with lymphomas.
- For some types of lymphoma or if certain treatments might be used, your doctor may also advise you to have tests to see if you've been infected with certain viruses, such as **hepatitis B virus (HBV)**, **hepatitis C virus (HCV)**, or **human immunodeficiency virus (HIV)**. Infections with these viruses may affect your treatment.

Tests of heart and lung function

These tests are not used to diagnose lymphoma, but they might be done if you are going to get certain chemotherapy drugs commonly used to treat lymphoma that could affect the heart or the lungs.

- 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/non-hodgkin-lymphoma/about/what-is-non-hodgkin-lymphoma.html
2. www.cancer.org/cancer/non-hodgkin-lymphoma/causes-risks-prevention/risk-factors.html
3. www.cancer.org/treatment/understanding-your-diagnosis/tests/testing-biopsy-and-cytology-specimens-for-cancer.html
4. www.cancer.org/treatment/understanding-your-diagnosis/tests/x-rays-and-other-radiographic-tests.html
5. www.cancer.org/treatment/understanding-your-diagnosis/tests/ct-scan-for-cancer.html
6. www.cancer.org/treatment/understanding-your-diagnosis/tests/mri-for-cancer.html
7. www.cancer.org/treatment/understanding-your-diagnosis/tests/ultrasound-for-cancer.html
8. www.cancer.org/treatment/understanding-your-diagnosis/tests/nuclear-medicine-scans-for-cancer.html
9. www.cancer.org/treatment/understanding-your-diagnosis/tests/understanding-your-lab-test-results.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.

National Cancer Institute. Physician Data Query (PDQ). Adult Non-Hodgkin Lymphoma Treatment. 2018. Accessed at <https://www.cancer.gov/types/lymphoma/hp/adult-nhl-treatment-pdq> on May 1, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: B-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf on April 30, 2018.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

Non-Hodgkin Lymphoma Stages

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

Tests used to gather information for staging can include:

- Physical exam
- Biopsies of enlarged lymph nodes or other abnormal areas
- Blood tests
- Imaging tests, such as PET and CT scans
- Bone marrow aspiration and biopsy (often but not always done)
- Lumbar puncture (spinal tap – this may not need to be done)

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 based on 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 (IE).

Stage II

Either of the following means the disease is stage II:

- The lymphoma is in 2 or more groups of lymph nodes on the same side of (above or below) the diaphragm (the thin band of muscle that separates the chest and abdomen). For example, this might include nodes in the underarm and neck area (II) but not the combination of underarm and groin nodes (III).
- The lymphoma is in a group of lymph node(s) and in one area of a nearby organ (IIE). It may also affect other groups of lymph nodes on the same side of the diaphragm.

Stage III

Either of the following means the disease is stage III:

- 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 for stage II lymphomas, as bulky disease might need more intensive treatment.

Staging small lymphocytic lymphoma (SLL)/chronic lymphocytic leukemia (CLL)

The system above is most often used to stage this lymphoma if it is only in lymph nodes. But if the disease is affecting the blood or bone marrow, it is often staged using the systems for CLL. See [Chronic Lymphocytic Leukemia Stages](#)¹.

How staging might affect treatment

The stage of a lymphoma is important when determining a person's treatment options, but it is more important for some types of lymphoma than for others. For many of the more common types of NHL, treatment is based in part on whether the lymphoma is "limited" (stage I or stage II non-bulky) or "advanced" (stage III or IV). For stage II bulky lymphomas, certain other factors (known as *prognostic factors*) are used to help determine if the lymphoma should be treated as limited or advanced.

For some other types of NHL, such as fast-growing lymphomas like Burkitt lymphoma, the stage is less important when deciding on treatment.

See [Treating B-cell Non-Hodgkin Lymphomas](#)² and [Treating T-cell Non-Hodgkin Lymphomas](#)³ for more on this.

Hyperlinks

1. www.cancer.org/cancer/chronic-lymphocytic-leukemia/detection-diagnosis-staging/staging.html
2. www.cancer.org/cancer/non-hodgkin-lymphoma/treating/b-cell-lymphoma.html
3. www.cancer.org/cancer/non-hodgkin-lymphoma/treating/t-cell-lymphoma.html

References

American Joint Committee on Cancer. Hodgkin and Non Hodgkin Lymphoma In: *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017:937

Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: The Lugano classification. *J Clin Oncol*. 2014;32:3059-3068.

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.

National Cancer Institute. Physician Data Query (PDQ). Adult Non-Hodgkin Lymphoma Treatment. 2018. Accessed at https://www.cancer.gov/types/lymphoma/hp/adult-nhl-treatment-pdq#section/_1 on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: B-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf on May 2, 2018.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

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. They 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. Talk with your doctor about how these numbers may apply to you, as he or she is familiar with your situation.

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 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, is found in two or more lymph node areas on the same side of the diaphragm, or is 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 71%. 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 two common types of NHL - diffuse large B-cell lymphoma and follicular lymphoma - based on people diagnosed between 2008 and 2014.

Diffuse large B-cell lymphoma

SEER Stage	5-Year Relative Survival Rate
Localized	72%
Regional	72%
Distant	55%
All SEER stages combined	63%

Follicular lymphoma

SEER Stage	5-Year Relative Survival Rate
Localized	95%
Regional	90%
Distant	84%
All SEER stages combined	88%

Understanding the numbers

- **These numbers apply only to the stage of the cancer when it is first diagnosed.** They do not apply later on if the cancer grows, spreads, or comes back after treatment.
- **People now being diagnosed with NHL may have a better outlook than these numbers show.** Treatments improve over time, and these numbers are based on people who were diagnosed and treated at least five years earlier.
- **These numbers don't take everything into account.** Survival rates are grouped based on how far the cancer has spread, but your age, overall health, [the type of NHL¹](#), how well the cancer responds to treatment, and other factors (see below)

can also affect your outlook.

Prognostic factors for non-Hodgkin lymphoma

For some types of lymphoma the stage isn't too helpful in determining a person's outlook. In these cases, other factors can give doctors a better idea about a person's prognosis.

International Prognostic Index (IPI)

The International Prognostic Index (IPI) was first developed to help doctors determine the outlook (prognosis) for people with fast-growing (aggressive) lymphomas. However, it has proven useful for most other lymphomas as well (other than slow-growing [indolent] follicular lymphomas, which are discussed below). The IPI allows doctors to plan treatment better than they could just based on the type and stage of the lymphoma. This has become more important as new, more effective treatments have been developed that sometimes have more side effects. The index helps doctors figure out whether these treatments are needed.

The index depends on 5 factors:

- The patient's age
- The stage of the lymphoma
- Whether or not the lymphoma is in organs outside the lymph system
- Performance status (PS) – how well a person can complete normal daily activities
- The blood level of lactate dehydrogenase (LDH), which goes up with the amount of lymphoma in the body

Good prognostic factors

Age 60 or below

Stage I or II

No lymphoma outside of lymph nodes, or lymphoma in only 1 area outside of lymph nodes

PS: Able to function normally

Poor prognostic factors

Age above 60

Stage III or IV

Lymphoma is in more than 1 organ of the body outside of lymph nodes

PS: Needs a lot of help with daily activities

Serum LDH is normal

Serum LDH is high

Each poor prognostic factor is assigned 1 point. 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 divides people with lymphomas into 4 risk groups:

- Low risk (0 or 1 poor prognostic factors)
- Low-intermediate risk (2 poor prognostic factors)
- High-intermediate risk (3 poor prognostic factors)
- High risk (4 or 5 poor prognostic factors)

Follicular Lymphoma International Prognostic Index (FLIPI)

The IPI is useful for most lymphomas, but it's not as helpful for follicular lymphomas, which tend to be slower growing. Doctors have developed the Follicular Lymphoma International Prognostic Index (FLIPI) specifically for this type of lymphoma. It uses slightly different prognostic factors than the IPI.

Good prognostic factors

Age 60 or below

Stage I or II

Blood hemoglobin 12 g/dL or above

4 or fewer lymph node areas affected

Serum LDH is normal

Poor prognostic factors

Age above 60

Stage III or IV

Blood hemoglobin level below 12 g/dL

More than 4 lymph node areas affected

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.

*SEER= Surveillance, Epidemiology, and End Results

Hyperlinks

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

References

National Comprehensive Cancer Network, Clinical Practice Guidelines in Oncology (NCCN Guidelines®), B-cell Lymphomas, Version 2.2019 -- March 6, 2019. Accessed at www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf on March 21, 2019.

Noone AM, Howlader N, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2015, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2015/, based on November 2017 SEER data submission, posted to the SEER web site, April 2018.

Solal-Celigny P, Roy P, Colombat P, et al. Follicular Lymphoma International Prognostic Index. *Blood*. 2004;104:1258-1265.

Last Medical Review: August 1, 2018 Last Revised: April 4, 2019

Questions to Ask About Non-Hodgkin Lymphoma

It's important to have honest, open discussions with your cancer care team. They want to answer all of your questions so you can make informed treatment and life decisions. For instance, consider these questions:

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?
- What are my [treatment options](#)²? What do you recommend, and why?
- Do we need to treat the lymphoma right away?
- Should I get a [second opinion](#)³ before starting treatment? Can you suggest a doctor or cancer center?
- What should I do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?
- What risks or side effects are there to the treatments you suggest?
- How might treatment affect my daily activities?
- What's my outlook for survival?
- What are the chances of the lymphoma coming back with these treatment plans?
- What would we do if the treatment doesn't work or if the lymphoma comes back?

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 to you, but getting answers to the ones that do may be helpful.

- How will we know if the treatment is working?
- Is there anything I can do to help manage [side effects](#)⁴?
- What symptoms or side effects should I tell you about right away?
- How can I reach you on nights, holidays, or weekends?
- Are there any limits on what I can do?
- Can you suggest a mental health professional I can see if I start to [feel](#)

[overwhelmed, depressed, or distressed](#)⁵?

After treatment

- What type of [follow-up](#)⁶ will I need after treatment?
- What symptoms should I watch for?
- How will we know if the lymphoma has come back? What would my options be if that happens?

Along with these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so that you can plan your work or activity schedule. Or you may want to ask about [clinical trials](#)⁷ for which you qualify.

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 [The Doctor-Patient Relationship](#)⁸.

Hyperlinks

1. www.cancer.org/cancer/non-hodgkin-lymphoma/about/types-of-non-hodgkin-lymphoma.html
2. www.cancer.org/cancer/non-hodgkin-lymphoma/treating.html
3. www.cancer.org/treatment/finding-and-paying-for-treatment/choosing-your-treatment-team/seeking-a-second-opinion.html
4. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html
5. www.cancer.org/treatment/treatments-and-side-effects/emotional-side-effects.html
6. www.cancer.org/cancer/non-hodgkin-lymphoma/after-treatment/follow-up.html
7. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
8. www.cancer.org/treatment/understanding-your-diagnosis/talking-about-cancer/the-doctor-patient-relationship.html

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

Written by

The American Cancer Society medical and editorial content team
(www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

American Cancer Society medical information is copyrighted material. For reprint requests, please see our Content Usage Policy (www.cancer.org/about-us/policies/content-usage.html).

cancer.org | 1.800.227.2345



[cancer.org](https://www.cancer.org) | 1.800.227.2345

Non-Hodgkin Lymphoma Treatment

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

How is non-Hodgkin lymphoma treated?

Depending on the type and stage (extent) of the lymphoma and other factors, treatment options for people with NHL might include:

- [Chemotherapy for Non-Hodgkin Lymphoma](#)
- [Immunotherapy for Non-Hodgkin Lymphoma](#)
- [Targeted Therapy Drugs for Non-Hodgkin Lymphoma](#)
- [Radiation Therapy for Non-Hodgkin Lymphoma](#)
- [High-Dose Chemotherapy and Stem Cell Transplant for Non-Hodgkin Lymphoma](#)
- [Surgery for Non-Hodgkin Lymphoma](#)

Common treatment approaches

Treatment approaches for NHL depend on the type of cancer, how advanced it is, as well as your health and other factors.

Another important part of treatment for many people is palliative or supportive care. This can help prevent or treat problems such as infections, low blood cell counts, or some symptoms caused by the lymphoma.

- [Treating B-Cell Non-Hodgkin Lymphoma](#)
- [Treating T-Cell Non-Hodgkin Lymphoma](#)
- [Treating HIV-Associated Lymphoma](#)

- [Palliative and Supportive Care for Non-Hodgkin Lymphoma](#)

Who treats non-Hodgkin lymphoma?

Based on your treatment options, you may have different types of doctors on your treatment team. These doctors could include:

- A **medical oncologist** or **hematologist**: a doctor who treats lymphoma with chemotherapy, immunotherapy, and targeted therapy.
- A **radiation oncologist**: a doctor who treats cancer with radiation therapy.
- A **bone marrow transplant doctor**: a doctor who specializes in treating cancer or other diseases with bone marrow or stem cell transplants.

You might have many other specialists on your treatment team as well, including physician assistants, nurse practitioners, nurses, nutrition specialists, social workers, and other health professionals.

- [Health Professionals Associated With Cancer Care](#)¹

Making treatment decisions

It's important to discuss all of your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. In choosing a treatment plan, consider your health and the type and stage of the lymphoma.

It's also very important to ask questions if there is anything you're not sure about.

If time permits, it is often a good idea to seek a second opinion. A second opinion can give you more information and help you feel more confident about the treatment plan you choose.

- [Questions to Ask About Non-Hodgkin Lymphoma](#)²
- [Seeking a Second Opinion](#)³

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-of-

the art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they're not right for everyone.

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

- [Clinical Trials](#)⁴

Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your cancer or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used along with your regular medical care. Alternative treatments are used instead of a doctor's medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

- [Complementary and Alternative Medicine](#)⁵

Help getting through cancer treatment

Your cancer care team will be your first source of information and support, but there are other resources for help when you need it. Hospital- or clinic-based support services are an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained specialists.

- [Find Support Programs and Services in Your Area](#)⁶

Choosing to stop treatment or choosing no treatment at all

For some people, when treatments have been tried and are no longer controlling the cancer, it could be time to weigh the benefits and risks of continuing to try new treatments. Whether or not you continue treatment, there are still things you can do to help maintain or improve your quality of life.

Some people, especially if the cancer is advanced, might not want to be treated at all. There are many reasons you might decide not to get cancer treatment, but it's important to talk to your doctors and you make that decision. Remember that even if you choose not to treat the cancer, you can still get supportive care to help with pain or other symptoms.

- [If Cancer Treatments Stop Working](#)⁷
- [Palliative or Supportive Care](#)⁸

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

Chemotherapy for Non-Hodgkin Lymphoma

Chemotherapy (chemo) is the use of anti-cancer drugs that are usually injected into a vein (IV) or taken by mouth. These drugs enter the bloodstream and reach almost all areas of the body, making this treatment very useful for lymphoma.

When might chemo be used?

Chemo is the main treatment for most people with non-Hodgkin lymphoma (NHL). Depending on the [type](#)¹ and the [stage](#)² of the lymphoma, chemo may be used alone or combined with other treatments, such as [immunotherapy drugs](#) or [radiation](#)

[therapy](#).

Which chemo drugs are used to treat non-Hodgkin lymphoma?

Many chemo drugs are useful in treating lymphoma. Often, several drugs are combined. The number of drugs, their doses, and the length of treatment depend on the type and stage of the lymphoma. Here are some of the drugs more commonly used to treat lymphoma (divided into groups based on how they work):

Alkylating agents

- Cyclophosphamide
- Chlorambucil
- Bendamustine
- Ifosfamide

Corticosteroids

- Prednisone
- Dexamethasone

Platinum drugs

- Cisplatin
- Carboplatin
- Oxaliplatin

Purine analogs

- Fludarabine
- Pentostatin
- Cladribine (2-CdA)

Anti-metabolites

- Cytarabine (ara-C)
- Gemcitabine
- Methotrexate
- Pralatrexate

Anthracyclines

- Doxorubicin (Adriamycin)
- Liposomal doxorubicin (Caelyx)

Others

- Vincristine
- Mitoxantrone
- Etoposide (VP-16)
- Bleomycin

Often drugs from different groups are combined. One of the most common combinations is called CHOP. This includes the drugs cyclophosphamide, doxorubicin (also known as hydroxydaunorubicin), vincristine (Oncovin) and prednisone. Another common combination leaves out doxorubicin and is called CVP.

Chemo is often combined with an [immunotherapy drug](#), especially rituximab (Rituxan).

Doctors give chemo in cycles, in which a period of treatment is followed by a period of rest to allow the body time to recover. Each chemo cycle generally lasts for several weeks. Most chemo treatments are given on an outpatient basis (in the doctor's office or clinic or hospital outpatient department), but some might require a hospital stay.

Sometimes a patient may get one chemo combination for several cycles and later switch to a different one if the first combination doesn't seem to be working.

Intrathecal chemo

Most chemo drugs given systemically (IV or by mouth) can't reach the cerebrospinal fluid (CSF) and tissues around the brain and spinal cord. To treat lymphoma that might have reached these areas, chemo may also be given into the CSF. This is called

intrathecal chemo. The chemo drugs most often used for intrathecal chemo are methotrexate and cytarabine.

Possible side effects

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

- [Hair loss](#)³
- [Mouth sores](#)⁴
- [Loss of appetite](#)⁵
- [Nausea and vomiting](#)⁶
- [Diarrhea](#)⁷ or [constipation](#)⁸
- Increased chance of [infection](#)⁹ (from a shortage of white blood cells)
- [Bleeding or bruising](#)¹⁰ after minor cuts or injuries (from a shortage of platelets)
- [Fatigue](#)¹¹ and [shortness of breath](#)¹² (from too few red blood cells)

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

There are often ways to lessen these side effects. For example, drugs can be given to prevent or reduce nausea and vomiting.

Certain chemo drugs can have other possible side effects. For example:

- Platinum drugs such as cisplatin can cause nerve damage ([neuropathy](#)¹³), leading to numbness, tingling, or even pain in the hands and feet.
- Ifosfamide can damage the bladder. The risk of this can be lowered by giving it along with a drug called *mesna*.
- Doxorubicin can damage the heart. Your doctor may order a test of your heart function (like a MUGA scan or echocardiogram) before starting you on this drug.
- Bleomycin can damage lungs. Doctors often test lung function before starting someone on this drug.
- Many chemo drugs can affect [fertility](#)¹⁴ (the ability to have children).
- Some chemo drugs can raise your risk of developing leukemia several years later.

Tumor lysis syndrome is a possible side effect when chemo is started, especially in patients with large or fast-growing lymphomas. Killing the lymphoma cells releases their contents into the bloodstream. This can overwhelm the kidneys, which can't get rid of all

of these substances at once. This can lead to the build-up of certain minerals in the blood and even kidney failure. The excess minerals can lead to heart and nervous system problems. Doctors work to prevent this by giving the patient extra fluids and certain drugs, such as sodium bicarbonate, allopurinol, and rasburicase.

Ask your health care team about what side effects you can expect based on the specific drugs you will receive. Be sure to tell your doctor or nurse if you do have side effects, as there are often ways to help with them. For example, drugs can be given to prevent or reduce nausea and vomiting.

Other drugs used to treat lymphoma

Other types of drugs can also be useful in treating some types of lymphoma. These drugs work differently from standard chemo drugs. For example, [immunotherapy](#) and [targeted therapy](#) drugs are helpful for some lymphomas.

Mucosa-associated lymphoid tissue (MALT) lymphoma, which usually starts in the stomach, is linked to infection with the bacterium *H. pylori*. Treatment of this infection can often make the lymphoma go away. This is most often done with a combination of **antibiotics** along with drugs called **proton pump inhibitors**, which lower stomach acid levels.

In a similar way, splenic marginal zone B-cell lymphoma is sometimes linked to infection with the hepatitis C virus. Treating the infection with **anti-viral drugs** can sometimes shrink these lymphomas, or even make them go away.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see [Chemotherapy](#)¹⁵.

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)¹⁶.

Hyperlinks

1. www.cancer.org/cancer/non-hodgkin-lymphoma/about/types-of-non-hodgkin-lymphoma.html
2. www.cancer.org/cancer/non-hodgkin-lymphoma/detection-diagnosis-staging/staging.html

3. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/hair-loss.html
4. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/mouth-problems.html
5. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/eating-problems/poor-appetite.html
6. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/nausea-and-vomiting.html
7. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/stool-or-urine-changes/diarrhea.html
8. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/stool-or-urine-changes/constipation.html
9. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/infections.html
10. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/low-blood-counts/bleeding.html
11. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/fatigue.html
12. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/low-blood-counts/anemia.html
13. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/peripheral-neuropathy.html
14. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/fertility-and-sexual-side-effects.html
15. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy.html
16. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.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.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: B-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 5.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: T-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf on May 2, 2018.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

Immunotherapy for Non-Hodgkin Lymphoma

Immunotherapy is treatment that either boosts the patient's own immune system or uses man-made versions of the normal parts of the immune system to kill lymphoma cells or slow their growth.

Monoclonal antibodies

Antibodies are proteins made by your immune system to help fight infections. Man-made versions, called *monoclonal antibodies*, can be designed to attack a specific target, such as a substance on the surface of lymphocytes (the cells in which lymphomas start).

Several monoclonal antibodies are now used to treat non-Hodgkin lymphoma (NHL).

Antibodies that target CD20

A number of monoclonal antibodies target the CD20 antigen, a protein on the surface of B lymphocytes. These include:

- **Rituximab (Rituxan):** This drug is often used along with [chemotherapy](#) (chemo) for some types of NHL, but it may also be used by itself.
- **Obinutuzumab (Gazyva):** This drug is often used along with chemo as a part of the treatment for small lymphocytic lymphoma/chronic lymphocytic leukemia (SLL/CLL). It can also be used along with chemo in treating follicular lymphoma.
- **Ofatumumab (Arzerra):** This drug is used mainly in patients with SLL/CLL that is no longer responding to other treatments.
- **Ibritumomab tiuxetan (Zevalin):** This drug is made up of a monoclonal antibody that is attached to a radioactive molecule. The antibody brings radiation directly to the lymphoma cells.

These drugs are given into a vein (IV), often over several hours. They all can cause reactions during the infusion (while the drug is being given) or several hours afterward. Most reactions are mild, such as itching, chills, fever, nausea, rashes, fatigue, and headaches. More serious reactions can include chest pain, heart racing, swelling of the face and tongue, cough, trouble breathing, feeling dizzy or lightheaded, and feeling faint. Because of these kinds of reactions, drugs to help prevent them are given before each infusion.

There is also a form of rituximab that is given as a shot under the skin. It can take 5-7 minutes to inject the drug, but this is much shorter than the time it normally takes to give the drug by vein. It is approved for use in patients with follicular lymphoma, diffuse large B-cell lymphoma, and chronic lymphocytic leukemia. Possible side effects include local skin reactions, like redness, where the drug is injected, infections, low white blood cell counts, nausea, fatigue, and constipation.

All of these drugs can cause inactive hepatitis B infections to become active again, which can lead to severe or life-threatening liver problems. Your doctor may check your blood for signs of an old hepatitis B infection before you start treatment. These drugs can also increase your risk of certain serious infections for many months after the drug is stopped. Other side effects can depend on which drug is given. Ask your doctor what you can expect.

Antibodies targeting CD52

Alemtuzumab (Campath) is an antibody directed at the CD52 antigen. It is useful in some cases of SLL/CLL and some types of peripheral T-cell lymphomas. This drug is infused into a vein (IV), usually 3 times a week for up to 12 weeks. The most common side effects are fever, chills, nausea, and rashes. It can also cause very low white blood cell counts, which increases the risk for serious infections. Antibiotic and antiviral

medicines are given to help protect against them, but severe and even life-threatening infections can still occur. Rare but serious side effects can include strokes, as well as tears in the blood vessels in the head and neck.

Antibodies that target CD30

Brentuximab vedotin (Adcetris) is an anti-CD30 antibody attached to a chemotherapy drug. The antibody acts like a homing signal, bringing the chemo drug to lymphoma cells, where it enters the cells and kills them.

Brentuximab can be used to treat some types of T-cell lymphoma, either as the first treatment (typically along with chemo) or if the lymphoma if it has come back after other treatments. This drug is infused into a vein (IV), typically every 3 weeks. Common side effects can include nerve damage (neuropathy), low blood counts, fatigue, fever, nausea and vomiting, infections, diarrhea, and cough.

Immune checkpoint inhibitors

Immune system cells normally have substances that act as checkpoints to keep them from attacking other healthy cells in the body. Cancer cells sometimes take advantage of these checkpoints to avoid being attacked by the immune system.

Drugs such as **pembrolizumab (Keytruda)** work by blocking these checkpoints, which can boost the immune response against cancer cells. Pembrolizumab can be used to treat primary mediastinal large B-cell lymphoma (PMBCL) that has not responded to or has come back after other therapies.

Immunomodulating drugs

Drugs such as **thalidomide (Thalomid)** and **lenalidomide (Revlimid)** are thought to work against certain cancers by affecting parts of the immune system, although exactly how they work isn't clear. They are sometimes used to help treat certain types of lymphoma, usually after other treatments have been tried.

These drugs are taken daily as pills. Side effects of can include low white blood cell counts (with an increased risk of infection) and neuropathy (painful nerve damage), which can sometimes be severe and may not go away after treatment. There is also an increased risk of serious blood clots (that start in the leg and can travel to the lungs), especially with thalidomide. Thalidomide can also cause drowsiness, fatigue, and severe constipation.

These drugs can cause severe birth defects if taken during pregnancy. Given this risk, the company that makes these drugs puts restrictions on access to them to prevent women who are or might become pregnant from being exposed to them.

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.

Axicabtagene ciloleucel (Yescarta) is a type of CAR T-cell therapy approved by the FDA to treat people with diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma and diffuse large B-cell lymphoma arising from follicular lymphoma after at least two other kinds of treatment have been tried. Because this treatment can have serious side effects, it is only given in medical centers that have special training with this treatment. Potentially life-threatening side effects can include high fever, chills, flu-like symptoms, and serious neurological changes. Other severe side effects include infection, low blood cell counts, and a weakened immune system.

Tisagenlecleucel (Kymriah) is another type of CAR T-cell therapy approved to treat people with diffuse large B cell lymphoma, high grade B cell lymphoma, and diffuse large B cell lymphoma arising from follicular lymphoma after trying at least two other kinds of treatment. Potentially life-threatening side effects can include fever, headache, low blood pressure, a fast heartrate, and trouble breathing. Other severe side effects include infection, diarrhea, swelling, and nausea. This drug must also be given in centers with specialized training.

To learn more, see [CAR T-Cell Therapies](#)¹.

More information about immunotherapy

To learn more about how drugs that work on the immune system are used to treat cancer, see [Cancer Immunotherapy](#)².

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)³.

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/car-t-cell1.html
2. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy.html
3. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

References

FDA approves pembrolizumab for treatment of relapsed or refractory PMBCL. (2018, June 13). Retrieved from <https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm610670.htm>

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.

National Cancer Institute. Physician Data Query (PDQ). Adult Non-Hodgkin Lymphoma Treatment. 2018. Accessed at <https://www.cancer.gov/types/lymphoma/hp/adult-nhl-treatment-pdq> on May 3, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: B-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 5.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: T-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf on May 2, 2018.

Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. *N Engl J Med*. 2017;377(26):2531-2544.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

Schuster S., et al. Primary Analysis of Juliet: A Global, Pivotal, Phase 2 Trial of CTL019 in Adult Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma. 59th American Society of Hematology Annual Meeting and Exposition. Abstract #577.

Value in Using CAR T Cells for DLBCL. *Cancer Discov.* 2018;8(2): 131-132; DOI: 10.1158/2159-8290.CD-NB2017-179.

Last Medical Review: August 1, 2018 Last Revised: November 30, 2018

Targeted Therapy Drugs for Non-Hodgkin Lymphoma

As researchers have learned more about the changes in lymphoma cells that help them grow, they have developed newer drugs to specifically target these changes. These targeted drugs work differently from standard chemotherapy (chemo) drugs. Sometimes they work when standard chemo drugs don't, and they often have different (and less severe) side effects.

Proteasome inhibitors

These drugs work by stopping enzyme complexes (proteasomes) in cells from breaking down proteins important for keeping cell division under control. They are more often used to treat multiple myeloma, but can be helpful in treating some types of non-Hodgkin lymphoma (NHL) as well.

Bortezomib (Velcade) is a proteasome inhibitor used to treat some lymphomas, usually after other treatments have been tried. Bortezomib is given as an infusion into a vein (IV) or an injection under the skin (subcutaneous, or sub-q), typically twice a week for 2 weeks, followed by a rest period. Side effects can be similar to those of standard chemo drugs, including low blood counts, nausea, loss of appetite, and nerve damage.

Histone deacetylase (HDAC) inhibitors

HDAC inhibitors are drugs that can affect what genes are active by interacting with proteins in chromosomes called *histones*.

Romidepsin (Istodax) can be used to treat both peripheral and skin T-cell lymphomas. It is usually given after at least one other treatment has been tried. This drug is given as an IV infusion, usually once a week for 3 weeks in a row, followed by a week off. Side effects tend to be mild, but can include lowered blood cell counts and effects on heart rhythm.

Belinostat (Beleodaq) can be used to treat peripheral T-cell lymphomas, usually after at least one other treatment has been tried. It is given as an IV infusion, usually daily for 5 days in a row, repeated every 3 weeks. Common side effects include nausea, vomiting, tiredness, and low red blood cell counts (anemia).

Kinase inhibitors

These drugs block *kinases*, which are proteins in cells that normally relay signals (such as telling the cell to grow). Many different types of kinases exist, and there are two that are targeted by specific drugs used to treat NHL: Bruton's tyrosine kinase (BTK) and PI3K.

Bruton's tyrosine kinase (BTK) inhibitors

BTK is a protein that normally helps some lymphoma cells (B cells) to grow and survive.

Ibrutinib (Imbruvica) blocks the BTK protein. This drug can be used to treat several types of NHL, including mantle cell lymphoma, marginal zone lymphoma, and small lymphocytic lymphoma. It's taken by mouth as capsules, once a day. Common side effects include diarrhea or constipation, nausea and vomiting, fatigue, swelling, decreased appetite, and low blood counts. This drug is currently approved for use after other treatments have been tried, and it's now being studied for use earlier in treatment.

Calquence (acalabrutinib) is another drug that blocks BTK. It is used to treat mantle cell lymphoma, after at least one other treatment has been tried. This drug is taken by mouth as capsules, twice a day. Common side effects are headache, diarrhea, bruising, fatigue, muscle pain, and low blood counts. More serious side effects can include bleeding (hemorrhage), infections, and irregular heartbeat (atrial fibrillation).

PI3K inhibitors

PI3K is a protein that sends signals in cells and controls cell growth.

Idelalisib (Zydelig) blocks the PI3K-delta protein. This drug has been shown to help treat follicular lymphoma and small lymphocytic lymphoma after other treatments have

been tried. It's taken as a pill twice a day. Common side effects include diarrhea, fever, fatigue, nausea, cough, pneumonia, belly pain, chills, rash and low blood counts. Less often, more serious side effects can also occur.

Copanlisib (Aliqopa) is another drug that blocks PI3K. It can be used to treat follicular lymphoma that comes back after other treatments have been tried. It's given as an infusion into a vein, typically once a week for 3 weeks, followed by a week off. Common side effects include high blood sugar levels, nausea, diarrhea, feeling weak, high blood pressure, low levels of white blood cells (with increased risk of infection), and low levels of blood platelets (with increased risk of bruising or bleeding). Less common side effects include infections, inflammation in the lungs, and severe skin reactions.

Duvelisib (Copiktra) blocks two kinase proteins called PI3K-delta and PI3K-gamma. It's been shown to help treat follicular lymphoma and small lymphocytic lymphoma after other treatments have been tried. It's a pill taken twice a day. Common side effects include diarrhea, fever, fatigue, nausea, cough, pneumonia, belly pain, joint/muscle pain and rash. Low blood counts, including low red blood cell counts (anemia) and low levels of certain white blood cells (neutropenia) are also common. Less often, more serious side effects can occur, such as liver damage, severe diarrhea, lung inflammation (pneumonitis), serious allergic reactions, severe skin problems.

More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see [Targeted Cancer Therapy](#)¹.

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)².

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/targeted-therapy.html
2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.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.

National Cancer Institute. Physician Data Query (PDQ). Adult Non-Hodgkin Lymphoma Treatment. 2018. Accessed at <https://www.cancer.gov/types/lymphoma/hp/adult-nhl-treatment-pdq> on May 3, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: B-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 5.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: T-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf on May 2, 2018.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

Wang ML, Rule S, Martin P, et al. Targeting BTK with ibrutinib in relapsed or refractory mantle-cell lymphoma. *N Engl J Med*. 2013;369:507-516.

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

Radiation Therapy for Non-Hodgkin Lymphoma

Radiation therapy uses high-energy rays to kill cancer cells.

When might radiation therapy be used for non-Hodgkin lymphoma?

Radiation might be used to treat non-Hodgkin lymphoma (NHL) in some different situations:

- It can be used as the main treatment for some types of NHL if they are found early (stage I or II), because these tumors respond very well to radiation.
- For more advanced lymphomas and for some lymphomas that are more aggressive, radiation is sometimes used along with chemotherapy.
- People who are getting a stem cell transplant may get radiation to the whole body along with high-dose chemotherapy, to try to kill lymphoma cells throughout the body.
- Radiation therapy can be used to ease (palliate) symptoms caused by lymphoma that has spread to internal organs, such as the brain or spinal cord, or when a tumor is causing pain because it's pressing on nerves.

How is radiation therapy given?

When radiation is used to treat NHL, it's most often done with a carefully focused beam of radiation, delivered from a machine outside the body. This is known as *external beam radiation*.

Before your treatment starts, your radiation team will take careful measurements to find the correct angles for aiming the radiation beams and the proper dose of radiation. This planning session, called *simulation*, usually includes getting imaging tests such as CT or MRI scans.

Most often, radiation treatments are given 5 days a week for several weeks. The treatment is much like getting an x-ray, but the radiation is stronger. The procedure itself is painless. Each treatment lasts only a few minutes, although the setup time – getting you into place for treatment – usually takes longer.

Radiation can also be given as a drug in some cases. (See [Immunotherapy for Non-Hodgkin Lymphoma](#) for more details.)

Possible side effects

The side effects of radiation therapy depend on where the radiation is aimed. **Common side effects** include:

- [Skin changes](#)¹ in areas getting radiation, ranging from redness to blistering and

peeling

- [Feeling tired](#)²
- [Nausea](#)³
- [Diarrhea](#)⁴

Nausea and diarrhea are more common if the abdomen (belly) is treated with radiation.

Radiation given to several areas, especially after chemotherapy, can [lower blood cell counts](#)⁵ and increase the [risk of infections](#)⁶.

Radiation to the head and neck area can lead to [mouth sores](#)⁷ and [trouble swallowing](#)⁸. Some people later have problems with [dry mouth](#)⁹.

Often these effects go away shortly after treatment is finished.

Side effects tend to be worse if radiation and chemotherapy are given together.

Radiation techniques are much more advanced and can limit the radiation exposure to nearby organs, but **long-term serious side effects** are possible:

- Radiation to the chest might damage the lungs and lead to trouble breathing. It can also affect the heart, and may increase the chance of a heart attack later on.
- Radiation to the neck can lead to thyroid problems later in life. This can lead to fatigue and weight gain.
- Side effects of brain radiation therapy may become serious 1 or 2 years after treatment and may include headaches and problems such as memory loss, personality changes, and trouble concentrating.
- Other types of cancer can form in the area that received radiation. For example, radiation to the chest may increase the risk of lung cancer (especially in smokers) and of breast cancer, but this is rare.

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see [Radiation Therapy](#)¹⁰.

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)¹¹.

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/skin-problems.html
2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/fatigue.html
3. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/nausea-and-vomiting.html
4. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/stool-or-urine-changes/diarrhea.html
5. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/low-blood-counts.html
6. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/infections.html
7. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/mouth-problems.html
8. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/eating-problems/swallowing-problems.html
9. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/mouth-problems/dry-mouth.html
10. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/radiation.html
11. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.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.

National Cancer Institute. Physician Data Query (PDQ). Adult Non-Hodgkin Lymphoma Treatment. 2018. Accessed at <https://www.cancer.gov/types/lymphoma/hp/adult-nhl-treatment-pdq> on May 3, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: B-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: T-

cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf on May 2, 2018.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

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

A stem cell transplant (also known as a bone marrow transplant) lets doctors give higher doses of chemotherapy, sometimes along with radiation therapy.

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

But with a stem cell transplant, doctors can give high doses of chemo because the patient receives a transplant of blood-forming stem cells to restore the bone marrow afterwards.

Stem cell transplants are sometimes used to treat lymphoma patients who are in remission or who have a relapse during or after treatment. Although only a small number of people with lymphoma are treated with this therapy, this number is growing.

Types of stem cell transplants

There are 2 main types of stem cell transplants (SCTs) based on where the stem cells come from.

- In an **autologous stem cell transplant**, the patient's own stem cells are used. They are collected several times in the weeks before treatment. The cells are

frozen and stored while the person gets treatment (high-dose chemo and/or radiation) and then are given back into the patient's blood by an IV (catheter in the vein).

- In an **allogeneic stem cell transplant**, the stem cells come from someone else (a donor). Usually this is a brother or sister, although the source may be an unrelated donor or umbilical cord blood. The donor's tissue type (also known as the HLA type) needs to match the patient's tissue type as closely as possible to help prevent the risk of major problems with the transplant. Regardless of the source, the stem cells are frozen and stored until they are needed for the transplant.

Autologous SCTs are used more often than allogeneic SCTs to treat lymphoma. Still, using the patient's own cells may not be an option if the lymphoma has spread to the bone marrow or blood. If that happens, it may be hard to get a stem cell sample that is free of lymphoma cells.

Allogeneic transplants are used less often for lymphoma because they can have severe side effects that make them hard to tolerate, especially for patients who are older or who have other medical problems. It can also be hard to find a matched donor.

A stem cell transplant is a complex treatment that can cause life-threatening side effects. If the doctors think a person might benefit from a transplant, it should be done at a cancer center where the staff has experience with the procedure and with managing the recovery phase.

More information about stem cell transplant

To learn more about stem cell transplants, including how they are done and their potential side effects, see [Stem Cell Transplant for Cancer](#)¹.

For more general information about side effects and how to manage them, see [Managing Cancer-related Side Effects](#)².

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/stem-cell-transplant.html
2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.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.

National Cancer Institute. Physician Data Query (PDQ). Adult Non-Hodgkin Lymphoma Treatment. 2018. Accessed at <https://www.cancer.gov/types/lymphoma/hp/adult-nhl-treatment-pdq> on May 3, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: B-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: T-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf on May 2, 2018.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

Surgery for Non-Hodgkin Lymphoma

Surgery is often used to get a biopsy sample to diagnose and classify a lymphoma, but it's rarely used as a form of treatment.

Rarely, surgery may be used to treat lymphomas that start in the spleen or in certain organs outside the lymph system, such as the thyroid or stomach, and that have not spread beyond these organs. But for treating lymphoma that's completely confined to one area, [radiation therapy](#) is usually preferred over surgery.

For more information about treating cancer with surgery, see [Cancer Surgery](#)¹.

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/surgery.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.

National Cancer Institute. Physician Data Query (PDQ). Adult Non-Hodgkin Lymphoma Treatment. 2018. Accessed at <https://www.cancer.gov/types/lymphoma/hp/adult-nhl-treatment-pdq> on May 3, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: B-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 5.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: T-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf on May 2, 2018.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

Palliative and Supportive Care for Non-Hodgkin Lymphoma

For most people with non-Hodgkin lymphoma (NHL), treatment of the lymphoma itself is the main concern. But patients can also often benefit from care aimed at helping with problems related to the NHL and its treatment. For example, some people with NHL have problems with infections or low blood counts. Although treating the NHL may help these problems over time, other therapies may be needed as well.

Treatments to prevent infections

Antibiotics and anti-virals

Patients getting certain chemotherapy drugs (such as fludarabine and other purine analogs) and the antibody drug alemtuzumab (Campath) have a high risk of infections seen mainly in people with impaired immune systems, like infection with CMV (a virus) and *Pneumocystis pneumonia* (PCP, which is caused by a type of fungus). An anti-viral drug like acyclovir is often given to try to prevent CMV infections. To help prevent PCP, a sulfa antibiotic is often given (trimethoprim with sulfamethoxazole, which is also known by brand names such as Septra and Bactrim). Other treatments are available for people who are allergic to sulfa drugs.

Antibiotics and anti-viral drugs are also given to treat infections. Often, active infections require higher doses or different drugs than those used to prevent infections.

Intravenous immunoglobulin (IVIG)

Some people with NHL have low levels of antibodies (immunoglobulins) to fight infections. This can lead to lung and/or sinus infections that keep coming back. The level of antibodies in the blood can be checked with a blood test, and if it is low, antibodies from donors can be given into a vein (IV) to help prevent infections. This is called *intravenous immunoglobulin* or *IVIG*. IVIG is often given once a month at first, but may be able to be given less often based on blood tests of antibody levels.

For more information on infections, see [Infections in People With Cancer](#)¹.

Treatments for low blood counts

Low white blood cell count: White blood cells, especially a certain kind of white blood cell called *neutrophils*, are needed to fight infection. Having too few neutrophils (neutropenia) can lead to serious or even life threatening infections. If you become neutropenic from chemotherapy (chemo), you may be treated with injections of a white blood cell growth factor, such as filgrastim (Neupogen) or pegfilgrastim (Neulasta), to boost your neutrophil count. This lowers the risk of serious infections and can allow chemo to continue on time. If you are neutropenic and have signs or symptoms of infection (like a fever), you will be treated with antibiotics.

Low platelet count: Platelets help blood to clot, which stops bleeding. If platelet counts get very low, it can lead to serious bleeding. Transfusions of platelets can often help prevent this.

In NHL, low platelet counts can also be caused by the cells being destroyed by abnormal antibodies. This is called *immune thrombocytopenia*. Before diagnosing this, the doctor often needs to check the bone marrow to make sure that there isn't another cause for the low platelet counts. In immune thrombocytopenia, giving platelet transfusions doesn't usually help because the antibodies just destroy the new platelets, too. This can be treated by drugs that affect the immune system, like corticosteroids and IVIG. Another option is to remove the spleen, since after the antibodies stick to the platelets, they are actually destroyed in the spleen. A third option is treatment with a drug that tells the body to make more platelets, like eltrombopag (Promacta) or romiplostim (Nplate).

Low red blood cell count: Some people develop low red blood cell counts (anemia) from NHL or its treatment. This can lead to feeling tired, lightheaded, or short of breath. Anemia that is causing symptoms can be treated with red blood cell transfusions. Drugs that boost red blood cell production can also be used, but these are linked to worse outcomes, and so are generally only used for people who decline blood transfusions.

In NHL, abnormal antibodies can also lower red blood cell counts. This is called *autoimmune hemolytic anemia* (AIHA). It can be treated with drugs that affect the immune system, like corticosteroids and IVIG. Removing the spleen is also an option. If the patient is being treated with the chemo drug fludarabine (Fludara) when the AIHA develops, the drug may be the cause, and so the fludarabine will be stopped.

Palliative care

Whether your lymphoma is being treated or not, it's important to have treatment to relieve your symptoms. This type of treatment, sometimes called *palliative care*, can be given along with cancer treatment as well as [if cancer treatment is no longer working²](#).

Sometimes, the treatments you get to control your symptoms are similar to the treatments used to treat cancer. For example, when lymph nodes become enlarged, they may press on nerves and cause pain. Radiation therapy to these areas may help relieve the pain. You might also be given pain medicines, ranging from ibuprofen and similar drugs to more potent medicines such as opioids (like morphine).

Nausea and loss of appetite can be treated with drugs and high-calorie food supplements. If the lymphoma has spread to the lungs, you may get short of breath. Oxygen may be used to help treat this.

It's important that you tell your health care team about any symptoms you have, including any side effects from treatment. There are often ways to help control or lessen these symptoms. This is an important part of your overall treatment plan.

For more information on palliative care and getting help with side effects, see [Palliative or Supportive Care](#)³.

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/infections.html
2. www.cancer.org/treatment/treatments-and-side-effects/if-cancer-treatments-stop-working.html
3. www.cancer.org/treatment/treatments-and-side-effects/palliative-care.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.

National Cancer Institute. Physician Data Query (PDQ). Adult Non-Hodgkin Lymphoma Treatment. 2018. Accessed at <https://www.cancer.gov/types/lymphoma/hp/adult-nhl-treatment-pdq> on May 3, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: B-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 5.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: T-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf on May 2, 2018.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

Treating B-Cell Non-Hodgkin Lymphoma

Non-Hodgkin lymphoma (NHL) is generally divided into main 2 types, based on whether it starts in B lymphocytes (B cells) or T lymphocytes (T cells). There are many different types of B-cell lymphomas. Treatment usually depends both on the [type of lymphoma](#)¹ and the [stage \(extent\) of the disease](#)², but many other factors can be important as well.

Diffuse large B-cell lymphoma

Diffuse large B-cell lymphoma (DLBCL) tends to grow quickly. Most often, the treatment is [chemotherapy](#) (chemo), usually with a regimen of 4 drugs known as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), plus the [monoclonal antibody](#) rituximab (Rituxan). This regimen, known as R-CHOP, is most often given in cycles 3 weeks apart. Because this regimen contains the drug doxorubicin, which can damage the heart, it may not be suitable for patients with heart problems, so other chemo regimens may be used instead.

Stage I or II

For DLBCL that is only in 1 or 2 lymph node groups on the same side of the diaphragm (the thin muscle that separates the chest from the abdomen), R-CHOP is often given for

3 to 6 cycles, which might be followed by radiation therapy to the affected lymph node areas.

Stage III or IV

Most doctors will give 6 cycles of R-CHOP as first-line treatment. After several cycles, doctors may get imaging tests such as a PET/CT scan to see how well treatment is working. People who have a higher risk of the lymphoma coming back later in the tissues around the brain and spinal cord may be treated with chemo injected into the spinal fluid (called *intrathecal chemotherapy*). Another option is to give high doses of methotrexate intravenously. (This drug can pass into the spinal fluid.)

For younger patients with a higher risk of the lymphoma coming back based on the International Prognostic Index (IPI) score, [high-dose chemo followed by a stem cell transplant](#) might be an option. But it's not yet clear if transplants are better as the initial treatment. Most doctors feel that if a transplant is done as part of the first treatment, it should be done in a clinical trial.

If the lymphoma doesn't go away completely with treatment or if it recurs (comes back) after treatment, doctors will usually suggest another chemo regimen. Several different regimens can be used, and they may or may not include rituximab. If the lymphoma shrinks with this treatment, it might be followed by a stem cell transplant if possible, as it offers the best chance of curing the lymphoma. Stem cell transplants are not effective unless the lymphoma responds to chemo. Unfortunately, not everyone is healthy enough for a stem cell transplant.

CAR T cell therapies such as tisagenlecleucel (Kymriah®) or axicabtagene ciloleucel (Yescarta™) can be considered if 2 or more chemo regimens have been tried. Clinical trials of new treatments may be another good option for some people.

DLBCL can be cured in about half of all patients, but the stage of the disease and the IPI score can have a large effect on this. Patients with lower stages have better survival rates, as do patients with lower IPI scores.

Primary mediastinal B-cell lymphoma

This lymphoma, which starts in the space between the lungs (the mediastinum), is treated like early stage diffuse large B-cell lymphoma. A common treatment is 6 courses of CHOP chemo plus rituximab (R-CHOP). This may be followed by radiation to the mediastinum. Often a PET/CT scan is done after the chemo to see if there's any lymphoma remaining in the chest. If no active lymphoma is seen on the PET/CT, the

patient may be observed without further treatment. If the PET/CT scan is positive (shows possible active lymphoma), radiation may be needed. Sometimes, the doctor will order a biopsy of the chest tumor to confirm that lymphoma is still present before starting radiation.

Another treatment option is 6 cycles of dose-adjusted etoposide, doxorubicin and cyclophosphamide with vincristine, prednisone and rituximab (DA-EPOCH-R) which typically does not require any radiation.

If the primary mediastinal B cell lymphoma does come back or does not respond to chemo, immunotherapy with the drug pembrolizumab may be an option.

Follicular lymphoma

This type of lymphoma often grows slowly and responds well to treatment, but it is very hard to cure. It often comes back after treatment, although it can take many years to do so. It's not always clear if the lymphoma needs to be treated right away, especially if the lymphoma isn't causing problems other than mildly swollen lymph nodes. Some people may never need treatment at all. For those who do, sometimes it might be years before treatment is needed.

Stage I and early-stage II

If treatment is needed for follicular lymphoma that is only in 1 lymph node group or in 2 nearby groups that are both above or below the diaphragm (the thin muscle separating the chest from the abdomen), the preferred treatment is [radiation therapy](#) to the lymph node areas affected by lymphoma (called *involved site radiation*). Other choices include treatment with [chemo](#) plus a [monoclonal antibody](#) (rituximab [Rituxan] or obinutuzumab [Gazyva]), or rituximab alone, which might be followed by radiation therapy.

Stages III, IV, and most stage II bulky lymphomas

If treatment is needed, the most common option is a monoclonal antibody (rituximab or obinutuzumab) combined with chemo. The chemo can be a single drug (such as bendamustine) or a combination of drugs, such as the CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CVP (cyclophosphamide, vincristine, prednisone) regimens.

If some lymph nodes are very large from the lymphoma, radiation may be used to reduce symptoms. This is most often used for patients who are too sick to be treated with chemo.

The radioactive monoclonal antibody ibritumomab (Zevalin) is also an option for initial treatment, although this is more often used as a second-line treatment.

For patients who may not be able to tolerate more intensive chemo regimens, rituximab alone, rituximab with milder chemo drugs (such as chlorambucil or cyclophosphamide), or rituximab with lenalidomide may be good options .

If the lymphoma shrinks or goes away with the initial treatment, doctors may advise either close follow-up or further treatment. This might include continuing the monoclonal antibody (rituximab or obinutuzumab) for up to 2 years, or treatment with ibritumomab. Further treatment may lower the chance that the lymphoma will come back later and may help some patients live longer, but it can also have side effects.

If follicular lymphoma doesn't respond to the initial treatment or if it comes back later, it may be treated with different chemo drugs, [targeted drugs](#), monoclonal antibodies, or some combination of these. If the lymphoma responds to this treatment, a [stem cell transplant](#) may be an option.

A small portion of follicular lymphomas, known as *grade 3B lymphomas*, tend to grow quickly, more like diffuse large B-cell lymphoma (DLBCL). Some follicular lymphomas can also change (transform) into or return as DLBCL. For these lymphomas, your doctor will review which treatments you may have already had to decide which is the next best treatment option.

Small lymphocytic lymphoma (and chronic lymphocytic leukemia)

Small lymphocytic lymphoma (SLL) and chronic lymphocytic leukemia (CLL) are considered different versions of the same disease. The main difference is where the cancer cells are (the blood and bone marrow for CLL, and the lymph nodes and spleen for SLL). CLL and SLL tend to grow slowly, but are very hard to cure.

Treatment for SLL is similar to that of CLL, which is described in detail in [Treating Chronic Lymphocytic Leukemia](#)³.

If the lymphoma isn't growing quickly or causing any problems, it can be watched closely without treatment for a time. If treatment is needed, it depends on the stage.

When the lymphoma is only in one lymph node or lymph node area (stage I), it may be treated with radiation therapy alone.

For more advanced disease, the treatment is often the same as what is used for CLL.

(See [Treating Chronic Lymphocytic Leukemia⁴](#).) Chemo, with or without rituximab or obinutuzumab (Gazyva) is one option for first-line treatment. Chlorambucil, fludarabine, or bendamustine are some of the chemo drugs that are used. The targeted drug ibrutinib (Imbruvica) is another option, as is rituximab alone (without chemo). Which treatment is used depends on a person's age and health, as well as on whether the cancer cells have certain chromosome changes.

If the lymphoma doesn't respond or comes back after initial treatment, different chemo drugs, targeted drugs, and/or other monoclonal antibodies may be used as second-line treatment.

Mantle cell lymphoma

This type of lymphoma has often spread widely when it's first found. Although it doesn't usually grow as quickly as some other fast-growing lymphomas, it often doesn't respond as well to treatment, either. Because current treatments for this type of lymphoma are very unlikely to cure it, patients might want to consider taking part in a [clinical trial⁵](#).

If the lymphoma has only spread to 1 lymph node group or to 2 nearby groups on the same side of the diaphragm (stage I and some stage II), which is rare, it can sometimes be treated with radiation therapy. Another option is to treat with chemo plus rituximab. Mantle cell lymphomas that have spread more widely when they are first diagnosed are treated with chemo plus rituximab.

When possible, the chemo treatment is intense, using regimens such as:

- Hyper-CVAD: cyclophosphamide, vincristine, doxorubicin (Adriamycin), and dexamethasone, alternating with high-dose methotrexate plus cytarabine)
- "Dose-intensified" R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), alternating with rituximab and cytarabine
- RDHAP (Rituximab, dexamethasone, cytarabine, cisplatin)

If the lymphoma responds well to these initial treatments, a stem cell transplant may be a good option followed by rituximab for 3 years.

Less intense chemo regimens, such as bendamustine with rituximab may be used for people who are older or who have other health issues.

For mantle cell lymphomas that don't respond or that come back after initial treatment, chemo with drugs such as bendamustine, bortezomib (Velcade), cladribine, fludarabine,

or lenalidomide (Revlimid) may be used, sometimes along with other chemo drugs or with rituximab. Another option includes the use of a [targeted drug](#), such as ibrutinib (Imbruvica) or acalabrutinib (Calquence). Other targeted drugs such as venetoclax (Venclexta) and idelalisib (Zydelig) have also shown promising results in some early studies. Still, because second-line treatment is not always helpful, patients might want to consider entering a [clinical trial](#)⁶.

Extranodal marginal zone B-cell lymphoma – mucosa-associated lymphoid tissue (MALT) lymphoma

Gastric (stomach) MALT lymphoma, the most common type, often occurs as a result of a chronic infection with the bacterium *H. pylori*, and it often responds to treatment of the infection. Because of this, gastric lymphomas are treated differently from other lymphomas in this group.

Stages I and II gastric lymphoma in people who test positive for *H. pylori*

Early-stage gastric MALT lymphomas are treated with antibiotics combined with drugs that block acid secretion by the stomach (called *proton pump inhibitors*). Usually the drugs are given for 10 to 14 days. This may be repeated after a couple of weeks. Examination of the stomach lining using upper endoscopy (where a flexible tube with a viewing lens is passed down the throat and into the stomach) is then repeated at certain intervals to see if the *H. pylori* is gone and if the lymphoma has shrunk. About 2 out of 3 of these lymphomas go away completely with antibiotic treatment, but it can sometimes take several months to be effective. In cases where symptoms need to be relieved before the antibiotics take effect or where antibiotics don't shrink the lymphoma, radiation therapy to the area is often the preferred treatment. The monoclonal antibody rituximab may be another option.

Stages I and II gastric lymphoma in people who test negative for *H. pylori*

For these early-stage gastric MALT lymphomas, treatment is usually either radiation therapy to the stomach or rituximab.

Stage III or IV gastric lymphoma

For more advanced gastric MALT lymphomas, which are rare, treatment is often similar to that for follicular lymphoma (see above). Lymphomas that are not growing quickly may be watched and not treated right away. If the lymphoma is large, is causing symptoms, or is growing, it can be treated with radiation therapy to the stomach,

rituximab, chemo, chemo plus rituximab, or the targeted drug ibrutinib (Imbruvica). The chemo drugs used are the same as those used for follicular lymphoma, and may include single agents such as chlorambucil or fludarabine or combinations such as CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CVP (cyclophosphamide, vincristine, prednisone).

Non-gastric MALT lymphoma

For MALT lymphomas that start in sites other than the stomach (non-gastric lymphomas), treatment depends on the location of the lymphoma and how much it has spread. Early-stage lymphomas can often be treated with radiation to the area containing the lymphoma. In certain sites (such as the lungs, breast, or thyroid), surgery may be an option. For more advanced disease (stage III or IV), treatment is generally the same as for stage III and IV gastric MALT lymphoma and follicular lymphoma (see above).

Nodal marginal zone B-cell lymphoma

This rare type of lymphoma is generally slow growing (indolent), and it often doesn't need to be treated right away. If it does need treatment, it is usually treated the same way as follicular lymphoma (which also tends to grow slowly).

Stage I and early-stage II

If treatment is needed for lymphoma that is only in 1 lymph node group or in 2 nearby groups on the same side of the diaphragm (the thin muscle separating the chest from the abdomen), the preferred treatment is radiation therapy to the lymph node areas affected by lymphoma (called *involved site radiation*). Other choices include treatment with rituximab (Rituxan), chemo, or both, which might be followed by radiation therapy.

Stages III, IV, and most stage II bulky lymphomas

If treatment is needed, the most common option is rituximab combined with chemo. The chemo can be a single chemo drug (such as bendamustine or fludarabine) or a combination of drugs, such as the CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CVP (cyclophosphamide, vincristine, prednisone) regimens. If the lymphoma shrinks, a total of 6 cycles of chemo plus rituximab is usually given.

Other options for initial treatment include rituximab alone or chemo alone (either one or several drugs). If some lymph nodes are very large from the lymphoma, radiation may be used to reduce symptoms. This is most often used for patients who are too sick to be

treated with chemo.

The radioactive monoclonal antibody ibritumomab tiuxetan (Zevalin) is also an option for initial treatment, although this is more often used as a second treatment.

For patients who may not be able to tolerate more intensive (stronger) chemo regimens, rituximab alone, milder chemo drugs (such as chlorambucil or cyclophosphamide), or both may be good options.

If the lymphoma shrinks or goes away with the initial treatment, doctors may advise either close follow-up or further treatment. This might include either rituximab for up to 2 years or treatment with ibritumomab tiuxetan. Further treatment may lower the chance that the lymphoma will come back later and may help some patients live longer, but it can also have side effects.

If the lymphoma doesn't respond to the initial treatment or if it comes back later, it may be treated with different chemo drugs, monoclonal antibodies, targeted drugs, or some combination of these. If the lymphoma responds to this treatment, a stem cell transplant may be an option.

Nodal marginal zone B-cell lymphoma can also change into a fast-growing diffuse large B-cell lymphoma (DLBCL), which would require more aggressive chemotherapy (see above).

Splenic marginal zone B-cell lymphoma

This is typically a slow-growing lymphoma. If it is not causing symptoms, it is often watched closely without treating it right away.

About 1 in 3 people with this type of lymphoma have chronic hepatitis C virus (HCV) infection. Treating the infection with anti-viral drugs can often cause these lymphomas to go into remission.

If that doesn't work, or if a person isn't infected with HCV, surgery to remove the spleen can sometimes lead to a long-term remission. This can be very helpful in relieving symptoms if the spleen is enlarged. Treatment with rituximab may be another option.

If the disease is more advanced or progresses, it's usually treated with chemo with or without rituximab (similar to what is used for advanced stage follicular lymphoma, which is described above). Another option might be the targeted drug ibrutinib (Imbruvica).

Sometimes this lymphoma can transform into an aggressive large-cell lymphoma, which then requires more intensive chemo.

Burkitt lymphoma

This is a very fast-growing lymphoma that is similar to a type of acute lymphocytic leukemia. It is usually treated in the hospital with intensive chemo, which usually includes at least 5 chemo drugs. Rituximab may also be added. Some examples of chemo regimens used for this lymphoma include:

- **Hyper-CVAD** (cyclophosphamide, vincristine, doxorubicin [Adriamycin], and dexamethasone), alternating with methotrexate and cytarabine (ara-C)
- **CODOX-M** (cyclophosphamide, vincristine [Oncovin], doxorubicin, and high-dose methotrexate), alternating with **IVAC** (ifosfamide, etoposide [VP-16], and cytarabine [ara-C])
- **EPOCH** (etoposide, prednisone, vincristine [Oncovin], cyclophosphamide, and doxorubicin)

Because this lymphoma tends to invade the area around the brain and spinal cord, the chemo drug methotrexate is often given into the spinal fluid (called *intrathecal therapy*). This may not be needed if high-dose methotrexate is given as a part of the main chemotherapy regimen.

An important part of the initial treatment of this disease is making sure a person gets plenty of fluids, as well as drugs like allopurinol, to help prevent tumor lysis syndrome (described in [Chemotherapy for Non-Hodgkin Lymphoma](#)).

If the lymphoma doesn't go away or if it comes back after treatment, another chemo regimen might be tried. If the lymphoma goes into remission, the doctor might suggest a stem cell transplant.

Lymphoplasmacytic lymphoma (Waldenstrom macroglobulinemia)

The main treatment for this lymphoma is usually chemo or rituximab. For more detailed information see [Treating Waldenstrom Macroglobulinemia](#)⁷.

Hairy cell leukemia

This is a slow-growing lymphoma that tends to invade the spleen and lymph nodes as

well as the blood. Patients without symptoms often don't need to be treated right away. When treatment is needed, most often the chemo drugs cladribine (2-CdA) or pentostatin are used. For more detailed information, see [Treating Chronic Lymphocytic Leukemia](#)⁸.

Primary central nervous system (CNS) lymphoma

This lymphoma begins in the brain or spinal cord. It often develops in older people or those with immune system problems caused by AIDS or drugs given to keep transplanted organs from being rejected.

Most patients are treated with chemo and/or radiation. One problem with treating this disease is that most chemo drugs commonly used to treat lymphoma don't reach the brain when given intravenously (IV). For people in reasonably good health, high IV doses of the drug methotrexate have been shown to be the most effective treatment. This is given along with the drug leucovorin and IV fluids, which help limit serious side effects. Other chemo drugs, such as cytarabine, may be added. Rituximab may be added as well. For those who aren't able to tolerate this treatment, other, less intensive chemo regimens or radiation therapy alone may be tried.

An issue with radiation therapy to the brain, especially in older patients, is that it can often cause mental changes. Doctors limit the dose of radiation to try to lessen this problem.

If CNS lymphoma keeps growing or comes back after treatment, further options may include chemo (using different drugs), radiation therapy, or a stem cell transplant if the person is healthy enough.

Primary intraocular lymphoma (lymphoma of the eye)

Most often doctors treat these cancers with radiation therapy, chemotherapy (chemo), or a combination of the two.

[External beam radiation therapy](#) is given if the cancer is limited to the eye. Radiation to both eyes may be recommended if lymphoma is found in both eyes. Because these lymphomas are commonly linked with lymphoma of the brain (CNS lymphoma), they have sometimes already spread outside the eye or to the brain when the cancer is first diagnosed. If this is the case, radiation therapy to the brain and spinal cord may be included because it can help prevent the lymphoma from spreading there or help destroy cancer cells that are there but haven't been seen by imaging. Problems with thinking, concentration, and memory are possible side effects from radiation to the brain

and spinal cord.

Depending on the type of lymphoma, **chemo** may be used alone or in combination with radiation therapy, especially if it has grown outside the eye or spread to other places in the body. Chemo can be given into a vein (systemic chemo), directly into the cerebrospinal fluid (intrathecal chemo), or directly into the eye (intraocular chemo). Intraocular chemo gets higher doses of the drug to the tumor without causing severe side effects in other parts of the body. Methotrexate is the most commonly used chemo drug, but others can be used as well. **Monoclonal antibodies** such as rituximab may also be given directly into the eye. The best combination and dosage of drugs is not yet known, and the choice may be influenced by the type of lymphoma. Sometimes systemic chemo may be given along with therapy given directly to the eye such as external radiation or intraocular chemo.

If the lymphoma does not respond to treatment or if it comes back (recurs), **high-dose chemotherapy followed by a stem cell transplant** may be an option for some people.

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

Hyperlinks

1. www.cancer.org/cancer/non-hodgkin-lymphoma/about/b-cell-lymphoma.html
2. www.cancer.org/cancer/non-hodgkin-lymphoma/detection-diagnosis-staging/staging.html
3. www.cancer.org/cancer/chronic-lymphocytic-leukemia/treating.html
4. www.cancer.org/cancer/chronic-lymphocytic-leukemia/treating.html
5. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
6. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
7. www.cancer.org/cancer/waldenstrom-macroglobulinemia/treating.html
8. www.cancer.org/cancer/chronic-lymphocytic-leukemia/treating.html
9. https://www.uptodate.com/contents/treatment-and-prognosis-of-primary-central-nervous-system-lymphoma?search=lymphoma%20of%20the%20eye&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H26

References

Batchelor T. Treatment and prognosis of primary central nervous system lymphoma. UpToDate website. https://www.uptodate.com/contents/treatment-and-prognosis-of-primary-central-nervous-system-lymphoma?search=lymphoma%20of%20the%20eye&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H26 (www.uptodate.com/contents/treatment-and-prognosis-of-primary-central-nervous-system-lymphoma?search=lymphoma%20of%20the%20eye&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H26)⁹. Updated Jun 27, 2018. Accessed January 24, 2019.

Dunleavy K, Pittaluga S, Maeda LS, et al. Dose-Adjusted EPOCH-Rituximab Therapy in Primary Mediastinal B-Cell Lymphoma. *The New England journal of medicine*. 2013;368(15):1408-1416. doi:10.1056/NEJMoa1214561.

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.

Grimm SA, McCannel CA, Omuro AM, et al. Primary CNS lymphoma with intraocular involvement: International PCNSL Collaborative Group Report. *Neurology*. 2008;71:1355-1360.

Karcioglu ZA, Haik BG. Chapter 67: Eye, orbit, and adnexal structures. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014

National Cancer Institute. Physician Data Query (PDQ). Adult Non-Hodgkin Lymphoma Treatment. 2018. Accessed at <https://www.cancer.gov/types/lymphoma/hp/adult-nhl-treatment-pdq> on May 3, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: B-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf on May 2, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 5.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf on May 2, 2018.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

Last Medical Review: August 1, 2018 Last Revised: January 29, 2019

Treating T-Cell Non-Hodgkin Lymphoma

Non-Hodgkin lymphoma (NHL) is generally divided into main 2 types, based on whether it starts in B lymphocytes (B cells) or T lymphocytes (T cells). There are many different types of T-cell lymphomas, and treatment can vary based on [which type you have](#)¹.

T-lymphoblastic lymphoma/leukemia

This disease can occur in both children and adults, and it can be considered either a lymphoma or a type of [acute lymphoblastic leukemia \(ALL\)](#)², depending on how much of the bone marrow is involved. (Leukemias have more bone marrow involvement.)

Regardless of whether it's labeled as a lymphoma or a leukemia, this is a fast-growing disease that's treated with intensive chemotherapy (chemo), when possible.

Combinations of many drugs are used. These can include cyclophosphamide, doxorubicin (Adriamycin), vincristine, L-asparaginase, methotrexate, prednisone, and, sometimes, cytarabine (ara-C). Because of the risk of spread to the brain and spinal cord, a chemo drug such as methotrexate is also given into the spinal fluid. Some doctors suggest maintenance chemo for up to 2 years after the initial treatment to reduce the risk of recurrence. High-dose chemo followed by a stem cell transplant may be another option.

Treatment is typically given in the hospital at first. During this time, patients are at risk for tumor lysis syndrome (described in [Chemotherapy for Non-Hodgkin Lymphoma](#)), so they are given plenty of fluids and drugs like allopurinol.

For more details on treatment, see [Treating Acute Lymphocytic Leukemia \(Adults\)](#)³ and [Treating Childhood Leukemia](#)⁴.

Although this lymphoma is fast-growing, if it hasn't spread to the bone marrow when it's

first diagnosed, the chance of cure with chemo is quite good. But it is harder to cure once it has spread to the bone marrow.

Peripheral T-cell lymphomas

Cutaneous T-cell lymphomas (mycosis fungoides, Sezary syndrome, and others)

Treatment of these skin lymphomas is discussed in [Treating Lymphoma of the Skin](#)⁵.

Adult T-cell leukemia/lymphoma

This lymphoma is linked to infection with the HTLV-1 virus. There are 4 subtypes, and treatment depends on which subtype you have.

- The **smoldering and chronic subtypes** grow slowly. Like other slow-growing lymphomas (such as follicular lymphoma and small lymphocytic lymphoma), these subtypes are often watched without treatment as long as they aren't causing problems other than mildly swollen lymph nodes. If treatment is needed, one option is interferon and the anti-viral drug zidovudine to fight the HTLV-1 infection. If the lymphoma is affecting the skin, it may be treated with radiation. Another option is chemo, using the CHOP regimen (cyclophosphamide, doxorubicin, vincristine, and prednisone) or other combinations.
- The **acute subtype** also can be treated with either anti-viral drugs or chemo (typically the CHOP regimen). If it responds well to treatment, a stem cell transplant might be considered.
- Anti-viral therapy is not helpful for the **lymphoma subtype**, so it is typically treated with chemotherapy. It can also involve the tissues around the brain and spinal cord, so chemo is given into the spinal fluid (intrathecal chemo) as well. Treatment after chemo may include a stem cell transplant.

Because there is no clear standard treatment for this disease, patients might want to consider enrolling in a [clinical trial](#)⁶, if one is available.

Angioimmunoblastic T-cell lymphoma

This fast-growing lymphoma might be treated first with steroids (such as prednisone or dexamethasone) alone, especially in older patients who might have trouble tolerating chemo. This treatment can reduce fever and weight loss, but the effect is often

temporary. If [chemo](#) is needed, combinations such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) may be used. Another option might be the chemo combination of cyclophosphamide, doxorubicin, and prednisone, along with the [monoclonal antibody](#) brentuximab vedotin (Adcetris). If the lymphoma is only in one area, [radiation therapy](#) may be an option.

Standard doses of chemo rarely produce long-term remissions, so a [stem cell transplant](#) is often suggested after initial chemotherapy if a person can tolerate it.

Extranodal natural killer/T-cell lymphoma, nasal type

This rare lymphoma is often confined to the nasal passages. Patients with stage I or II disease who aren't healthy enough for chemotherapy may be treated with radiation therapy alone. Most other patients are treated with chemoradiation (chemo and radiation given together) or chemo followed by radiation. Several different chemo combinations can be used.

If the lymphoma doesn't go away completely, a stem cell transplant may be done if possible.

Enteropathy-associated T-cell lymphoma

This lymphoma generally develops in the small intestine or colon. Intensive chemo using several drugs is usually the main treatment. Often CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) is the chemo used. If the lymphoma is only in one area, radiation therapy may be used as well. But if these treatments work, a hole (perforation) can develop in the intestines (as the lymphoma cells die), so surgery might be done first to remove the part of the intestines containing the lymphoma. Surgery may also be needed before chemo or radiation if a person is diagnosed with this lymphoma because it caused a perforation or intestinal blockage (obstruction). A stem cell transplant may be an option if the lymphoma responds to chemo.

Anaplastic large cell lymphoma (ALCL)

This fast-growing lymphoma mainly affects lymph nodes and is treated with [chemo](#) regimens such as CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone). Another option might be the chemo combination of cyclophosphamide, doxorubicin, and prednisone, along with the [monoclonal antibody](#) brentuximab vedotin (Adcetris). Doctors might recommend [radiation therapy](#) as well for some patients.

This lymphoma often responds well to treatment, and long-term survival is common, especially if the lymphoma cells have too much of the ALK protein. If the cells lack the ALK protein or if the lymphoma returns after initial treatment, a [stem cell transplant](#) may be an option. Another option for lymphomas that no longer respond to initial treatment is brentuximab vedotin (Adcetris).

For ALCL that develops in the capsule (normal protective scar tissue) that forms around a breast implant, experts typically recommend removing the implant and the capsule surrounding it. Additional treatment might include chemo, sometimes with radiation.

Peripheral T-cell lymphoma, unspecified

These lymphomas are generally treated the same way as diffuse large B-cell lymphoma (DLBCL). [Chemo](#) with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or other drug combinations is used. For early-stage disease, [radiation therapy](#) may be added. Another option for some of these lymphomas might be the chemo combination of cyclophosphamide, doxorubicin, and prednisone, along with the [monoclonal antibody](#) brentuximab vedotin (Adcetris). A [stem cell transplant](#) may be recommended when possible.

If other treatments are no longer working, newer chemo drugs such as pralatrexate (Folotyn), [targeted drugs](#) such as bortezomib (Velcade), belinostat (Beleodaq), or romidepsin (Istodax), or [immunotherapy](#) drugs such as alemtuzumab (Campath) and denileukin diftitox (Ontak) may be tried.

The outlook for these lymphomas is usually not as good as in DLBCL, so taking part in a [clinical trial](#)⁷ of newer treatments is often a good option.

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

Hyperlinks

1. www.cancer.org/cancer/non-hodgkin-lymphoma/about/t-cell-lymphoma.html
2. www.cancer.org/cancer/acute-lymphocytic-leukemia.html
3. www.cancer.org/cancer/acute-lymphocytic-leukemia/treating.html
4. www.cancer.org/cancer/leukemia-in-children/treating.html

5. www.cancer.org/cancer/skin-lymphoma/treating.html
6. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
7. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.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.

National Cancer Institute. Physician Data Query (PDQ). Adult Non-Hodgkin Lymphoma Treatment. 2018. Accessed at <https://www.cancer.gov/types/lymphoma/hp/adult-nhl-treatment-pdq> on May 3, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: T-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf on May 2, 2018.

Ondrejka S and Jagadeesh D. Enteropathy-Associated T-Cell Lymphoma. *Curr Hematol Malig Rep*. 2016;11(6):504-513. doi: 10.1007/s11899-016-0357-7.

Rizvi MA, Evens AM, Tallman MS, et al. T-cell non-Hodgkin lymphoma. *Blood*. 2006;107:1255-1264.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

Last Medical Review: August 1, 2018 Last Revised: November 19, 2018

Treating HIV-Associated Lymphoma

People with [HIV infections](#)¹ are at increased risk for non-Hodgkin lymphoma. Although people with HIV tend to get more aggressive forms of lymphoma such as diffuse large

B-cell lymphoma, primary CNS lymphoma, or Burkitt lymphoma, their outlook has improved a great deal in recent years. The use of highly active anti-retroviral therapy (HAART) to treat HIV has helped patients to better tolerate treatments such as chemo and immunotherapy.

A major problem in the past was that patients with HIV infection tended to have low blood cell counts to begin with, which made it hard to treat them with full doses of chemo. This problem has been relieved somewhat by the use of HAART and by the use of drugs to help the patient's body make new blood cells. Still, doctors give chemo cautiously and monitor blood counts closely. HIV can lower the number of white blood cells known as CD4-positive cells. People with low CD4 counts can have more problems when treated with rituximab, so some experts don't use this drug for patients who have low CD4 counts.

Most experts believe that the prognosis (outlook) for a person with HIV-associated lymphoma relates at least as much to the HIV infection as to the lymphoma. Modern anti-HIV therapy can often control the immune deficiency in patients with AIDS, so the outlook for patients who develop lymphoma has improved.

The treatment of the lymphoma itself depends on the specific type of lymphoma.

Hyperlinks

1. www.cancer.org/cancer/cancer-causes/infectious-agents/hiv-infection-aids.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.

National Cancer Institute. Physician Data Query (PDQ). Adult Non-Hodgkin Lymphoma Treatment. 2018. Accessed at <https://www.cancer.gov/types/lymphoma/hp/adult-nhl-treatment-pdq> on May 3, 2018.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: B-cell Lymphomas. Version 3.2018. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf on May 2, 2018.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

Written by

The American Cancer Society medical and editorial content team
(www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

American Cancer Society medical information is copyrighted material. For reprint requests, please see our Content Usage Policy (www.cancer.org/about-us/policies/content-usage.html).

cancer.org | 1.800.227.2345



[cancer.org](https://www.cancer.org) | 1.800.227.2345

After Non-Hodgkin Lymphoma Treatment

Living as a Cancer Survivor

For many people, cancer treatment often raises questions about next steps as a survivor.

- [Living as a Non-Hodgkin Lymphoma Survivor](#)

Cancer Concerns After Treatment

Treatment may remove or destroy the lymphoma, but it is very common to have questions about cancer coming back or treatment no longer working.

- [Second Cancers After Non-Hodgkin Lymphoma](#)
-

Living as a Non-Hodgkin Lymphoma Survivor

For many people with non-Hodgkin lymphoma, treatment can destroy the lymphoma. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about the lymphoma coming back. (When cancer comes back after treatment, it is called [recurrence](#)¹.) This is a very common worry if

you've had cancer.

For some people, the lymphoma may [never go away completely](#)². These people may get regular treatments with chemo, radiation, or other therapies to help keep the lymphoma in check for as long as possible and to help relieve symptoms. Learning to live with lymphoma that doesn't go away can be difficult and very stressful.

Follow-up care

There are many types of non-Hodgkin lymphomas, which can require [different treatments](#)³ and can have very different outlooks. Your care after treatment will depend on the type of lymphoma you have, what type of treatment you receive, and how well treatment works.

Even if you've completed treatment, your doctors will still want to watch you closely. It's very important to go to all of your follow-up appointments, because lymphoma can sometimes come back even many years after treatment.

Some [treatment side effects](#)⁴ might last a long time or might not even show up until years after you have finished treatment. Your doctor visits are a good time to ask questions and talk about any changes or problems you notice or concerns you have.

Exams and tests

During your follow-up visits, your doctor will ask you about any symptoms you are having, examine you, and may order blood or imaging tests. Your doctor will probably want to see you regularly, usually every few months for the first year or so and gradually less often after that.

Imaging tests may be done, based on the type, location, and stage of lymphoma. For example, CT scans or PET/CT scans may be used to monitor the size of any remaining tumors, or to look for possible new tumors.

You may need frequent blood tests to check that you have recovered from treatment and to look for possible signs of problems such as lymphoma recurrence. Blood counts can also sometimes become abnormal because of a disease of the bone marrow called *myelodysplasia*, which can sometimes lead to leukemia. Some chemotherapy drugs can cause this disease. For more on this, see [Myelodysplastic Syndromes](#)⁵. It's also possible for a person to develop leukemia a few years after being treated for lymphoma.

Ask your doctor for a survivorship care plan

Talk with your doctor about developing a survivorship care plan for you. This plan might include:

- A suggested schedule for follow-up exams and tests
- A schedule for other tests you might need in the future, such as early detection (screening) tests for other types of cancer, or tests to look for long-term health effects from your cancer or its treatment
- A list of possible late- or long-term side effects from your treatment, including what to watch for and when you should contact your doctor
- Diet and physical activity suggestions

Keeping health insurance and copies of your medical records

Even after treatment, it's very important to keep health insurance. Tests and doctor visits cost a lot, and even though no one wants to think of their cancer coming back, this could happen.

At some point after your treatment, you might find yourself seeing a new doctor who doesn't know about your medical history. It's important to keep copies of your medical records to give your new doctor the details of your diagnosis and treatment. Learn more in [Keeping Copies of Important Medical Records](#)⁶.

Can I lower my risk of the lymphoma progressing or coming back?

If you have (or have had) lymphoma, you probably want to know if there are things you can do that might lower your risk of the lymphoma growing or coming back, such as exercising, eating a certain type of diet, or taking nutritional supplements. Unfortunately, it's not yet clear if there are things you can do that will help.

Adopting healthy behaviors such as [not smoking](#)⁷, [eating well](#)⁸, [getting regular physical activity](#)⁹, and [staying at a healthy weight](#)¹⁰ might help, but no one knows for sure. However, we do know that these types of changes can have positive effects on your health that can extend beyond your risk of lymphoma or other cancers.

About dietary supplements

So far, no [dietary supplements](#)¹¹ (including vitamins, minerals, and herbal products) have been shown to clearly help lower the risk of lymphoma progressing or coming back. This doesn't mean that no supplements will help, but it's important to know that

none have been proven to do so.

Dietary supplements are not regulated like medicines in the United States – they do not have to be proven effective (or even safe) before being sold, although there are limits on what they're allowed to claim they can do. If you're thinking about taking any type of nutritional supplement, talk to your health care team. They can help you decide which ones you can use safely while avoiding those that might be harmful.

If the lymphoma comes back

If the lymphoma does come back at some point, your treatment options will depend on the type of lymphoma, where it is, what treatments you've had before, how long it's been since treatment, and your current health and preferences.

For more general information on dealing with a recurrence, see [Coping With Cancer Recurrence](#)¹².

Could I get a second cancer after treatment?

People who've had non-Hodgkin lymphoma can still get other cancers. In fact, lymphoma survivors are at higher risk for getting some other types of cancer. Learn more in [Second Cancers After Non-Hodgkin Lymphoma](#).

Getting emotional support

Some amount of feeling depressed, anxious, or worried is normal when lymphoma is a part of your life. Some people are affected more than others. But everyone can benefit from help and support from other people, whether friends and family, religious groups, support groups, professional counselors, or others. Learn more in [Life After Cancer](#)¹³.

Hyperlinks

1. www.cancer.org/treatment/survivorship-during-and-after-treatment/understanding-recurrence.html
2. www.cancer.org/treatment/survivorship-during-and-after-treatment/when-cancer-doesnt-go-away.html
3. www.cancer.org/cancer/non-hodgkin-lymphoma/treating.html
4. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html
5. www.cancer.org/cancer/myelodysplastic-syndrome.html

6. www.cancer.org/treatment/survivorship-during-and-after-treatment/be-healthy-after-treatment/keeping-copies-of-important-medical-records.html
7. www.cancer.org/healthy/stay-away-from-tobacco.html
8. www.cancer.org/healthy/eat-healthy-get-active/eat-healthy.html
9. www.cancer.org/healthy/eat-healthy-get-active/get-active.html
10. www.cancer.org/healthy/eat-healthy-get-active/take-control-your-weight.html
11. www.cancer.org/treatment/treatments-and-side-effects/complementary-and-alternative-medicine/dietary-supplements.html
12. www.cancer.org/treatment/survivorship-during-and-after-treatment/understanding-recurrence/coping-with-cancer-recurrence.html
13. www.cancer.org/treatment/survivorship-during-and-after-treatment/be-healthy-after-treatment/life-after-cancer.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.

Roschewski MJ, Wilson WH. Chapter 106: Non-Hodgkin Lymphoma. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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

Second Cancers After Non-Hodgkin Lymphoma

Cancer survivors can be affected by a number of health problems, but often a major concern is facing cancer again. If a cancer comes back after treatment it is called a *recurrence*. But some cancer survivors may develop a new, unrelated cancer later. This is called a *second cancer*.

People who have had non-Hodgkin lymphoma (NHL) can get any type of second cancer, but they have an increased risk of certain cancers, including:

- [Melanoma skin cancer](#)¹
- [Lung cancer](#)²
- [Kidney cancer](#)³
- [Kaposi sarcoma](#)⁴
- Cancers of the head/neck area (includes the [lip, tongue, floor of the mouth, throat](#)⁵, [salivary glands](#)⁶, and [voice box](#)⁷)
- [Colon cancer](#)⁸
- [Thyroid cancer](#)⁹
- [Bone](#)¹⁰ and [soft tissue cancer](#)¹¹
- [Bladder cancer](#)¹²
- [Leukemia](#)¹³ and [myelodysplastic syndrome](#)¹⁴
- [Hodgkin disease](#)¹⁵

Radiation therapy to the chest increases the risk of breast cancer in women who were treated before age 30. [Mesothelioma](#)¹⁶, a rare cancer of the outer lining of the lung, is also increased in those who were treated with chest radiation.

Follow-up after treatment

After completing treatment for NHL, you should still see your doctor regularly and may have tests to look for signs that the cancer has come back. Let your doctors know if you have any new symptoms or problems, as they could be due to the lymphoma coming back or from a new disease or cancer.

Women who were treated with chest radiation prior to the age of 30 have an increased risk of breast cancer. The American Cancer Society recommends yearly breast MRIs in addition to mammograms and clinical breast exams beginning at age 30 for these women.

The Children's Oncology Group has guidelines for the follow-up of patients treated for cancer as a child, teen, or young adult, including screening for second cancers. These can be found at www.survivorshipguidelines.org¹⁷.

Lymphoma survivors should also follow the [American Cancer Society recommendations for the early detection of cancer](#)¹⁸, such as those for colorectal, lung, and breast cancer. Most experts don't recommend any other testing to look for second cancers unless you have symptoms.

Can I lower my risk of getting a second cancer?

There are steps you can take to lower your risk and stay as healthy as possible. For example, it's important to [stay away from tobacco products](#)¹⁹. Smoking increases the risk of many cancers, including some of the second cancers seen in people who have had lymphoma.

To help maintain good health, lymphoma survivors should also:

- Get to and stay at a [healthy weight](#)²⁰
- Stay [physically active](#)²¹
- Eat a [healthy diet](#)²², with an emphasis on plant foods
- Limit [alcohol](#)²³ to no more than 1 drink per day for women or 2 per day for men

These steps may also lower the risk of some other health problems.

See [Second Cancers in Adults](#)²⁴ for more information about causes of second cancers.

Hyperlinks

1. www.cancer.org/cancer/melanoma-skin-cancer.html
2. www.cancer.org/cancer/lung-cancer.html
3. www.cancer.org/cancer/kidney-cancer.html
4. www.cancer.org/cancer/kaposi-sarcoma.html
5. www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer.html
6. www.cancer.org/cancer/salivary-gland-cancer.html
7. www.cancer.org/cancer/laryngeal-and-hypopharyngeal-cancer.html
8. www.cancer.org/cancer/colon-rectal-cancer.html
9. www.cancer.org/cancer/thyroid-cancer.html
10. www.cancer.org/cancer/bone-cancer.html
11. www.cancer.org/cancer/soft-tissue-sarcoma.html
12. www.cancer.org/cancer/bladder-cancer.html
13. www.cancer.org/cancer/leukemia.html
14. www.cancer.org/cancer/myelodysplastic-syndrome.html
15. www.cancer.org/cancer/hodgkin-lymphoma.html
16. www.cancer.org/cancer/malignant-mesothelioma.html
17. <http://www.survivorshipguidelines.org/>
18. www.cancer.org/healthy/find-cancer-early/cancer-screening-guidelines.html
19. www.cancer.org/healthy/stay-away-from-tobacco.html

20. www.cancer.org/cancer/cancer-causes/diet-physical-activity/body-weight-and-cancer-risk.html
21. www.cancer.org/cancer/cancer-causes/diet-physical-activity.html
22. www.cancer.org/cancer/cancer-causes/diet-physical-activity.html
23. www.cancer.org/cancer/cancer-causes/diet-physical-activity/alcohol-use-and-cancer.html
24. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/second-cancers-in-adults.html

References

Children's Oncology Group. Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancers. V 4.0 (Oct 2013). Accessed at www.survivorshipguidelines.org on May 2, 2018.

Dores GM, Coté TR, Travis LB. New Malignancies Following Hodgkin Lymphoma, Non-Hodgkin Lymphoma, and Myeloma. In: Curtis RE, Freedman DM, Ron E, Ries LAG, Hacker DG, Edwards BK, Tucker MA, Fraumeni JF Jr. (eds). *New Malignancies Among Cancer Survivors: SEER Cancer Registries, 1973-2000*. National Cancer Institute. NIH Publ. No. 05-5302. Bethesda, MD, 2006. Accessed on May 2, 2018 at http://seer.cancer.gov/archive/publications/mpmono/MPMonograph_complete.pdf.

Tward JD, Wendland MM, Shrieve DC, Szabo A, Gaffney DK. The risk of secondary malignancies over 30 years after the treatment of non-Hodgkin lymphoma. *Cancer*. 2006;107:108-115.

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

Written by

The American Cancer Society medical and editorial content team
(www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

American Cancer Society medical information is copyrighted material. For reprint

requests, please see our Content Usage Policy (www.cancer.org/about-us/policies/content-usage.html).

cancer.org | 1.800.227.2345