



PROVIDING THE LATEST INFORMATION FOR  
PATIENTS & CAREGIVERS

# Hodgkin Lymphoma



Revised **2024**

---

## A six-word narrative about living with blood cancer from patients in our LLS Community

---

Stay strong and keep moving forward. Find the positive in every day. Be your own best patient advocate. Changed my life for the better. Accept, learn and focus on present. Learning to live a different life. Sudden and life changing—be positive. Waiting, worrying, anxiousness/happy I'm alive! Embrace a new normal each day. 5 years, 41 infusions, constant fatigue. Patience, positive attitude, hope and faith. Test to test, I will survive! Treatment, fatigue, treatment, fatigue and survival. Love life, live better every day. I don't look back only forward. So far, so good, live life. Meditation, mindfulness, wellness, faith, nutrition and optimism. Finding the joy while living with uncertainty. Watch, wait, treat, regroup, rest, re-energize. Blessed to be doing so well! Eye opening needed learning and healing. Feel great: uncertain travel plans annoying. Renewed faith, meditation, diet, mindfulness, gratitude. Watchful waiting can be watchful worrying. Scary, expensive, grateful, blessings, hope, faith. Thank god for stem cell transplants! Do not know what to expect. Extraordinarily grateful, I love my life. Diagnosed; frightened; tested; treating; waiting; hoping. I'm more generous, impatient less often. Embrace your treatment day after day. Live today, accept tomorrow, forget yesterday. Strength you never realized you had. Challenging to our hearts and minds. Life is what we make it. Live life in a beautiful way.



Discover what thousands already have at  
[www.LLS.org/Community](http://www.LLS.org/Community)

Join our online social network for people who are living with or supporting someone who has a blood cancer. Members will find

- Thousands of patients and caregivers sharing experiences and information, with support from knowledgeable staff
- Accurate and cutting-edge disease updates
- The opportunity to participate in surveys that will help improve care.

## Inside This Booklet

- 3** Introduction
- 3** Hodgkin Lymphoma Basics
- 5** Signs and/or Symptoms
- 6** Diagnosis
- 8** Hodgkin Lymphoma Subtypes
- 10** Staging
- 14** Treatment Planning
- 17** Treatment for Classical Hodgkin Lymphoma
- 23** Drug Information
- 29** Monitoring Treatment Response and Assessing Measurable Residual Disease
- 33** Treatment for Nodular Lymphocyte-Predominant B-cell Lymphoma (NLPBL)
- 34** Treatment for Relapsed or Refractory Classical Hodgkin Lymphoma in Adults
- 36** Hodgkin Lymphoma in Children and Adolescents
- 41** Hodgkin Lymphoma and Young Adults
- 41** Hodgkin Lymphoma and Pregnancy
- 41** Hodgkin Lymphoma in Older Adults
- 42** Monitoring After Completion of Treatment
- 43** Clinical Trials for Blood Cancers
- 45** Financial Concerns
- 45** Side Effects and Complications
- 48** Survivorship
- 53** Incidence, Causes and Risk Factors
- 55** Normal Blood and Bone Marrow
- 58** The Lymphatic System
- 59** Resources and Information
- 62** Health Terms
- 68** References

## Acknowledgements

The Leukemia & Lymphoma Society appreciates the review of this material by:

**Ann S. LaCasce, MD, MMSc**

Director, Dana-Farber/Mass General Brigham Fellowship in Hematology/Oncology,  
Associate Professor of Medicine, Harvard Medical School  
Boston, MA  
and

**Sharon Castellino MD, MSc**

Professor of Pediatrics, Emory University School of Medicine  
Member, Winship Cancer Institute  
Director, Leukemia/Lymphoma Program  
The Aflac Cancer & Blood Disorders Center  
Children's Healthcare of Atlanta  
Atlanta, GA

Support for this publication is provided by Pfizer Oncology.

This publication is designed to provide accurate and authoritative information about the subject matter covered. It is distributed as a public service by The Leukemia & Lymphoma Society (LLS), with the understanding that LLS is not engaged in rendering medical or other professional services. LLS carefully reviews content for accuracy and confirms that all diagnostic and therapeutic options are presented in a fair and balanced manner without particular bias to any one option.

## List of Figures and Tables

### Figures

- 4 **Figure 1.** Hodgkin Lymphoma and the Lymphatic System
- 14 **Figure 2.** Hodgkin Lymphoma Stages
- 53 **Figure 3.** Age-Specific Incidence Rates for Hodgkin Lymphoma, 2015-2019
- 57 **Figure 4.** Blood Cell and Lymphocyte Development

### Tables

- 9 **Table 1.** World Health Organization: Classification of Hodgkin Lymphoma Subtypes
- 13 **Table 2.** Lugano Classification System for Hodgkin Lymphoma (HL)
- 15 **Table 3.** Risk Factors for Early-Stage (Stage I and II) Favorable or Unfavorable Hodgkin Lymphoma According to EORTC and GHLSG
- 16 **Table 4.** Adverse Prognostic Factors for Advanced-Stage Classical Hodgkin Lymphoma
- 23 **Table 5.** Drug Classes and Drug Mechanisms
- 25 **Table 6.** Some Drugs Used in the Treatment of Hodgkin Lymphoma
- 28 **Table 7.** Some Drug Combinations Used to Treat Hodgkin Lymphoma
- 31 **Table 8.** Some Treatment Approaches for Classical Hodgkin Lymphoma in Adults Based on Stage
- 35 **Table 9.** Some Treatment Approaches for Relapsed or Refractory Hodgkin Lymphoma
- 38 **Table 10.** Some Drug Combinations Used to Treat Children and Adolescents Who Have Classical Hodgkin Lymphoma Based on Risk Group
- 39 **Table 11.** Some Drug Combinations Used to Treat Children and Adolescents Who Have Relapsed or Refractory Classical Hodgkin Lymphoma

# Introduction

“Lymphoma” is a general term for a group of blood cancers that originate in the lymphatic system. The lymphatic system is part of the body’s immune system. It is made up of tissues and organs that produce, store and carry white blood cells throughout the body to fight infections and diseases.

There are two major types of lymphoma: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Both types are further classified into subtypes. Knowing your subtype is important because your treatment is based on the subtype. A discussion of HL subtypes begins on page 8.

This booklet provides information about HL for patients and their families. It also includes brief descriptions of normal blood and bone marrow and the lymphatic system, as well as definitions of medical terms.

Advances in the treatment of HL are resulting in improved remission (a decrease or disappearance of the signs and symptoms of the disease) and cure rates. According to the National Cancer Institute, up to 90% of all newly diagnosed cases of HL can be cured with chemotherapy and/or radiation. New treatment approaches are being studied in clinical trials for patients of all ages and at all stages of the disease.

**All LLS publications mentioned in this booklet are free and can be viewed, downloaded or ordered online at [www.LLS.org/booklets](http://www.LLS.org/booklets).**

**Feedback.** Visit [www.LLS.org/PublicationFeedback](http://www.LLS.org/PublicationFeedback) to give suggestions about this booklet.

New treatments may have been approved since this book was printed.  
Check [www.LLS.org/DrugUpdates](http://www.LLS.org/DrugUpdates) or call (800) 955-4572.

## Hodgkin Lymphoma Basics

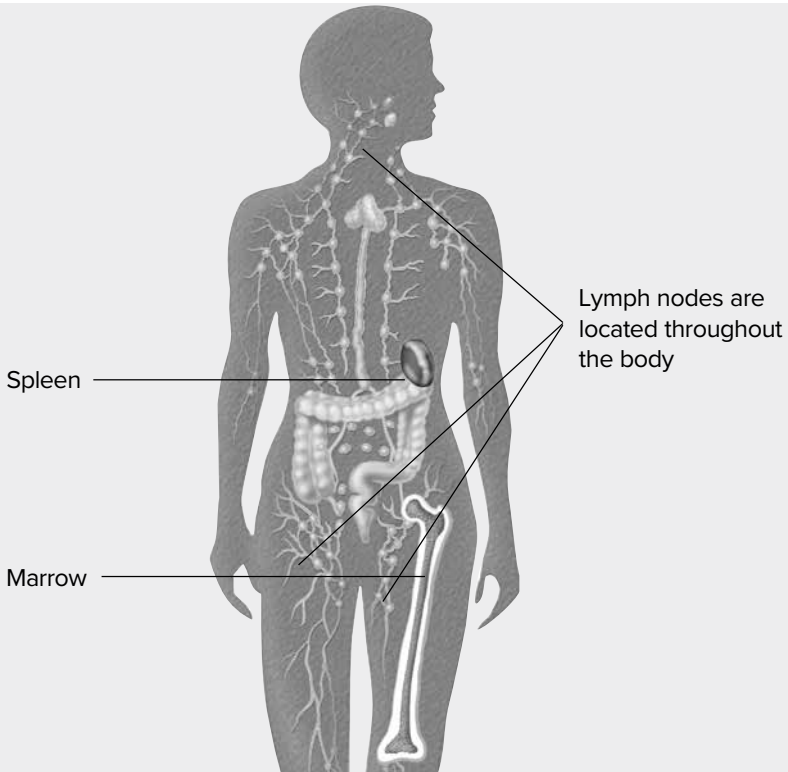
Hodgkin lymphoma (HL) was named after Dr. Thomas Hodgkin, a British pathologist. In 1832, Hodgkin described several cases of people with symptoms of a cancer involving the lymph nodes. The disease was called “Hodgkin’s disease.” It was officially renamed “Hodgkin lymphoma” when it became clear that it is caused by a change in the DNA (deoxyribonucleic acid) of lymphocytes in the lymphatic system.

A lymphocyte is a type of white blood cell. In lymphoma, a lymph node or other lymphatic structure undergoes a change, called a “mutation.” The abnormal cell, referred to as a “lymphoma cell” or an “HL cell,” begins to multiply. Lymphoma cells may then build up in one or more lymph nodes or in other lymphoid tissues and organs, such as the spleen. They may form a mass (tumor), invade

neighboring tissues, or travel from one group of lymph nodes to the next. Over time, the lymphoma cells can spread to tissues and organs outside the lymphatic system.

In HL, the accumulation of abnormal lymphocytes results in masses that are usually found in the lymph nodes and other sites in the body. See **Figure 1**, below.

### Figure 1. Hodgkin Lymphoma and the Lymphatic System



The lymphatic system is part of the immune system. The normal immune system helps to protect the body from infection. The marrow, lymph nodes and spleen are parts of the immune system. There are about 600 lymph nodes throughout the body.

Lymph nodes and other lymphoid tissues that are commonly involved in lymphoma are those around the ears and jaw, in the tonsils and adenoids, in the front and back of the neck, above and below the collar bone, in the armpit, near the elbow, in the chest, in the abdomen, in the pelvis and in the groin. The spleen contains many clusters of lymphocytes that can become malignant and grow, leading to the enlargement of the spleen. The gut-associated (intestinal) lymph tissue may also be the site of lymphoma development.

Hodgkin lymphoma is distinguished from other types of lymphoma primarily by the presence of what are called Reed-Sternberg cells, named after the scientists who first identified them. Reed-Sternberg cells are large, abnormal B lymphocytes that often have more than one nucleus and an owl-like appearance. These cells can be observed under a microscope and further identified by special pathology tests. This essential information helps doctors determine a patient's HL subtype.

## Signs and/or Symptoms

Signs and/or symptoms are changes in the body that may indicate disease. A sign is a change that the doctor sees during an examination or in a laboratory test result. A symptom is a change that a patient can see and/or feel.

A person who has signs or symptoms that suggest the possibility of lymphoma is usually referred to a specialist called a “hematologist-oncologist.” A hematologist is a doctor who has special training in disorders of the blood, and an oncologist is a doctor who has special training in cancer. Doctors with training in both hematology and oncology have particular expertise in treating blood cancers such as leukemia, lymphoma and myeloma.

It is important to point out that the signs and symptoms of HL can also be caused by other, less serious conditions. Check with your doctor if you have any of the following signs and/or symptoms:

- Painless, swollen lymph nodes in the neck, underarm or groin\*
- Unexplained fever (above 100.4 °F)\*\*
- Drenching night sweats\*\*
- Unexplained weight loss (more than 10% of your body weight)\*\*
- Itchy skin without a rash or other explanation
- Fatigue, extreme tiredness or lack of energy
- Loss of appetite
- Persistent cough and shortness of breath (due to enlarged lymph nodes in the chest)
- Abdominal pain or swelling and feeling of fullness (due to an enlarged spleen)
- Occasional pain in lymph nodes after drinking alcohol

\*Make sure to let your doctor know if you recently received a COVID-19 vaccine, as some people have enlarged lymph nodes afterwards.

\*\*Indicates a “B symptom.” B symptoms are an important part of staging HL and determining a patient's prognosis (chance of recovery).

# Diagnosis

If you have signs or symptoms that suggest that you may have HL, exams and tests will be done to find out if you have the disease and, if so, to determine the exact subtype. Obtaining a precise diagnosis helps your doctor to:

- Estimate how your disease will progress
- Determine the appropriate treatment

**Patient Evaluation.** If you have signs or symptoms of lymphoma, your doctor will perform a physical examination and take a thorough medical history. Your medical history may include information about past illnesses, injuries, treatments and medications. Some illnesses run in families, so your doctor may also ask about the health of your blood relatives.

The doctor will ask about any signs and/or symptoms you are experiencing and then conduct a physical examination. It is important for the doctor to be aware of any of the following signs and/or symptoms, including, but not limited to: fevers, night sweats, unexplained weight loss, itchy skin, fatigue, and occasional pain in lymph nodes after drinking alcohol.

During the physical examination, the doctor may listen to your lungs and heart and carefully examine your body for any indications of infection and disease. The physical examination should include the doctor's assessment of all accessible lymph node groups in the neck, underarms and groin. The doctor will also palpate (check by feeling) the size of organs such as the spleen and liver.

**Biopsy.** A biopsy, generally of an enlarged lymph node, is needed to diagnose HL. Biopsy is the removal of cells for examination by a pathologist or hematopathologist; these are doctors who have special training in diagnosing blood diseases by studying cells under a microscope.

There are several different types of biopsies. These procedures are used to detect cancer in cells and tissues:

- Fine needle aspiration/fine needle biopsy—a thin, hollow needle is inserted through the skin into the lymph node or other suspicious area, then a small sample of cells and fluid (called “aspirate”) is suctioned out
- Core needle biopsy—similar to a fine needle biopsy, but uses a larger needle to remove a small core of tissue
- Incisional biopsy—a surgeon will cut into the skin to remove a small area of tissue
- Excisional biopsy—a surgeon will cut through the skin to remove an entire lymph node

The lymph node tissue sample that can be obtained through a fine needle aspiration is not sufficient for the hematopathologist to make a conclusive



diagnosis. The preferred and most common type of biopsy is called an incisional or excisional biopsy, in which part of, or the whole lymph node is typically removed (excised). If the lymph node is just under the skin, the biopsy procedure is usually simple and can sometimes be done with a numbing medication (local anesthetic). If the lymph node is inside the chest or abdomen (stomach area), the patient may be sedated or receive general anesthesia.

The hematopathologist examines the samples using a microscope to look for cancer cells. If Reed-Sternberg cells are found in the lymph node sample, the hematopathologist will make a diagnosis of “classical HL” (often abbreviated as “cHL”). In the past, there was another less common but distinct subtype of Hodgkin lymphoma, called “nodular lymphocyte-predominant Hodgkin lymphoma” (NLPHL); however, that subtype has been reclassified as nodular lymphocyte-predominant B-cell lymphoma (NLPBL).

Hodgkin lymphoma may be difficult to diagnose because the Reed-Sternberg cells may comprise only 0.1 to 10 percent of the biopsy tissue sample, so it is important for it to be analyzed by a specialist with experience in diagnosing HL. Pathology slides may be sent to a specialty center for confirmation of the diagnosis.

Slides are prepared from the biopsy sample by placing the tissue in a preservative and staining it with dyes. Then the cells are examined under a microscope. The distinctive patterns of lymph node abnormalities that are characteristic of HL are visible under the microscope and can help the hematopathologist categorize the patient’s disease into one of several HL subtypes (see **Table 1** on page 9).

**Biomarker Tests.** These tests use a sample of tissue, blood, or other body fluid to check for certain genes, proteins, or other molecules that may be a sign of a disease or condition such as cancer. Biomarker testing can also be used to check for certain changes in a gene or chromosome that may increase a person’s risk of developing cancer or other diseases. Biomarker testing may be done with other procedures, such as biopsies, to help diagnose some types of cancer. It may also be used to help plan treatment, find out how well treatment is working, make a prognosis, or predict whether cancer will come back or spread to other parts of the body. Also called molecular profiling and molecular testing, these types of tests include:

**Immunophenotyping.** This laboratory test can detect specific cancer cells based on the types of antigens or proteins on the surface of the cells. Immunophenotyping is used to help diagnose specific types of leukemia and lymphoma.

In this test, a sample of cells is treated with special antibodies that only bind to cells that have a specific antigen on them. The cells are then passed through a laser beam. If the cells have the special antibodies attached to them, they will give off light.

Depending on the specific type of lymphoma, the lymphoma cells can have different antigens on their surfaces. Certain antigens, called “cluster of differentiation (CD) proteins,” are helpful in identifying lymphoma cells. In the majority of patients with classical HL, the antigens called CD30 and CD15 are found on the surface of the Reed-Sternberg cells. Nodular lymphocyte-predominant B-cell lymphoma cells usually express antigens CD45 and CD20, but not antigens CD15 or CD30.

Some of these tests may be repeated both during and after treatment to measure whether the treatment is working.

**Next Generation Sequencing and Liquid Biopsies.** Next generation sequencing (NGS) tests can rapidly examine stretches of DNA (deoxyribonucleic acid). This technology can detect mutations and other genetic abnormalities in DNA extracted from blood or bone marrow samples. Due to the small number of Reed-Sternberg cells, performing genetic analysis from tumor samples in Hodgkin lymphoma can be difficult.

The use of NGS and liquid biopsies are currently under investigation in clinical trials. These methods have the potential to become a complement to tissue biopsy in the near future. They could be particularly useful in cases in which a tumor mass is difficult to biopsy or when there is very little tissue removed through biopsy.

## Hodgkin Lymphoma Subtypes

The World Health Organization (WHO) classifies Hodgkin lymphoma (HL) into two main subtypes:

- Classical Hodgkin lymphoma (cHL)
- Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL)\*

\*Note: The WHO continues to use the term NLPHL (so as not to interfere with ongoing clinical trials) but states that “NLPHL may be more accurately called nodular lymphocyte-predominant B-cell lymphoma (NLPBL).” WHO is preparing to adopt this new name. NLPBL will be considered a separate disease and not a Hodgkin lymphoma subtype.

Classical Hodgkin lymphoma (cHL) is characterized by the presence of Reed-Sternberg cells. About 95 percent of HL patients have the classical subtype, so it is often simply referred to as “Hodgkin lymphoma.” Classical Hodgkin lymphoma is further classified into four subtypes (see **Table 1** on page 9), each with distinctive characteristics. Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is distinguished by the presence of lymphocyte-predominant cells, sometimes termed “popcorn cells,” which are a variant of Reed-Sternberg cells. When the doctor is making treatment decisions, the HL subtype is an important consideration.

**Table 1. World Health Organization: Classification of Hodgkin Lymphoma Subtypes**

Hodgkin Lymphoma Subtype	Features
<b>Classical Hodgkin Lymphoma (cHL)</b>	<ul style="list-style-type: none"> <li>• Accounts for 95% of all HL cases</li> </ul>
Nodular Sclerosis	<ul style="list-style-type: none"> <li>• Accounts for 70% of cHL cases</li> <li>• Most common subtype in young adults</li> <li>• Involved lymph nodes contain elements of fibrous tissue (sclerosis)</li> <li>• Similar incidence in males and females</li> <li>• Highly curable</li> <li>• B symptoms in approximately 40% of cases</li> </ul>
Mixed Cellularity	<ul style="list-style-type: none"> <li>• Accounts for 20%-25% of cHL cases</li> <li>• More prevalent in children, older adults and patients with HIV infection</li> <li>• Most common in males</li> <li>• Involved lymph nodes contain RS cells and several other cell types</li> <li>• B symptoms common</li> <li>• Associated with EBV infection</li> </ul>
Lymphocyte-rich	<ul style="list-style-type: none"> <li>• Accounts for about 5% of cHL cases</li> <li>• Involved lymph nodes contain numerous normal-appearing lymphocytes and RS cells</li> <li>• Usually diagnosed at an early stage</li> <li>• More common in males</li> <li>• B symptoms are rare</li> </ul>
Lymphocyte-depleted	<ul style="list-style-type: none"> <li>• Rarest cHL subtype</li> <li>• Involved lymph nodes contain few normal lymphocytes but numerous RS cells</li> <li>• More prevalent in older adults and patients with HIV infection</li> <li>• Usually diagnosed at an advanced stage</li> <li>• B symptoms common</li> <li>• Associated with EBV infection</li> </ul>
<b>*Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL)</b>	<ul style="list-style-type: none"> <li>• Accounts for 5% of all HL cases</li> <li>• Most common in age range 30 to 50 years</li> <li>• More common in males</li> <li>• Slow growing and disease can relapse many years later (eg, indolent NHL); highly curable</li> <li>• Small risk of transformation to aggressive NHL (7% of cases)</li> </ul>

Abbreviations: cHL, classical Hodgkin lymphoma; EBV, Epstein-Barr virus; HIV, human immunodeficiency virus; HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; NLPHL, nodular lymphocyte-predominant Hodgkin lymphoma; RS cell, Reed-Sternberg cell.

Definitions: Nodular sclerosis, hardening of the lymph nodes; mixed cellularity, presence of RS cells and other types of cells; indolent, slow to develop or heal.

**\*Note:** NLPHL has been reclassified as Nodular Lymphocyte-Predominant B-cell Lymphoma (NLPBL). In the near future it will be considered a separate disease and not a Hodgkin lymphoma subtype.

# Staging

After a person is diagnosed with HL, doctors use imaging and blood tests, and sometimes bone marrow biopsies, to determine if the cancer cells have spread within the lymphatic system and/or to other parts of the body. This determination, called “staging,” provides valuable information for treatment planning. A series of tests are done to help determine the patient’s stage of HL.

**Imaging Tests.** Imaging tests make “pictures” (images) of the inside of the body and can show where the cancer is located. One example is the simple imaging test called an “x-ray.” Imaging tests are a very important part of the staging and management of HL. Your doctor may first order imaging tests when your medical history and physical examination suggest a possible diagnosis of HL. The imaging test(s) may show enlarged lymph nodes in the chest or abdomen, or both. Tumor masses can also occur outside the lymph nodes in the lungs, bones or other body tissue.

It is important to note that imaging tests, as is the case with virtually all medical tests, can sometimes have “false positive” results. For example, findings that appear to show tumor masses could actually be related to something else, like infection or inflammation. Therefore, these tests need to be interpreted carefully, taking into consideration all aspects of the patient’s situation.

The imaging tests may include:

- **Chest x-ray.** This test produces a black and white “picture” of the inside of the chest that shows the heart, lungs, airways and blood vessels. It is often one of the first tests performed to evaluate symptoms of cough, chest pressure, or shortness of breath. It may show a mass between the lungs (the area between the lungs is called the “mediastinal” area). Although not commonly used for this purpose, the doctor can also see lymph nodes on an x-ray image and note if any lymph nodes are enlarged.
- **Computed tomography (CT) scan.** A CT scan, also referred to as a “CAT scan,” uses special x-ray equipment to take multiple images of areas inside the body from different angles. A computer then processes this information and produces one detailed picture. For certain CT procedures, a special dye (called a “contrast” dye) is used to highlight specific areas inside the body, resulting in clearer pictures. The patient may drink the contrast dye, and/or it may be injected into a vein. Patients may have CT scans of all the areas where lymph nodes are present, which could include the neck, arms, chest, abdomen and/or pelvis, to identify areas of disease involvement. A CT scan can also show whether there is lymphoma in the lungs, liver and other organs.
- **Positron emission tomography-computed tomography (PET-CT) scan.** This procedure combines a PET scan with a CT scan. A PET-CT scan provides a more detailed image of areas inside the body than either scan can produce

alone. A PET scan is an imaging technique that produces a 3D image of functional processes in the body. It is sometimes referred to as an “FDG-PET scan” because a small amount of fluorodeoxyglucose (FDG), a radioactive glucose, is injected into the patient and absorbed by tissue cells. The imaging device detects the radiation given off by the FDG and produces color-coded images that show differences between normal and cancerous tissues: areas with cancerous tissue appear brighter or “lit up” in the scan. The images from a PET-CT scan frequently help doctors to identify an appropriate biopsy site. Before treatment, doctors may view PET-CT scans to determine the stage of HL. After treatment, PET-CT scans may be used to assess treatment response.

- **Magnetic resonance imaging (MRI) scan (in select cases).** The scanners for MRIs use powerful magnetic fields and radio waves that are processed by a computer to create clear and detailed cross-sectional images (slices) of the body. These “slices” can then be displayed on a video monitor and/or saved on a disk for future analysis. MRI scans are rarely used to diagnose HL; however, doctors may use them for close examination of the spinal cord or the brain if there is a possibility that the disease has spread to these areas. Since MRI imaging does not use radiation, it may also be used during pregnancy to protect the unborn baby.

**Blood Tests.** Blood tests cannot be used to detect HL, but they can help the doctor obtain information about the stage of the disease and determine if patients can tolerate certain treatments.

- **Complete blood count (CBC).** This test measures the number of blood cells in a sample, including red blood cells, white blood cells and platelets. Low numbers of red blood cells, white blood cells or platelets may indicate that lymphoma is present in the bone marrow and/or blood. Additional tests may be done to determine the ratio between two different types of white blood cells (lymphocytes and monocytes), which can help to predict the outcome of the disease.
- **Comprehensive metabolic panel (CMP).** This test measures 14 different substances in the blood. It can detect a range of abnormalities in blood sugar and nutrient balance, and also evaluate liver and kidney health.
- **Erythrocyte sedimentation rate (ESR).** This test is done to determine the rate at which the red blood cells settle to the bottom of a tube. This “sedimentation” rate is a measure of how much inflammation is in the body. Inflammation is the body’s attempt to heal itself. The ESR may be higher than normal for some people with HL.
- **Lactate dehydrogenase (LDH).** This is a protein, normally present in most cells, which is released into the blood when a cell is damaged. A high level of LDH in the blood may indicate a number of conditions. The LDH level can be higher than normal in people with HL when the cancer is more active and causing more damage to cells.

- **Liver and kidney function tests.** These tests measure chemicals that are made or processed by the liver and kidneys. High or low levels of these chemicals in the liver may signal that the cancer has spread to the liver. High levels of creatinine in the kidneys may mean that HL (or some other disease) has damaged the kidneys.
- **Human immunodeficiency virus (HIV) and hepatitis B testing.** Tests for both HIV and hepatitis B are a recommended part of the pretreatment workup for patients with HL, because these diseases can affect cancer treatment. If a patient has HIV, treating it will improve how well the cancer therapy works. Hepatitis B can also affect how well some cancer treatments work.

**Heart and Lung Tests.** Some HL treatments may damage the heart and/or lungs. The healthcare team may decide to do heart and lung function tests before treatment, in order to plan appropriately.

**Pregnancy Test.** Some cancer treatments can harm an unborn baby, so a pregnancy test is recommended before undergoing treatment. Treatment options may depend on the results. See *Hodgkin Lymphoma and Pregnancy* on page 41.

**Bone Marrow Tests.** Some patients who have been diagnosed with HL may need to undergo a bone marrow aspiration and biopsy. These tests are not typically used to diagnose HL, but they may be done after diagnosis to see if there are lymphoma cells in the bone marrow. The doctor will decide if these procedures are necessary. That determination will be based on considerations including the location of the disease in the body (see **Figure 2** on page 14). A bone marrow aspiration and biopsy may not be required for patients who have early-stage HL with low-risk (favorable) clinical features, for example, no B symptoms or “bulky” disease (a large mass in the chest or a lymph node mass greater than 10 centimeters). A visualizing PET scan may also eliminate the need for a bone marrow biopsy to assess the disease.

**Stages of HL.** Staging for HL is based on the Lugano classification (see **Table 2** on page 13). These classifications were determined at meetings of lymphoma specialists, where the systems were developed and adopted for use in patients. Hodgkin lymphoma usually starts in the upper body (above the diaphragm), in lymph nodes found in the neck, chest or armpits. The diaphragm is the thin muscle below the lungs and heart that separates the chest from the abdomen.

For example, stage IIB would indicate that the patient has:

- Involvement of two lymph node sites near each other (for example, enlarged lymph nodes in the neck and collarbone area or in the neck and the armpit)
- Fever, excessive sweating and/or weight loss (B symptoms)

Patients in the B symptom category sometimes require more aggressive treatments. It is important to note that even patients with stage IV (advanced stage) HL are frequently cured with treatment, despite having lymphoma in many areas of the body.

**Table 2. Lugano Classification System for Hodgkin Lymphoma (HL)**

### **Stage I**

- HL cells found in a single lymph node region (this can include one node or a group of adjacent nodes) above the diaphragm, OR
- HL cells found in one organ or site outside the lymphatic system

### **Stage II**

- HL cells found in two or more lymph node regions on the same side of the diaphragm, either above or below, OR
- HL cells found in a lymph node area and a nearby organ outside the lymphatic system, on the same side of the diaphragm

### **Stage III**

- HL cells found in lymph node regions on both sides of the diaphragm (above and below), possibly with localized involvement of an organ outside the lymphatic system or the spleen

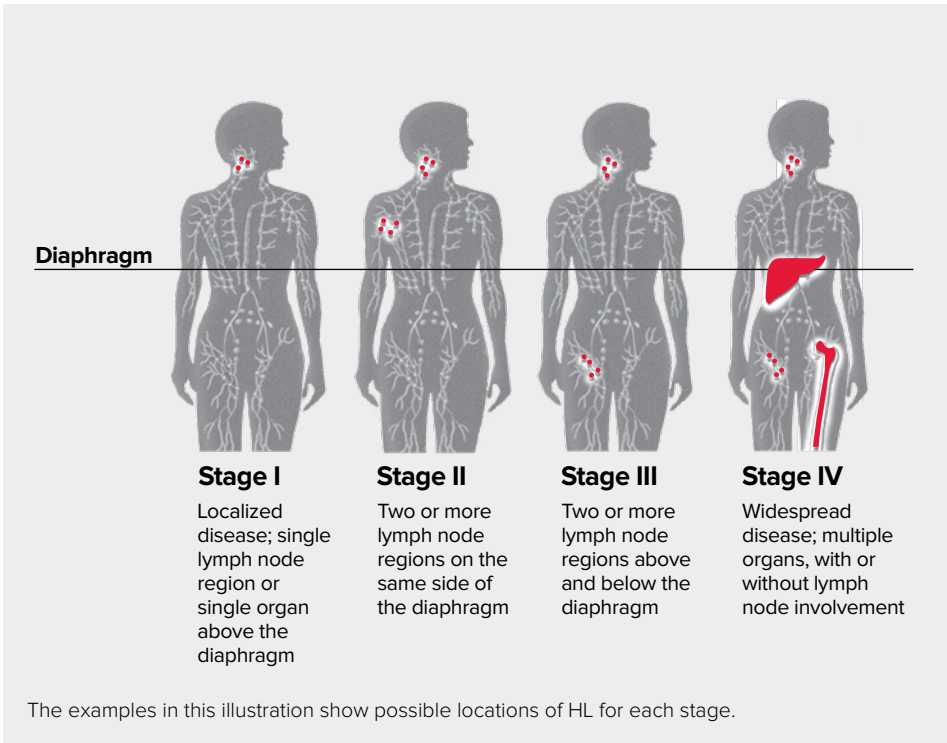
### **Stage IV**

- HL cells found to have spread widely into one or more organs outside the lymphatic system and possibly into nearby lymph nodes, OR
- HL cells found in one organ outside the lymphatic system and also in distant lymph nodes

In addition to the stage number, the letters A, B, E or S may be used to further classify the stage of HL.

- **Category A:** The patient does not have B symptoms (fever, drenching night sweats and/or unexplained weight loss greater than 10 percent of body weight over 6 months).
- **Category B:** The patient has B symptoms.
- **Category E:** The patient has HL cells in organs or tissues outside the lymphatic system.
- **Category S:** The patient has HL cells in the spleen.

**Figure 2. Hodgkin Lymphoma Stages**



## Treatment Planning

Hodgkin lymphoma (HL) cases are generally classified into subgroups called early-stage favorable, early-stage unfavorable, and advanced stage.

**Early-Stage: Stage I or II Hodgkin Lymphoma.** Different scoring systems are used to determine early-stage favorable or unfavorable HL.

Within these scoring systems you will see the terms “mediastinal” and “extranodal.” Mediastinal refers to the area between the two lungs. Extranodal indicates an area or organ outside of the lymph nodes.

One scoring system is from the National Comprehensive Cancer Network (NCCN), an alliance of leading cancer centers in the United States. NCCN has developed Clinical Practice Guidelines for healthcare providers who treat HL.



The NCCN Clinical Practice Guidelines look at the factors below to determine favorable (no risk factors) or unfavorable (one or more risk factors) for early-stage I-II HL:

- Bulky mediastinal disease or bulky disease greater than 10 cm
- B symptoms (fever, night sweats, weight loss)
- Erythrocyte sedimentation rate (ESR) greater than 50 mm/hr
- More than 3 nodal sites of disease

The European Organization for the Research and Treatment of Cancer (**EORTC**) and the German Hodgkin Lymphoma Study Group (**GHLSG**), two additional cancer research organizations outside the United States, also provide scoring systems to define risk factors for early-stage Hodgkin lymphoma.

Having none of the risk factors listed below is considered favorable, whereas having one or more of the risk factors is considered unfavorable.

**Table 3. Risk Factors for Early-Stage (Stages I and II) Favorable or Unfavorable Hodgkin Lymphoma According to EORTC and GHLSG**

EORTC	GHLSG
Large mediastinal mass	Large mediastinal mass
Erythrocyte sedimentation rate (ESR) of 50 or higher	Erythrocyte sedimentation rate (ESR) of 50 or higher
4 or more involved regions	3 or more involved regions
Age greater than 50 years	Extranodal disease

EORTC, European Organization for the Research and Treatment of Cancer; GHLSG, German Hodgkin Lymphoma Study Group.

**Advanced Stage: Stage III or IV Hodgkin Lymphoma.** The International Prognostic Score (IPS) is the most common risk stratification tool, used both nationally and internationally, for advanced Hodgkin lymphoma. Seven factors (shown in **Table 4**, on page 16) provide a basis for recommending either aggressive or less-intensive treatment options. The IPS assigns a point for each of the adverse prognostic factors that are present at diagnosis.

#### **Table 4. Adverse Prognostic Factors for Advanced-Stage Classical Hodgkin Lymphoma**

- Being male
- Age 45 years or older
- Stage IV disease
- Albumin level below 4 g/dL (grams per deciliter); albumin is a type of protein in the blood
- Hemoglobin level below 10.5 g/dL (grams per deciliter); hemoglobin is a protein in red blood cells that carries oxygen
- A higher-than-normal white blood cell count, generally equal to or greater than 15,000/uL (microliters)
- A lower-than-normal lymphocyte count (a type of white blood cell), generally below 600/uL (microliters) or less than 8% of the total white blood cell count

**Treatment Goals.** The main goal of treatment for patients with HL is to cure them of the disease. More than 80 percent of all patients diagnosed with HL can be cured by current treatment approaches. The cure rate is higher, approaching 90 percent, in younger patients and in those with early-stage favorable HL. Even in cases of advanced stage HL, the disease is often highly curable.

Most patients become long-term survivors of the disease. Other treatment goals are to:

- Maximize cures in all stages of the disease
- Minimize both short-term and long-term side effects and complications
- Weigh the risks of toxicity against treatment benefits

Typically, the team that works together to treat the patient consists of the hematologist-oncologist, a nurse practitioner and/or a physician assistant, a registered nurse, a social worker and sometimes a nurse navigator, and a financial counselor. Patients are carefully assessed, and treatment is tailored to the individual needs of each patient. Factors evaluated in treatment planning for HL patients include:

- Disease subtype
- Disease stage and category
- Whether the disease is refractory (does not respond to treatment) or has relapsed (recurred after treatment)
- Patient's age
- Coexisting diseases or conditions (for example, heart or kidney disease, diabetes)

**Fertility Concerns.** While many treatments for HL have little or no adverse effect on fertility, some cancer treatments can limit a person's ability to conceive or have a baby in the future. Adults of childbearing age, as well as parents of children and adolescents diagnosed with HL, are encouraged to ask their doctors for information on ways to help decrease the risk of infertility.

It may be helpful to speak to a fertility specialist before starting cancer treatment. Some methods of fertility preservation include:

- **Sperm Banking.** Males who want to conceive children after treatment may choose to store their semen in a sperm bank for later use.
- **Egg or Ovarian Tissue Freezing.** A female's eggs can be removed, frozen and stored for later use. The eggs could be fertilized with sperm before freezing. Another option is for a part of the ovary that contains eggs to be removed, frozen and stored.
- **Ovarian Transposition.** This less commonly used method, called "oophoroxy," is an option for females who will be treated with radiation therapy. An ovary is surgically transposed (moved) out of the range of the radiation beam in order to protect it.

**For more information, see the free LLS booklet *Fertility and Cancer*.**

## Treatment for Classical Hodgkin Lymphoma

New treatments may have been approved since this book was printed. Check [www.LLS.org/DrugUpdates](http://www.LLS.org/DrugUpdates) or call (800) 955-4572.

Before treatment begins, your doctor will discuss treatment options with you. Treatment options may include standard therapy or a clinical trial. Standard therapy is treatment that is accepted by medical experts as proper treatment for a certain type of disease. A clinical trial is a research study that evaluates how well a new medical treatment works in people. A clinical trial may be your best treatment option, so it is important to discuss all your treatment options with your doctor. See page 43 for more information about clinical trials for blood cancers.

It is important to seek treatment in a center where doctors are experienced in the care of patients with Hodgkin lymphoma (HL). If time allows, you may want to seek a second opinion from another doctor or treatment center. Choosing your cancer treatment is a very important decision. It can affect the length and the quality of your life. A second opinion may help you feel more confident about your chosen treatment plan.

**For more information, see the free LLS booklet *Choosing A Specialist or Treatment Center*.**

**Treatment Overview.** Most patients with newly diagnosed HL have a high likelihood of being cured with appropriate treatment. The main treatment options for classical HL (cHL) are chemotherapy alone, or a “combined modality therapy” consisting of chemotherapy followed by radiation therapy. The treatment for nodular lymphocyte-predominant B-cell lymphoma (formerly called nodular lymphocyte-predominant Hodgkin lymphoma) requires a different treatment approach. For more information on the treatment of NLPBL, see page 33.

**Chemotherapy.** Chemotherapy drugs kill fast-growing cells throughout the body, including both cancer cells and normal, healthy cells. Several types of chemotherapy drugs work in different ways to eliminate lymphoma cells or stop new lymphoma cells from forming. Therefore, in many cases, more than one chemotherapy drug is used to treat HL.

Chemotherapy is usually given in treatment cycles. Each cycle is made up of a certain number of days of treatment followed by a rest period of a few days or weeks in between each cycle. In most cases, treatment is administered over the course of 1 to 3 days, depending on the particular combination of drugs.

A rest period of a few days to a few weeks following a treatment cycle allows the body to recover from the effects of chemotherapy. Then another cycle begins. Generally, a treatment cycle lasts 3 or 4 weeks. The number of cycles in a chemotherapy regimen will depend on:

- Which drugs are used
- The stage and subtype of HL
- How well the disease responds to treatment

Some chemotherapy drugs are given to the patient by intravenous (IV) infusion, which means they are injected slowly over a period of time, into a vein. These chemotherapy drugs are generally given through a thin, soft tube that may be called a “central venous line,” “catheter,” or “central line.” The central line is often attached to a “port” (surgically placed under the skin in the patient’s upper chest) that allows access to the central line. See *Health Terms* on pages 62-67.

**Radiation Therapy.** Radiation therapy, also known as “radiotherapy,” uses high-energy x-rays or other types of radiation to kill cancer cells in a small, targeted area of the body. Because radiation can also harm normal cells, when possible radiation therapy is directed only at the affected lymph node areas in order to reduce long-term side effects.

Involved-site radiation therapy (ISRT) is often used to treat HL. It selectively treats the lymph nodes or sites where the cancer is located. With a special machine, carefully focused beams of radiation are directed at the cancer. This is also called “external beam therapy” (EBT). The size of the targeted area is restricted

to minimize radiation exposure to adjacent, uninvolved organs, and to decrease the side effects associated with radiation therapy.

**For more information, see the free LLS booklet *External Beam Radiation Therapy*.**

In recent years, proton therapy has been introduced in a limited number of cancer centers to treat HL found in the chest. This therapy uses a beam of protons instead of photons or electrons as the source of radiation, and it allows for precise delivery of the radiation to the malignant (cancerous) tissue. Proton therapy does not replace other therapies and not all patients need proton therapy. It is unclear if proton therapy is superior to standard radiation therapy.

A simulation session is needed for planning before radiation treatment starts. During the simulation session, CT or PET scans are used to take “pictures” of the tumor. Based on these scans, the treatment team takes careful measurements to determine the angles for aiming the radiation beams and the amount of radiation needed. The goal is to focus the radiation on the cancer to limit the effect on healthy tissues and organs.

During radiation treatments, you will lie on a table in the same position you were in for the simulation session. You will be alone while the radiation therapist operates the machine from a nearby room. The treatment is similar to the treatment you undergo during an x-ray; however, radiation is stronger than x-ray. Each treatment session lasts only a few minutes, but the entire session can take between 15 and 30 minutes due to the setup of the equipment.

Imaging techniques such as MRI and PET-CT scans can enhance treatment planning, and the exposure of uninvolved organs can be either reduced or avoided. Other specialized imaging techniques include:

- **Four-dimensional computed tomography (4D-CT)**, which can adjust for movement of tumors near the breastbone (sternum), caused by the patient breathing. This is valuable for accurately treating tumors located on or near organs that move, such as those in the chest and abdomen.
- **Image-guided radiation therapy (IGRT)**, which can improve how well the radiation beam targets some tumors. The machine used for IGRT delivers radiation and, at the same time, takes images of the tumor and normal body structures. These images allow for adjustments to the beam position or radiation dose, improving the accuracy of treatment and reducing harm to normal tissue.
- **Three-dimensional conformal radiation therapy (3D-CRT)**, which uses images from scans to precisely plan the treatment area and design the radiation beams to conform to the shape of the tumor. This allows for the use of higher doses of radiation while sparing normal tissue.

- **Intensity-modulated radiation therapy (IMRT)**, which is a type of 3D-CRT. It uses smaller beams, and the strength of the beams can be changed to give higher doses to certain parts of the tumor.

If radiation therapy is being considered, patients are encouraged to carefully review the benefits and risks of these different approaches with their treating doctor.

**Immunotherapy.** This type of therapy uses the patient's own immune system to fight cancer. Immunotherapy can be used to treat some people with HL. The following immunotherapies are in use or under study for HL treatment:

**Monoclonal Antibody Therapy.** This is a type of targeted therapy. When the body's immune system identifies something harmful, such as bacteria or a virus, it produces antibodies. Antibodies are proteins that help fight infection. Monoclonal antibodies are made in a laboratory and are a type of protein that can bind to only one substance. By design, they can only attack a specific target, typically a substance on cancer cells (though sometimes they are designed to bind to a substance on immune cells, in order to improve their function). This targeting can reduce damage to normal, healthy cells. In patients with classical HL, the malignant Reed-Sternberg cells typically express a protein called CD30. **Brentuximab vedotin (Adcetris®)**, given by IV, is classified as an antibody-drug conjugate: it's an anti-CD30 monoclonal antibody attached to a chemotherapy drug. It binds to cells that express CD30 and then enters the cancer cells. Once inside the cancer cells, it releases the chemotherapy drug. By targeting only cells that express CD30, fewer normal cells are harmed.

**Immune checkpoint inhibitors.** Checkpoints are molecules found on T cells, a type of white blood cell. T cells circulate throughout the body looking for signs of infection and diseases, including cancer. When a T cell comes near any type of cell, it probes (looks for) certain proteins on the cell's surface. If the T cell determines that it is a normal, healthy cell, it moves on to check other cells. If the proteins indicate that the cell is foreign or cancerous, the T cell attacks it. But cancer cells can sometimes send misleading signals to these checkpoints, telling the T cells that they are not harmful. Checkpoint inhibitors work by blocking the signals that cancer cells send to T cells. When the signals are blocked, it is more likely the T cells will distinguish the cancer cells from healthy cells and begin an attack. **Nivolumab (Opdivo®)** and **pembrolizumab (Keytruda®)**, both given by IV, can be used for some patients with HL that has become refractory (come back or spread during treatment), or that has relapsed (returned) after the patient has completed other treatments. Nivolumab plus chemotherapy may soon be FDA-approved for pediatric and adult patients with previously untreated advanced stage HL.

New types of monoclonal antibodies and checkpoint inhibitors are being studied in clinical trials to treat Hodgkin lymphoma. See *Clinical Trials for Blood Cancers* on page 43.

**Chimeric Antigen Receptor (CAR) T-Cell Therapy.** This is a type of immunotherapy that uses a patient's own T cells (a type of white blood cell) to identify and attack cancer cells. Blood is taken from the patient, and the T cells are separated out from the patient's blood and sent to a laboratory, where they are genetically modified so they will attack cancer cells. The engineered T cells are then multiplied and later reinfused into the patient's bloodstream. CAR T-cell therapy is currently under study in clinical trials for relapsed and refractory HL. See *Clinical Trials for Blood Cancers* on page 43.

**For more information, see the free LLS booklet *Chimeric Antigen Receptor (CAR) T-Cell Therapy*.**

See **Table 6** on pages 25-27 for drug information.

**Stem Cell Transplantation.** Some patients may benefit from stem cell transplantation. It is not used as an initial treatment for HL but may be recommended for people who have refractory or relapsed HL.

The goal of stem cell transplantation is to cure the patient by destroying the cancer cells with high doses of chemotherapy. These high doses of chemotherapy, however, can severely damage the stem cells in the bone marrow where new blood cells are made. Stem cell transplantation allows doctors to give patients high doses of chemotherapy and then replace the damaged stem cells with healthy stem cells.

There are two main types of stem cell transplantation:

- Autologous stem cell transplantation—a procedure in which stem cells are removed from a patient, frozen and stored, and then returned to the patient's bloodstream after the patient has had intensive chemotherapy
- Allogeneic stem cell transplantation—a procedure in which patients undergo chemotherapy and then receive stem cells from a donor

**Autologous Stem Cell Transplantation.** In almost all cases, this is the type of stem cell transplantation used to treat HL. It remains the standard therapy for relapsed and refractory cases of HL.

The first step is to collect the patient's own stem cells after initial treatment is completed and the patient's disease is in remission. After the patient's blood is collected, the stem cells are removed from the patient's blood and are frozen and stored until they are needed for transplantation. The patient is then given high doses of chemotherapy to destroy any lymphoma cells that were not killed

during the initial treatment. After the high-dose chemotherapy is completed, the stem cells are returned to the patient's bloodstream by IV infusion (a procedure similar to a blood transfusion). The goal is to "rescue" the bone marrow from the effects of the high doses of chemotherapy, reintroducing healthy stem cells into the system in order to restore normal blood cell production.

**Allogeneic Stem Cell Transplantation.** This type of transplantation uses stem cells donated from someone other than the patient. It has been successful in some patients with HL after several relapses of the disease, but it is not commonly used as a treatment for HL. It is generally only done if the disease relapses after autologous transplantation.

Talk to your doctor to find out if stem cell transplantation is a treatment option for you.

**For more information, see the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.**



# Drug Information

**Table 5. Drug Classes and Drug Mechanisms**

<b>Alkylating Agents (DNA-Damaging Drugs)</b>	These drugs interfere with a cell's DNA and inhibit cancer cell growth.
<b>Antibody-Drug Conjugates (ADCs)</b>	Antibody-drug conjugates are immunotherapy drugs designed to target specific proteins (antigens) on the surfaces of cancer cells. Other immunotherapy drugs are coupled with a chemotherapy drug or attached to a radioactive particle, so they are also called “antibody-drug conjugates.” They circulate throughout the body until they attach to the target antigen and then deliver the toxic substance to the cancer cell.
<b>Antimetabolites</b>	Antimetabolites mimic the building blocks of DNA or RNA that cancer cells need to survive and grow. When the cancer cell uses an antimetabolite instead of the natural substances, it cannot produce normal DNA or RNA, and the cancerous cell dies.
<b>Antitumor Antibiotics</b>	Antitumor antibiotics prevent cell division by either binding to DNA to prevent the cancer cells from duplicating, or by inhibiting RNA synthesis.
<b>Checkpoint Inhibitors</b>	These drugs block proteins called checkpoints, such as PD-1 and PD-L1, allowing the immune system to better find and attack cancer cells.
<b>Chimeric Antigen Receptor (CAR) T-Cell Therapy</b>	This is a type of cellular immunotherapy that consists of modifying a patient's own immune cells to recognize and attack cancer cells.
<b>Corticosteroids</b>	These synthetic hormones—relatives of the natural hormone cortisol—can kill malignant lymphocytes. They are believed to work by blocking cell metabolism through their effect on specific genes.

<b>DNA-Repair Enzyme Inhibitors</b>	These drugs attack the cancer cell proteins that normally repair damage to the DNA, making the cancer cell more susceptible to damage, and also blocking growth.
<b>Immunomodulators</b>	These drugs influence the immune system function by suppressing or stimulating immune response.
<b>Mitotic Inhibitors</b>	These drugs prevent mitosis (cell division) by blocking it.
<b>Monoclonal Antibodies</b>	Monoclonal antibodies are laboratory-produced proteins that target specific antigens on the cancer cell's surface to interfere with the cell's function and destroy it. Once the antibody finds and attaches to its target, it can "recruit" (harness) other parts of the immune system to destroy cancer cells that contain the antigen. Some monoclonal antibodies work by themselves and are therefore known as "naked antibodies." Some monoclonal antibodies are combined with a toxin or radioactive substance. See "Antibody-Drug Conjugates."
<b>mTOR Inhibitors</b>	These drugs block a protein called mTOR, which helps control cell growth and division.
<b>Topoisomerase Inhibitors</b>	These drugs block certain enzymes that break and reconnect DNA strands, and are needed for cell growth and division.

**Table 6. Some Drugs Used in the Treatment of Hodgkin Lymphoma**

For more details about each drug listed below, see the Package Insert and/or the Full Prescribing Information for each medication (available on the internet).

<b>Drug Name</b> <b>Type of Drug</b> <b>Administration</b>	<b>Indications</b>
<b>Bendamustine (Belrapzo<sup>®</sup>, Bendeka<sup>®</sup>, Treanda<sup>®</sup>)</b> Alkylating agent Intravenous (IV)	Used in the treatment of relapsed or refractory cHL or NLPBL
<b>Bleomycin (Blenoxane<sup>®</sup>)</b> Antitumor antibiotic Intravenous (IV), intramuscular (IM), subcutaneous (SC) injection	FDA-approved for the treatment of Hodgkin lymphoma (HL) as a single agent or in combination
<b>Brentuximab vedotin (Adcetris<sup>®</sup>)</b> Antibody-drug conjugate Intravenous (IV)	FDA-approved for the treatment of adult patients: <ul style="list-style-type: none"> <li>○ With previously untreated Stage III or IV classical HL (cHL), in combination with doxorubicin, vinblastine, and dacarbazine</li> <li>○ With cHL at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation</li> <li>○ With cHL after failure of auto-HSCT or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates</li> </ul> FDA-approved for the treatment of pediatric patients: <ul style="list-style-type: none"> <li>○ 2 years and older with previously untreated high-risk cHL, in combination with doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide</li> </ul>

<b>Carboplatin (Paraplatin®)</b> Alkylating agent Intravenous (IV)	Used in the ICE regimen
<b>Carmustine (BiCNU®)</b> Alkylating agent Intravenous (IV)	FDA-approved for the treatment of patients with relapsed or refractory HL in combination with other approved drugs
<b>Cyclophosphamide (Cytoxan®)</b> Alkylating agent Oral (PO) or intravenous (IV)	FDA-approved for the treatment of HL
<b>Dacarbazine (DTIC-Dome®)</b> Alkylating agent Intravenous (IV)	FDA-approved for second-line treatment of HL in combination with other agents. Also used as initial therapy for some patients.
<b>Dexamethasone</b> Corticosteroid Oral (PO) or intravenous (IV)	FDA-approved for the treatment of many kinds of cancer
<b>Doxorubicin (Adriamycin®)</b> Antitumor antibiotic Intravenous (IV)	FDA-approved for the treatment of HL
<b>Etoposide (Etopophos®)</b> Topoisomerase inhibitor Oral (PO) or intravenous (IV)	Used in the ABVE, ABVE-PC, BEACOPP, BrECADD and ICE regimens
<b>Everolimus (Afinitor®)</b> mTOR inhibitor Oral (PO)	Used for the treatment of relapsed or refractory cHL
<b>Gemcitabine (Gemzar®)</b> Antimetabolite Intravenous (IV)	Used in the GCD, GDP, GVD, IGEV, GEMOX regimens
<b>Ifosfamide (Ifex®)</b> Alkylating agent Injection, intravenous (IV)	Used in the ICE regimen
<b>Lenalidomide (Revlimid®)</b> Immunomodulator Oral (PO)	Treatment of relapsed or refractory cHL
<b>Melphalan (Alkeran®)</b> Alkylating agent Oral (PO) or intravenous (IV)	Used for the treatment of relapsed or refractory cHL

<p><b>Nivolumab (Opdivo®)</b> Checkpoint inhibitor Intravenous (IV)</p>	<p>FDA-approved for treatment of adult patients with cHL that has relapsed or progressed after</p> <ul style="list-style-type: none"> <li>○ Autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin</li> <li>○ 3 or more lines of systemic therapy that includes autologous HSCT</li> </ul>
<p><b>Pembrolizumab (Keytruda®)</b> Checkpoint inhibitor Intravenous (IV)</p>	<p>FDA-approved for treatment of adult patients:</p> <ul style="list-style-type: none"> <li>○ With relapsed or refractory cHL</li> <li>○ For use at an additional recommended dosage</li> </ul> <p>Treatment of pediatric patients:</p> <ul style="list-style-type: none"> <li>○ With refractory cHL, or cHL that has relapsed after 2 or more lines of therapy</li> </ul>
<p><b>Prednisone</b> Corticosteroid Oral (PO)</p>	<p>Treatment of HL and many other cancers</p>
<p><b>Procarbazine (Matulane®)</b> Alkylating agent Oral (PO)</p>	<p>Treatment of advanced HL in combination</p>
<p><b>Rituximab (Rituxan®)</b> Monoclonal antibody Intravenous (IV)</p>	<p>Treatment of NLPBL</p>
<p><b>Vinblastine (Velban®)</b> Antimitotic Intravenous (IV)</p>	<p>FDA-approved for the treatment of advanced HL as a single agent or in combination</p>
<p><b>Vincristine (Oncovin®)</b> Antimitotic Intravenously (IV)</p>	<p>FDA-approved for the treatment of HL in combination</p>
<p><b>Vinorelbine (Navelbine®)</b> Mitotic inhibitor Intravenous (IV)</p>	<p>Used in the GVD regimen</p>

Abbreviations: cHL, classical Hodgkin lymphoma; FDA, United States Food and Drug Administration; HSCT, hematopoietic stem cell transplant; NLPBL, nodular lymphocyte-predominant B-cell lymphoma; PO, oral.

New treatments may have been approved since this book was printed.  
Check [www.LLS.org/DrugUpdates](http://www.LLS.org/DrugUpdates) or call (800) 955-4572.

**Off-Label Prescribing.** Drugs that are not FDA-approved for HL can be used as an “off-label” treatment. “Off-label” prescribing is when a doctor gives a drug that is *not* FDA-approved to treat a patient’s condition, but *is* FDA-approved for another condition, if the doctor feels it will benefit the patient. This is a common practice.

**Table 7. Some Drug Combinations Used to Treat Hodgkin Lymphoma**

- A+AVD—brentuximab vedotin plus doxorubicin, vinblastine, dacarbazine
- \*ABVD—doxorubicin, bleomycin, vinblastine, dacarbazine
- \*ABVE—doxorubicin, bleomycin, vincristine, etoposide
- \*ABVE-PC—doxorubicin, bleomycin, vincristine, etoposide, prednisone, cyclophosphamide
- \*AEPA—brentuximab vedotin, etoposide, prednisone, doxorubicin
- AVD—doxorubicin, vinblastine, dacarbazine
- \*AVPC—doxorubicin, vincristine, prednisone, cyclophosphamide
- \*BEACOPP—bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone
- BeGEV—bendamustine, gemcitabine, vinorelbine
- BrECADD—brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone
- \*BV-AVE-PC—brentuximab vedotin, doxorubicin, vincristine, etoposide, prednisone, cyclophosphamide
- \*CAPDAC—cyclophosphamide, brentuximab vedotin, prednisone, dacarbazine
- CHOP—cyclophosphamide, doxorubicin, vincristine, prednisone
- \*COPDAC—cyclophosphamide, vincristine, prednisone, dacarbazine
- \*COPP—cyclophosphamide, vincristine, procarbazine, prednisone
- COPP-ABV— cyclophosphamide, vincristine, prednisone, procarbazine, doxorubicin, bleomycin, vinblastine
- DHAP—dexamethasone, cytarabine, cisplatin
- Escalated BEACOPP— bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone; given in higher doses in a shorter time period
- ESHAP—etoposide, methylprednisolone, high-dose cytarabine, cisplatin
- GDP—gemcitabine, dexamethasone, cisplatin
- GEMOX—gemcitabine, oxaliplatin
- GVD—gemcitabine, vinorelbine, liposomal doxorubicin

- ICE—ifosfamide, carboplatin, etoposide
- IGEV—ifosfamide, gemcitabine, vinorelbine
- N+AVD—nivolumab, doxorubicin, vinblastine, dacarbazine
- \*OEPA—vincristine, etoposide, prednisone, doxorubicin
- OPPA—vincristine, procarbazine, prednisone, doxorubicin
- R-CHOP—rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone

**\*Indicates drug combinations also used in children and adolescents with Hodgkin lymphoma.**

## Monitoring Treatment Response and Assessing Measurable Residual Disease

During and at the end of treatment, patients need to be monitored to check their response to therapy. The doctor will run tests to see how well the treatment is working. Treatment response is important in predicting long-term outcomes. Patients who fail to reach complete disease remission with the first-line (initial) treatment have a worse prognosis (predicted future outcome). So there is potential value in identifying these patients early in the course of their disease.

Imaging tests are used to distinguish between tumor and fibrous (scar) tissue. PET-CT scans help doctors determine if the disease is responding to treatment. A PET scan is typically performed after two cycles of therapy (interim PET) and at the end of therapy. The results of the interim PET often help the doctors determine the subsequent therapies. PET-CT has become the standard method for assessment of treatment response in most types of lymphoma.

The Deauville score is the internationally recognized way of using PET-CT to assess treatment response. This scale determines the “FDG uptake” (the absorption of this radioactive material by tissues) in the involved sites. The Deauville score is then used to determine if any treatment modifications are needed. A score of 1, 2 or 3 is considered negative, meaning there are no areas of concern. A score of 4 or 5 is considered positive, which suggests there are malignant (cancerous) areas of concern. The treatment team can determine how well the lymphoma is responding to treatment by observing whether this score increases or decreases as treatment progresses. FDG uptake can also occur in sites of inflammation or infection and must be interpreted carefully by your medical team.

Measurable residual disease (MRD) refers to cancer cells that may remain in the body after treatment ends. Besides the use of PET-CT scans to identify residual disease, there are other methods that are under study which may be used to complement these imaging techniques.

Over the last decade, technologies to detect, genotype (analyze the genetic makeup), and monitor cancer through the blood have been developed and hold promise for revolutionizing the way in which some types of cancer are diagnosed and managed.

“Liquid biopsies” rely on the detection of tumor DNA from the blood plasma of patients. Tumor DNA is either secreted directly into the bloodstream by tumor cells or released by these cells during cell death. Next-generation sequencing (NGS) tests can detect mutations and other genetic abnormalities in the tumor DNA extracted and can also assess MRD during and after treatment in a non-invasive manner. In recent studies, higher tumor DNA concentrations were correlated with higher tumor volume measured by PET-CT scans. These new methods of MRD assessment can identify residual disease beyond the sensitivity of imaging tests and have the potential of complementing PET-CT scans in evaluating treatment response.

These methods are being explored in research studies and are not currently used in clinical practice.

**For more information, see the free LLS booklet *Measurable Residual Disease (MRD)*.**

If your doctors conclude that the treatment is working, you will either continue with the same treatment or become a candidate for less intensive therapy. For instance, your treatment team may decide that you will not receive radiation therapy after completing chemotherapy. If the treatment does not appear to be working, your treatment plan may be changed.

**Treatments by Stage.** Treatment options for cHL vary depending on the stage of the disease. Speak to members of your healthcare team to understand the stage of your disease and what it means for your treatment.



**Table 8. Some Treatment Approaches for Classical Hodgkin Lymphoma in Adults Based on Stage**

**Early-Stage (Stages I-II) Classical Hodgkin Lymphoma**

- Chemotherapy combinations
  - ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine)
  - Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
  - AVD (doxorubicin, vinblastine, dacarbazine)
- Chemotherapy combinations with or without radiation therapy. Radiation can be used at the end of a chemotherapy regimen depending on how well the patient responded to the chemotherapy.

**Advanced-Stage (Stages III-IV) Classical Hodgkin Lymphoma**

- Chemotherapy combinations
  - A+AVD (brentuximab vedotin + AVD)
  - ABVD
  - ABVD followed by escalated BEACOPP
  - BrECADD
  - Escalated BEACOPP
  - N+AVD (nivolumab + AVD)
- Occasionally, chemotherapy is followed by involved-site radiation therapy (ISRT).

See **Table 7** on pages 28-29 for information on drug combinations and page 37 for pediatric regimens.

**Treatment of Early-Stage (Stages I-II) Favorable HL.** The current treatment approach is to administer chemotherapy alone (without radiation therapy), or a combined modality therapy (combination chemotherapy followed by radiation therapy to areas of the body where lymphoma was found).

For many years, ABVD has been the most commonly used chemotherapy regimen in adults for early-stage favorable HL. ABVD is associated with very low rates of risk for later development of leukemia or infertility than many other chemotherapy combinations used for adults.

Current clinical practice guidelines for treatment of early-stage favorable HL suggest that at least 90 percent of patients can be cured with as few as two courses of ABVD followed by low-dose radiation therapy.

Older patients (over 60 years of age) with early favorable HL may benefit from omitting the bleomycin in ABVD to avoid pulmonary (lung) toxicity. Older patients who are not candidates for chemotherapy may have radiation therapy alone.

Concerns about the late effects of radiation therapy (especially an increased risk of developing a second cancer and/or cardiac disease) have led some oncology groups to recommend the use of chemotherapy alone for some patients, particularly when the risk of developing a second cancer is considered to be significant. Patients who are at a higher risk of developing a second cancer include females younger than age 30 years who have a family history of breast cancer, and those who will have radiation therapy involving their breast tissue. See *Long-Term and Late Effects of Treatment* starting on page 48.

**Treatment of Early-Stage (Stages I-II) Unfavorable HL.** For patients in this category, the disease is considered to be high-risk yet potentially curable. Initial treatment usually consists of either a combined modality therapy (chemotherapy plus radiation therapy) or chemotherapy alone. Treatment generally involves more cycles of chemotherapy than for those in the favorable category. Results of PET-CT scans done both during and after treatment may affect decisions about the type and duration of chemotherapy and the use of radiation therapy. Some drug combinations used for treatment of these patients (see **Table 7** on pages 28-29) include:

- ABVD
- ABVD followed by BEACOPP

**Treatment of Advanced-Stage (Stages III-IV) HL.** Even in advanced stages, HL is potentially curable. In general, patients with advanced-stage HL are treated with more intense regimens of combination chemotherapy. Some drug combinations used for the treatment of these patients (see **Table 7** on pages 28-29) include:

- Brentuximab vedotin + AVD
- Escalated BEACOPP
- ABVD
- BrECADD
- ABVD followed by BEACOPP
- Nivolumab + AVD

Dose-escalated BEACOPP results in good cure rates, but it puts patients at a slightly higher risk of developing leukemia or other second cancers. Patients are also at a much higher risk of infertility; for this reason, it is less commonly used. The BrECADD and N+AVD regimens are used in certain circumstances for ages 18 to 61.

Use of radiation therapy is limited to a small number of patients, including those who have areas of bulky disease (large masses) at diagnosis or those who have evidence of residual disease observed on PET-CT scans after treatment. Even in these cases, the role of radiation therapy for advanced-stage HL varies.

# Treatment for Nodular Lymphocyte-Predominant B-cell Lymphoma (NLPBL)

*Note that nodular lymphocyte-predominant Hodgkin lymphoma (NLPBL) has been reclassified as nodular lymphocyte-predominant B-cell lymphoma (NLPBL) and is no longer considered a distinct subtype of Hodgkin lymphoma. The following information is being provided while this change is being put into practice.*

The cancer cells in NLPBL are a variant of Reed-Sternberg cells. They are larger than Reed-Sternberg cells and are sometimes called “popcorn” cells because their unique shape is similar to pieces of popcorn.

NLPBL tends to progress more slowly than classical HL, so the treatment approach is usually different. About 75 percent of patients with NLPBL have stage I disease at diagnosis. It is rare for NLPBL patients to have B symptoms or disease involvement outside the lymph nodes; mediastinal masses and bulky disease are also rare.

Because NLPBL is associated with an excellent long-term survival rate, the risk of overtreatment is an important consideration for these patients. Overtreatment may lead to problems and harmful side effects caused by cancer therapies that are not needed. One option for some patients is the “watch-and-wait” approach (also called “active surveillance”), in which patients are closely monitored for disease progression without getting any treatment until symptoms appear or begin to change. Other options for early-stage NLPBL without any B symptoms or bulky disease are the use of radiation therapy alone or, occasionally, surgical removal.

Combination chemotherapy may be needed in more advanced stages of the disease, with **rituximab (Rituxan®)** added to the regimen in some cases. Rituximab is a monoclonal antibody designed to bind to cells expressing CD20. Rituximab is often combined with chemotherapy drugs. It is sometimes used to treat NLPBL because CD20 is expressed by the lymphoma cells in this type of disease. In rituximab therapy, the monoclonal antibodies attach to and kill the lymphoma cells.

Common treatments used in advanced NLPBL include:

- **R + ABVD**—rituximab plus doxorubicin, bleomycin, vinblastine, dacarbazine
- **R + B**—rituximab plus bendamustine
- **R-CHOP**— rituximab plus cyclophosphamide, doxorubicin, vincristine, prednisone
- **R-CVP**—rituximab plus cyclophosphamide, vinblastine, prednisone
- **Rituximab** alone

NLPBL can sometimes recur many years (or even decades) after initial treatment. In a small percentage of patients (8% to 14%), it can transform into diffuse large B-cell lymphoma (DLBCL), a type of non-Hodgkin lymphoma that is usually aggressive. NLPBL is more likely to transform into DLBCL if, at the time of diagnosis, the patient presents with large tumors (bulky disease) or if lymphoma is found below the diaphragm or in the spleen. For patients with a suspected relapse of NLPBL, another biopsy should be considered to rule out transformation to DLBCL. Patients with refractory or relapsed NLPBL can be treated with second-line therapies including rituximab, chemotherapy, radiation therapy, and/or autologous stem cell transplantation.

See **Table 6** on pages 25-27 for drug information.

New treatments may have been approved since this book was printed.  
Check [www.LLS.org/DrugUpdates](http://www.LLS.org/DrugUpdates) or call (800) 955-4572.

## Treatment for Relapsed or Refractory Classical Hodgkin Lymphoma in Adults

Most patients with classical HL are cured by their initial (first-line) treatment.

However, in a small percentage of patients—especially those with advanced stage HL—the disease relapses or is refractory. Relapse means the disease comes back after a remission following treatment. Refractory means the disease has not responded to treatment. For patients whose disease is relapsed or refractory, HL is still potentially curable.

When patients are not cured with initial therapy, second-line treatment options include:

- Alternate chemotherapy combinations
- Antibody-drug conjugate therapy with brentuximab vedotin
- Checkpoint inhibitors, such as nivolumab or pembrolizumab
- Autologous stem cell transplantation (see pages 21-22)

Talk with your treatment team to see if participating in a clinical trial is an appropriate option for you. See *Clinical Trials for Blood Cancers* on pages 43-44 or visit [www.LLS.org/CTSC](http://www.LLS.org/CTSC) for more information.

**Table 9. Some Treatment Approaches for Relapsed or Refractory Hodgkin Lymphoma**

### **Second-Line Therapies**

- BeGEV (gemcitabine/bendamustine/vinorelbine)
- Brentuximab vedotin
- Brentuximab vedotin + bendamustine
- Brentuximab vedotin + nivolumab
- DHAP (dexamethasone, cisplatin, high-dose cytarabine)
- GVD (gemcitabine, vinorelbine, liposomal doxorubicin)
- GVD + pembrolizumab
- ICE (ifosfamide, carboplatin, etoposide)
- ICE + brentuximab vedotin
- ICE + nivolumab
- IGEV (ifosfamide, gemcitabine, vinorelbine)
- Pembrolizumab
- Pembrolizumab + ICE

### **Third-Line Therapies**

- Bendamustine
- Bendamustine + carboplatin + etoposide
- Everolimus
- GCD (gemcitabine, cisplatin, dexamethasone)
- GEMOX (gemcitabine, oxaliplatin)
- Lenalidomide
- Nivolumab
- Vinblastine

Source: National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines. Hodgkin Lymphoma, Version 1.2024.

See **Table 6** on pages 25-27 for drug information.

# Hodgkin Lymphoma in Children and Adolescents

Hodgkin lymphoma (HL) is commonly diagnosed in children and young adults between the ages of 15 and 34, but it can occur in younger children between the ages of 3 and 15. It is very rare in infants.

Children and adolescents with HL have special needs for their treatment and care. Usually, specialized cancer centers for children and adolescents are best equipped to address their needs. These centers offer the advantage of having doctors called “pediatric oncologists,” who have specialized training in treating children with cancer.

According to the National Comprehensive Cancer Network (NCCN), the term “pediatric” includes any patient aged 18 years or younger, whereas the adolescent and young adult patient is defined as aged 15 to 39 years at the time of initial diagnosis. Adolescents with HL may be treated with either pediatric or adult protocols.

It is important for parents of children diagnosed with HL to talk to members of the oncology team about the:

- Specific subtype of the disease (see *Hodgkin Lymphoma Subtypes* on pages 8-9)
- Stage of the disease (see *Staging* on pages 10-14)
- Risk of treatment-related fertility issues (see *Fertility Concerns* on page 17)
- Risk group (low-risk, intermediate-risk or high-risk). Risk group is based on the stage, tumor size (sometimes called “bulk”), and whether or not the patient has B symptoms (fever, night sweats, weight loss)
- Other risk factors

Doctors use all of this information about the patient’s disease to determine the most effective treatment approach. They can develop treatment plans that limit the amount of therapy required to bring about remission. It is important for adult patients as well as parents of children who will be undergoing treatment, to discuss the planned therapy with members of the oncology team in order to learn about the following:

- Treatment schedule
- Drugs that will be used
- Potential need for radiation therapy, in some cases
- Potential side effects and long-term effects

The option of participating in a clinical trial should also be discussed. See *Clinical Trials for Blood Cancers* on pages 43-44.

Usually, one or more of the below treatment approaches, called “pediatric regimens,” are used for children with HL:

- **Chemotherapy**—the use of potent drugs to kill or damage cancer cells
- **Image-guided radiation therapy (IGRT)**—the use of high energy x-rays or other types of radiation to kill cancer cells. In IGRT, imaging scans are used for both treatment planning and during radiation therapy sessions, allowing for adjustments to improve accuracy.
- **Targeted therapy**—the use of drugs such as antibody-drug conjugates (ADCs) to target specific proteins on cancer cells, stopping their growth and spread
- **Immunotherapy**—the use of drugs such as monoclonal antibodies and immune checkpoint inhibitors to encourage one’s own immune system to work more effectively to identify and kill cancer cells
- **Surgery**—in rare cases of NLPBL (formerly called NLPHL), doctors may completely remove a single lymph node
- **High-dose chemotherapy with stem cell transplantation**— see *Stem Cell Transplantation* on pages 21-22

Children and adolescents are treated with dose-intensive regimens that are adjusted based on monitoring of early-treatment response. A patient who responds quickly to initial treatment is considered a rapid early responder (RER). A patient who responds slowly to treatment is considered a slow early responder (SER).

The following is a list of some of the many drug combinations used in first-line therapy for children and adolescents::

- **ABVE**—doxorubicin, bleomycin, vincristine, etoposide
- **ABVE-PC**—doxorubicin, bleomycin, vincristine, etoposide, prednisone, cyclophosphamide
- **ABVD**—doxorubicin, bleomycin, vincristine, dacarbazine
- **BEACOPP**—bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone
- **Bv-AVE-PC**—brentuximab vedotin, doxorubicin, vincristine, etoposide, prednisone, cyclophosphamide
- **COPP/ABV**—cyclophosphamide, vincristine, procarbazine, prednisone, doxorubicin, bleomycin, vinblastine
- **Escalated BEACOPP**—bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone

- **OEPA/COPDAC**—(for males) vincristine, etoposide, prednisone, doxorubicin followed by cyclophosphamide, vincristine, prednisone, dacarbazine
- **OPPA/COP**—(for females) vincristine, procarbazine, prednisone, doxorubicin followed by cyclophosphamide, vincristine, procarbazine, prednisone

See **Table 6** on pages 25-27 for information about individual drugs and their indications, and **Table 7** on page 28 for information on additional drug combinations.

New treatments may have been approved since this book was printed. Check [www.LLS.org/DrugUpdates](http://www.LLS.org/DrugUpdates) or call (800) 955-4572.

Some protocols include drug therapy followed by radiation therapy.

**Table 10. Some Drug Combinations Used to Treat Children and Adolescents Who Have Classical Hodgkin Lymphoma Based on Risk Group**

<b>Low-Risk Disease</b> (non-bulky stage IA or IIA)	<b>Intermediate-Risk Disease</b> (non-bulky stage IB or IIB, bulky stage IA or IIA, stage IIAE, stage IIIA)	<b>High-Risk Disease</b> (stage IIB with bulk, stage IIIB, stage IV)
ABV	COPP/ABV	BV plus DHAP
COPP	ABVE-PC	BV-AVE-PC
OEPA	OEPA or OPPA plus COPP or COPDAC	ABVE-PC
ABVD		OEPA or OPPA plus COPP or COPDAC
		BEACOPP (may be followed by COPP/ABV or ABVD)

Abbreviations used in headings: A, absence of fever, night sweats, unexplained weight loss; B, presence of fever, night sweats, unexplained weight loss; E, extranodal, meaning disease that has spread outside the lymph nodes to the organs. Bulky disease is a mass of 6 centimeters or more (10 centimeters in adults).

Risk groups based on Children’s Oncology Group criteria and *NCCN Clinical Practice Guidelines in Oncology - Pediatric Hodgkin Lymphoma*.



**Treatments for Children and Adolescents with Relapsed or Refractory Classical Hodgkin Lymphoma.** According to the National Cancer Institute (NCI), treatment options for children and adolescents whose disease has relapsed (come back after treatment) or is refractory (did not respond to initial treatment) include:

- Chemotherapy with or without steroids (such as dexamethasone or prednisone), targeted therapy (such as rituximab for NLPBL, brentuximab, or bortezomib), or both chemotherapy and targeted therapy
- Immunotherapy (such as pembrolizumab or nivolumab)
- High-dose chemotherapy with autologous stem cell transplantation, which uses the patient’s own stem cells; brentuximab vedotin may also be given
- Radiation therapy may be given after autologous stem cell transplantation, or if the cancer has not responded to other treatments and the area with cancer has not been treated before
- High-dose chemotherapy with allogeneic stem cell transplantation, which uses a donor’s stem cells
- Targeted therapy (such as brentuximab vedotin) for patients who have relapsed after an autologous stem cell transplant
- A clinical trial of anti-CD30 CAR T-cell therapy
- A clinical trial of immunotherapy (such as pembrolizumab)

**Table 11. Some Drug Combinations Used to Treat Children and Adolescents Who Have Relapsed or Refractory Classical Hodgkin Lymphoma**

<b>Re-Induction Therapy Options</b> (in alphabetical order)	<b>Subsequent Therapy Options</b> (in alphabetical order)	<b>Maintenance</b> (post-transplant)
Brentuximab vedotin + bendamustine	Bortezomib, ifosfamide, vinorelbine	For certain patients with high-risk disease: brentuximab vedotin
Brentuximab vedotin + gemcitabine	EPIC (etoposide, prednisolone, ifosfamide, cisplatin)	
Brentuximab vedotin + nivolumab	GDP (gemcitabine, dexamethasone, cisplatin)	
DHAP (dexamethasone, cytarabine, cisplatin)	ICE (ifosfamide, carboplatin, etoposide)	

GV (gemcitabine, vinorelbine)	Nivolumab	
IGEV (ifosfamide, gemcitabine, vinorelbine)	Pembrolizumab	
IV (ifosfamide, vinorelbine)		

Source: NCCN Guidelines Version 2.2023 for Pediatric Hodgkin Lymphoma.

NOTE: For relapsed or refractory nodular lymphocyte-predominant B-cell lymphoma (NLPBL), NCCN refers to the Guidelines for Adults.

See **Table 6** on pages 25-26 for drug information and page 33 for NLPBL information.

Children may experience treatment-related side effects, both in the short and long term. Some effects include second cancers, cardiovascular disease, hypothyroidism (underactive thyroid) and fertility issues. Side effects can affect learning, growth, cognitive development and psychosocial development. With regular screenings and survivorship care following active treatment, these and other possible long-term and late effects can be managed. When children return to school, families will face new challenges because their main focus, up to that point, had been getting through treatment. By being aware of possible side effects, parents can work with school personnel to help their children cope and manage their schoolwork.

**For more information, see the free LLS booklet *Learning & Living with Cancer: Advocating for your child's educational needs*.**

**Visit [www.LLS.org/FamilyWorkbook](http://www.LLS.org/FamilyWorkbook) to find information for children and families on topics such as talking with your child about cancer; coping with hair loss; siblings; long-term and late effects; and more.**

**Also visit [www.LLS.org/SurvivorshipWorkbook](http://www.LLS.org/SurvivorshipWorkbook) to access workbooks for children and adolescents, for young adults, and for adults.**

## Hodgkin Lymphoma and Young Adults

As with adolescents, young adults (generally considered through age 39 years) with HL may be treated with either pediatric or adult protocols. Additional studies are needed to determine preferred regimens for this population, and also how to best integrate new treatments. Notably, young adults face certain challenges unique to their age group, such as concerns about fertility, work, school, finances, health insurance, dating, parenting, etc.

**For more information, see the free LLS booklets *A Teen's Guide to Everything Cancer* and *Young Adults and Cancer*.**

## Hodgkin Lymphoma and Pregnancy

Because HL primarily affects adolescents and young adults, it is one of the most common types of cancer diagnosed during pregnancy. If a person is pregnant when diagnosed with HL, the treatment options depend on several factors, including: the trimester at the time of diagnosis; the stage and aggressiveness of the disease; and whether or not the patient has significant symptoms. Patients are encouraged to work closely with their hematologist-oncologist as well as a high-risk obstetrician (also called a maternal-fetal medicine specialist).

If possible, treatment should be delayed until at least the second trimester (the second 3 months) of pregnancy, because the risks of treatment to the fetus are greatest during the first trimester. For patients in their second and third trimesters, doctors may consider delaying treatment until after delivery of the baby (watchful waiting), if they determine that a delay in therapy would not impair the mother's health. Combination chemotherapy regimens given after the first trimester appear to be safe for both the mother and the baby. Treatment choices for pregnant patients with HL must be individualized, taking into consideration the patient's wishes, the symptoms and stage of the disease, and the length of time until delivery can occur safely. The timing of delivery should be carefully planned by the treatment team.

## Hodgkin Lymphoma in Older Adults

Older adults, generally defined as age 60 and older, make up approximately 20 percent of HL cases. Older adults are more likely to be diagnosed with the HL subtypes called "Mixed Cellularity" and "Lymphocyte-depleted." See **Table 1** on page 9.

The presentation of HL in older adults is similar to that of younger patients. The most commonly found symptom is swollen lymph nodes, with or without

B symptoms (unexplained fever, drenching night sweats, unexplained weight loss). See *Signs and/or Symptoms* on page 5.

The goal of treatment for HL in older adults is cure, with minimal harmful effects. Older adults need to be carefully evaluated for coexisting conditions as well as fitness for chemotherapy. Geriatric assessment (comprehensive evaluation of an older adult's health) is recommended to screen for frailty. Cardiac and pulmonary testing help determine a patient's suitability for certain treatments, such as an anthracycline-based therapy like doxorubicin (which can affect the heart) and/or bleomycin (which can affect the lungs).

Individualized treatment planning is essential for patients who are older than 60 years. Older adults can have more medical problems caused by treatment and a higher risk of death. It is important for patients to clearly communicate their priorities (for example, maintaining independence) and for the treatment team to understand a patient's preferences when discussing treatment options.

## Monitoring After Completion of Treatment

A PET-CT scan (see page 10) is the most accurate way to evaluate treatment response and remission status after completion of treatment. Imaging with a PET-CT scan should occur at least 3 weeks after the last chemotherapy treatment because if the scan is done earlier, temporary treatment-related inflammation could be mistaken for lymphoma masses.

Because of the risk of recurrence, periodic examination of HL patients is necessary for years after treatment. Most relapses occur within the first 2 years after completion of treatment, so follow-up visits during this time period will be more frequent, typically every 3 to 6 months. After 2 years, follow-up visits are generally scheduled every 6 to 12 months for the next 3 years until 5 years after completion of treatment.

There are long-term risks associated with HL therapy, so patients need to plan to continue their annual follow-up visits with a doctor who will monitor them for potential late complications of HL treatments, including second cancers and cardiovascular disease. See *Long-Term and Late Effects of Treatment* on pages 48-50. Many comprehensive cancer centers now have "survivorship clinics" to provide patients with individualized recommendations and follow-up planning after treatment ends.

The patient's history, as well as a physical examination and blood tests, are effective assessment tools for follow-up purposes. Unless new symptoms or signs suggesting relapse are evident, follow-up CT or PET-CT scans are not recommended for ongoing monitoring of potential disease recurrence because of high false-positive rates. The decision about whether to perform imaging tests

should be made on an individual basis, after the healthcare provider discusses the implications of their use with the patient. New technologies that seek to complement imaging techniques to assess treatment response are currently under study in clinical trials (see *Monitoring Treatment Response and Assessing Measurable Residual Disease* on pages 29-30.)

## Clinical Trials for Blood Cancers

Every new cancer drug goes through a series of carefully controlled research studies before it can become part of standard cancer care. These research studies are called clinical trials and they are used to find better ways to care for and treat people with cancer.

In the United States, the FDA (U.S. Food and Drug Administration) requires that all new drugs and other treatments be tested in clinical trials before they can be used. At any given time, there are thousands of cancer clinical trials taking place. Doctors and researchers are always looking for new and better ways to treat cancer.

Researchers use cancer clinical trials to study new ways to:

- Treat cancer using
  - A new drug
  - An approved drug to treat a different kind of cancer
  - A new combination of drugs
  - A new way of giving a drug—by mouth (pill), intravenously (IV)
- Manage cancer symptoms and ease treatment side effects
- Find and diagnose cancer
- Keep cancer from coming back after treatment
- Manage long-term side effects

By taking part in a clinical trial, patients can see doctors who are experts in their disease, gain access to new, cutting-edge therapies, and provide helpful information for future patients. The treatments and information we have today are due in large part to patients being willing to join clinical trials. Anyone interested in being part of a clinical trial are encouraged to speak with their hematologist-oncologist about whether a clinical trial might be right for them. During this conversation it may help to:

- Have a list of questions to ask about the risks and benefits of each trial (visit [www.LLS.org/WhatToAsk](http://www.LLS.org/WhatToAsk) for lists of suggested questions).
- Ask a family member or friend to go with you to your doctor visit—both for support and to take notes.

Clinical trials can be difficult to navigate and figure out, but The Leukemia & Lymphoma Society is here to help. Pediatric and adult patients and caregivers can work with **Clinical Trial Nurse Navigators** who will help find potential clinical trials, overcome barriers to enrollment and provide support throughout the entire clinical trial process. Our Clinical Trial Nurse Navigators are registered nurses who are experts in pediatric and adult blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about your treatment goals
- Help you understand the clinical-trial process, including your rights as a patient
- Ask you for details about your diagnosis (like past treatments, treatment responses, and your cancer genetic profile), your current health, and your medical history—because these might impact whether you can take part in certain clinical trials
- Help you understand how your finances, insurance coverage, support network, and ability and willingness to travel might impact your choice of clinical trials
- Guide you and help you in your efforts to find and enroll in a clinical trial, including connecting you with trial sites
- Help deal with any problems you might have as you enroll in a trial
- Support you throughout the clinical trial process

**Call an LLS Information Specialist at (800) 955-4572 or visit [www.LLS.org/CTSC](http://www.LLS.org/CTSC) for more information about clinical trials and the Clinical Trial Support Center (CTSC) at LLS.**

**Also, for further information, see the free LLS booklet *Understanding Clinical Trials for Blood Cancers*.**

## Financial Concerns

Paying for healthcare is a major concern for many people living with Hodgkin lymphoma and other blood cancers. The cost of treatment can be a financial burden as well as a worry for patients and families. In some cases, financial challenges may limit access to medications and lower adherence to treatments. There may also be significant travel and lodging expenses. Please talk with your doctor and members of your healthcare team (e.g., financial counselor, social worker, patient navigator) about your financial and other concerns. There are often resources that can help.

Health insurance usually doesn't cover all the costs of your cancer care. However, there are resources from organizations, foundations and prescription assistance programs that may be able to help. Several major pharmaceutical manufacturers provide patient assistance or prescription assistance programs. These companies may be able to help by providing both insured and uninsured patients with either free or reduced-cost medications.

LLS offers a number of financial assistance programs, as funds are available, for eligible blood cancer patients. These LLS programs may assist with co-pays, travel expenses and non-medical needs. Please contact an LLS Information Specialist at (800) 955-4572 or visit [www.LLS.org/finances](http://www.LLS.org/finances) to learn about the variety of LLS financial assistance programs and other resources available to patients.

**For more information and resources to cope with the financial aspects of cancer care, see the free LLS booklet *Cancer and Your Finances*.**

## Side Effects and Complications

Most side effects in patients with Hodgkin lymphoma (HL) are temporary and subside once the body adjusts to treatment, or when treatment is completed. Chemotherapy drugs attack rapidly dividing cells throughout the body, including both cancer cells and normal, healthy cells. Cells in the bone marrow, in hair follicles, and in the lining of the mouth and intestines divide quickly and may be affected by chemotherapy. The side effects of chemotherapy may vary, depending on the drugs used.

**Low Blood Cell Counts.** Patients who are treated with chemotherapy may experience low blood cell counts. Chemotherapy is toxic to the healthy cells in the bone marrow and may cause a deficiency of:

- Red blood cells (the cells that carry oxygen), resulting in a condition called "anemia"

- Platelets (the cells that help blood clot), resulting in a condition called “thrombocytopenia”
- White blood cells (the cells that fight infection), and especially the type of white blood cell called a neutrophil, resulting in a condition called “neutropenia”

Read more about blood cells in *Normal Blood and Bone Marrow* on page 55.

If the number of white blood cells (particularly the type called “neutrophils”) drops severely and for an extended time, patients may develop infections that require antibiotic treatment and possible hospitalization. In some types of cancer, it is necessary to allow a patient’s blood cell counts to recover from these side effects before continuing treatment. Sometimes the patient’s chemotherapy dosages or the time between chemotherapy cycles needs to be adjusted.

However, because HL has a high potential for cure, a low white blood cell count is not a reason to delay treatment or reduce the treatment dosage. It is uncommon for patients to continue to have low blood cell counts for a long time after the completion of treatment. However, patients who undergo stem cell transplantation may continue to be at risk for infection.

Treatment with drugs that are designed to improve white blood cell counts, such as granulocyte-colony stimulating factor (G-CSF), may be considered for patients with some types of cancer. However, in HL regimens that include bleomycin, G-CSF is not typically recommended because its use may increase the potential for lung complications. Bleomycin can damage the lungs and cause a disease called “pulmonary fibrosis.” G-CSF is commonly recommended for use in regimens that combine brentuximab vedotin with chemotherapy drugs.

**Infection.** During treatment for HL, the deficiency of neutrophils can lead to infection from bacteria and fungi that are normally present in the environment, on the skin, and in the nose, mouth and colon. The risk of infection may increase because chemotherapy damages the lining of the mouth and intestines, making it easier for bacteria to enter the blood. When the white blood cell count is low and there is an increased risk of infection, antibiotics are given to prevent or treat infection.

Because the patient has an increased risk of developing infections, the medical staff, family and friends of the patient need to wash their hands frequently and vigorously and take other precautions to avoid exposing the patient to bacteria, viruses and other infection-causing agents. Caregivers of patients with central lines need to be meticulous in caring for these devices.

Patients at home should seek medical attention right away if any sign of infection develops. A rise in temperature to 100.4°F or higher, or the onset of chills, may be the only sign of infection in a patient with a very low white blood cell count. Other signs of infection may include: persistent coughing, tenderness at a site prone



to infection (such as the area surrounding the anus or the facial sinuses), sore throat, pain on urination, or frequent loose stools.

One of the notable features of HL is a decrease in immune-system function; that is, the cells of the immune system do not react in normal ways. As a result, patients are susceptible to certain types of infection. Herpes zoster (shingles) is an example of a viral disease that occurs with increased frequency in patients with HL. Chemotherapy and radiation therapy can make patients more susceptible to infections because these treatments lower blood cell counts and weaken immune-system cell function.

HL patients are advised to get certain vaccinations once they have finished their treatment, including vaccinations for pneumococcal pneumonia and influenza. There are two types of pneumococcal vaccines available for adults: a pneumococcal polysaccharide vaccine (PPSV23) and a pneumococcal conjugate vaccine (PCV13, PCV15, or PCV20). A COVID-19 vaccine is also recommended. Immunizations using live organisms or with high viral loads, such as the herpes zoster or shingles vaccine, should not be administered. Patients who have HL can receive the shingles vaccine Shingrix® because it is an “inactivated” rather than a “live” vaccine. Speak to your doctor for more information.

**Other Side Effects.** Reactions to chemotherapy and radiation therapy vary from person to person. Most side effects appear shortly after the initiation of treatment but should resolve once the treatment is completed.

Chemotherapy and immunotherapy side effects depend on various factors including the drug type, dose administered, length of treatment and the patient’s susceptibility. Certain drugs have a specific tendency to affect certain tissues—for example, vincristine tends to affect nerve tissue, and bleomycin may affect the lungs. In addition to low blood cell counts and infection, some common side effects of immunotherapy and chemotherapy are listed below.

Acid reflux	Appetite changes	Bloating
Cognitive issues (“chemo brain”)	Constipation	Cough
Diarrhea	Extreme fatigue	Fever
Hair loss	Mouth sores	Muscle and joint pain
Nausea	Neuropathy (numbness and pain, usually in the hands or feet)	Rash or itchiness
Shortness of breath	Taste changes	Vomiting

Radiation therapy side effects depend on the area treated. Many people experience fatigue after radiation therapy. The skin may look and feel as if it is mildly sunburned, and it may also become dry or sore and feel painful when touched. Patients may also have short-term hair loss in the area that was treated. Treatment to the head or neck can cause mouth sores, dry mouth and changes in taste. Chest radiation can cause a dry cough or a sensation of a lump in the throat when swallowing. Radiation in the abdomen may cause nausea, vomiting, diarrhea and cramps.

It is important for patients to tell the members of their treatment team about any side effects they are experiencing. Appropriate medications may help patients feel better, and some side effects can even be prevented.

**For more information, see the free LLS series of booklets *Side Effect Management*.**

## Survivorship

According to the National Cancer Institute:

“In cancer, survivorship focuses on the health and well-being of a person with cancer from the time of diagnosis until the end of life. This includes the physical, mental, emotional, social, and financial effects of cancer that begin at diagnosis and continue through treatment and beyond. The survivorship experience also includes issues related to follow-up care (including regular health and wellness checkups), late effects of treatment, cancer recurrence, second cancers, and quality of life. Family members, friends, and caregivers are also considered part of the survivorship experience.”

The information in this section applies to Hodgkin lymphoma survivors in general. See page 50 for additional information specific to childhood cancer survivors.

**Long-Term and Late Effects of Treatment.** Today, much is understood about the specific types of treatment for Hodgkin lymphoma (HL) and the risk for long-term or late effects. The most serious late effects experienced by long-term survivors of HL are second cancers, cardiovascular disease, lung damage, hypothyroidism (underactive thyroid) and fertility issues.

The incidence of these late effects appears to increase over time. However, the risk of late side effects may be lower with current treatments than it was with treatments used more than 10 years ago. For example, current treatments with radiation therapy tend to use less radiation and lower doses of radiation than in the past. Patients should be examined regularly by a hematologist-oncologist and should also be seen by a primary care doctor for a general health examination at least once a year.

**Second Cancer Risk.** Survivors of HL are at an increased risk for developing a second cancer later in life from chemotherapy and/or radiation therapy. It is important for patients who have been treated for HL to be routinely screened for signs of a second cancer.

- Radiation Therapy. The degree of risk for developing a second cancer is related to the amount of radiation therapy given during treatment. Lung and breast cancer are the most common second cancers in HL patients. Most of these cancers develop more than 10 years after the end of treatment. The risk of developing a second cancer is highest when radiation therapy is used as a part of first-line treatment.

Female patients younger than age 30 who have radiation therapy to the breast are at risk for developing breast cancer 15 to 20 years later. Male survivors of childhood cancer may also be at risk for developing second cancers, including breast cancer, though this is rare. Radiation therapy can also injure the lungs, especially in patients who receive the chemotherapy drug bleomycin. Bleomycin is the “B” in the commonly used chemotherapy regimen ABVD, which stands for Adriamycin® (doxorubicin), bleomycin, vinblastine and dacarbazine. Survivors who have had chest radiation therapy are also at risk for lung cancer. Smoking further increases this risk, so HL survivors are advised not to start smoking or, if they do smoke, to stop. The use of e-cigarettes (also known as vaping) can cause unhealthy side effects. The long-term effects of these products are unknown, so it’s best not to start their use.

- Chemotherapy. Use of chemotherapy with alkylating agents (such as cyclophosphamide or dacarbazine; see **Table 5** on pages 23-24 for drug class information) increases the risk of developing another type of blood cancer called acute myeloid leukemia (AML). Chemotherapy with alkylating agents can also significantly increase the risk of other malignancies such as lung, stomach and pancreatic cancer.

**Heart Disease.** Radiation therapy to the chest, and treatment with certain chemotherapy drugs (anthracyclines such as doxorubicin, and some alkylating agents) has been linked to heart problems, including cardiomyopathy (damage to the heart muscle), pericarditis (inflammation of the sac surrounding the heart), valve dysfunction, and myocardial infarction (classic heart attack). Radiation may also damage the lining of blood vessels. In large arteries, this damage may lead to accelerated atherosclerosis (buildup of plaque) and an increased risk of narrowing of the blood vessels and stroke. Radiation may also increase the risk of electrical conduction abnormalities, and lead to the need for a pacemaker. Heart disease induced by radiation therapy, if it occurs, is usually observed more than 5 to 10 years after the end of treatment, but symptoms may appear at any time.

**Lung Damage.** Radiation therapy to the chest and treatment with chemotherapy regimens that include bleomycin are both associated with acute lung toxicity and

can also lead to reduced lung function. Some reports suggest that the use of growth factors with chemotherapy drugs significantly increases the incidence of long-term lung problems. Risk factors include older age, cumulative bleomycin dose, lung radiation and prior history of lung disease.

**Thyroid Dysfunction.** Radiation therapy can injure the thyroid gland, causing decreased thyroid function (hypothyroidism). The resulting deficiency of thyroid hormones can disrupt heart rate, body temperature and metabolism. Symptoms of hypothyroidism include fatigue, weight gain, constipation, dry skin and sensitivity to cold temperatures. Hypothyroidism is reported in a number of long-term HL survivors who received neck or upper chest radiation therapy.

**Fertility.** Patients may have decreased fertility after treatment. The risk of infertility varies according to the type and amount of chemotherapy, the area of the body exposed to radiation therapy and the patient's age. With some chemotherapy regimens, fertility appears to be affected either minimally or not at all. The ABVD (see **Table 7** on pages 28-29) regimen, for example, rarely leads to sterility (the inability to have children) in males or females. Other regimens, such as BEACOPP, may cause immediate and permanent infertility in both males and females. In addition, females who have received chemotherapy with alkylating agents may experience premature menopause. These possible side effects of chemotherapy should be taken into consideration with respect to family planning before the start of treatment. There are fertility preservation options for both males and females, so speak to the healthcare team before starting treatment. **See *Fertility Concerns* on page 17 and for more information, see the free LLS booklet *Fertility and Cancer*.**

In couples of childbearing ages, if only one partner has received treatment and remains fertile, the incidence of pregnancy loss and the health of the newborn are very similar to those of healthy couples.

**Fatigue.** Fatigue is a common long-term effect for many people who receive chemotherapy, radiation therapy, or both. Fatigue in HL survivors has also been associated with underlying heart disease, anxiety, depression and other health problems. Exercise has been shown to improve fatigue related to chemotherapy. **For more information, see the free LLS booklet *Cancer-Related Fatigue*.**

**Concerns for Childhood HL Survivors.** Cancer treatments can harm a child's organs, tissues or bones and may cause delayed growth and other health problems later in life. Childhood cancer survivors may have complex and long-term health issues due to the treatments they received. While treatments for HL have led to greatly increased survival rates, some may cause significant long-term or late effects, involving:

- Cognition (the mental process of thinking, learning, remembering and using judgment)

- Physical development
- Psychological development

Factors that influence a child's risk for developing long-term or late effects include:

- Type and duration of treatment
- Sex
- Age at the time of treatment
- Overall health

The range and severity of these potential long-term and late effects vary. Some late effects become evident with the onset of puberty, growth and the normal aging process. Early intervention and healthy lifestyle practices (not smoking, good nutrition and exercise, regular screenings and follow-up care) may have a positive effect on the occurrence and/or severity of long-term and late effects.

It is important for parents to discuss possible late effects with members of their child's healthcare team so that the proper planning, evaluation and follow-up care can take place. See information for parents on page 53.

**Follow-Up Care.** Patients whose disease is in remission after completing treatment will continue to be examined regularly by their doctors. Careful periodic assessment of the patient's health may be required to evaluate the full effect of therapy, as well as to identify signs of disease relapse. Patients need to keep their doctors informed of any changes they notice in their health (for example, enlarged lymph nodes, fevers, night sweats, and the like). Over time, follow-up examinations may become less frequent.

Survivors of HL are encouraged to:

- Keep records of the treatments they have received. This information can help the doctor follow up on specific late effects that may be associated with those treatments and help the members of your healthcare team develop a schedule of follow-up examinations.
  - These records should include the following information: the patient's diagnosis; the names of all drugs taken; information about any radiation therapy, surgery or transplant received; information about any other treatments, and the names and dates of any significant complications and the treatment received for those complications.
  - Patients should periodically access treatment centers'/doctors' portals and review their electronic medical records themselves to be sure that the information in them is complete and up to date.

- Have regular screenings for heart disease and annual blood pressure and lipid/cholesterol monitoring. A baseline cardiac stress test, echocardiogram and carotid ultrasound (for patients treated with radiation to the neck) should be considered after completion of therapy.
- Have regular screenings for cancer. Cancers of the breast, lung, stomach, bone and soft tissues have been reported as early as 5 years after initial therapy for HL. If treated with radiation, an annual skin examination by a dermatologist and a monthly self-examination of the skin are recommended.
- Practice monthly breast self-examination, have a yearly breast examination by a healthcare professional and have an early baseline mammogram (within 8 to 10 years after therapy or by age 40, whichever occurs earlier). It is recommended that a breast MRI be added to mammography screening for females who received radiation in the chest area when they were between the ages of 10 and 30 years. Although some females may develop breast cancer after HL treatment, it can be detected early and treated, which provides the best chance for a cure.
- Have regular lung cancer screenings if a current or previous smoker and treated with chest radiation. Smoking further increases the risk of lung cancer and several other types of cancer, including acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS). If you smoke, ask your doctor for strategies to help you quit. The use of e-cigarettes (vaping) is also discouraged.
- Have a colonoscopy at least every 10 years. This is recommended for survivors aged 45 and older, or by age 40 for survivors at increased risk for colorectal cancer due to previous treatment. Colonoscopies may be recommended more frequently if polyps (growths) are found.
- Have regular thyroid function checkups, preferably by an endocrinologist (a doctor with specialized training to diagnose, treat and manage conditions related to hormones, glands and metabolism) every year to rule out hypothyroidism, especially in patients who were treated with radiation to the neck.
- Stay up to date with vaccinations appropriate for your age and circumstances. (Note that some people experience enlarged lymph nodes after receiving a COVID-19 vaccine.)
- Seek medical and psychosocial support for fatigue, depression and other long-term effects, if needed.

**For additional information, see the free LLS booklet *Navigating Life During and After a Blood Cancer Diagnosis: Adult, Young Adult, and Children and Adolescents*.**

For parents, the Children’s Oncology Group provides a downloadable Summary of Cancer Treatment template for you to fill out with the help of the members of your child’s healthcare team. Visit [www.survivorshipguidelines.org](http://www.survivorshipguidelines.org) to download a treatment template.

Also, many hospitals and treatment centers offer survivorship clinics that specialize in long-term follow-up care for cancer survivors. Children often begin visiting a survivorship clinic 2 years after finishing cancer treatment. However, the timeline can differ based on your child’s unique needs and medical history. Additionally, coordination between members of your child’s cancer survivorship healthcare team and primary care pediatrician is essential.

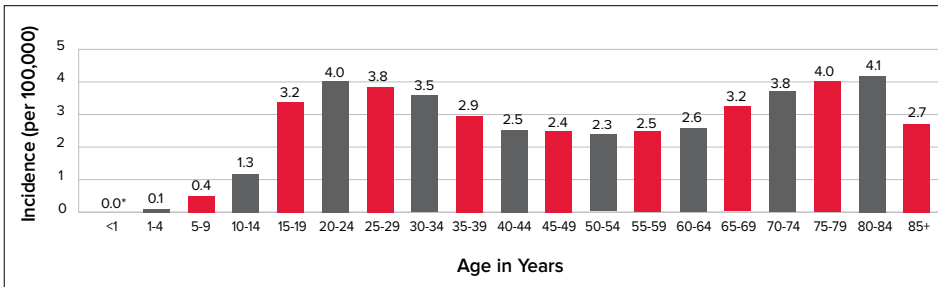
**Visit [www.LLS.org/FamilyWorkbook](http://www.LLS.org/FamilyWorkbook) to find information for children, adolescents, young adults and families.**

## Incidence, Causes and Risk Factors

Although Hodgkin lymphoma (HL) can occur in both adults and children, in most patients the disease is diagnosed between the ages of 15-34 years (see **Figure 3** below). For some HL subtypes, the risk of HL rises again after age 55. For older adults, the incidence is highest at ages 80-84 years. The disease is slightly more common among males than females.

Approximately 8,830 new cases of HL are expected to be diagnosed in 2023. This represents approximately 10% of all lymphomas in the United States. An estimated 159,867 people are living with or in remission from HL in the United States.

**Figure 3. Age-Specific Incidence Rates for Hodgkin Lymphoma, 2015-2019**



Source: SEER\*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. [Cited 2023 February 19]. Available from <https://seer.cancer.gov/explorer/>.

\*Estimates based on less than 16 cases are suppressed and not shown.

**Causes and Risk Factors.** In most cases, it is not clear what causes the genetic changes that lead to HL. There are, however, some known risk factors for HL. A “risk factor” is anything that increases a person’s chance of developing a disease. Having a risk factor, though, does not mean that a person will develop

the disease. Some people with several risk factors may never develop that disease, while others with no known risk factors for a disease do. It is known with certainty that HL is not contagious.

While the causes of HL are unknown, several factors are associated with an increased risk of developing HL, including:

- **Past Epstein-Barr virus infection.** The Epstein-Barr virus (EBV), known for causing mononucleosis, is associated with the development of some types of cancer, including HL. Infection with EBV in early childhood or having “mono” in the teenage years increases the risk of developing HL. But while the vast majority of the population has had prior infection with EBV, very few people actually develop HL.
- **Age.** People can develop HL at any age, but it is most common in adolescents and young adults. Certain subtypes may peak again in older adults.
- **Sex.** The risk of developing HL is slightly higher in males than females.
- **Family history.** There are occasional cases of familial clustering: having a first degree relative (parent or sibling) with HL may increase the risk of developing the disease compared with risk in the general population. There is a 10-fold higher risk in the case of same-sex siblings of patients with Hodgkin lymphoma.
- **Weakened immune system.** People infected with HIV, the virus that causes AIDS (acquired immunodeficiency syndrome), have an increased risk of developing HL. People who take medicines to suppress the immune system and people with autoimmune disease are also at a higher risk of developing HL.

Since many of these risk factors cannot be changed, there is no known way to prevent most cases of HL.

**For more information, see “Disease Registries and Other Disease Studies” at [www.LLS.org/ResourceDirectory](http://www.LLS.org/ResourceDirectory) under the heading “Blood Cancer—General Information,” or contact our Information Specialists at (800) 955-4572.**



# Normal Blood and Bone Marrow

**Blood.** Blood is the liquid that flows through a person's arteries and veins. It carries oxygen and nutrients throughout the body. It also carries away waste products. Blood is composed of plasma and cells.

**Plasma.** Plasma is largely made up of water, in which many chemicals are dissolved. These chemicals each have a special role. They include:

- Proteins
  - Albumin, the most common blood protein
  - Blood-clotting proteins (coagulation factors) made by the liver
  - Erythropoietin, a protein made by the kidneys that stimulates red blood cell production
  - Immunoglobulins, proteins that help the body fight infection
- Hormones, such as thyroid hormone and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate (B9) and vitamin B12
- Electrolytes, such as calcium, potassium and sodium

**Blood Cells.** Blood cells are formed in the bone marrow, a spongy tissue where blood cells grow and develop. Blood cells start as stem cells. The process of stem cells maturing into blood cells is called "hematopoiesis." The blood cells are suspended in the plasma. See **Figure 4** on page 57.

Once the stem cell is created, it will develop into one of the three types of blood cells:

1. Red blood cells (RBCs) (the cells that carry oxygen)

- These make up a little less than half of the body's total blood volume.
- They are filled with hemoglobin, the protein that picks up oxygen from the lungs and takes it around the body. It binds with carbon dioxide (CO<sub>2</sub>) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the CO<sub>2</sub> is removed from the lungs.

2. Platelets (the cells that help blood to clot)

- These are small cells (one-tenth the size of red blood cells).
- They help stop bleeding from an injury or cut.
- They stick to the torn surface of the vessel, clump together and plug up the bleeding site. They form a clot with the help of proteins, such as fibrin and electrolytes such as calcium.

3. White blood cells (WBCs). These are the cells that fight infections. They include:

- Neutrophils and monocytes. These cells, called “phagocytes,” ingest and destroy bacteria and fungi. Unlike red blood cells and platelets, monocytes can leave the bloodstream and enter tissues to attack invading organisms and fight off infection.
- Eosinophils and basophils. These WBCs respond to allergens or parasites.
- Lymphocytes. These WBCs, found mostly in the lymph nodes, spleen and lymphatic channels, are a key part of the immune system. Some enter the bloodstream. There are three major types of lymphocytes:
  - T lymphocytes (T cells)
  - B lymphocytes (B cells)
  - Natural killer cells (NK cells)

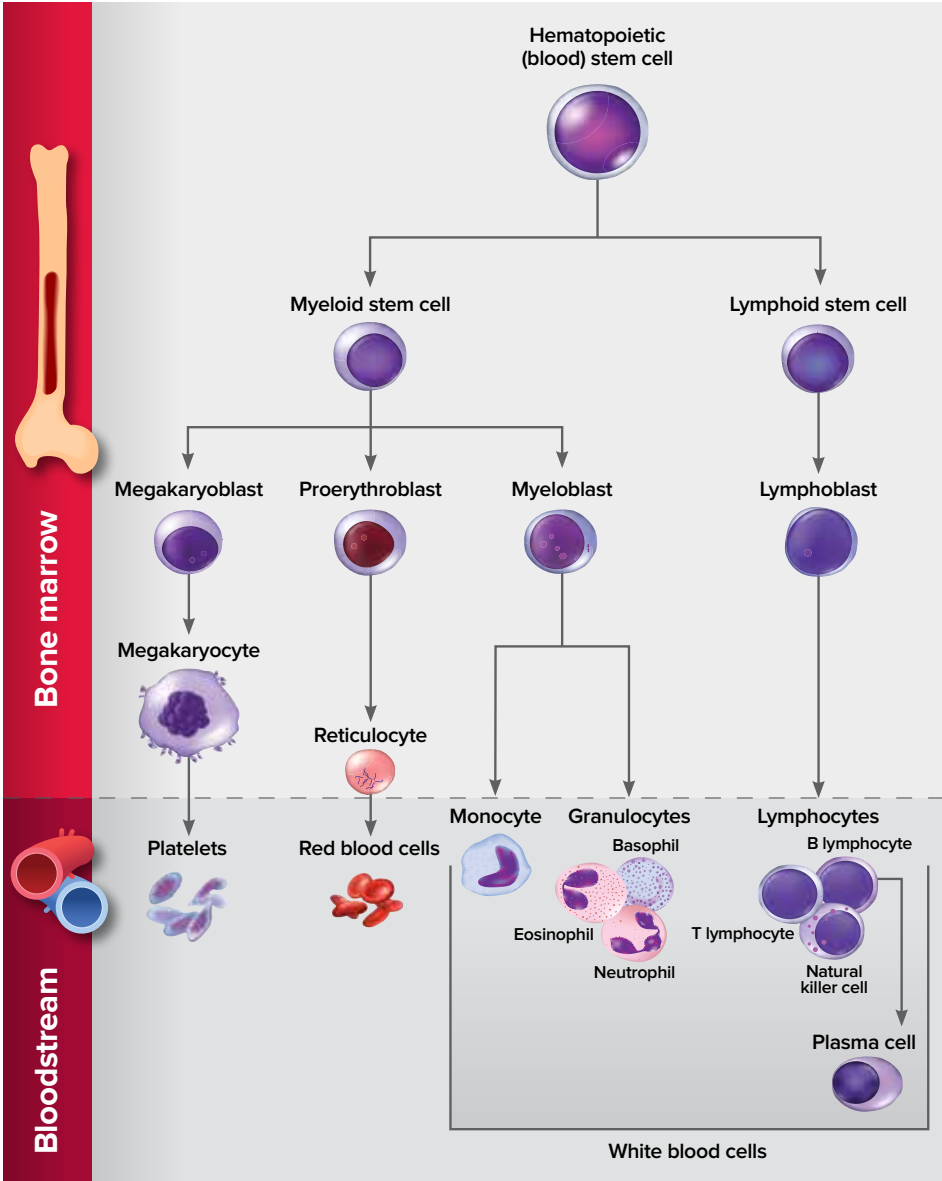
**Bone Marrow.** In healthy people, stem cells in the bone marrow produce new blood cells continuously. When blood cells are fully developed, they enter the bloodstream as it passes through the marrow and then circulate throughout the body.

In babies, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms and legs no longer have blood-forming marrow. In adults, marrow is only found in the spine (vertebrae), hip and shoulder bones, ribs, breastbone and skull.

Hematopoietic stem cells are found in the marrow. These stem cells are important because they can be used for transplants. Some stem cells enter the bloodstream and circulate. Doctors know how to stimulate the growth of these cells in the marrow and make them migrate into the bloodstream. Then a special technique called “apheresis” is used to separate them from the circulating blood so they can be collected and stored. Stem cells from the placenta and the umbilical cord of a newborn infant can also be harvested and used for future transplantation.

## Figure 4. Blood Cell and Lymphocyte Development

Most blood cells start as hematopoietic (blood) stem cells in the bone marrow. Hematopoietic stem cells are the most immature blood-forming cells. They must mature (go through many stages) to become a red blood cell, white blood cell or platelet. Some blood cells mature in the bone marrow. Other blood cells leave the bone marrow and travel to other parts of the body to develop into mature blood cells.



# The Lymphatic System

The lymphatic system comprises the tissues and organs that produce, store and carry lymphocytes (a type of white blood cell) that fight infection and other diseases. This system includes the bone marrow, spleen, and thymus. Lymph nodes and lymphatic vessels (a network of thin tubes that carry lymph and white blood cells.) See **Figure 1** on page 4.

The bone marrow is really two organs in one. It is (1) the organ that forms blood cells, and it is (2) the organ that forms lymphocytes, which make up part of the immune system.

The marrow produces three main types of lymphocytes. They are:

- B lymphocytes (B cells), which make antibodies in response to foreign antigens, especially microbes
- T lymphocytes (T cells), which mature in the thymus. The T lymphocytes have several functions, including assisting B lymphocytes to make antibodies against invading bacteria, viruses or other microbes. The antibody attaches to the microbe, making it possible for other white blood cells to recognize the antibody and pull it into the cell (ingest it) along with its attached microbe. The white blood cell then kills and ingests the microbe.
- Natural killer (NK) cells, which attack virus-infected cells or tumor cells without requiring an antibody or other substances. T cells and NK cells have other functions as well, and are important elements in research efforts to design immunotherapies to treat lymphoma and other cancers.

The lymphocytes circulate through channels called “lymphatics,” which connect the lymph nodes to each other throughout the body. The lymphatic channels collect into large ducts that empty into blood vessels. Lymphocytes enter the blood via these ducts. Most lymphocytes are found in the lymph nodes and other parts of the lymphatic system, such as the skin, spleen, tonsils and adenoids, intestinal lining, and (in young people) the thymus.

## Resources and Information

LLS offers free information and services for patients and families affected by blood cancers. This section lists various resources you may find helpful.

### For Help and Information

**Consult with an Information Specialist.** Information Specialists can assist you through cancer treatment, financial and social challenges and give accurate, up-to-date disease, treatment and support information. Our Information Specialists

are highly trained oncology social workers and nurses. Language services are available. For more information, please:

- Call: (800) 955-4572 (Monday through Friday, 9 a.m. to 9 p.m. ET)
- Email and Live chat: [www.LLS.org/InformationSpecialists](http://www.LLS.org/InformationSpecialists)

**Clinical Trials (Research Studies).** Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. Pediatric and adult patients and caregivers can work with our Clinical Trial Nurse Navigators who will help find clinical trials and provide personalized support throughout the entire clinical trial process. Visit [www.LLS.org/CTSC](http://www.LLS.org/CTSC) for more information.

**Nutrition Consultations.** Schedule a free one-on-one nutrition consultation with one of our registered dietitians who have expertise in oncology nutrition. Consultations are available to patients of all cancer types and their caregivers. Dietitians can assist with information about healthy eating strategies, side effect management and more. Please visit [www.LLS.org/nutrition](http://www.LLS.org/nutrition) for more information.

**Free Information Booklets.** LLS offers free education and support booklets for patients, caregivers and healthcare professionals that can either be read online or ordered. Please visit [www.LLS.org/booklets](http://www.LLS.org/booklets) for more information.

**Telephone/Web Education Programs.** LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit [www.LLS.org/programs](http://www.LLS.org/programs) for more information.

**Financial Assistance.** LLS offers financial support to eligible individuals with blood cancer for insurance premiums, co-pays, and non-medical expenses like travel, food, utilities, housing, etc. For more information, please:

- Call: (877) 557-2672
- Visit: [www.LLS.org/finances](http://www.LLS.org/finances)

**Podcast.** *The Bloodline with LLS* is here to remind you that after a diagnosis comes hope. Listen in as patients, caregivers, advocates, doctors and other healthcare professionals discuss diagnosis, treatment options, quality-of-life concerns, treatment side effects, doctor-patient communication and other important survivorship topics. Visit [www.LLS.org/TheBloodline](http://www.LLS.org/TheBloodline) for more information and to subscribe to access exclusive content, submit ideas and topics, and connect with other listeners.

**3D Models.** LLS offers interactive 3D images to help visualize and better understand blood cell development, intrathecal therapy, leukemia, lymphoma, myeloma, MDS, MPNs and lab and imaging tests. Visit [www.LLS.org/3D](http://www.LLS.org/3D) for more.

## Free Mobile Apps.

- LLS Coloring For Kids™—Allows children (and adults) to express their creativity and offers activities to help them learn about blood cancer and its treatment. Visit [www.LLS.org/ColoringApp](http://www.LLS.org/ColoringApp) to download for free.
- LLS Health Manager™—Helps you track side effects, medication, food and hydration, questions for your doctor, and more. Visit [www.LLS.org/HealthManager](http://www.LLS.org/HealthManager) to download for free.

**Suggested Reading.** LLS provides a list of selected books recommended for patients, caregivers, children and teens. Visit [www.LLS.org/SuggestedReading](http://www.LLS.org/SuggestedReading) to find out more.

## Connecting with Patients, Caregivers and Community Resources

**LLS Community.** The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. Visit [www.LLS.org/community](http://www.LLS.org/community) to join.

**Weekly Online Chats.** Moderated online chats can provide support and help cancer patients and caregivers reach out and share information. Please visit [www.LLS.org/chat](http://www.LLS.org/chat) for more information.

**Local Programs.** LLS offers community support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection® Program* (a peer-to-peer support program), local support groups and other great resources. For more information about these programs or to contact your region, please:

- Call: (800) 955-4572
- Visit: [www.LLS.org/LocalPrograms](http://www.LLS.org/LocalPrograms)

**Advocacy and Public Policy.** Working closely with dedicated volunteer advocates, LLS's Office of Public Policy elevates the voices of patients to state and federal elected officials, the White House, governors and even courts. Together, we advocate for safe and effective treatments. We pursue policies that would make care more accessible to all patients. And, most of all, we advocate for the hope for a cure. Want to join our work? Visit [www.LLS.org/advocacy](http://www.LLS.org/advocacy) for more information.

**Other Helpful Organizations.** LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. For more information, please visit [www.LLS.org/ResourceDirectory](http://www.LLS.org/ResourceDirectory) to view the directory.

## Additional Help for Specific Populations

**Información en Español (LLS information in Spanish).** Please visit [www.LLS.org/espanol](http://www.LLS.org/espanol) for more information.

**Language Services.** Let members of your healthcare team know if you need translation or interpreting services because English is not your native language, or if you need other assistance, such as a sign language interpreter. Often these services are free.

**Information for Veterans.** Veterans who were exposed to Agent Orange while serving in Vietnam; to airborne hazards and burn pits while serving in Iraq, Afghanistan and other areas of Southwest Asia; to contaminated water at Camp Lejeune between 1953-1987; or to ionizing radiation during service may be able to get help from the United States Department of Veterans Affairs. For more information, please:

- Call: the VA (800) 749-8387
- Visit: <https://www.va.gov/disability/eligibility/hazardous-materials-exposure/>

**Information for Firefighters.** Firefighters are at an increased risk of developing cancer. There are steps that firefighters can take to reduce the risk. Please visit [www.LLS.org/FireFighters](http://www.LLS.org/FireFighters) for resources and information.

**World Trade Center Health Program.** People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be able to get help from the World Trade Center (WTC) Health Program. People eligible for help include:

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were in the NYC disaster area and those who lived, worked or were in school in that area
- Responders to the Pentagon and the Shanksville, PA, crashes

For more information, please:

- Call: WTC Health Program at (888) 982-4748
- Visit: [www.cdc.gov/wtc/faq.html](http://www.cdc.gov/wtc/faq.html)

**Help for Depression.** Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time, for example, if you feel depressed every day for a 2-week period. For more information, please:

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at [www.nimh.nih.gov](http://www.nimh.nih.gov) and enter “depression” in the search box

## Health Terms

**Allogeneic Stem Cell Transplantation.** A treatment that uses donor stem cells to restore a patient's damaged and diseased bone marrow after they receive high doses of chemotherapy. **See the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.**

**Anemia.** A condition in which the number of red blood cells is below normal. This results in a diminished ability of the blood to carry oxygen. Severe anemia can cause a pale complexion, weakness, fatigue and shortness of breath.

**Antibody.** A type of protein created by blood cells in response to an antigen (a substance that causes a specific immune response in the body). Antibodies help the body fight against these "invaders" that make a person sick. Antibodies can also be made in the laboratory and are used to help identify and treat certain types of cancer.

**Antigen.** A foreign substance, usually a protein, that stimulates an immune response when it is ingested, inhaled, or comes into contact with the skin or mucous membranes. Examples of antigens are bacteria, viruses and allergens.

**Autologous Stem Cell Transplantation.** A treatment in which stem cells are removed from a patient, stored, and then returned to the patient's bloodstream after the patient receives intensive chemotherapy. **See the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.**

**B Symptoms.** Symptoms caused by the lymphoma, including high fevers, drenching night sweats, and rapid weight loss without dieting.

**Biopsy.** A procedure to remove cells or tissue from the body for examination by a pathologist. The pathologist may study the sample under a microscope or perform other tests on the cells or tissue.

**Bone Marrow.** The spongy tissue in the hollow central cavity of the bones, where blood cell formation occurs. It produces red blood cells, white blood cells and platelets. After puberty, the bone marrow in the spine, ribs, breastbone, hips, shoulders and skull is most active in blood cell formation. In adults, the bones of the hands, feet, legs and arms do not contain blood-forming marrow (in these sites, the bone marrow is filled with fat cells). When bone marrow cells have matured into blood cells, they enter the blood that passes through the bone marrow and are carried throughout the body in the bloodstream.



**Bone Marrow Aspiration.** A procedure in which a sample of liquid bone marrow is removed, usually from the hip (pelvic) bone. After medication is given to numb the skin and the surface of the bone underneath, a special needle is inserted into the bone to remove a liquid sample of bone marrow. The bone marrow sample is sent to a laboratory for examination by a pathologist. This procedure is almost always done at the same time as a bone marrow biopsy.

**Bone Marrow Biopsy.** A procedure in which a small sample of bone containing bone marrow is removed, usually from the hip (pelvic) bone. It differs from bone marrow aspiration in that a sample of actual bone is removed, rather than a liquid sample. After medication is given to numb the skin, a special hollow biopsy needle is used to remove a core sample of bone. The sample is sent to a laboratory to be examined under a microscope. This procedure is almost always done at the same time as a bone marrow aspiration.

**Bone Marrow Transplantation.** See Allogeneic Stem Cell Transplantation and Autologous Stem Cell Transplantation.

**Central Line (Central Venous Catheter).** A flexible tube used to administer medications, fluids or blood products in the body or to withdraw blood samples from the body. See Port.

**Chemotherapy.** Treatment with chemical substances that stop the growth of cancer cells, either by killing the cancer cells or by stopping them from dividing.

**Clinical Trial.** A carefully planned and monitored research study that examines how new treatment approaches work in patients. The goal of clinical trials for blood cancers is to develop new treatments, improve quality of life and increase survival time. A treatment that is proven safe and effective in a clinical trial is often approved by the United States Food and Drug Administration (FDA) for use as a new standard treatment, if it is either more effective or has fewer side effects than the current standard treatment.

**Colony-Stimulating Factor.** See Growth Factor.

**Combined Modality Therapy.** Two or more types of treatment used alternately or at the same time to treat a disease. For example, chemotherapy with involved-site radiation therapy (ISRT) is a combined modality therapy for patients with Hodgkin lymphoma.

**Computed Tomography (CT) Scan.** A procedure in which a series of

x-ray images are processed by a computer to create 3D views of tissues and organs in the body.

**Cycle of Treatment.** A period of treatment followed by a period of rest to allow the body to recover. A cycle comprises the time from the start of one round of treatment until the start of the next round of treatment. For example, chemotherapy given daily for 1 week, followed by 3 weeks of rest, may be one cycle of treatment.

**DNA.** The abbreviation for deoxyribonucleic acid, the genetic material found in all cells. It is passed to new cells during the process of cell division. A change or mutation in the DNA can lead to cell death, changes in cell function, and in some cases, cancer.

**Erythrocyte Sedimentation Rate (ESR).** A blood test that measures how quickly red blood cells (erythrocytes) settle to the bottom of a test tube in one hour. A sedimentation rate test is done to find out if inflammation is present in the body. It can also be used to determine how much a disease has progressed or how well a treatment is working.

**Extranodal Lymphoma.** Lymphoma that has spread outside the lymph nodes to the organs—for example, to the thyroid, lungs, liver, bones, stomach or central nervous system.

**FDA.** The abbreviation for the United States Food and Drug Administration. The FDA is responsible for assuring the safety, effectiveness and security of drugs, medical devices and the nation's food supply.

**G-CSF (Granulocyte-Colony Stimulating Factor).** See Growth Factor.

**Growth Factor.** A substance used to increase the number of neutrophils after chemotherapy.

**Hematologist.** A doctor who specializes in the treatment of blood diseases.

**Hematopathologist.** A doctor who has special training in identifying blood diseases by examining blood, bone marrow, lymph tissue and other tissue samples under a microscope.

**Immune System.** A complex network of cells, tissues and organs that work together to defend the body against infections and diseases.

**Immunophenotyping.** A lab test that can measure the number of blood cells in a sample as well as certain characteristics of cells, such as their

size and shape. It can also detect tumor markers on the surface of cells and identify specific types of leukemia and lymphoma cells.

**Immunotherapy.** The term for several treatment approaches used by doctors to harness the body's immune system to treat lymphoma and other diseases. **For more information, see the free LLS booklet *Immunotherapy*.**

**Late Effect.** A medical problem that either does not appear or is not noticed until years after treatment ends. A second, treatment-related cancer and heart disease are examples of late effects.

**Lymph Node.** A bean-shaped structure that is part of the body's immune system. Lymph nodes contain large numbers of lymphocytes and are connected with each other by small channels called "lymphatic vessels." There are hundreds of lymph nodes distributed throughout the body. In patients with lymphoma, malignant lymphocytes grow into masses that can cause the lymph nodes to become enlarged.

**Lymphatic System.** A network of tissues and organs that produce, store and carry white blood cells throughout the body to fight infections and diseases. The lymphatic system includes lymph nodes, lymphatic vessels (a network of thin tubes that carry lymph and white blood cells), bone marrow, the spleen and thymus.

**Magnetic Resonance Imaging (MRI) Scan.** A procedure that uses magnetic fields and radio waves to create images of the body's organs and tissues. It differs from a CT scan in that the patient is not exposed to x-rays or other sources of radiation.

**Mediastinal Mass.** A growth that forms in the area of the chest between the lungs. The organs in this area include the heart, the trachea, the esophagus and lymph nodes, but not the lungs.

**Monoclonal Antibody.** A type of synthetic protein that can bind to substances in the body, including substances on cancer cells. Monoclonal antibodies are used in cancer treatment to target cancer cells.

**MRI Scan.** See Magnetic Resonance Imaging (MRI) Scan.

**Mutation.** A change in the DNA (deoxyribonucleic acid) sequence of a cell. A mutation may be caused by an error in cell division, or it may be caused by contact with DNA-damaging substances in the environment. Certain mutations may lead to cancer or other diseases.

**Neutropenia.** A decrease below normal in the concentration of neutrophils, a type of white blood cell.

**Neutrophil.** A type of white blood cell that helps fight infection by ingesting microorganisms and releasing enzymes that kill microorganisms. People with some types of blood cancer, or who have received treatment (such as chemotherapy) for cancer, usually have low neutrophil counts. People with low neutrophil counts are very susceptible to infections.

**Oncologist.** A doctor who has special training in diagnosing and treating cancer.

**Pathologist.** A doctor who has special training in identifying diseases by studying cells and tissues under a microscope.

**PET Scan.** See Positron Emission Tomography (PET) Scan.

**PET-CT Scan.** See Positron Emission Tomography-Computed Tomography (PET-CT) Scan.

**Port.** A small device that is used to access a central venous line to withdraw blood from patients and to give them treatments, including intravenous fluids, drugs and/or blood transfusions. The port is placed under the skin, usually in the chest. It is attached to a central line (a thin, flexible tube) that is guided into a large vein. A central line and port may stay in place for weeks or months. See Central Line.

**Positron Emission Tomography (PET) Scan.** A procedure that uses a scanner to make detailed computerized pictures of areas inside the body. A small amount of radioactive glucose, a type of sugar called FDG, is also used. Because cancer cells absorb more sugar than normal cells, the glucose helps in locating cancer cells.

**Positron Emission Tomography-Computed Tomography (PET-CT) Scan.** A procedure that combines two powerful imaging techniques, a PET scan and a CT scan. The two scans are done at the same time with the same machine. The combined scans give more detailed pictures of areas inside the body than either scan alone. A PET-CT scan may be used to help diagnose cancer, plan treatment, or determine how well treatment is working.

**Prognostic Factor.** A condition or characteristic of a patient that can be used to estimate the chance of recovery from a disease.

**Radiation Therapy.** The use of x-rays and other forms of radiation in cancer treatment. Radiation therapy may be useful in the treatment of localized lymphoma masses.

**Refractory.** This term refers to particular cases of a disease, such as Hodgkin lymphoma and other cancers, that do not respond to treatment. A disease can be refractory in newly diagnosed or relapsed cases.

**Relapse.** The return of a disease after a period of improvement or remission.

**Remission.** A decrease or disappearance of the signs and symptoms of a disease. Remission usually follows treatment. The terms “complete” and “partial” are sometimes used to further define remission. Complete remission means that all evidence of the disease is gone. Partial remission means that the disease is significantly improved by treatment, but some evidence of the disease remains.

**Second-Line Therapy.** Treatment that is given when the initial (“first-line”) therapy does not work or stops working.

**Spleen.** An organ of the lymphatic system located in the left upper portion of the abdomen, just under the left side of the diaphragm. Blood and lymphatic fluid circulate through the spleen, which filters out debris such as bacteria and old blood cells.

**Staging.** The use of exams and tests to determine if and how far a cancer has spread throughout the body. Staging provides important information for treatment planning.

**Stem Cell Transplantation.** See Allogeneic Stem Cell Transplantation and Autologous Stem Cell Transplantation.

**Thrombocytopenia.** A decrease below normal in the number of platelets (thrombocytes) in the blood.

**Toxic.** Used to describe a substance that is poisonous or harmful to cells in the body.

**World Health Organization (WHO).** An agency of the United Nations that deals with major health issues around the world. The WHO sets standards for health care and medicines and publishes scientific papers and reports.

# References

Alaggio R, Amador C, Anagnostopoulos I, et al. The 5th edition of the World Health Organization classification of haematolymphoid tumours: lymphoid neoplasms. *Leukemia*. 2022;36:1720-1748.

<https://www.nature.com/articles/s41375-022-01620-2>

Ansell SM. Hodgkin lymphoma: 2023 update on diagnosis, risk-stratification, and management. *American Journal of Hematology*. 2022;97(11):1478-1488.

<https://doi.org/10.1002/ajh.26717>

Barrett A, Collins GP. Older patients with Hodgkin lymphoma: walking the tightrope of efficacy and toxicity. *Frontiers in Oncology*. 2023;12:1017787.

<https://doi.org/10.3389/fonc.2022.1017787>

Campo E, Jaffe ES, Cook JR, et al. The international consensus classification of mature lymphoid neoplasms: a report from the Clinical Advisory Committee. *Blood*. 2022;140(11): 1229-1253.

<https://ashpublications.org/blood/article/140/11/1229/485458/The-International-Consensus-Classification-of>

Cancer Therapy Advisor. Hodgkin lymphoma: pharmacologic treatment.

<https://www.cancertherapyadvisor.com/ddi/hodgkin-lymphoma-pharmacologic-treatment/> Accessed July 26, 2023.

Castellino SM, Giulino-Roth L, Harker-Murray P, et al. Children's Oncology Group's 2023 blueprint for research: Hodgkin lymphoma. *Pediatric Blood & Cancer*. 2023;70(suppl 6):e30580. <https://doi.org/10.1002/pbc.30580>

Castellino SM, Pei Q, Parsons SK, et al. Brentuximab vedotin with chemotherapy in pediatric high-risk Hodgkin's lymphoma. *New England Journal of Medicine*. 2022;387:1649-1660. <https://www.nejm.org/doi/full/10.1056/NEJMoa2206660>

Children's Oncology Group. In treatment with Hodgkin disease.

<https://www.childrensoncologygroup.org/in-treatment-with-hodgkin-disease> Accessed October 30, 2023.

Eichenauer DA, Engert A. How I treat nodular lymphocyte-predominant Hodgkin lymphoma. *Blood*. 2020;136(26):2987-2993.

<https://doi.org/10.1182/blood.2019004044>

Eichenauer DA, Engert A. Nodular lymphocyte-predominant Hodgkin lymphoma: a unique disease deserving unique management. *Hematology ASH Education Program*. 2017;(1):324-328. <https://doi.org/10.1182/asheducation-2017.1.324>

El-Galaly TC, Cottureau AS, Condoluci A, et al. Hodgkin lymphoma: recent progress in overall management. In: Gallamini A, Juweid M, eds. *Lymphoma*. Brisbane, Australia: Exon Publications; 2021. <https://doi.org/10.36255/exon-publications.lymphoma.2021>

Evens AM, Carter J, Loh KP, et al. Management of older Hodgkin lymphoma patients. *Hematology ASH Education Program*. 2019(1):233-242. <https://ashpublications.org/hematology/article/2019/1/233/422626/Management-of-older-Hodgkin-lymphoma-patients>

Herrera AF, LeBlanc ML, Castellino SM, et al. SWOG S1826, a randomized study of nivolumab(N)-AVD versus brentuximab vedotin(BV)-AVD in advanced stage (AS) classic Hodgkin lymphoma (HL). *Journal of Clinical Oncology*. 2023 ASCO Annual Meeting Abstract. 2023 41(17)(suppl):LBA4-LBA4. [https://ascopubs.org/doi/abs/10.1200/JCO.2023.41.17\\_suppl.LBA4](https://ascopubs.org/doi/abs/10.1200/JCO.2023.41.17_suppl.LBA4)

Houlihan OA, Buckley D, Maher GM, et al. Maternal and perinatal outcomes following a diagnosis of Hodgkin lymphoma during or prior to pregnancy: a systematic review. *BJOG An International Journal of Obstetrics and Gynaecology*. 2023;130(4):336-347. <https://obgyn.onlinelibrary.wiley.com/doi/10.1111/1471-0528.17347>

Kaseb H, Babiker HM. Hodgkin lymphoma. National Library of Medicine: Stat Pearls. Continuing Education Activity. July 10, 2022. <https://www.ncbi.nlm.nih.gov/books/NBK499969/>

LaCasce AS, Ng AK. Hodgkin lymphoma: epidemiology and risk factors. UpToDate. <https://www.uptodate.com/contents/hodgkin-lymphoma-epidemiology-and-risk-factors> Accessed July 10, 2023.

LaCasce AS, Ng AK, Aster JC. Clinical presentation and diagnosis of classic Hodgkin lymphoma in adults. UpToDate. <https://www.uptodate.com/contents/clinical-presentation-and-diagnosis-of-classic-hodgkin-lymphoma-in-adults> Accessed June 28, 2023.

Lew-Derivry L, Brice P, Bigenwald C, et al. Should adolescents and young adults with Hodgkin lymphoma be treated as children or adults? *Blood*. 2022(140)(suppl 1):1749-1750. <https://doi.org/10.1182/blood-2022-157046>

Lo AC, Dieckmann K, Pelz T, et al. Pediatric classical Hodgkin lymphoma. *Pediatric Blood & Cancer*. 2021 May;68(suppl 2):e28562. <https://doi.org/10.1002/pbc.28562>

Maco M, Kupcova K, Herman V, et al. Circulating tumor DNA in Hodgkin lymphoma. *Annals of Hematology*. 2022(101):2393-2403. <https://doi.org/10.1007/s00277-022-04949-x>

McClain KL, Kamdar K. Overview of Hodgkin lymphoma in children and adolescents. UpToDate. <https://www.uptodate.com/contents/overview-of-hodgkin-lymphoma-in-children-and-adolescents> Accessed June 28, 2023.

Medscape Oncology. Hodgkin lymphoma treatment protocols. <https://emedicine.medscape.com/article/2006680-overview> Accessed July 26, 2023.

Naresh KN. Proposal of 'reactive-lymphocyte/histiocyte rich large B-cell lymphoma' as an alternate term for 'nodular lymphocyte predominant Hodgkin lymphoma' that would also address its overlap with T-cell/histiocyte rich large B-cell lymphoma. *European Journal of Haematology*. 2022; (3)4:1449-1451. <https://onlinelibrary.wiley.com/doi/10.1002/jha2.560>

National Cancer Institute. SEER cancer stat facts: Hodgkin lymphoma. <https://seer.cancer.gov/statfacts/html/hodg.html> Accessed July 10, 2023

National Cancer Institute. External beam radiation therapy for cancer. <https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy/external-beam> Accessed August 10, 2023.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Adolescent and Young Adult (AYA) Oncology. Version 2.2024. [https://www.nccn.org/professionals/physician\\_gls/pdf/aya.pdf](https://www.nccn.org/professionals/physician_gls/pdf/aya.pdf) Accessed August 17, 2023.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Pediatric Hodgkin Lymphoma. Version 2.2023. [https://www.nccn.org/professionals/physician\\_gls/pdf/ped\\_hodgkin.pdf](https://www.nccn.org/professionals/physician_gls/pdf/ped_hodgkin.pdf) Accessed June 30, 2023.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Hodgkin Lymphoma. Version 2.2023. [https://www.nccn.org/professionals/physician\\_gls/pdf/hodgkins.pdf](https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf) Accessed June 28, 2023.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Hodgkin Lymphoma. Version 1.2024. [https://www.nccn.org/professionals/physician\\_gls/pdf/hodgkins.pdf](https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf) Accessed November 20, 2023.

National Comprehensive Cancer Network (NCCN) Guidelines for Patients. Hodgkin Lymphoma. 2023. <https://www.nccn.org/patients/guidelines/content/PDF/hodgkin-patient.pdf> Accessed June 28, 2023.

National Comprehensive Cancer Network (NCCN) Guidelines for Patients. Hodgkin Lymphoma in Children. 2023. <https://www.nccn.org/patients/guidelines/content/PDF/hodgkinlymphomainchildren-patient.pdf> Accessed August 23, 2023.



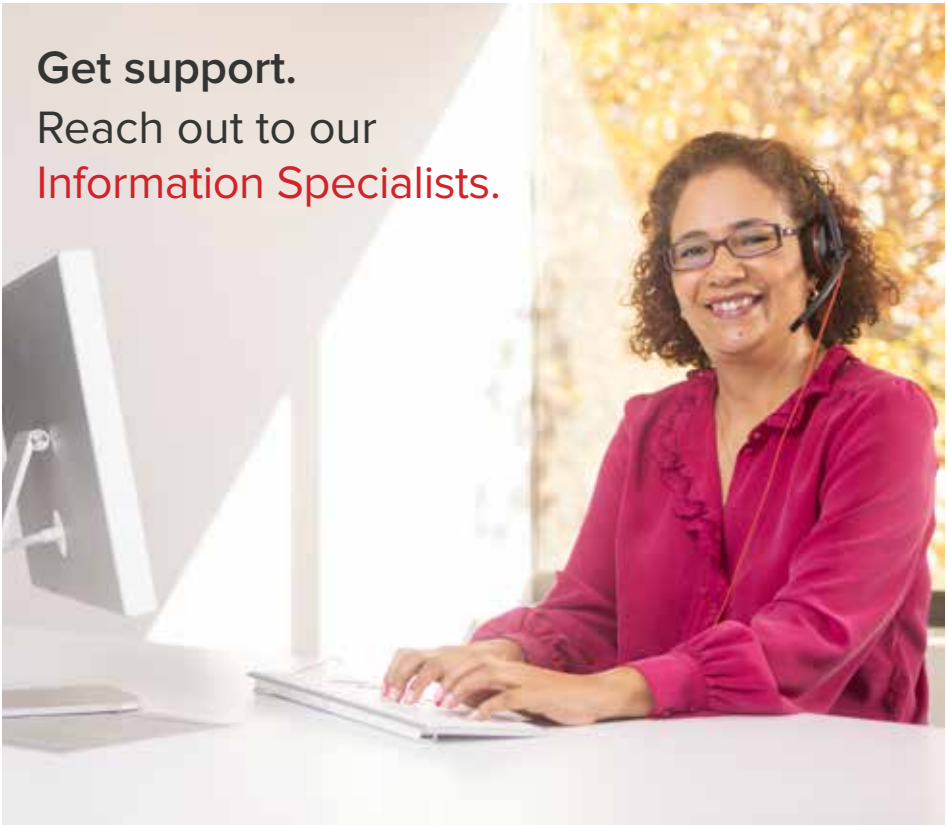
PDQ® Adult Treatment Editorial Board. *PDQ Hodgkin Lymphoma Treatment*. Bethesda, MD: National Cancer Institute. Updated March 23, 2023. <https://www.cancer.gov/types/lymphoma/hp/adult-hodgkin-treatment-pdq> Accessed June 29, 2023.

PDQ® Pediatric Treatment Editorial Board. *PDQ Childhood Hodgkin Lymphoma Treatment*. Bethesda, MD: National Cancer Institute. Updated June 6, 2023. <https://www.cancer.gov/types/lymphoma/hp/child-hodgkin-treatment-pdq> Accessed June 29, 2023.

Van Leeuwen FE, Ng AK. Long-term risk of second malignancy and cardiovascular disease after Hodgkin lymphoma treatment. *Hematology*. 2016(1):323-330. <https://doi.org/10.1182/asheducation-2016.1.323>



**Get support.**  
Reach out to our  
**Information Specialists.**



The Leukemia & Lymphoma Society® team consists of highly trained oncology social workers and nurses who are available by phone, email and live chat Monday through Friday, 9 a.m. to 9 p.m. (ET).

- Get one-on-one personalized support and information about blood cancers
- Know the questions to ask your doctor
- Discuss financial resources
- Receive individualized clinical-trial searches
- Get connected to resources

Contact us at  
**800.955.4572**  
or **www.LLS.org/**  
**InformationSpecialists**

(Language interpreters  
can be requested.)



For more information, please  
contact our Information Specialists  
**800.955.4572** (Language interpreters  
available upon request).

**National Office** 3 International Drive, Suite 200 Rye Brook, NY 10573

**The mission of The Leukemia & Lymphoma Society (LLS) is to cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families. Find out more at [www.LLS.org](http://www.LLS.org).**