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 Non-Hodgkin 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 in the body begin to grow out of control. Cells in nearly any part of the body can become cancer, and can spread to other areas of the body. To learn more about how cancers start and spread, see What Is Cancer?

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.

There are two types of lymphoma. They are treated differently, so it’s important to know which one you have. The information here focuses on non-Hodgkin lymphoma in adults.

For information on the other type of lymphoma, see Hodgkin Lymphoma. We also have
separate information about non-Hodgkin lymphoma in children and lymphoma of the skin.

The lymph system

To understand what lymphoma is, it helps to know about 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. The lymph system also helps fluids move through the body.

Lymphocytes

The lymph system is made up mainly of immune system cells that help the body fight infections. Most of these cells are lymphocytes, a type of white blood cell. 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.

Non-Hodgkin lymphoma can develop from either type of lymphocyte, but B-cell lymphomas are much more common in the United States than T-cell lymphomas. Different types of lymphoma can develop from each type of lymphocyte, based on how mature the cells are when they become cancerous and other factors.

Treatment for non-Hodgkin lymphoma depends on which type it is, so it’s important for doctors to find out the exact type of lymphoma you have.

How non-Hodgkin lymphoma starts and spreads

Lymph tissue is found in many places throughout the body, so lymphomas can start almost anywhere.
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.

There are many different types of non-Hodgkin lymphoma, which can start in different parts of the body. This can affect which symptoms a person has.

Non-Hodgkin lymphoma can also grow and spread at different rates, depending on which type it is:

- Some types of lymphoma tend to grow and spread slowly. These are known as **indolent lymphomas**. 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.
- Some types of lymphoma tend to grow and spread quickly. These are known as **aggressive lymphomas**, and they 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 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.

• **References**


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Types of Non-Hodgkin Lymphoma

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 cells

The more common types of lymphoma are listed below according to whether they start in B lymphocytes (B cells) or T lymphocytes (T cells). Some rarer forms of non-Hodgkin lymphoma are not listed here.

B-cell lymphomas

B-cell lymphomas make up most (about 85%) of NHL in the United States.

Diffuse large B-cell lymphoma (DLBCL)

This is the most common type of NHL in the United States, accounting for about 1 out of every 3 lymphomas. The lymphoma cells look fairly large when seen with a microscope.

DLBCL can affect people of any age, but it occurs mostly in older people. (The average age at the time of diagnosis is mid-60s.) It usually starts as a quickly growing mass in a lymph node deep inside the body, such as in the chest or abdomen, or in a lymph node you can feel, such as in the neck or armpit. It can also start in other areas such as the intestines, bones, or even the brain or spinal cord.

DLBCL tends to be a fast-growing (aggressive) lymphoma, but it often responds well to treatment. Overall, about 3 out of 4 people will have no signs of disease after the initial treatment, and many are cured.

A common subtype of DLBCL is primary mediastinal B-cell lymphoma. This type of
lymphoma occurs mostly in young women. It starts in the mediastinum (the area in the middle of the chest behind the breastbone). It can grow quite large and can cause trouble breathing because it often presses on the windpipe (trachea) leading into the lungs. It can also block the superior vena cava (the large vein that returns blood to the heart from the arms and head), which can make the arms and face swell. This is a fast-growing lymphoma, but it usually responds well to treatment.

There are several other subtypes of DLBCL, but these are rare.

**Follicular lymphoma**

About 1 out of 5 lymphomas in the United States is a follicular lymphoma. This is usually a slow-growing (indolent) lymphoma, although some follicular lymphomas can grow quickly.

The average age for people with this lymphoma is about 60. It’s rare in very young people. Usually, this lymphoma occurs in many lymph node sites throughout the body, as well as in the bone marrow.

Follicular lymphomas often respond well to treatment, but they are hard to cure. These lymphomas may not need to be treated when they are first diagnosed. Instead, treatment may be delayed until the lymphoma starts causing problems. Over time, some follicular lymphomas turn into a fast-growing diffuse large B-cell lymphoma.

**Chronic lymphocytic leukemia (CLL) /small lymphocytic lymphoma (SLL)**

CLL and SLL are closely related diseases. In fact, many doctors consider them different versions of the same disease. The same type of cancer cell (known as a *small lymphocyte*) is seen in both CLL and SLL. The only difference is where the cancer cells are found. In CLL, most of the cancer cells are in the blood and bone marrow. In SLL, the cancer cells are mainly in the lymph nodes and spleen.

Both CLL and SLL are usually slow-growing (indolent) diseases, although CLL, which is much more common, tends to grow more slowly. Treatment is the same for CLL and SLL. They are usually not curable with standard treatments, but many people can live a long time (even decades) with them. Sometimes, these can turn into a more aggressive (fast-growing) type of lymphoma over time.

For more information, see [Chronic Lymphocytic Leukemia](#).
Mantle cell lymphoma (MCL)

About 5% of lymphomas are mantle cell lymphomas. MCL is much more common in men than in women, and it most often appears in people older than 60. When MCL is diagnosed, it is usually widespread in the lymph nodes, bone marrow, and often the spleen.

MCL can be challenging to treat. It tends to grow faster than indolent (slow-growing) lymphomas, but it doesn’t usually respond to treatment as well as aggressive (fast-growing) lymphomas. But newer treatments might offer a better chance for long-term survival for patients now being diagnosed.

Marginal zone lymphomas

Marginal zone lymphomas account for about 5% to 10% of lymphomas. They tend to be slow-growing (indolent). The cells in these lymphomas look small under the microscope. There are 3 main types of marginal zone lymphomas:

Extranodal marginal zone B-cell lymphoma, also known as mucosa-associated lymphoid tissue (MALT) lymphoma: This is the most common type of marginal zone lymphoma. It starts in places other than the lymph nodes (extranodal). Most MALT lymphomas start in the stomach and are linked to infection by Helicobacter pylori (the bacteria that causes many stomach ulcers). MALT lymphoma might also start in the lung, skin, thyroid, salivary glands, or tissues surrounding the eye. Usually the lymphoma stays in the area where it begins and is not widespread. Many of these other MALT lymphomas have also been linked to infections with bacteria or viruses.

The average age of people with MALT lymphoma at the time of diagnosis is about 60. This lymphoma tends to grow slowly and is often curable if found early. Doctors often use antibiotics as the first treatment for MALT lymphoma of the stomach, because treating the Helicobacter pylori infection often cures the lymphoma.

Nodal marginal zone B-cell lymphoma: This is a rare disease, found mainly in older women. It starts and usually stays in the lymph nodes, although lymphoma cells can also sometimes be found in the bone marrow.

This lymphoma tends to be slow-growing (although not usually as slow as MALT lymphoma), and is often curable if found early.

Splenic marginal zone B-cell lymphoma: This is a rare lymphoma. Most often the lymphoma is found only in the spleen and bone marrow.
It is most common in older men, and often causes fatigue and discomfort due to an enlarged spleen. Because the disease is slow-growing, it might not need to be treated unless the symptoms become troublesome. This type of lymphoma has been linked to infection with the hepatitis C virus.

**Burkitt lymphoma**

This fast-growing lymphoma is named after the doctor who first described this disease in African children and young adults. It makes up about 1% to 2% of all lymphomas. It is rare in adults, but is more common in children. It’s also much more common in males than in females.

The cells in Burkitt lymphoma are medium-sized. A similar kind of lymphoma, Burkitt-like lymphoma, has slightly larger cells. Because it is hard to tell these lymphomas apart, the WHO classification combines them.

Different varieties of this lymphoma are seen in different parts of the world:

- In the African (or endemic) variety, Burkitt lymphoma often starts as a tumor of the jaw or other facial bones. It is often linked to infection with the Epstein-Barr virus (EBV, which can also cause infectious mononucleosis or “mono”). This type of Burkitt lymphoma is rare in the United States.
- In the type seen more often in the United States, the lymphoma usually starts in the abdomen (belly), where it forms a large tumor. It can also start in the ovaries, testicles, or other organs, and can spread to the brain and spinal fluid. It is not usually linked to EBV infection.

Burkitt lymphoma grows very quickly, so it needs to be treated right away. But more than half of patients can be cured by intensive chemotherapy.

**Lymphoplasmacytic lymphoma (Waldenstrom macroglobulinemia)**

This slow-growing lymphoma is not common, accounting for only 1% to 2% of lymphomas. The lymphoma cells are small and found mainly in the bone marrow, lymph nodes, and spleen. This lymphoma is discussed in detail in Waldenstrom Macroglobulinemia.

**Hairy cell leukemia**

Despite the name, hairy cell leukemia (HCL) is sometimes considered to be a type of
lymphoma. It is rare – about 700 people in the United States are diagnosed with it each year. Men are much more likely to get HCL than women, and the average age at diagnosis is around 50.

The cells are small B lymphocytes with projections coming off them that give them a “hairy” appearance. They are typically found in the bone marrow and spleen and in the blood.

Hairy cell leukemia is slow-growing, and some people may never need treatment. An enlarging spleen or low blood cell counts (due to cancer cells invading the bone marrow) are the usual reasons to begin treatment. If treatment is needed, it’s usually very effective.

Hairy cell leukemia is also talked about in Chronic Lymphocytic Leukemia.

**Primary central nervous system (CNS) lymphoma**

This lymphoma involves the brain or spinal cord (the central nervous system, or CNS). The lymphoma is also sometimes found in tissues around the spinal cord or the eye. Over time, it tends to become widespread in the central nervous system.

Primary CNS lymphoma is rare overall, but it’s more common in older people and in people with immune system problems, such as those who have had an organ transplant or who have AIDS. Most people develop headaches and confusion. They can also have vision problems; weakness or altered sensation in the face, arms, or legs; and in some cases, seizures.

Historically, the outlook for patients with primary CNS lymphoma has not been as good as for many other lymphomas, but this is at least partly because people with CNS lymphoma tend to be older or have other serious health problems. Still, some people do well with treatment.

For information about lymphoma of the eye (primary intraocular lymphoma), which is related to primary CNS lymphoma, see Eye Cancer (Melanoma and Lymphoma).

**T-cell lymphomas**

T-cell lymphomas make up less than 15% of non-Hodgkin lymphomas in the United States. There are many types of T-cell lymphoma, but they are all fairly rare.
Precursor T-lymphoblastic lymphoma/leukemia

This disease accounts for about 1% of all lymphomas. It can be considered either a lymphoma or a type of acute lymphoblastic leukemia (ALL), depending on how much of the bone marrow is involved (leukemias have more bone marrow involvement). The cancer cells are very early forms of T cells.

This lymphoma often starts in the thymus (a small organ behind the breastbone and in front of the heart, which is where many T cells are made), and can grow into a large tumor in the mediastinum (the area between the lungs). This can cause trouble breathing and swelling in the arms and face.

This lymphoma is most common in teens or young adults, with males being affected more often than females.

This lymphoma is fast-growing, but if it hasn’t spread to the bone marrow when it is first diagnosed, the chance of cure with chemotherapy is quite good.

Often, the lymphoma form of this disease is treated in the same way as the leukemia form. For more information, see Acute Lymphocytic Leukemia (Adults).

Peripheral T-cell lymphomas

These uncommon types of lymphomas develop from more mature forms of T cells.

Cutaneous T-cell lymphomas (mycosis fungoides, Sezary syndrome, and others): These lymphomas start in the skin. Skin lymphomas account for about 5% of all lymphomas. They are described in Lymphoma of the Skin.

Adult T-cell leukemia/lymphoma: This lymphoma is caused by infection with a virus called HTLV-1. It is rare in the United States, and much more common in Japan, the Caribbean, and parts of Africa – where infection with HTLV-1 is more common. It can affect the bone marrow (where new blood cells are made), lymph nodes, spleen, liver, skin, and other organs. There are 4 subtypes:

- The smoldering subtype tends to grow slowly and has a good prognosis.
- The chronic subtype also grows slowly and has a good prognosis.
- The acute subtype is the most common. It grows quickly like acute leukemia, so it needs to be treated right away.
- The lymphoma subtype grows more quickly than the chronic and smoldering types,
but not as fast as the acute type.

**Angioimmunoblastic T-cell lymphoma:** This lymphoma accounts for about 4% of all lymphomas. It is more common in older adults. It tends to involve the lymph nodes as well as the spleen or liver, which can become enlarged. People with this lymphoma usually have fever, weight loss, and skin rashes and often develop infections. This lymphoma often progresses quickly. Treatment is often effective at first, but the lymphoma tends to come back (recur).

**Extranodal natural killer/T-cell lymphoma, nasal type:** This rare type often involves the upper airway passages, such as the nose and upper throat, but it can also invade the skin, digestive tract, and other organs. It is much more common in parts of Asia and South America. Cells of this lymphoma are similar in some ways to natural killer (NK) cells, another type of lymphocyte.

**Enteropathy-associated intestinal T-cell lymphoma (EATL):** EATL is a lymphoma that occurs in the lining of the intestine. This lymphoma is most common in the small intestine, but can also occur in the colon. Symptoms can include severe abdominal (belly) pain, nausea, and vomiting. There are 2 subtypes of this lymphoma:

- **Type I EATL** occurs in some people with celiac disease (also called gluten-sensitive enteropathy). Celiac disease is an autoimmune disease in which eating gluten, a protein found mainly in wheat and barley, causes the immune system to attack the lining of the intestine and other parts of the body. Type I EATL is rare among people who have had celiac disease since childhood, and is more common in people diagnosed as older adults. This lymphoma is more common in men than women.

- **Type II EATL** is not linked to celiac disease and is less common than type I.

**Anaplastic large cell lymphoma (ALCL):** About 2% of lymphomas are of this type. It is more common in young people (including children), but it can also affect older adults. This type of lymphoma tends to be fast-growing, but many people with this lymphoma can be cured.

There are different forms of ALCL:

- **Primary cutaneous ALCL** only affects the skin. This is discussed in more detail in [Lymphoma of the Skin](#).

- **Systemic ALCL** can affect the lymph nodes and other organs, including the skin. Systemic ALCL is divided into 2 types based on whether the lymphoma cells have a change in the ALK gene. ALK-positive ALCL is more common in younger people and tends to have a better prognosis (outlook) than the ALK-negative type.
• **Breast implant-associated ALCL** is a rare type of ALCL that can develop in the breasts of women who have had implants. It seems to be more likely to occur if the implant surfaces are textured (as opposed to smooth).

**Peripheral T-cell lymphoma, not otherwise specified (PTCL, NOS):** This name is given to T-cell lymphomas that don’t readily fit into any of the groups above. Most people diagnosed with these lymphomas are in their 60s. These lymphomas often involve the lymph nodes, but they can affect the skin, bone marrow, spleen, liver, and digestive tract, as well. As a group, these lymphomas tend to be widespread and grow quickly. Some patients respond well to chemotherapy, but over time these lymphomas tend to become harder to treat.

**References**


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## 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 2018:

• About 74,680 people (41,730 males and 32,950 females) will be diagnosed with
NHL. This includes both adults and children.

- About 19,910 people will die from this cancer (11,510 males and 8,400 females). The average American’s risk of developing NHL during his or her lifetime is about 1 in 47. But each person’s risk can be affected by a number of risk factors.

NHL can occur at any age. In fact, it is one of the more common cancers among children, teens, and young adults. 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 for more key statistics.

- References


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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. 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 methods, including new ways to collect the stem cells before the transplant.

Autologous transplants (which use stem cells from the patient rather than from another person) 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 otherwise 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) 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:

- Phosphatidyl-inositol 3 kinase (PI3K) inhibitors, such as duvelisib and
**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](#).

**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](#).

**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.

Many new monoclonal antibodies are being developed as well. One example is epratuzumab, which targets the CD22 antigen on certain lymphoma cells.

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.

- **CAT-8015 (moxetumomab pasudotox)** targets the CD22 antigen on certain lymphoma cells, bringing along a toxin known as PE38. An earlier version of this drug showed a great deal of promise in treating hairy cell leukemia (HCL) in early clinical trials.

Several other ADCs are now being studied as well, including pinatuzumab vedotin and IMG529.

**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. 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. CAR T-cell therapy 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.

**Antibiotics**

Some types of lymphoma are strongly linked to infections. Researchers are finding that in some cases, treating the infection actually helps treat the lymphoma. For example, gastric MALT lymphoma, which is linked to infection by the bacteria Helicobacter pylori, can often be treated with antibiotics. MALT lymphoma of the tissues around the eye (called ocular adnexal marginal zone lymphoma) has been linked to infection with the bacterium Chlamydophila psittaci. Some research has shown that treating this infection with an antibiotic (doxycycline) might make this lymphoma get better or even go away. More studies may be needed before antibiotics become part of the standard treatment for this type of lymphoma.

- **References**

Ferreri AJ, Govi S, Pasini E, et al. Chlamydophila psittaci eradication with doxycycline as first-line targeted therapy for ocular adnexae lymphoma: Final results of an


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 something that affects your chance of getting a disease such as 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.

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, and thyroid cancer.

Patients treated with radiation therapy for some other cancers, such as Hodgkin lymphoma, 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) 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**. 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.
- *Chlamydophila 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 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 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 surfaces (as opposed to smooth surfaces).

- **References**


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.

Still, 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. But NHL is not one of the cancer types often caused by these inherited mutations. In other words, having a family history of lymphoma does not 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.

For some types of lymphoma, some of the gene changes that led to the 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.

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


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, AIDS, and Cancer.

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* 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 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 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 may help protect against lymphoma, but more research is needed to confirm this.

- References


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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.

- **What Should You Ask Your Doctor 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, 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** 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.

- **References**


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. Some common signs and symptoms include:

- Enlarged lymph nodes
- Fever
- Sweating and chills
- Weight loss
- Fatigue (extreme tiredness)
- Swollen abdomen (belly)
- Feeling full after only a small amount of food
- Chest pain or pressure
- Shortness of breath or cough

Swollen lymph nodes

Non-Hodgkin lymphoma can cause lymph nodes to become enlarged. When this occurs in 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), they 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.

General symptoms
Non-Hodgkin lymphoma often causes general symptoms, such as:

- Fever
- Sweating and chills, especially at night
- Unexplained weight loss
- Feeling very tired
- Severe or frequent infections
- Easy bruising or bleeding

**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.)

Having one or more of the symptoms above doesn’t mean you definitely have lymphoma. In fact, many of these symptoms 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.

• References


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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.

**Medical history and physical exam**

Your doctor will want to get a thorough medical history, including information about your symptoms, possible risk factors, 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 in the part of the body near the swollen lymph nodes.

The doctor also might order blood tests to look for signs of infection or other problems. 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**

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 nodes shrink. If the nodes stay the same or continue to grow, the doctor might order a biopsy. Either a small piece of a node or, more commonly, the entire node is removed for viewing under the microscope and for other lab tests.

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**

A biopsy is the only way to confirm a person has NHL. 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. 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, the patient will be sedated or given general anesthesia (drugs are used to put the patient into a deep sleep). This method almost always provides enough of a sample to diagnose the exact type of non-Hodgkin lymphoma.

**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). 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).

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 to diagnose and classify lymphoma, even after a needle biopsy has been done.

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 patients 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 withdrawn and looked at under the microscope to check for lymphoma cells.

Lab tests on biopsy samples
All biopsy samples and fluids are looked at under a microscope 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, samples of cells are treated with antibodies that stick to certain proteins on cells. For immunohistochemistry, the cells are then looked at under a microscope to see if the antibodies stuck to them (meaning they have these proteins), For flow cytometry, a special machine is used to look for the antibodies.

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 under the microscope. 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 looked at under a microscope to see if the chromosomes have any abnormalities. A drawback of this test is that it usually takes about 2 to 3 weeks because the cells must grow in lab dishes for a couple of weeks before their chromosomes are ready to be viewed under the microscope.
- **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, which is why this test is now used in many medical centers.
- **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.

**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 to look for enlarged lymph nodes in this area.

**Computed tomography (CT) scan**

A CT scan 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 under a microscope.

**Magnetic resonance imaging (MRI) scan**

Like CT scans, MRI scans 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 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. (It can't be used to look at lymph nodes in the chest because the ribs block the sound waves.)

**Positron emission tomography (PET) scan**

For a [PET scan](#), 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.

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

- They can help tell if an enlarged lymph node contains lymphoma.
- They can help spot small areas in the body that might be lymphoma, even if the area looks normal on a CT scan.
- They can help tell if a lymphoma is responding to 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 take up the radioactive sugar.
- They can be used after treatment in helping decide whether an enlarged lymph node still contains lymphoma or is just scar tissue.

**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 not usually done unless a person is having bone pain or has lab test 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 picked up 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 measure the amounts of certain types of cells and chemicals in the blood. They 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 kidney and liver function.
  - 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.

**References**

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. Doctors also use a cancer’s stage when talking about survival statistics.

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 but not the combination of underarm and groin nodes (II).
- 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.

How staging might affect treatment

The stage of a lymphoma is often 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 and Treating T-cell Non-Hodgkin Lymphomas for more on this.

- References

Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation,


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

**Living as a Cancer Survivor**

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

- Living as a Brain or Spinal Cord Tumor Survivor

Survival rates tell you what portion 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
about how likely it is that your treatment will be successful. Some people will want to
know the survival rates for their cancer, and some people won’t. If you don’t want to
know, you don’t have to.

**What is a 5-year survival rate?**

Statistics on the outlook for a certain type of cancer are often given as 5-year survival
rates. The 5-year survival rate is the percentage of people who live at least 5 years after
being diagnosed with cancer. For example, a 5-year survival rate of 70% means that an
estimated 70 out of 100 people who have that cancer are still alive 5 years after being
diagnosed. Keep in mind, however, that many of these people live much longer than 5
years after diagnosis.

**Relative survival rates** are a more accurate way to estimate the effect of cancer on
survival. These rates compare people with a certain type of cancer to similar people in
the overall population. For example, if the 5-year relative survival rate for a type of
cancer is 80%, it means that people who have that type of cancer are, on average,
about 80% as likely as people who don’t have that cancer to live for at least 5 years
after being diagnosed.

But remember, all survival rates are estimates – your outlook can vary based on a
number of factors specific to you.

**Cancer survival rates don’t tell the whole story**

Survival rates are often based on previous outcomes of large numbers of people who
had the disease, but they can’t predict what will happen in any particular person’s case.
There are a number of limitations to remember:

- The numbers below are among the most current available. But to get 5-year (or 10-
year) survival rates, doctors have to look at people who were treated at least 5 (or
10) years ago. As treatments are improving over time, people who are now being
diagnosed with non-Hodgkin lymphoma (NHL) may have a better outlook than
these statistics show.
- These statistics are based on when the cancer was first diagnosed. They do not
apply to cancers that later come back or spread, for example.
- The outlook for people with lymphoma varies by the type and stage (extent) of the
lymphoma – in general, the survival rates are higher for people with earlier stage cancers. But other factors can also affect a person’s outlook (see below). The outlook for each person is specific to their circumstances. Your doctor can tell you how these numbers may apply to you, as he or she is familiar with your particular situation.

Survival rates for non-Hodgkin lymphoma

The overall 5-year relative survival rate for people with NHL is 70%, and the 10-year relative survival rate is 60%. But it’s important to keep in mind that survival rates can vary widely for different types and stages of 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 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 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 (serum) level of lactate dehydrogenase (LDH), which goes up with the amount of lymphoma in the body

<table>
<thead>
<tr>
<th>Good prognostic factors</th>
<th>Poor prognostic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 60 or below</td>
<td>Age above 60</td>
</tr>
<tr>
<td>Stage I or II</td>
<td>Stage III or IV</td>
</tr>
<tr>
<td>No lymphoma outside of lymph nodes, or lymphoma in only 1 area outside of lymph nodes</td>
<td>Lymphoma is in more than 1 organ of the body outside of lymph nodes</td>
</tr>
<tr>
<td>PS: Able to function normally</td>
<td>PS: Needs a lot of help with daily activities</td>
</tr>
<tr>
<td>Serum LDH is normal</td>
<td>Serum LDH is high</td>
</tr>
</tbody>
</table>

Each poor prognostic factor is assigned 1 point. People with no poor prognostic factors would have a score of 0, while those with all of the 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)

In the studies used to develop the index, about 75% of people in the lowest risk group lived at least 5 years, whereas only about 30% of people in the highest risk group lived at least 5 years. These numbers show the difference the index scores can make, but the IPI was devised in the early 1990s. Newer treatments have been developed since then, so current survival rates are likely to be higher.

**Revised International Prognostic Index**

A more recent version of the IPI is based on people with fast-growing lymphomas who have received more modern treatment, including a newer drug called rituximab (Rituxan), which is described in Immunotherapy for Non-Hodgkin Lymphoma. The revised IPI uses the same factors but divides patients into only 3 risk groups:

- Very good (no poor prognostic factors)
- Good (1 or 2 poor prognostic factors)
- Poor (3 or more poor prognostic factors)

In the study used to develop this index, about 95% of people in the very good risk group lived at least 4 years, whereas only about 55% of people in the poor risk group lived at least 4 years.

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.

**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.

<table>
<thead>
<tr>
<th>Good prognostic factors</th>
<th>Poor prognostic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 60 or below</td>
<td>Age above 60</td>
</tr>
<tr>
<td>Stage I or II</td>
<td>Stage III or IV</td>
</tr>
</tbody>
</table>
Blood hemoglobin 12 g/dL or above  Blood hemoglobin level below 12 g/dL
4 or fewer lymph node areas affected  More than 4 lymph node areas affected
Serum LDH is normal  Serum LDH is high

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

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

The study used to develop the FLIPI produced the following survival rates:

<table>
<thead>
<tr>
<th>Risk group</th>
<th>5-year survival rate</th>
<th>10-year survival rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk</td>
<td>91%</td>
<td>71%</td>
</tr>
<tr>
<td>Intermediate-risk</td>
<td>78%</td>
<td>51%</td>
</tr>
<tr>
<td>High-risk</td>
<td>53%</td>
<td>36%</td>
</tr>
</tbody>
</table>

These rates reflect the number of people who lived for at least 5 or 10 years after being diagnosed – many people lived longer than this. The rates were based on people diagnosed with follicular lymphoma in the 1980s and 1990s. Newer treatments have been developed since then, so current survival rates are likely to be higher.

Remember, all of these survival rates are only estimates – they can’t predict what will happen to any individual person. We understand that these statistics can be confusing and may lead you to have more questions. Talk to your doctor to better understand your specific situation.

- References


What Should You Ask Your Doctor About Non-Hodgkin Lymphoma?

It’s important to have honest, open discussions with your cancer care team. You should feel free to ask any question, no matter how minor it might seem. For instance, consider these questions:

**When you’re told you have non-Hodgkin lymphoma**

- What type of non-Hodgkin lymphoma 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? What do you recommend, and why?
- Do we need to treat the lymphoma right away?
- Should I get a second opinion 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?
• 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?

After treatment

• What type of follow-up 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 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.

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For additional assistance please contact your American Cancer Society
1-800-227-2345 or [www.cancer.org](http://www.cancer.org)
Non-Hodgkin Lymphoma Treatment

If you’ve been diagnosed with non-Hodgkin lymphoma (NHL), your cancer care team will discuss treatment options with you. It’s important to think carefully about your choices. You will want to weigh the benefits of each treatment option against the possible risks and side effects.

Which treatments are used for non-Hodgkin lymphoma?

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

- Chemotherapy
- Immunotherapy
- Targeted therapy
- Radiation therapy
- Stem cell transplant
- Surgery (in rare cases)

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.

To learn about the most common approaches to treating different types of NHL, see:

- Treating B-cell non-Hodgkin lymphomas
- Treating T-cell non-Hodgkin lymphomas
- Treating HIV-associated lymphoma

What types of doctors treat non-Hodgkin lymphoma?
Based on your treatment options, you may have different types of doctors on your treatment team. These doctors could include:

- A **hematologist**: a doctor who treats disorders of the blood, including lymphomas.
- A **medical oncologist**: a doctor who treats cancer with medicines.
- A **radiation oncologist**: a doctor who treats cancer with radiation therapy.

Many other specialists might be part of your treatment team as well, including physician assistants (PAs), nurse practitioners (NPs), nurses, nutrition specialists, social workers, and other health professionals. See [Health Professionals Associated With Cancer Care](#) for more on this.

## 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 best decision for you. 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 you’re not sure about something. You can find some good questions to ask in [What Should You Ask Your Doctor About Non-Hodgkin Lymphom?](#)

## Getting a second opinion

If time allows, you may also want to get a second opinion. This can give you more information and help you feel more certain about the treatment plan you choose. If you aren’t sure where to go for a second opinion, ask your doctor for help.

## 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. Sometimes 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 are 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. See [Clinical Trials](#) to learn more.
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 dangerous.

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. See Complementary and Alternative Medicine to learn more.

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 can be 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, support groups, 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 on call 24 hours a day, every day.

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.

- References
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 and the stage 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

**Others**

- Vincristine
- Doxorubicin (Adriamycin)
- 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 may 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 may 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*
- *Mouth sores*
- *Loss of appetite*
- *Nausea and vomiting*
- *Diarrhea* or *constipation*
- Increased chance of *infection* (from a shortage of white blood cells)
- *Bleeding or bruising* after minor cuts or injuries (from a shortage of platelets)
Fatigue and shortness of breath (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), 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 (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.

To learn more about chemo, see the Chemotherapy section of our website.

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.

**References**


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**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 \textit{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).

\textbf{Antibodies that target CD20}

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

- \textbf{Rituximab (Rituxan)}: This drug is often used along with chemotherapy for some types of NHL, but it may also be used by itself.
- \textbf{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.
- \textbf{Ofatumumab (Arzerra)}: This drug is used mainly in patients with SLL/CLL that is no longer responding to other treatments.
- \textbf{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. These are usually 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 hepatitis B infections that were inactive 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.

**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 lymphoma, especially 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.

**Interferon**

Interferon is a chemical made by white blood cells that can help boost the immune system. Some studies have suggested that giving man-made interferon can make some types of lymphomas shrink or stop growing.

Common side effects of this treatment include fatigue, fever, chills, headaches, muscle and joint aches, and mood changes. Because of the side effects, interferon is not used very often. It might be given to some patients in addition to chemotherapy.

**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.

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

For more on immunotherapy, see Cancer Immunotherapy.

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. Most CAR T-cell therapies are still being studied and only available in clinical trials. There is one CAR T-cell therapy that is FDA approved to treat certain kinds of large B-cell lymphoma.

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.

To learn more, see CAR T-Cell Therapies.
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 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.

For more general information about targeted therapy, see [Targeted Therapy](#).

- **References**


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** in areas getting radiation, ranging from redness to blistering and peeling
- **Feeling tired**
- **Nausea**
- **Diarrhea**

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** and increase the risk of infections.

Radiation to the head and neck area can lead to **mouth sores** and **trouble swallowing**. Some people later have problems with **dry mouth**.
Often these effects go away shortly after treatment is finished.

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

Possible long-term side effects of radiation therapy can be more serious:

- Radiation to the chest might damage the lungs and lead to trouble breathing. It can also affect the heart, making you more likely to have 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. Radiation to the neck may also increase the risk of stroke many years later.
- Side effects of brain radiation therapy usually become most 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. This happens rarely.

To learn more about radiation therapy, see the Radiation Therapy section of our website.

- References


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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.

- 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.

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

- **References**


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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.

- References


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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.

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 refuse to have 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 working.
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 the Palliative or Supportive Care section of our website.

- **References**


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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 and the stage (extent) of the disease, 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. 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. The main treatment is usually about 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. Often, the doctor will order a biopsy of the chest tumor to confirm that lymphoma is still present before starting radiation.

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]), chemo alone, 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.

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 (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, 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 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 3 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, the treatment is the same as for DLBCL (see above).
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.

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 Leukemia.) 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 trial.

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
- R-CHOP followed by rituximab plus ifosfamide, carboplatin, and etoposide (known as RICE)

Less intense chemo regimens may be used for people who are older or who have other health issues.

If the lymphoma responds well to initial treatment, a stem cell transplant may be a good option.

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.

**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 \textit{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.

\textbf{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.

\textbf{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).

\textbf{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).

\textbf{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
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.

**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.

**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.

Treatment of lymphoma of the eye (primary intraocular lymphoma) is discussed in Treating Eye Cancer.

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.

- **References**


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Treating T-Cell Non-Hodgkin Lymphomas

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.

Precursor 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), 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 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) and Treating Childhood Leukemia.

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.

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, 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. 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 are not fit 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). 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 the monoclonal antibody brentuximab vedotin (Adcetris).

For anaplastic large cell lymphoma associated with a breast implant, experts typically
recommend removing the implant and the capsule surrounding it (that contains the lymphoma). 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. Stem cell transplants 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 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.

- **References**


Treating HIV-Associated Lymphoma

People with HIV infections 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.

- References

Lippincott Williams & Wilkins; 2015.


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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.) This is a very common worry if you’ve had cancer.

For some people, the lymphoma may never go away completely. 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 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 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. 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*](https://example.com).

**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](https://example.com), [eating well](https://example.com), [getting regular physical activity](https://example.com), and [staying at a healthy weight](https://example.com) 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](https://example.com) (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.

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.

- References


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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
- Lung cancer
- Kidney cancer
- Kaposi sarcoma
- Cancers of the head/neck area (includes the lip, tongue, floor of the mouth, throat, salivary glands, and voice box)
- Colon cancer
- Thyroid cancer
- Bone and soft tissue cancer
- Bladder cancer
- Leukemia and myelodysplastic syndrome
- Hodgkin disease

Radiation therapy to the chest increases the risk of breast cancer in women who were treated before age 30. Mesothelioma, 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.org.

Lymphoma survivors should also follow the American Cancer Society recommendations for the early detection of cancer, 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. 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
- Stay physically active
- Eat a healthy diet, with an emphasis on plant foods
- Limit alcohol 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 for more information about causes of second cancers.

References


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