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PATIENTS & CAREGIVERS

# Hodgkin Lymphoma



Revised **2022**

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

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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.



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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.

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### Acknowledgement

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# 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 7

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.

Approximately 8,830 new cases of HL were expected to be diagnosed in 2021. As of 2017, the latest year for which statistics are available, an estimated 152,671 people are either living with or in remission from HL.<sup>1</sup>

Advances in the treatment of HL are resulting in improved remission and cure rates. New treatment approaches are being studied in clinical trials for patients of all ages and at all stages of the disease.

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<sup>1</sup>Source: *Facts 2020-2021*. The Leukemia and Lymphoma Society. April 2021.

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## Hodgkin Lymphoma Basics

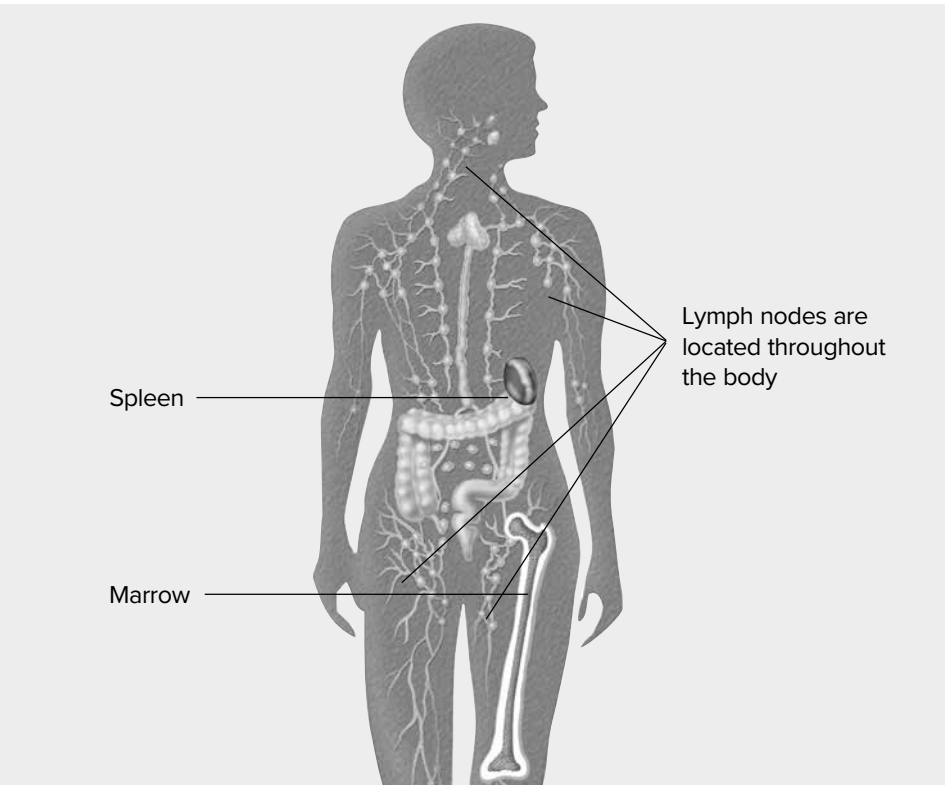
Hodgkin lymphoma (HL) was named after Dr. Thomas Hodgkin, a British pathologist who, in 1832, described several cases of people with symptoms of a cancer involving the lymph nodes. The disease was called “Hodgkin’s disease” until it was officially renamed “Hodgkin lymphoma,” when it became clear that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

When a normal lymphocyte, a type of white blood cell, undergoes a change (mutation) in a lymph node or other lymphatic structure, 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 malignant lymphocytes results in masses that are typically found in the lymph nodes and other sites in the body. See **Figure 1**, below.

Hodgkin lymphoma is distinguished from other types of lymphoma primarily by the presence of two types of cells, referred to as Hodgkin cells and 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. Hodgkin cells are larger than normal lymphocytes, but smaller than Reed-Sternberg cells. These differences can be observed under a microscope and further identified by special pathology tests. This is important information that helps doctors determine a patient's HL subtype.

### 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.

## 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 and/or symptoms that suggest the possibility of lymphoma is usually referred to a specialist called a “hematologist-oncologist.” This is a doctor who has special training in diagnosing and 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, especially after bathing or drinking alcohol
- 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

\*Indicates a “B symptom.” B symptoms are an important part of staging HL and determining a patient’s prognosis (chance of recovery). See page 13.

## 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. The 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 these signs and/or symptoms, including, but not limited to, high 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 measurement of all accessible lymph node groups in the neck, underarms and groin, as well as palpation (checking by feeling) of the size of organs such as the spleen and liver.

**Lymph Node Biopsy.** A biopsy of an enlarged lymph node is needed to diagnose HL. The preferred and most common type of biopsy is called an “excisional biopsy,” in which 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), you may be sedated or receive general anesthesia.

The biopsy samples will be sent to a hematopathologist, a doctor who has special training in diagnosing blood diseases by studying cells under a microscope. The hematopathologist examines the samples using a microscope to look for cancer cells. If Hodgkin and Reed-Sternberg cells are found in the lymph node sample, the hematopathologist will make a diagnosis of “classical HL” (often abbreviated as “cHL”). There is another, less common but distinct subtype of Hodgkin lymphoma, called “nodular lymphocyte-predominant Hodgkin lymphoma” (NLPHL); a diagnosis of NLPHL is made if the hematopathologist finds a specific type or pattern of lymphocytes that indicate this subtype of the disease.

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 8**).

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

Liquid biopsies rely on the detection of tumor-derived cell-free DNA from the blood plasma of patients, also called circulating tumor DNA (ctDNA). Sequencing ctDNA can be useful in several ways, such as:

- Identifying tumor-derived mutations through the blood
- Evaluating response to treatment and detecting minimal/measurable residual disease (MRD) during or after therapy is completed (see more information on MRD on page 22)
- Identifying patients whose disease is likely to relapse

This method is currently under investigation in clinical trials, and it could become a complementary method to tissue biopsy in the near future. It could be particularly useful in cases where a tumor mass is difficult to biopsy or when there is very little tissue removed through biopsy.

**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, the 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 antibodies attached to them, they will give off light.

Depending on the 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, CD30 and CD15 are found on the surface of the Hodgkin and Reed-Sternberg cells. Nodular lymphocyte-predominant Hodgkin lymphoma cells usually express CD45 and CD20, but not CD15 or CD30.

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



# Hodgkin Lymphoma Subtypes

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

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

Classical Hodgkin lymphoma (cHL) is characterized by the presence of both Hodgkin and Reed-Sternberg cells. 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. 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 8), each with different characteristics. When the doctor is making treatment decisions, the HL subtype is a very 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; 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.

# 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 important information for treatment planning. A series of tests are done to help determine the stage of HL.

**Imaging Tests.** Imaging tests make “pictures” (images) of the inside of the body and can show where the cancer is located. They 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 (this is called the “mediastinal” area). Healthcare professionals can also see lymph nodes on an x-ray image and note if any 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, 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 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 also 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 your 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 the 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.
- **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. The “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, that is released into the blood when a cell is damaged. A high level of LDH in the blood signals cell damage. The LDH level can be higher than normal in people with HL when the cancer is more active and doing 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 process) has damaged the kidneys.

- **Human immunodeficiency virus (HIV) and hepatitis B testing.** Tests for both HIV and hepatitis B should be part of the pretreatment workup for patients with HL, since 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 weaken or 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 should be given before undergoing treatment. Treatment options may depend on the results. See *Hodgkin Lymphoma and Pregnancy* on page 28.

**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 13). 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). Also, a visualizing PET scan may eliminate the need for a bone marrow biopsy to assess the disease.

**Stages of HL.** Staging for HL is based on the Lugano classification, which is derived from the Ann Arbor staging system (see **Table 2** on page 12). These classifications come from 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

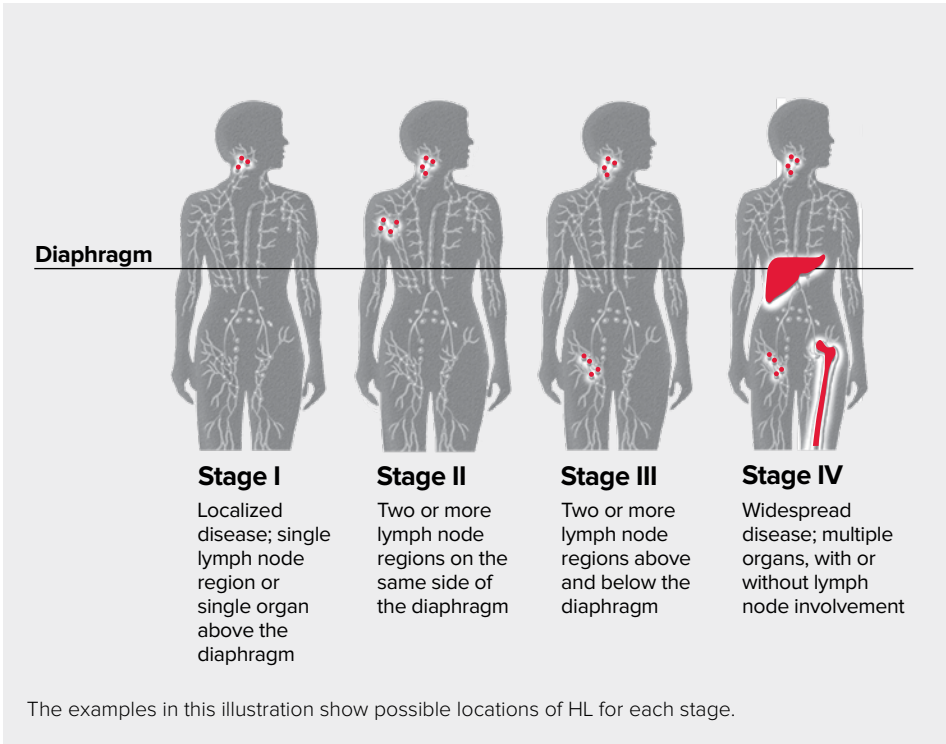
**Stage IV**

- HL cells 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 these three subgroups:

- Early-stage favorable: stage I to II with no unfavorable risk factors
- Early-stage unfavorable: stage I to II with one or more of the following unfavorable risk factors
  - Bulky disease: a mass in the chest that is one-third the width of the chest, or any lymph node mass greater than 10 centimeters
  - Involvement of 3 or more lymph nodes
  - B symptoms: fever, drenching night sweats and/or unexplained weight loss greater than 10 percent of body weight over 6 months
  - Extranodal disease: involvement of an organ outside the lymphatic system
  - Erythrocyte sedimentation rate (ESR) of 50 or higher

- Advanced stage: stage III to IV
  - Seven factors (shown in **Table 3**, below) provide a basis for recommending either aggressive or less-intensive treatment options.

About 30% of patients present with early-stage favorable HL; the other 70% of patients present with more advanced disease.

### **Table 3. 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)
- Hemoglobin level below 10.5 g/dL
- Leukocytosis: white blood cell count equal to or greater than 15,000/uL (microliter)
- Lymphocytopenia: lymphocyte count less than 8% of the white blood cell count and/or lymphocyte count less than 600/uL

The International Prognostic Score (IPS) assigns a point for each of the adverse prognostic factors that are present at diagnosis. The IPS helps doctors to determine the course of treatment and the prognosis for patients with advanced-stage (stages III to IV) disease.

**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, should 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 "oophorexy," 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.

See the free LLS booklet *Fertility and Cancer* for more details.

## Treatment for 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.

Patients have two main treatment options: standard care or treatment in a clinical trial. Be sure to talk with members of your healthcare team about the best treatment option for you.

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.

**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 only or a “combined modality therapy” consisting of chemotherapy followed by radiation therapy. The treatment for nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) requires a different treatment approach. For more information on the treatment of NLPHL, see *Treatment Options for Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL)* on page 24.

**Chemotherapy.** Chemotherapy drugs kill fast-growing cells throughout the body, including both cancer cells and normal, healthy cells. Different 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 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 the 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 by intravenous (IV) infusion, which means they are injected slowly, over a period of time, into a vein. The infusion, called a “continuous infusion,” may take a few hours or up to a few days to complete. These chemotherapy drugs are generally given through a thin, soft tube 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 *Central Line and Port in Health Terms* on page 45.

**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. Since radiation can also harm normal cells, whenever possible,

radiation therapy is directed only at the affected lymph node areas in order to reduce the long-term side effects.

Involved-site radiation therapy (ISRT) is sometimes used to treat HL. It selectively treats the lymph nodes where the cancer started and the cancerous masses near those nodes. 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. In recent years, proton therapy has been introduced to treat HL found in the chest. This therapy uses a beam of protons instead of electrons as the source of radiation and it allows for precise delivery of the radiation to the malignant tissue.

In many cases, a simulation session is needed for planning before 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, but the radiation is stronger. Each treatment session is only a few minutes, but the entire session can last between 15 and 30 minutes due to the set up of the equipment.

With careful planning, the exposure of uninvolved organs can be either reduced or avoided. Imaging techniques such as MRI and PET-CT scans can enhance treatment planning. 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
- 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.
- Three-dimensional conformal radiation therapy (3D-CRT), which uses photon beams that focus precisely on the tumor and avoid the surrounding healthy tissue

If radiation therapy is being considered, the benefits and risks of these different approaches should be carefully reviewed with the treating doctor.

**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 a type of protein made in the laboratory 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.

**Brentuximab vedotin (Adcetris®).** In patients with classical HL, the malignant Hodgkin and Reed-Sternberg cells typically express a protein called CD30. Brentuximab vedotin is an anti-CD30 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.

Brentuximab vedotin, given intravenously (IV), is approved for the treatment of adult patients with:

- Previously untreated stage III or IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine
- Classical Hodgkin lymphoma at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (post auto-HSCT) consolidation
- Classical Hodgkin lymphoma 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
- Certain other lymphomas with CD30 expression

**Immunotherapy.** This type of therapy uses the patient's immune system to fight cancer. Immunotherapy can be used to treat some people with HL.

Immune checkpoint inhibitors are a type of immunotherapy. 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 across 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®)** are checkpoint inhibitors, both given by IV, that 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). These drugs are also used to treat certain other types of cancer in which their effects on the immune system can be helpful.

**Nivolumab** is approved by the FDA (Food and Drug Administration) for the treatment of adult patients with classical Hodgkin lymphoma that has relapsed or progressed after:

- Autologous hematopoietic stem cell transplantation (auto-HSCT) and brentuximab vedotin, OR
- Three or more lines of systemic therapy that includes autologous HSCT.

**Pembrolizumab** is FDA-approved for the treatment of:

- Adult patients with relapsed or refractory cHL
- Pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy.

New types of monoclonal antibodies and checkpoint inhibitors are being studied in clinical trials to treat Hodgkin lymphoma.

#### **Table 4. Some Treatment Approaches for Classical Hodgkin Lymphoma**

##### **Early-stage classical Hodgkin lymphoma (cHL)**

- Chemotherapy combinations
  - ABVD—Adriamycin® (doxorubicin), bleomycin, vinblastine, dacarbazine
  - Escalated BEACOPP—bleomycin, etoposide, Adriamycin® (doxorubicin) cyclophosphamide, vincristine, procarbazine, prednisone
  - AVD—Adriamycin® (doxorubicin), vinblastine, dacarbazine
- Combination chemotherapy, administered either 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 cHL**

- Chemotherapy combinations
  - A+AVD—Adecetris® (brentuximab vedotin) plus Adriamycin® (doxorubicin), vinblastine, dacarbazine
  - ABVD
  - ABVD followed by escalated BEACOPP
- Occasionally, chemotherapy is followed by involved-site radiation therapy (ISRT)

**Relapsed/Refractory cHL** (A biopsy may be done before these treatments can begin)

- Further chemotherapy is given, such as
  - ICE—ifosfamide, carboplatin, etoposide
  - DHAP—dexamethasone, high-dose Ara-C (cytarabine), Platinol® (cisplatin)
  - ESHAP—etoposide, methylprednisolone, high-dose cytarabine, cisplatin
  - GDP—gemcitabine, dexamethasone, Platinol® (cisplatin)
  - GVD—gemcitabine, vinorelbine, liposomal doxorubicin
  - IGEV—ifosfamide, gemcitabine, vinorelbine
  - C-MOPP—cyclophosphamide, vincristine, procarbazine, prednisone
  - MINE—etoposide (Etopophos®), ifosfamide, mesna (Mesnex®), mitoxantrone (Novantrone®)
  - GCD—gemcitabine (Gemzar®), carboplatin, dexamethasone
  - Bendamustine (Bendeka®)
  - Bendamustine, carboplatin, etoposide
  - Everolimus (Afinitor®)
  - GEMOX—gemcitabine, oxaliplatin
- Brentuximab vedotin (Adcetris®), either alone or in combination with chemotherapy or other agents
- Stem cell transplantation
- Nivolumab (Opdivo®)\*
- Pembrolizumab (Keytruda®)\*

Radiation can be used either for palliative purposes or for radiation of sites of partial response to chemotherapy.

\*These treatments are for patients whose disease relapsed after autologous stem cell transplantation and brentuximab vedotin or for patients who are not eligible for transplant based on comorbidities or failure of second-line chemotherapy.

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.

**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 intensive chemotherapy
- Allogeneic stem cell transplantation, a procedure in which patients undergo intensive 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. The stem cells are removed from the patient's bone marrow (found inside the bones), 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.

**Brentuximab vedotin** is sometimes also given to patients before autologous stem cell transplantation, or, in select patients, it is administered as maintenance treatment after transplantation (see page 18 for more information).

**Allogeneic Stem Cell Transplantation.** This type of transplantation 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 an autologous transplantation.

Talk to your doctor to find out if stem cell transplantation is a treatment option for you. **See the free LLS booklet *Blood and Marrow Stem Cell Transplantation for more information about autologous and allogeneic stem cell transplantations.***

**Monitoring Treatment Response and Assessing Minimal/Measurable Residual Disease.** During and at the end of treatment, patients need to be monitored to check their response to therapy. The doctor runs 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, 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 inform the subsequent therapies. PET-CT has become the standard method for assessment of treatment response in most types of lymphoma.

The Deauville score, based on a five-point scale developed in 2009, is now an 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 or 2 is considered negative, meaning there are no areas of concern. A score of 4 or 5 is considered positive, which suggests there are malignant areas of concern. A score of 3 can be considered either positive or negative depending on the situation. The treatment team can determine how well the lymphoma is responding to treatment by observing whether this score increases or decreases as treatment progresses.

Minimal/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 and monitor cancer through the blood have been developed and hold the promise to revolutionize the way in which some types of cancer are diagnosed and managed. These methods, known as “liquid biopsies” rely on the detection of tumor-derived cell-free DNA (ctDNA) from the blood plasma of patients. ctDNA is either secreted directly into the bloodstream by tumor cells or released by these cells during cell death. Next-generation sequencing tests can detect mutations and other genetic abnormalities in the tumor DNA extracted and assess MRD during and after treatment in a non-invasive manner. In recent studies, higher ctDNA concentrations were correlated with higher tumor volume measured by PET-CT scans. This new method of MRD assessment can identify residual disease beyond the sensitivity of imaging tests and has the potential of complementing PET-CT scans in evaluating treatment response.



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 treatment. 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.

**Treatment of Early-Stage (Stage I-II) Favorable HL.** The cure rate for patients in this category exceeds 90 percent. 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** (see **Table 4** on page 19) has been the most commonly used chemotherapy regimen for these patients. ABVD poses less of a risk for later development of leukemia or infertility than many other chemotherapy combinations used for adults. Another treatment regimen is escalated **BEACOPP** (see **Table 4** on page 19).

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.

Concerns about the late effects of radiation therapy (especially an increased risk of developing a second cancer) 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 and 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* on page 33.

**Treatment of Early-Stage (Stage I-II) Unfavorable HL.** For patients in this category, the disease is considered to be high risk. Initial treatment usually consists of either a combined modality therapy (chemotherapy plus radiation therapy) or chemotherapy alone. Treatment is generally more intense for these patients 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 4** on page 19) include:

- **ABVD**
- **ABVD** followed by **escalated BEACOPP**

**Treatment of Advanced-Stage (Stage III-IV) HL.** Even in advanced stages, HL is curable. In general, patients with advanced-stage HL are treated with more intense regimens of combination chemotherapy. Some drug combinations used for treatment of these patients (see **Table 4** on page 19) include:

- **Brentuximab vedotin + AVD**
- **ABVD**
- **ABVD** followed by **escalated BEACOPP**
- **Escalated BEACOPP**

Dose-escalated BEACOPP results in a good cure rate, 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, and it is less commonly used for this reason.

Use of radiation therapy is limited to a small number of patients, those who have areas of bulky disease (large masses) at diagnosis or 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 Options for Nodular Lymphocyte-Predominant Hodgkin lymphoma (NLPHL).** This is a rare subtype of HL that accounts for only about 5 percent of all HL cases. The cancer cells in NLPHL are a variant of Reed-Sternberg cells. They are larger and are sometimes called “popcorn” cells because their unique shape is similar to pieces of popcorn.

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

Because NLPHL 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 from cancer therapies that are not needed. One option for some patients is the “watch-and-wait” approach, in which the patient is closely monitored for disease progression without getting any treatment until symptoms appear or begin to change. Other options for early-stage NLPHL without any B symptoms or bulky disease are the surgical removal of involved lymph nodes and the use of radiation therapy alone.

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

Common treatments used in NLPHL include:

- **ABVD + rituximab (Rituxan®)**—Adriamycin® (doxorubicin), bleomycin (Blenoxane®), vinblastine, dacarbazine plus rituximab
- **CHOP + rituximab (Rituxan®)**—cyclophosphamide, doxorubicin, vincristine, prednisone plus rituximab
- **CVP + rituximab (Rituxan®)**—cyclophosphamide, vinblastine, prednisone plus rituximab
- **Rituximab (Rituxan®)** alone

NLPHL 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. NLPHL 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 NLPHL, another biopsy should be considered to rule out transformation to DLBCL. Patients with refractory or relapsed NLPHL can be treated with a second-line therapy that includes rituximab, either with or without chemotherapy or radiation therapy.

## Treatment for Relapsed or Refractory Cases of cHL

Most patients with classical HL are cured by their initial (first-line) treatment. However, in a significant 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 these patients, HL is still potentially curable.

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

- Alternate chemotherapy combinations
- Monoclonal antibody therapy with brentuximab vedotin
- Checkpoint inhibitors, nivolumab and pembrolizumab
- Autologous stem cell transplantation (see page 21)

**Alternate Chemotherapy Combinations.** Some chemotherapy-based regimens used to treat patients with refractory or relapsed classic HL (see **Table 4** on page 19) include:

- **ICE**
- **DHAP**

- **ESHAP**
- **GDP**
- **GVD**
- **IGEV**
- **C-MOPP**
- **MINE**
- **GCD**
- **Brentuximab vedotin (Adcetris®)\***
- **Nivolumab (Opdivo®)\***
- **Pembrolizumab (Keytruda®)\***

**\*See pages 18-19 for prescribing information.**

## **Hodgkin Lymphoma in Children and Adolescents**

Hodgkin lymphoma (HL) is diagnosed in most patients between the ages of 15 and 34. 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 these needs. These centers offer the advantage of having doctors called “pediatric oncologists,” who specialize in treating children with cancer and therefore understand their unique needs.

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 page 7)
- Stage of the disease (see *Staging* on page 9)
- Risk of treatment-related fertility issues (see *Fertility Concerns* on page 15)
- 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 and parents of children who will be undergoing treatment to discuss their children’s planned therapy with members of the oncology team in order to learn about the treatment schedule and the drugs that will be used, as well as their potential side effects and long-term effects.

Usually, one or more of the following treatment approaches are used for children with HL:

- Chemotherapy
- Image-guided radiation therapy
- Targeted therapy (monoclonal antibodies)
- Surgery (if doctors believe that a mass can be completely removed)
- High-dose chemotherapy with stem cell transplantation

Children and adolescents are treated with dose-intensive regimens that are adjusted based on monitoring of early treatment response. The following is a list of just some of the many drug combinations used:

- **ABVE**—Adriamycin® (doxorubicin), bleomycin (Blenoxane®), vincristine, etoposide (Etopophos®)
- **ABVE-PC**—Adriamycin® (doxorubicin), bleomycin (Blenoxane®), vincristine, etoposide (Etopophos®), prednisone, cyclophosphamide
- **Escalated BEACOPP**—bleomycin (Blenoxane®), etoposide (Etopophos®), Adriamycin® (doxorubicin), cyclophosphamide, vincristine, procarbazine, prednisone
- **COPP/ABV**—cyclophosphamide, vincristine, procarbazine, prednisone, Adriamycin® (doxorubicin), bleomycin (Blenoxane®), vinblastine
- **VAMP/COP**—vincristine, Adriamycin® (doxorubicin), methotrexate and prednisone alternating with cyclophosphamide, vincristine and prednisone
- **Stanford V**—Adriamycin® (doxorubicin), vinblastine, mechlorethamine (Mustargen®), vincristine, bleomycin (Blenoxane®), etoposide (Etopophos®), prednisone

Children may experience treatment-related side effects, both in the short and long term. Some effects include second cancers, cardiovascular disease, hypothyroidism and fertility issues. Side effects can affect learning, growth, cognitive development and psychosocial development. 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 *Learning & Living with Cancer: Advocating for your child's educational needs*. Also visit [www.LLS.org/FamilyWorkbook](http://www.LLS.org/FamilyWorkbook) to find information for children and families.**

## 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 life-threatening symptoms. Patients should work with their hematologist-oncologist as well as a high-risk obstetrician.

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, if they determine that a delay in therapy would not impair the mother's health. Combination chemotherapy regimens with non-antimetabolite drugs, given after the first trimester, appear to be safe for both the mother and the baby. Other treatment choices include symptom management with corticosteroids or vinblastine alone until the time of delivery. 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.

## Monitoring After Completion of Treatment

A PET-CT scan (see page 9) is the most accurate way to evaluate treatment response and remission status after completion of treatment. Imaging testing 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 page 33. 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 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 professional 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 Minimal/Measurable Residual Disease* on page 22.)

## 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 (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 (pill, intravenously/IV etc.)
- 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 should talk to 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. Patients and caregivers can work with Clinical Trial Nurse Navigators who will help find potential clinical trials, overcome the barriers to enrollment and provide support throughout the entire clinical-trial process. Our Clinical Trial Nurse Navigators are registered nurses who are experts in blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about your treatment goals
- Help you to understand the clinical-trial process, including your rights as a patient
- Ask you for details about your diagnosis (such as 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 to 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

**Please 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 at LLS.**

**Also, visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Understanding Clinical Trials for Blood Cancers*.**



# 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, hair follicles and 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 often have low blood cell counts. Chemotherapy is toxic to the healthy cells in the bone marrow and may cause a severe deficiency of:

- Red blood cells, resulting in a condition called “anemia”
- Platelets, resulting in a condition called “thrombocytopenia”
- White blood cells
  - Neutrophil deficiency results in a condition called neutropenia.
  - Monocyte deficiency results in a condition called monocytopenia.

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 need 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. 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 in 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 and monocytes can lead to infection from bacteria and fungi that are normally present in the environment, on the skin and in the nose, mouth or 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 or ports need to be meticulous in cleaning 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 important features of HL is a decrease in immune-system function. 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). 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. COVID-19 vaccines are also recommended. 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 side effects depend on various factors including the drug type, dose administered, length of treatment and the patient’s susceptibility. Treatment with chemotherapy drugs may cause low blood cell counts, mouth sores, nausea, vomiting, acid reflux, bloating, constipation, diarrhea, extreme fatigue, neuropathy (numbness and pain, usually in the hands or feet), fever, cough and hair loss. Certain drugs have a specific tendency to affect certain tissues—for example, vincristine tends to affect nerve tissue, and bleomycin may affect the lungs.

- Radiation therapy side effects depend on the area treated. Many people experience fatigue. The skin may look and feel as if it is mildly sunburned and it may also become dry, 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. Some side effects can be prevented and appropriate medications may help patients feel better.

**Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view, print or order the free LLS series of booklets *Side Effect Management*.**

## Survivorship

**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 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. 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. It is important for patients who have been treated for HL to be routinely screened for signs of a second cancer.

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 second cancer is highest when radiation therapy is used as a part of first-line treatment.

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 (however, males who have had HL in childhood do not appear to have the same risk for developing cancer in the breast/chest area as female childhood cancer survivors). 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.

Use of chemotherapy with alkylating agents increases the risk of developing another type of leukemia called “acute myeloid leukemia (AML)”. Chemotherapy 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 and an increased risk of narrowing of the blood vessels and stroke. 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). This is reported in about 50 percent of long-term HL survivors who received neck or upper chest radiation therapy. Symptoms of hypothyroidism include weight gain, constipation, dry skin and sensitivity to cold temperatures.

**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. Other regimens, such as BEACOPP (see **Table 4** on page 19), 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 15 and see the free LLS booklet *Fertility and Cancer* for more information.

In couples of childbearing age, if only one partner has received treatment, 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*.**

**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, etc.) 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 to follow up on specific late effects that may be associated with those treatments, and also help the members of your healthcare team to 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 soon as 5 years after initial therapy for HL.
- Practice monthly breast self-examination, have 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 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.
- Have a colonoscopy every 10 years. This is recommended for survivors age 50 and older, or by age 40 for survivors at increased risk for colorectal cancer due to previous treatment.
- Have regular thyroid function checkups (at least every year) to rule out hypothyroidism, especially in patients who were treated with radiation to the neck
- Seek medical and psychosocial support for fatigue, depression and other long-term effects, if needed

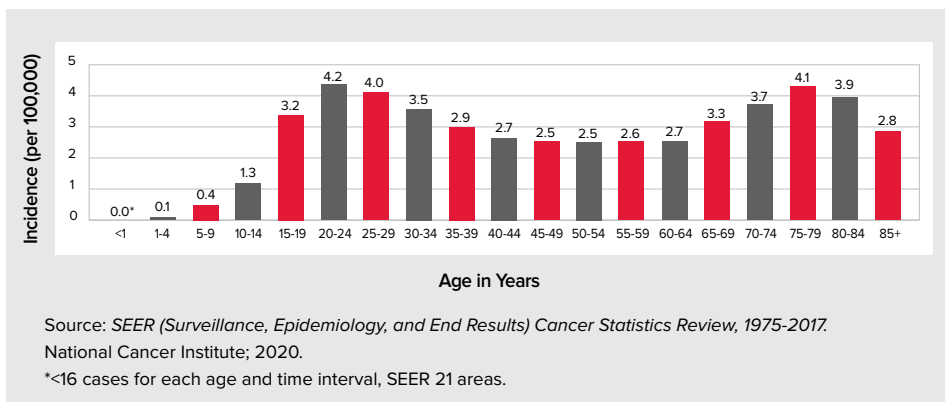
**For additional information, see the free LLS booklet *Navigating Life During and After a Blood Cancer Diagnosis: Adults*. Also visit [www.LLS.org/FamilyWorkbook](http://www.LLS.org/FamilyWorkbook) to find information for children and families.**

## 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 20-24 years and 75-79 years (see **Figure 3** below). The disease is more common among males than females.

Approximately 8,830 new cases of HL were expected to be diagnosed in 2021.

**Figure 3. Age-Specific Incidence Rates for Hodgkin Lymphoma, 2013-2017**



**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 many people are infected with EBV, very few actually develop HL.
- Age. People can develop HL at any age, but it is most common in adolescents and young adults (ages 15 to 29 years) and in older adults (ages 75 to 79 years).
- 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 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.

**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. This is the most common blood protein.

- Blood-clotting proteins (coagulation factors). They are made by the liver.
- Erythropoietin. It is made by the kidneys and stimulates red blood cell production.
- Immunoglobulins. These are cells that fight infection.
- Hormones, such as thyroid and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin B<sub>12</sub>
- 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 39.

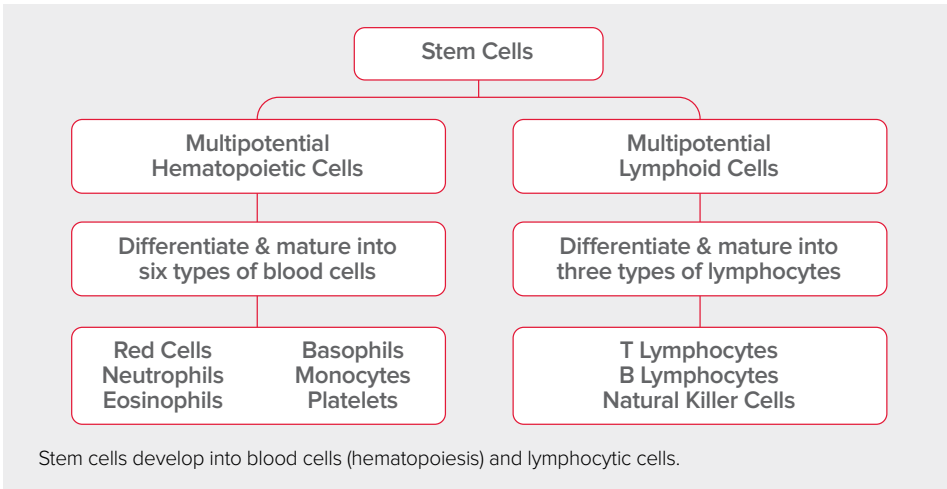
Once the blood cell is created, it will develop into one of the three types of blood cells.

These are:

1. Red blood cells (the cells that carry oxygen); they
  - Make up a little less than half of the body’s total blood volume
  - 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 (cells that help blood clot); they
  - Are small cells (one-tenth the size of red blood cells)
  - Help stop bleeding from an injury or cut
  - 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) are cells that fight infections. The several types of WBCs include:
  - Neutrophils and monocytes. These are “phagocytes” (eating cells) that 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.



**Figure 4. Blood Cell & Lymphocyte Development**



- Eosinophils and basophils. These WBCs respond to allergens or parasites.
- Lymphocytes. WBCs found mostly in the lymph nodes, spleen and lymphatic channels, they 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 (NK cells)

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 circulates 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 transplanted. Some stem cells enter the bloodstream and circulate; there are not enough of them to be counted in standard blood tests. Doctors know how to stimulate the growth of these cells in the marrow and have 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.

# The Lymphatic System

The 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 mediation. 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 to patients, caregivers and families affected by blood cancers. This section of the book lists various resources that can be helpful to you. Use this information to learn more, to ask questions and to make the most of your healthcare team members' knowledge and skills.

## For Help and Information

**Consult With an Information Specialist.** Information Specialists are highly trained oncology social workers, nurses and health educators. They offer up-to-date disease and treatment information. Language services are available. For more information, please:

- Call: (800) 955-4572 (Monday through Friday, 9 am to 9 pm ET)
- Email or live chat: [www.LLS.org/InformationSpecialists](http://www.LLS.org/InformationSpecialists)

**Clinical Trials Support Center (CTSC).** Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. Patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist them throughout the entire clinical-trial process. Please visit [www.LLS.org/CTSC](http://www.LLS.org/CTSC) for more information.

**One-on-One Nutrition Consultations.** Access free one-on-one nutrition consultations provided by a registered dietitian who has experience in oncology nutrition. Dietitians assist callers with information about healthy eating strategies, side effect management, and survivorship nutrition. They also provide additional nutrition resources. Visit [www.LLS.org/nutrition](http://www.LLS.org/nutrition) for more information and to schedule a consult.

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

**Financial Assistance.** LLS offers financial support including insurance premium and medication co-pay assistance as well as travel and other needs to eligible individuals with blood cancer. For more information, please:

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

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

**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.

### **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. Please visit [www.LLS.org/SuggestedReading](http://www.LLS.org/SuggestedReading) to view the titles.

### **Community Resources and Networking**

**LLS Community.** This is 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. Please 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 to reach out and share information. Please visit [www.LLS.org/chat](http://www.LLS.org/chat) for more information.

**LLS Chapters.** LLS offers 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, local education programs and other great resources. For more information about these programs or to contact the nearest chapter, please:

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

**Advocacy.** The LLS Office of Public Policy (OPP) engages volunteers in advocating for policies and laws that encourage the development of new treatments and improve access to quality medical care. For more information:

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

**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. Please visit [www.LLS.org/ResourceDirectory](http://www.LLS.org/ResourceDirectory) for more information.

### **Additional Help for Specific Populations**

**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 the service of a sign language interpreter. Often these services are free.

**Information for Veterans.** Veterans who were exposed to Agent Orange while serving in Vietnam may be able to get help from the United States Department of Veterans Affairs. Please visit [www.publichealth.va.gov/exposures/agentorange](http://www.publichealth.va.gov/exposures/agentorange) or call the Department of Veterans Affairs at (877) 222-8387 for more information.

**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 (WTC) Survivors.** People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be eligible for 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, lived, worked or were in school in the 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)

**People Suffering from Depression.** Treating depression has benefits for cancer patients. Contact your doctor 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

**Alkylating Agent.** A type of chemotherapy drug that kills cancer cells by damaging the cells' DNA, which prevents the cells from dividing (reproducing).

**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 Hodgkin 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.

**Differentiation.** The process in which immature cells develop and mature into cells with specific functions. Stem cells mature into red blood cells, platelets or white blood cells through this process. See Hematopoiesis.

**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.

**Eosinophil.** A type of white blood cell that helps fight allergies and certain parasitic infections.

**Erythrocyte.** See Red Blood Cell.

**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.

**Granulocyte.** A type of white blood cell that has a large number of granules in the cell body. Neutrophils, eosinophils and basophils are types of granulocytes.



**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.

**Hematopoiesis.** The formation of all types of blood cells in the bone marrow. For more information on the process of blood cell development, see *Normal Blood and Bone Marrow* on page 37.

**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 Facts*.**

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

**Leukocyte.** See White Blood Cell.

**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, and the spleen and thymus.

**Lymphocyte.** A type of white blood cell that is made in the bone marrow and is found in the blood and in lymph tissue. There are three major types of lymphocytes: 1) B lymphocytes, which produce antibodies to help combat infectious agents like bacteria, viruses and fungi; 2) T lymphocytes, which have several functions, including assisting B lymphocytes to make antibodies; and 3) natural killer (NK) cells, which can attack virus-infected cells or tumor cells.

**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.

**Monoclonal Antibody Therapy.** Type of immunotherapy using proteins made in the laboratory to target cancer cells. They either attach to antigens on the cancer cells or trigger an immune system reaction against them.

**Monocyte/Macrophage.** A type of white blood cell that is made in the bone marrow and travels through the blood to tissues in the body where it becomes a macrophage. Macrophages surround and kill microorganisms, ingest foreign material, remove dead cells and boost immune system functions.

**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.

**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.

**Phagocyte.** A type of white blood cell that protects the body from infection by eating and killing microorganisms such as bacteria and fungi. Neutrophils and monocytes are the two main types of phagocytes.

**Platelet.** A small, colorless blood cell that helps control bleeding. Platelets travel to and accumulate at the site of a wound. Their sticky surface helps them to form clots at the site of the wound and stop bleeding. This process is called clotting. Platelets make up about one tenth of the volume of red blood cells. Also called “thrombocyte.”

**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.

**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.

**Red Blood Cell.** A type of blood cell that contains a protein called hemoglobin that carries oxygen from the lungs to all parts of the body. Red blood cells make up about 40 to 45 percent of the volume of the blood in healthy individuals. Red blood cells are also called “erythrocytes.”

**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.

**Sedimentation Rate.** 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. This test is also called “erythrocyte sedimentation rate” or ESR.

**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.** A cell from which other types of cells develop. For example, red blood cells, white blood cells and platelets develop from blood-forming stem cells. See Hematopoiesis.

**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.

**White Blood Cell.** Any one of the five major types of infection-fighting blood cells, including: neutrophils, eosinophils, basophils, monocytes and lymphocytes. White blood cells are also called “leukocytes.” They are part of the body’s immune system.

**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.

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