Overall, non-Hodgkin lymphoma (NHL) is the seventh most common cancer affecting adults in the United States. The incidence of NHL in the United States nearly doubled between 1975 and 2013, while the rates have plateaued over the last several years. Currently, more than 74,000 new cases are diagnosed each year.

NHL is not a single cancer, but rather a group of several closely related cancers, called lymphoid neoplasms. The most recent 2016 revision of the World Health Organization (WHO) classification of lymphoid neoplasms estimates that there are approximately 85 subtypes of NHL. Among these, three lymphoma subtypes make up the majority of NHLs. These most common types of NHL in the United States are diffuse large B-cell lymphoma (DLCBL; 21%), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL; 18%), and follicular lymphoma (FL; 11%). Although the various types of NHL share many common characteristics, they differ in certain features, including their appearance under the microscope, their molecular features and growth patterns, their impact on the body, and how they respond to different types of treatment. For more in-depth information on NHL, please see the Lymphoma Research Foundation’s (LRF’s) booklet Understanding Non-Hodgkin Lymphoma: A Guide for Patients, Survivors, and Loved Ones at lymphoma.org/publications or call the LRF Lymphoma Helpline at 800-500-9976 to order a copy.

NHL is broadly categorized into two groups: B-cell lymphomas and natural killer (NK)/T-cell lymphomas. B-cell lymphomas develop from abnormal B cells and account for about 90 percent of all NHLs. NK/T-cell lymphomas develop from abnormal T cells or NK cells and account for about 10 percent of all NHLs. NHL subtypes are also classified as either indolent (slow-growing) or aggressive (fast-growing).

Common signs and symptoms of NHL include swelling of the lymph nodes (which is often but not always painless), fever, night sweats, unexplained weight loss, and lack of energy. While most people with these symptoms will not have NHL, anyone with persistent symptoms (lasting more than several weeks) should be discussed and seen by a physician.

**DIAGNOSIS AND STAGING**

A biopsy (a procedure that collects a sample of the tumor) of an affected lymph node is the only way to make a definite diagnosis of NHL. A pathologist (doctor who specializes in the diagnosis of diseases by studying the cells from a patient’s body fluids and tissue samples) or a hematopathologist (pathologist who has undergone additional training in the diagnosis of blood cancers, including lymphoma) who is experienced in diagnosing lymphoma should review the biopsy. There are multiple subtypes of NHL, many of which are very uncommon, and highly specialized procedures and tests may be needed in order to make an accurate diagnosis. An accurate diagnosis and knowing the exact NHL subtype help identify appropriate treatment options to most effectively treat the patient’s particular subtype of lymphoma.

Generally speaking, NHL is systemic (throughout the body). Staging is a process used to describe where the cancer is located and how widely the cancer has spread. The Lugano classification of the Ann Arbor staging system is used for most NHLs. To stage a lymphoma, the physician may order imaging tests such as abdominal and chest computed tomography (CT) scans or a positron emission tomography (PET) scan. A CT scan allows the physician to see inside the chest and abdomen, locating the tumor. PET scans are a form of imaging that incorporates a special dye that contains tracers and are used to track changes with the cancer. Other staging tests may...
include a bone marrow biopsy, spinal tap, endoscopy/colonoscopy, and magnetic resonance imaging (MRI). Physicians may also request blood tests and an echocardiogram to help evaluate overall health.

**RISK FACTORS**
The characteristics that make a person possibly more susceptible to developing any type of disease are called risk factors. Having one or more risk factors does not mean a person will develop NHL. People with a family history appear to be at slightly higher risk of developing lymphoma, often of the same subtype. Nonetheless, the likelihood of two first-degree relatives having lymphoma remains very small. In fact, most people with the known risk factors never develop NHL, and many people diagnosed with NHL do not have any of these risk factors. The causes of NHL in most cases remain unknown. Nevertheless, known risk factors for NHL include:

- A weakened immune system caused by an inherited immune disorder (for example, hypogammaglobulinemia or Wiskott-Aldrich syndrome) or infection with human immunodeficiency virus (HIV; the virus that causes AIDS)
- An autoimmune disease (for example, Crohn’s disease, rheumatoid arthritis, systemic lupus erythematosus, or psoriasis)
- Treatment for autoimmune diseases, especially with methotrexate and tumor necrosis factor-inhibitor therapy
- Treatment with certain drugs used after organ transplantation
- Infections with certain viruses (for example, Epstein-Barr virus [EBV], human T-cell lymphotropic virus type 1 [HTLV-1], or hepatitis C virus [HCV])
- Infection with the bacteria *H. pylori, Campylobacter jejuni,* or *Chlamydia psittaci*
- Older age—Like most cancers, NHL is much more common in adults older than 60 years, although it may develop in children and adults of all ages
- Male (for unknown reasons, NHL is slightly more common in men than in women)
- Exposure to certain chemicals such as some herbicides (for example, Agent Orange) and pesticides, and some chemotherapy drugs used to treat other cancers or autoimmune diseases
- Treatment with radiation therapy for other cancers, including NHL

**TREATMENT OPTIONS**
For patients who do not show any signs or symptoms of lymphoma an active surveillance approach may be taken. Active surveillance is also known as watchful waiting (observation with no treatment [drug therapy, radiation therapy, or stem cell transplantation] given) and the lymphoma is monitored with regular checkups. For patients who show symptoms or for those whose lymphoma begins to progress after a period of active surveillance, a multitude of highly effective treatment options exist for patients with NHL, including:

- Chemotherapy (common treatments are bendamustine or CHOP [cyclophosphamide, doxorubicin, vincristine, and prednisone])

**TYPES AND SUBTYPES OF NHL**
The classification of lymphoma is complicated and has evolved over the years. NHL subtypes are grouped according to which kind of lymphocyte is affected [B cells or NK/T cells] and how quickly the cancer grows (aggressive or indolent). Within each type of lymphoma (for example, B cell), there are many subtypes. There are more subtypes of NHL than those listed here. Please consult with a physician if you are not sure of your subtype. Knowing as much as possible about your lymphoma subtype, treatment options and their potential side effects can empower you to take charge of your health and better communicate with your physician. New research studies are defining different subsets that impact treatment decisions. The following list includes selected lymphoid malignancies in the current WHO classification.

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**Aggressive B-cell NHLs include the following subtypes:**

- Burkitt lymphoma
- Diffuse large B-cell lymphoma (DLBCL)
- High-grade B-cell lymphoma, also known as double-hit lymphoma (DHL)
- Mantle cell lymphoma (MCL), sometimes classified as indolent

**Aggressive T-cell NHLs include the following subtypes:**

- Peripheral T-cell lymphoma (PTCL)
- Anaplastic large cell lymphoma (ALCL)
- Angioimmunoblastic T-cell lymphoma (AITL)
- Adult T-cell leukemia/lymphoma (ATLL)

**Indolent B-cell NHLs include the following subtypes:**

- Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
- Follicular lymphoma (FL)
- Marginal zone lymphoma (MZL)
- Lymphoplasmacytic lymphoma/Waldenström macroglobulinemia (WM)

**Indolent T-cell NHLs include the following subtypes:**

- Cutaneous T-cell lymphoma (CTCL)
- Mycosis fungoides (MF)
• Immunotherapy (includes the use of monoclonal antibodies, antibody-drug conjugates, radioimmunotherapy, immunomodulatory drugs, and chimeric antigen receptor [CAR] T-cell therapy)
• Targeted therapies
• Radiation therapy
• Stem cell transplantation

The physician considers many factors when deciding the most appropriate form of treatment, including the type and subtype of NHL; the stage of the lymphoma; the symptoms (if any); the prior therapies; the patient’s age and overall health (for example, other conditions the patient may have); and the patient’s goals for treatment.

Sometimes after an initial treatment, the lymphoma may relapse (returns after treatment) or become refractory (does not respond to treatment). However, numerous treatment options exist for patients with relapsed/refractory NHL.

TREATMENTS UNDER INVESTIGATION

Many treatments at different stages of drug development are currently being tested in clinical trials for various subtypes of NHL. It is critical to remember that today’s scientific research is continuously evolving. Treatment options may change as new treatments are discovered and current treatments are improved. Therefore, it is important that patients check with their physician or with LRF for any treatment updates that may have recently emerged.

CLINICAL TRIALS

Clinical trials are crucial in identifying effective drugs and determining optimal doses for patients with lymphoma. Patients interested in participating in a clinical trial should view the Understanding Clinical Trials fact sheet on LRF’s website at www.lymphoma.org/publications, talk to their physician, or contact the LRF Helpline for an individualized clinical trial search by calling 800-500-9976 or emailing helpline@lymphoma.org.

FOLLOW-UP

Patients with lymphoma should have regular visits with a physician who is familiar with their medical history and the treatments they may have received. Medical tests (such as blood tests, CT scans, and PET scans) may be required at various times during remission to evaluate the need for additional treatment. Some treatments can cause long-term effects or late side effects, which can vary based on duration and frequency of treatments, age, gender, and the overall health of each patient at the time of treatment. A physician will check for these effects during follow-up care. Visits may become less frequent the longer the lymphoma remains in remission.

Patients and their caregivers are encouraged to keep copies of all medical records and test results as well as information on the types, amounts, and duration of all treatments received. This documentation will be important for keeping track of any effects resulting from treatment or potential lymphoma recurrences. LRF’s award-winning Focus On Lymphoma mobile app (lymphoma.org/mobileapp) and Lymphoma Care Plan (lymphoma.org/publications) can help patients manage this documentation.

PATIENT AND CAREGIVER SUPPORT SERVICES

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. One-to-one peer support programs, such as LRF’s Lymphoma Support Network, connects patients and caregivers with volunteers who have experience with non-Hodgkin lymphoma, similar treatments, or challenges, for mutual emotional support.

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Patient Education

LRF offers a wide range of opportunities to learn about lymphoma.

• Ask the Doctor About Lymphoma is a national series of two-hour, topic-specific, community-based programs that combine a presentation by a medical doctor with an extensive question-and-answer session.
• Living with Lymphoma podcast helps the lymphoma community better understand how to cope with the unique circumstances that a diagnosis of lymphoma presents.
• Lymphoma Workshops are regional, full-day educational programs that provide the latest information about lymphoma, current treatment options, and patient support issues.
• The North American Educational Forum on Lymphoma is held annually and provides critical information on treatment options, patient support issues, and the latest in lymphoma research.
• Webinars are hour-long, interactive programs that provide an opportunity to learn more about lymphoma, treatments, and promising research from leading lymphoma experts.
Patient Publications
LRF offers a series of print and digital patient education publications. LRF offers comprehensive guides on non-Hodgkin lymphoma (NHL), Hodgkin lymphoma (HL), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), and the transplantation process in lymphoma, along with a variety of lymphoma- and topic-specific fact sheets. Contact the LRF Helpline at (800) 500-9976 or visit our website at lymphoma.org/publications.

Mobile App
Focus On Lymphoma is the first mobile application (app) that provides patients and caregivers comprehensive content based on their lymphoma subtype and tools to help manage their lymphoma such as, keep track of medications and blood work, track symptoms, and document treatment side effects. The Focus On Lymphoma mobile app is available for download for iOS and Android devices in the Apple App Store and Google Play. For additional information on the mobile app, visit FocusOnLymphoma.org.

To learn more about any of these resources, visit our website at lymphoma.org, or contact the LRF Helpline at 800-500-9976 or helpline@lymphoma.org.

Resources
LRF offers a wide range of resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma including our award-winning mobile app. LRF also provides many educational activities, from in-person meetings to webinars for people with lymphoma, as well as patient guides and e-Updates that provide the latest lymphoma-specific news and treatment options.