



PROVIDING THE LATEST INFORMATION FOR  
PATIENTS & CAREGIVERS

# Hodgkin Lymphoma



Revised **2018**

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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

This booklet provides information about Hodgkin lymphoma (HL) for patients and their families. “Lymphoma” is a general term for a group of blood cancers that start in the lymphatic system. For easier reading and understanding, brief descriptions of normal blood and marrow, the lymphatic system, and definitions of health terms are included towards the end of the booklet. You may wish to glance through those sections first, to find out how a normal, healthy system functions (so that you can better understand the ways in which disease impacts it) and to learn some of the medical terms used here. See *Normal Blood and Marrow and the Lymphatic System* on page 31 and *Health Terms* on page 38.

An estimated 8,500 people living in the United States are expected to be diagnosed with Hodgkin lymphoma in 2018. There are an estimated 191,423 people either living with, or in remission from, HL.

Advances in the treatment of HL are resulting in improved remission and cure rates. The disease is now curable in at least 80 percent of patients. New approaches to therapy are being studied in clinical trials for patients of all ages and at all stages of the disease.

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## Lymphoma

Lymphoma is a general name for a group of cancers that affect the lymphatic system, which is part of the body’s immune system. There are two major types of lymphoma, Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL).

Both Hodgkin and non-Hodgkin lymphoma are further classified into subtypes. Knowing the subtype of your disease is important because the prognosis and treatment approach are based on the subtype. See *Subtypes of Hodgkin Lymphoma* on page 6.

You can find information about non-Hodgkin lymphoma in the free LLS booklet *Non-Hodgkin Lymphoma*.

# About Hodgkin Lymphoma

Hodgkin lymphoma was named for 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 the disease results from a change in the DNA (deoxyribonucleic acid) of a lymphocyte, a type of white blood cell.

Alterations to the DNA in the lymphocyte produces a malignant (cancerous) change that—if untreated—results in the uncontrolled growth of abnormal lymphocytes. In Hodgkin lymphoma (HL), the accumulation of abnormal lymphocytes results in tumor masses that are found in the lymph nodes and other sites in the body (see *Signs and Symptoms*, below).

Hodgkin lymphoma is distinguished from other types of lymphoma by the presence of Hodgkin and Reed-Sternberg (RS) cells, named for the scientists who first identified them. Reed-Sternberg cells are large, abnormal B lymphocytes, which often have more than one nucleus (multinuclear) and an owl-like appearance. Hodgkin cells are larger than normal lymphocytes but smaller than RS 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.

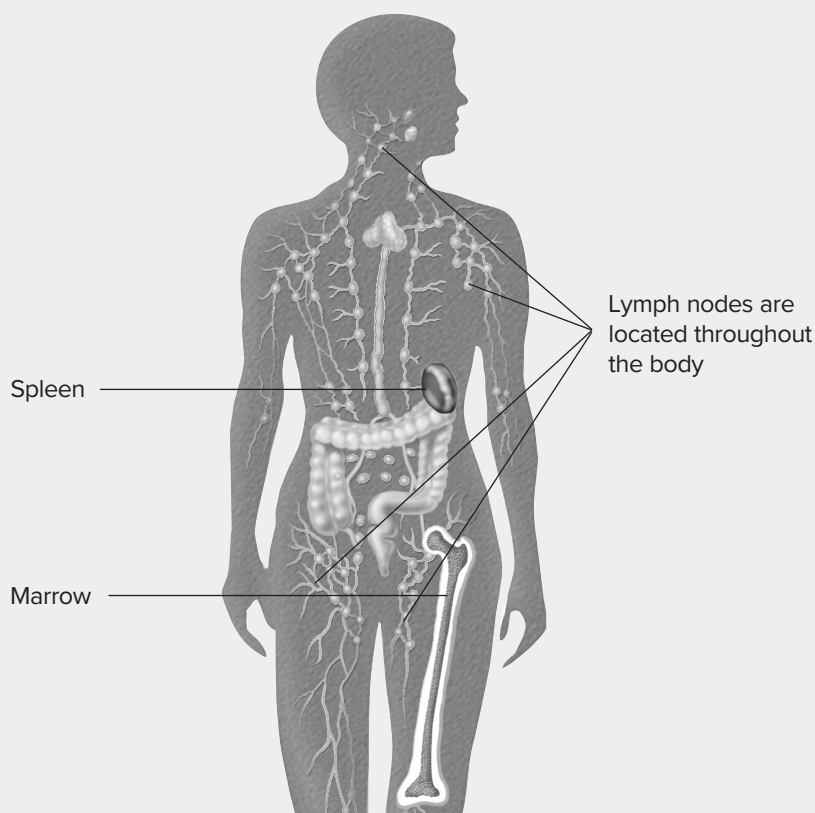
This booklet provides detailed information including diagnosis, staging and treatment of the more common HL subtypes. For those who want to better understand the concepts and terms in this booklet, there is a section towards the end of this booklet entitled *Normal Blood and Marrow and the Lymphatic System* on page 31 and also a glossary, *Health Terms* on page 38.

## Signs and Symptoms

A person with signs or symptoms that suggest the possibility of lymphoma is referred to a doctor called a “hematologist-oncologist.” Doctors who specialize in cancer are called “oncologists”. Doctors who specialize in blood diseases are called “hematologists.” Doctors who specialize in blood-related cancers like Hodgkin lymphoma (HL) are called “hematologist-oncologists.”

The signs and symptoms of HL can also be associated with other, less serious diseases. The doctor will order tests to make a definitive diagnosis (see *Diagnosis* on page 5).

## 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.

**Figure 1.** 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.

The most common early sign of HL is the painless swelling of one or more of the several hundred lymph nodes in the body (see **Figure 1** on *page 4*). In HL

- Most patients will have one or more affected lymph nodes in the upper part of the body—usually in the neck or upper chest.
- Sometimes the affected lymph node is in the armpit, abdomen or groin.
- The disease can also affect areas outside of the lymph nodes in other tissues.

Many patients have no symptoms at all. Signs and symptoms of HL may include B symptoms, which are significant to the prognosis and staging of the disease (B symptoms listed below are indicated with an asterisk). The other HL symptoms do not have the same prognostic importance and are not considered B symptoms. Signs and symptoms associated with HL are

- Drenching night sweats\*
- Unexplained weight loss\*
- Unexplained fever\*
- Persistent fatigue
- Persistent cough and shortness of breath (if the HL is located in the chest)
- Itchy skin
- Decreased appetite
- Abdominal pain or swelling and feeling of fullness (due to an enlarged spleen)
- Occasional pain in lymph nodes after drinking alcohol (uncommon but specific symptom).

\*Indicates a B symptom.

## Diagnosis

An accurate diagnosis of the subtype of Hodgkin lymphoma (HL) is important. Obtaining a precise diagnosis helps the doctor

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

**Patient Evaluation.** The healthcare provider takes a comprehensive medical history and asks questions regarding symptoms, including the absence or presence of B symptoms. Physical examination includes measurement of all accessible lymph node groups (neck, underarms and groin) as well as checking by feeling (palpating) the size of organs such as the spleen and liver.

**Lymph Node Biopsy.** A biopsy of an involved lymph node or other tumor site is needed to establish the diagnosis of HL. A needle biopsy, also known as “fine-needle aspiration,” of the lymph node is usually not sufficient to make a definitive diagnosis. The entire lymph node or part of the lymph node is typically surgically removed so that the hematopathologist has enough tissue to make a firm diagnosis. This procedure is known as an “excisional biopsy” (excision means “cutting out”). A doctor who examines lab samples and helps with diagnosis is called a “pathologist”; a doctor who specializes in blood diseases is called a “hematopathologist.”

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

Slides are prepared from the biopsy specimen by placing the tissue in preservative and staining it with dyes. Then the cells are examined under a microscope. The distinctive patterns of lymph node changes that are characteristic of HL are visible under the microscope and can help the hematopathologist to categorize the patient’s HL into one of several subtypes (see **Table 1** on *page 7*).

**Immunophenotyping.** A technique called “immunophenotyping” is used to distinguish HL from other types of lymphoma or other cancerous or noncancerous conditions. The hematopathologist looks for the presence of certain antigens or markers on the surface of the cells in order to identify Hodgkin and RS cells and confirm a diagnosis of HL.

Some of these tests may be repeated both during and after therapy to measure the effects of treatment.

## Subtypes of Hodgkin Lymphoma

The World Health Organization (WHO) divides Hodgkin lymphoma (HL) into two main subtypes. They are

- 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 (RS) cells. Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is characterized by the presence of lymphocyte-predominant cells, sometimes termed “popcorn cells,” which are a variant of RS cells. About 95 percent of HL patients have cHL (however, cHL is often simply referred to as “Hodgkin lymphoma”). Classical Hodgkin lymphoma is further classified into four subtypes (see **Table 1**, on *page 7*), each with different characteristics. When the doctor is making treatment decisions, the patient’s HL subtype is a very important consideration.



The World Health Organization’s Classification of Hodgkin Lymphoma Subtypes

Hodgkin Lymphoma Subtype	Features
Classical Hodgkin Lymphoma (cHL)	
Nodular Sclerosis	<ul style="list-style-type: none"><li>• Accounts for 70% of cHL cases</li><li>• Most common type in young adults</li><li>• Involved lymph nodes contain elements of fibrous tissue (sclerosis)</li><li>• Incidence similar in males and females</li><li>• Highly curable</li><li>• B symptoms in approximately 40% of cHL cases</li></ul>
Mixed Cellularity	<ul style="list-style-type: none"><li>• Accounts for 20%-25% of cHL cases</li><li>• Most common in older adults</li><li>• Most common in males</li><li>• More prevalent in patients with HIV infection</li><li>• Involved lymph nodes contain RS cells and several other cell types</li><li>• B symptoms common</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>• Median age range 30-37 years</li><li>• More prevalent in patients with HIV infection</li><li>• Usually diagnosed at an advanced stage</li><li>• B symptoms common</li></ul>
Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL)	<ul style="list-style-type: none"><li>• Accounts for 5% of all HL cases</li><li>• Most common in age range 30 to 50</li><li>• More common in males</li><li>• Slow growing and can relapse many years later like indolent NHL; highly curable</li><li>• Small risk of transformation to aggressive NHL (7% of cases)</li></ul>

**Table 1.** 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.

# Staging and Prognosis Factors

Doctors use physical examinations, imaging tests, blood tests and, sometimes, bone marrow biopsies to determine the extent of the disease. This determination is called “staging.” Staging provides important information for treatment planning. Prognosis is the likely outcome of a disease along with the chance of recovery or recurrence.

**Imaging Tests.** The physical examination and imaging tests help the doctor evaluate

- The location and distribution of lymph node enlargement
- Whether organs other than lymph nodes are involved
- Where there are very large masses of tumors in one site or another.

Imaging tests are a very important part of the staging and management of Hodgkin lymphoma (HL). A doctor may first order imaging tests when a patient’s 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 lung, bone or other body tissue.

The imaging tests may include

- A chest x-ray. This 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 document a mass between the lungs (this is called the “mediastinal” area). Healthcare professionals can see lymph nodes on an x-ray and note if there is any enlargement.
- A CT scan. A CT scan, also referred to as a “CAT scan,” uses special x-ray equipment to take multiple images from different angles around the body. A computer then processes this information and produces an image that shows a cross section of the area being examined. Patients may have CT scans of all the areas where lymph nodes are present, which may include the neck, chest, abdomen and pelvis, to identify areas of disease. A CT scan can also show whether there is involvement of the lungs, liver and other organs. A diagnostic CT scan should, at minimum, include all involved areas identified as abnormal on a previous PET scan. This information is helpful in staging HL.
- A positron emission tomography scan-computed tomography (PET-CT) scan. A combination PET and CT scan. A PET scan is an imaging technique that produces a three-dimensional (3D) image of functional processes in the body. This type of scan 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 of the body that highlight differences in the glucose accumulation in normal organs and

potentially cancerous tissues. Certain organs in the body absorb glucose at a higher rate than others. Cancer grows at a faster rate than normal tissue, so cancerous tissue also absorbs more of the radioactive glucose. Cancer spots appear brighter or “light up” in the scan. The images from a PET-CT scan frequently help the specialist to identify an appropriate biopsy site.

A PET-CT scan is also used to assess the response to therapy. A negative PET-CT finding after two courses of therapy has been identified as an important prognostic indicator.

- Magnetic resonance imaging (MRI), in select cases. Magnetic resonance imaging scanners use powerful magnetic fields and radio waves that are linked to 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 saved on a disk for future analysis. This test is rarely used in diagnosing HL, however, MRI is used for close examination of the spinal cord or the brain if a doctor is concerned that the disease may have involved these areas.

**Blood Tests.** Blood tests are used to

- Assess blood counts, including red blood cells, white blood cells, and platelets. Sometimes, anemia associated with HL can be mistakenly diagnosed as iron-deficiency anemia (a blood condition, characterized by a lack of red blood cells, that can be corrected with iron supplements). In addition, tests that compare the ratio between two different types of white blood cells (lymphocytes and monocytes) can help to predict the outcome of the disease.
- Determine whether lymphoma cells are present in the blood and whether the immunoglobulins (antibodies) made by lymphocytes are either deficient or abnormal
- Check indicators of inflammation and disease severity such as blood protein levels, including albumin and lactate dehydrogenase (LDH), as well as uric acid levels and erythrocyte sedimentation rate (ESR). High levels of either of the following may indicate cancer or another health problem.
  - Lactate dehydrogenase is a protein found in most cells and LDH levels increase when cells and tissues are damaged
  - Erythrocyte sedimentation rate is used to determine if there is inflammation.
- Assess kidney and liver functions

**Human immunodeficiency virus and Hepatitis B Testing.** Receiving the appropriate human immunodeficiency virus (HIV) treatment is an important part of HL treatment as it will improve how well the cancer therapy works. Hepatitis B can also affect how well some cancer treatments work. Both tests should be part of the pretreatment workup.

**Heart and Lung Tests.** Some HL treatments may weaken or damage the heart and lungs. The healthcare team may decide to test how well these organs work before treatment, in order to plan appropriate treatment.

**Pregnancy Test.** Some cancer treatments can harm an unborn baby, so a pregnancy test may be required for women of reproductive age before they can start certain treatments. Treatment options may depend on the results. See *Pregnancy and Hodgkin Lymphoma* on page 22.

**Bone Marrow Tests.** Some patients who have been diagnosed with HL may undergo a bone marrow aspiration and biopsy. The doctor will decide if these procedures are necessary. That determination will be based on considerations, such as the location of the disease in the body (see **Figure 1** on page 4). A bone marrow aspiration and biopsy may not be required for patients with early-stage favorable disease with low-risk clinical features, such as HL that manifests without B symptoms or bulky disease (large masses of lymphocytes).

Patients with newly diagnosed HL who are undergoing pretreatment staging with PET-CT scans may not need a bone marrow aspiration and biopsy, particularly if the scan findings are negative or if they display a uniform pattern of bone marrow uptake (“uptake” refers to the areas of cell activity that light up in the scan). Some of these tests may be repeated, both during and after therapy, to measure the response to treatment.

See *Health Terms* on page 38 for expanded definitions of some of the tests mentioned here.

**Staging.** Staging for HL is based on the Ann Arbor staging system (see **Figure 2** on page 11).

**Stage I.** One lymph node or a group of adjacent nodes

**Stage II.** Involvement of two or more lymph node regions on the same side of the diaphragm

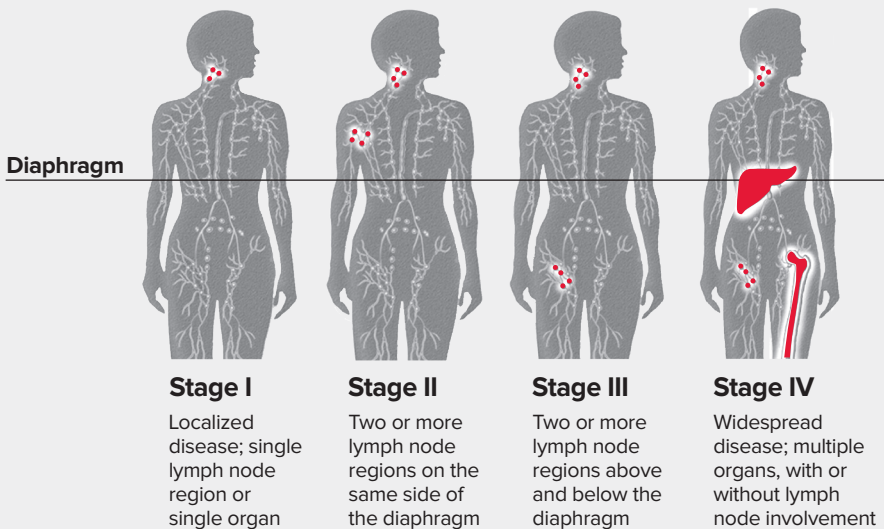
**Stage III.** Involvement of lymph nodes on both sides of the diaphragm (for example, neck, chest and abdomen)

**Stage IV.** Involvement of lymph nodes on both sides of the diaphragm and/or involvement of organs such as the lungs, spleen, liver, bones, or bone marrow

Each stage is subdivided and assigned to one of the following categories:

- Category A indicates no symptoms are present.
- Category B indicates the presence of the following B symptoms:
  - Unexplained fevers (higher than 100.4°F)
  - Drenching night sweats
  - Unexplained weight loss of more than 10 percent of body weight within 6 months prior to diagnosis
- Category E indicates involvement of organs or tissues beyond the lymph system.
- Category S indicates involvement of the spleen.

### Hodgkin Lymphoma Stages



**Figure 2.** This illustration shows the location of Hodgkin lymphoma in the body for each stage.

Staging for HL, based on the Ann Arbor staging system, would mean that stage IIB indicates that the patient has

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

Patients in the B category often require aggressive treatment.

# Treatment Planning

**Prognosis Factors.** Hodgkin lymphoma (HL) is generally classified into the following three subgroups that are based on the Ann Arbor staging system and either the presence or the absence of certain prognostic factors. The subgroups are

- Early-stage favorable: Disease is stage I to II with no unfavorable risk factors
- Early-stage unfavorable: Disease is stage I to II with unfavorable risk factors
- Advanced-stage: Disease is stage III to IV.

**Prognostic Factors for Early-Stage Hodgkin Lymphoma.** Early-stage favorable Hodgkin lymphoma (HL) patients are designated as such if they have either stage I or stage II disease and no adverse or unfavorable risk factors. Sometimes, patients with early-stage favorable HL are given less intensive treatment regimens. However, the use of staging information to modify therapy varies.

Early-stage unfavorable HL risk factors include

- B symptoms—fever, drenching night sweats, unexplained weight loss greater than 10 percent of body weight over 6 months
- Extranodal disease—masses located outside of the lymph nodes or lymph system
- Bulky disease—a chest mass that is greater than one third of the chest diameter as visualized on x-ray OR any lymph node mass greater than 10 cm in diameter
- Three or more sites of lymph node involvement
- Erythrocyte sedimentation rate that is greater than or equal to 50 millimeters per hour (50 mm/hr).

**Prognostic Factors for Advanced-Stage Classical Hodgkin Lymphoma.** An international collaboration among several cancer research groups in North America and Europe evaluated thousands of patients with advanced-stage classical Hodgkin lymphoma (cHL) (stages III and IV) and identified seven unfavorable prognostic factors (see **Table 2** on *page 13*).

These factors can provide a basis for recommending either more or less aggressive treatment, including stem cell transplantation for patients with high-risk disease. The International Prognostic Score (IPS) is defined by the number of adverse prognostic factors present at diagnosis. The IPS helps doctors to determine the course of treatment and the prognosis for patients with advanced-stage (stage III to IV) disease.

# Adverse Prognostic Factors for Advanced-Stage Classical Hodgkin Lymphoma

- Being male
- Age 45 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 greater than 15,000/mm<sup>3</sup>
- Lymphocytopenia: lymphocyte count less than 8% of the white blood cell count and/or lymphocyte count less than 600/mm<sup>3</sup>

**Table 2.** The International Prognostic Score (IPS) assigns a point for each adverse factor present at diagnosis.

Clinical trials to identify other prognostic indications for HL patients are under way. In fact, treatment for HL is also changing due to new drugs and research findings from clinical trials. See *Research and Clinical Trials* on page 23. Before treatment begins, it is important to consider getting a second opinion at a cancer center with an HL-specific expert.

Cure is the goal of treatment for patients with HL. 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 those with early-stage favorable disease. Even if the disease recurs, many patients can be cured with further treatment.

Most patients become long-term survivors of the disease. Treatment goals are to

- Maximize cure for all stages
- 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, 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. Treatment-planning factors for HL patients include

- Disease subtype
- Disease stage and category

- Identifying if the disease is refractory (does not respond to treatment) or relapsed (has recurred after treatment)
- Patient age
- Coexisting diseases or conditions (for example, heart or kidney disease, diabetes).

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

It may be helpful to speak to a fertility specialist before starting cancer treatment. Some methods of fertility preservation that are available to men and women include

- Sperm Banking. Men who want to father children after treatment may choose to store their semen for later use.
- Egg Freezing. A woman's eggs can be removed, frozen and stored for later use. A woman's eggs can be fertilized with sperm before freezing. Also, a part of the ovary that contains eggs can be frozen and stored.
- Ovarian Transposition. Called "oophorexy," this method is used for women who will be treated with radiation therapy. An ovary is surgically moved out of the range of the radiation beam in order to protect it.

See the free LLS booklet *Fertility Facts* for more details.

## Treatment

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A patient has two options for treatment: standard care or a clinical trial. It is important to talk to the healthcare team about the best treatment option.

Chemotherapy alone or chemotherapy together with radiation therapy (called "combined modality therapy") are commonly administered treatment approaches for Hodgkin lymphoma (HL).

**Chemotherapy.** Chemotherapy is the mainstay of treatment for HL. A combination chemotherapy regimen consists of two or more chemotherapy drugs. Generally, the drugs are dissolved in fluid and usually administered via a peripheral intravenous (IV) line. If finding an accessible vein is problematic, a central line (a port, or a percutaneously inserted central venous catheter (a PICC or PIC line) may be used for some HL patients. Percutaneous means "through the skin."



Chemotherapy is given in cycles of treatment that are separated by periods of rest. Chemotherapy drugs can have strong side effects so the body needs time to recover in between treatment cycles. Typically, the cycles are between 3 and 4 weeks long but they vary in length, depending on the drugs employed.

**Radiation Therapy.** Radiation therapy, also known as “radiotherapy (RT),” consists of the use of special machines that produce high-energy rays capable of killing the HL cells. Radiation therapy alone was a standard treatment option for patients with early-stage disease for many decades. However, there are often long-term serious side effects of radiation, and this treatment approach has changed.

There are different types of radiation therapy.

- Involved-site radiation therapy (ISRT) uses external beam radiation to treat the lymph nodes where the cancer started and the cancer near those nodes. The size of the radiation area is restricted to minimize radiation exposure to adjacent uninvolved organs and the potential toxicity associated with this type of therapy.
- Involved-field radiation therapy (IFRT) treats lymph node regions that are affected by HL. However, IFRT includes a much larger treatment area and is not used as often as ISRT.

With careful radiation therapy planning, the exposure of uninvolved organs can be either reduced or avoided. Imaging techniques such as magnetic resonance imaging (MRI) and positron emission tomography-computed tomography (PET-CT) can enhance treatment planning. Other specialized imaging techniques include

- Four-dimensional computed tomography (4D-CT) which can account for tumor movement from breathing, in tumors near the breastbone (sternum).
- 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 match the shape of the tumor.

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

Some Treatment Approaches for Classical Hodgkin Lymphoma

Early-stage classical Hodgkin lymphoma (cHL)

- Chemotherapy combinations
  - ABVD (Adriamycin® [doxorubicin], bleomycin, vinblastine, dacarbazine)
  - Dose-escalated BEACOPP (bleomycin, etoposide, Adriamycin [doxorubicin], cyclophosphamide, Oncovin® [vincristine], procarbazine, prednisone), for early-stage unfavorable cHL
- Combination chemotherapy is administered with or without radiation therapy

Advanced-stage cHL

- Chemotherapy combinations
  - ABVD
  - A+AVD (Adcetris® [brentuximab vedotin], Adriamycin [doxorubicin], vinblastine, dacarbazine)
  - Dose-escalated BEACOPP, in selected younger patients
- Occasionally, chemotherapy is followed by involved-site radiation therapy (ISRT)

Relapsed/Refractory cHL

- Further chemotherapy is given, such as
  - ICE (ifosfamide, carboplatin, etoposide)
  - DICE (dexamethasone, ifosfamide, cisplatin, etoposide)
  - ESHAP (etoposide, methylprednisolone, Ara-C, cisplatin)
  - GND (gemcitabine [Gemzar®], Navelbine® [vinorelbine], Doxil® [liposomal doxorubicin])
- Brentuximab vedotin (Adcetris, either alone or in combination with chemotherapy or other agents)
- Stem cell transplantation
- Nivolumab (Opdivo®)
- Pembrolizumab (Keytruda®)

Table 3. This table includes treatment approaches for classical Hodgkin lymphoma.

**Early-Stage Favorable Hodgkin Lymphoma Treatment.** The cure rate for patients diagnosed in early-stage favorable HL (either stage I or stage II with no unfavorable risk factors) exceeds 90 percent. The current treatment approach is to administer combined modality therapy (combination chemotherapy either alone or with reduced amounts of radiation). This approach has resulted in less toxicity and improved outcome. To date, **ABVD** (Adriamycin® [doxorubicin], bleomycin, vinblastine, dacarbazine) is the most effective and least toxic regimen available. It poses less of a risk for later development of leukemia or infertility than many other adult chemotherapy combinations.

Current 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 a reduced dose of radiation.

Other treatment regimens omit radiation therapy altogether and treat with chemotherapy alone. Rarely, the use of PET-CT scan results, either during or after treatment, can guide the treatment team about whether or not radiation therapy should be included; however, most patients do not receive radiation. Concerns about the late effects of radiation therapy (especially an increased risk of developing secondary cancers) have led some oncology groups to recommend chemotherapy alone for some patients, particularly when the risk of developing a secondary cancer is considered to be high. Patients who are at higher risk of a secondary cancer include women younger than 35 years and those with a family history of breast cancer, or for whom the radiation therapy would involve breast tissue. See *Long-Term and Late Effects of Treatment* on page 27.

**Early-Stage Unfavorable Hodgkin Lymphoma Treatment.** Patients in this category (stages I and II with unfavorable risk factors) are considered to have a higher-risk disease. These patients are also treated with chemotherapy, either alone or with radiation therapy. Treatment generally requires at least four to six cycles of combination chemotherapy, sometimes followed by radiation therapy. Again, PET-CT scan results, both during and after therapy, may affect the nature and length of chemotherapy and the use of radiation. Drug combinations used for treatment include

- **ABVD**
- **Dose-escalated BEACOPP:** bleomycin, etoposide, Adriamycin [doxorubicin], cyclophosphamide, Oncovin® [vincristine], procarbazine, prednisone

**Advanced-Stage Hodgkin Lymphoma.** Hodgkin lymphoma is potentially curable, even in late stages. In general, patients with advanced-stage HL (stage III or IV disease) are treated with six cycles of combination chemotherapy. Drug combinations used for treatment include

- **ABVD**
- **A+ABVD** (Adcetris [brentuximab vedotin], Adriamycin [doxorubicin], vinblastine, dacarbazine)
- **Dose-escalated BEACOPP**, sometimes used.

Dose-escalated BEACOPP results in a good cure rate but patients carry a small risk of developing leukemia or other secondary cancers. Patients are also at a much higher risk of infertility, and for this reason, it is less commonly used. It may be used for patients who have advanced HL.

Radiation therapy is reserved for the few patients with initial sites of bulky disease (large masses) or residual cancer observed on PET-CT scans. Even in these situations, the role of radiation therapy for advanced disease is variable.

**Treatment Response Monitoring.** During treatment, patients need to be monitored to check their response to therapy. Response to treatment is important in predicting long-term outcomes. Patients who fail to reach complete remission with first-line treatment have a worse prognosis, so there is great value in identifying these patients early in the course of their disease.

Imaging tests are used to distinguish between tumor and fibrous (scar) tissue. The PET scan is typically better than a CT scan in determining that difference and the combination PET-CT scan has become the standard for assessment of treatment response in most types of lymphoma.

A five-point scale called the “Deauville criteria,” developed in 2009, is now an internationally recognized way of using PET-CT in the initial staging and assessment of treatment response. This scale determines the FDG uptake (the absorption of, in this case radioactive material, by tissues) in the involved sites. These scans need to be carefully evaluated in order to assess response and decide if any treatment modifications are appropriate.

**Relapsed or Refractory Hodgkin Lymphoma.** In most patients, ABVD results in shrinkage of disease. However, in some cases, HL may return, even after patients have achieved a remission. The return of the disease is referred to as “a relapse,” or “relapsed disease.” For these patients, HL is still potentially curable.

A small percentage of patients have disease that either does not respond or is resistant to initial treatment, a condition called “refractory” HL. Approximately 10 percent of patients with early-stage HL and 20 to 30 percent of patients who have advanced disease either respond briefly and then their disease relapses,

or they do not respond at all to standard chemotherapy combinations, and these patients experience progression of the disease. These patients often require further treatment which typically consists of high-dose chemotherapy followed by autologous (using the patient's own cells) stem cell transplantation (SCT).

The following are treatments approved for relapsed and refractory cHL.

**Brentuximab vedotin (Adcetris®)**, a monoclonal antibody-drug combination, given intravenously (IV), is approved by the Federal Drug Administration (FDA) for the treatment of previously untreated stage III or stage IV classical Hodgkin lymphoma (cHL), in combination with chemotherapy. Brentuximab vedotin is also approved for the treatment of HL after failure of autologous hematopoietic stem cell (auto-HSCT) transplant or after failure of at least two prior multiagent chemotherapy regimens in patients who are not auto-HSCT candidates as well as in patients whose cHL is at high risk of relapse or progression as post-auto-HSCT consolidation. See [www.LLS.org/drugs](http://www.LLS.org/drugs) for more information.

**Nivolumab (Opdivo®)**, a monoclonal antibody and PD-1 checkpoint inhibitor, which allows the immune system to reactivate against the lymphoma and is given IV. It is FDA-approved for treatment of adult patients with cHL that has either relapsed or progressed after three or more lines of systemic therapy that included autologous stem cell transplantation. It is also for approved for the treatment of patients who have undergone hematopoietic stem cell transplantation (HSCT) and post-transplantation treatment with brentuximab vedotin. See [www.LLS.org/drugs](http://www.LLS.org/drugs) for more information.

**Pembrolizumab (Keytruda®)**, a monoclonal antibody and anti-PD-1 checkpoint inhibitor, given IV, is approved by the FDA for the treatment of adult and pediatric patients with refractory cHL, and for those who have relapsed after three or more prior lines of therapy. See [www.LLS.org/drugs](http://www.LLS.org/drugs) for more information.

**Stem Cell Transplantation.** Stem cell transplantation may provide a cure for many patients with relapsed HL.

High-dose chemotherapy with stem cell transplantation is not recommended for initial treatment because

- The results of treatment with primary **ABVD** and other combination regimens are very good.
- High-dose chemotherapy and stem cell transplantation are higher-risk treatments.

**Autologous Stem Cell Transplantation.** High-dose chemotherapy with autologous (using the patient's own cells) stem cell transplantation remains the standard therapy for relapsed and refractory HL. This treatment can provide a better-than 50 percent long-term survival for patients, although specific outcomes can vary depending on patient-specific risk factors. **Brentuximab vedotin** is also

sometimes given to treat patients before transplant or administered in select patients as maintenance treatment after autologous stem cell transplantation.

**Allogeneic Stem Cell Transplantation.** Some patients with HL who have relapsed several times have been treated successfully with allogeneic (using cells from a donor) stem cell transplantation. However, this treatment has significant risks. Other patients may benefit from a reduced-intensity allogeneic transplant, a treatment that uses lower doses of chemotherapy than a standard allogeneic transplant. Data are being collected to compare this treatment to other treatments.

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 transplants.

**Nodular Lymphocyte-Predominant Hodgkin Lymphoma Treatment.** Nodular lymphocyte-predominant hodgkin lymphoma (NLPHL) accounts for about 5 percent of all HL diagnoses. In some ways, the characteristics of NLPHL are more similar to those of slow-growing (indolent) non-Hodgkin lymphoma than they are to those of cHL. Treatment plans for patients with the NLPHL subtype are different from those prescribed for patients with cHL. About 75 percent of patients with NLPHL are diagnosed with stage I disease. Patients rarely have B symptoms, disease involvement outside of the lymph nodes, mediastinal masses or bulky disease.

Even though NLPHL is associated with an excellent long-term survival, to avoid unnecessary side effects, it is important not to over-treat these patients. On the other hand, some patients may relapse many years after treatment.

The preferred treatment choice for early-stage NLPHL is radiation therapy alone. For more advanced disease, combination chemotherapy may be needed, and **rituximab (Rituxan®)** may be added to the regimen. Common chemotherapy combinations used in treating NLPHL include

- **ABVD**
- **CHOP** (cyclophosphamide, doxorubicin, Oncovin [vincristine], prednisone)
- **CVP** (cyclophosphamide, vincristine, prednisone)
- **Rituximab (Rituxan).**

Transformation to diffuse large B-cell lymphoma (DLBCL) is reported in 7 percent of patients from 4 to 8 years after an initial NLPHL diagnosis. Patients with suspected relapse of NLPHL should have another biopsy performed in order to rule out a change from early-stage NLPHL to DLBCL. Patients with refractory or relapsed NLPHL can be treated with second-line therapy that includes rituximab, either with or without chemotherapy or radiation therapy. Some patients may develop chronic indolent disease and may not require aggressive treatment unless they have obvious symptoms.

**Childhood Hodgkin Lymphoma.** Hodgkin lymphoma comprises about 7 percent of childhood cancers. In the United States, the incidence of HL is age-related and is highest among adolescents age 20 to 24 years (4.0 cases per 100,000 per year).

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

- Specific subtype of the disease (see *Subtypes of Hodgkin Lymphoma* on page 6)
- Stage of the disease (see *Staging and Prognostic Factors* on page 8)
- Fertility concerns (see *Fertility Concerns* on page 14)
- Other potential risk factors
- Potential response to treatment—measured with imaging such as PET-CT scans.

Doctors make use of all this information about the patient's disease to determine the most effective therapy. They can develop treatment plans that limit the amount of therapy required to bring about remission. It is important for patients to discuss the planned therapy with members of the oncology team to learn about the drugs, potential side effects and long-term effects and the treatment schedule.

Children and young adults with HL are usually treated with one or more of the following approaches:

- Chemotherapy
- Radiation therapy
- Targeted therapy (monoclonal antibodies)
- Surgery (if a mass can be completely removed)
- High-dose chemotherapy with stem cell transplant.

Children are treated with response-based, dose-dense regimens. Some of the following drug combinations may be used:

- **ABVD**
- **AV-PC** (Adriamycin [doxorubicin], vincristine [Oncovin®], prednisone, cyclophosphamide)
- **ABVE** (Adriamycin [doxorubicin], bleomycin, vincristine [Oncovin], and etoposide)
- **ABVE-PC** (Adriamycin [doxorubicin], bleomycin, vincristine [Oncovin], etoposide, prednisone, cyclophosphamide)
- **BEACOPP**

- **OEPA/COPDac** (Oncovin [vincristine], etoposide, prednisone, Adriamycin [doxorubicin], cyclophosphamide, Oncovin [vincristine], prednisone, dacarbazine)
- **OEPA/COPP** (Oncovin [vincristine], etoposide, prednisone, Adriamycin [doxorubicin], cyclophosphamide, Oncovin [vincristine], prednisone, procarbazine).

Advances in treating childhood HL, which have improved the cure rate and quality of life for survivors, are due in large part to the research of pediatric cooperative groups. The focus of ongoing research and clinical trials is to

- Further improve the cure rate, especially for children with advanced HL
- Improve quality of life
- Minimize the risk of long-term and late effects associated with treatment (eg, infertility, impaired cardiac function, secondary cancers)
- Improve the overall survival rate.

The free LLS booklet *Understanding Side Effects of Drug Therapy* has useful information about medication side effects.

**Pregnancy and Hodgkin Lymphoma.** Given that it affects primarily young adults, HL is one of the most common cancers reported in pregnancy. To avoid radiation exposure, staging should be done with ultrasound imaging or whole-body MRI.

Radiation therapy or chemotherapy should generally be avoided because of the risk of toxic effects to the fetus. However, data from some case studies suggest that treatment with **ABVD** seems to be safe, especially in the second and third trimesters. Other treatment options include either observation or symptom control with corticosteroids or single-agent vinblastine treatment up to delivery. Treatment choice must be individualized, taking into consideration the mother's wishes, disease symptoms, the stage of the HL, 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 Therapy.** Following completion of therapy, a PET-CT scan is the most accurate assessment to confirm remission status. This scan should occur at least 3 weeks after the last chemotherapy treatment to avoid treatment-related inflammation, which would be detected on a PET scan.

Periodic examination for recurrence in HL patients is necessary for years after treatment. Most patients who relapse do so within the first two years after completion of therapy. 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 should plan to continue their annual follow-up visits with a healthcare professional who will monitor them for potential late complications of HL treatments, including



secondary cancers and cardiovascular disease. See *Long-Term and Late Effects of Treatment* on page 27. Many comprehensive cancer centers now have a survivorship clinic to provide individualized recommendations and help guide follow-up planning.

A patient's history and physical examination are effective assessment tools for follow-up purposes. After the last treatment, physical examinations and blood tests are recommended to be performed every 3 to 6 months for 1 to 2 years and then every 6 to 12 months for the next 3 years. After that, they can be done annually. Follow-up CT or PET-CT scans are not recommended for ongoing monitoring of disease recurrence because of high false-positive rates, unless new symptoms or signs suggesting relapse are evident. The decision whether to perform imaging should be made on an individual basis and after the implications of imaging tests have been discussed by the patient and healthcare professional.

## Research and Clinical Trials

New approaches under study in clinical trials for HL treatment, many of which are being supported by LLS research programs, hold the promise of increasing the rate of remission and finding a cure for HL.

**Clinical Trials.** Every new drug or treatment regimen available today has been through a series of studies called “clinical trials” before it became a part of standard therapy. Clinical trials are carefully designed and reviewed by expert clinicians and researchers to ensure safety and scientific accuracy. Participation in a carefully conducted clinical trial may be the best available therapy. Patient participation in past clinical trials has resulted in the therapies we have today.

LLS Information Specialists, at (800) 955-4572, can offer guidance on how patients can work with their doctors to determine if a specific clinical trial is an appropriate treatment option. Information Specialists can provide information and conduct individualized clinical-trial searches for patients, family members and healthcare professionals. When appropriate, Information Specialists refer patients for personalized clinical-trial navigation by trained nurses, which is available through our Clinical Trial Support Center.

**Research Approaches.** There are clinical trials for both newly diagnosed patients and patients with relapsed or refractory disease. A number of approaches are under study in clinical trials for the treatment of patients with HL.

**Genetic Studies.** HL is a rare disease. Nonetheless, it may affect more than one person in the same family. The existence of this familial clustering supports the theory that there is a genetic basis of HL susceptibility. Studies of familial HL are under way to obtain a better understanding of the genetic causes of the disease and to determine which genetic variations are responsible for recurring HL in families. This information may help doctors predict a person's risk of developing

HL, and also help scientists discover biological pathways that can be targeted with novel treatments.

**Interim Positron Emission Tomography-Computed Tomography as a Decision Tool for Risk-Adapted Therapy.** Recent studies have focused on assessing the role of interim and “restaging” PET-CT scans in patients with Hodgkin lymphoma. Accurate mid-treatment restaging is expected to enable tailoring of treatment, allowing healthcare professionals to improve remission rates while minimizing toxicities. Some of these studies are comparing different chemotherapy regimens (such as **ABVD** and **BEACOPP**) in both advanced- and early-stage disease. At the same time, PET-CT is used to help doctors to determine which patients will benefit most from more intensive treatment versus treatment de-escalation.

**Monoclonal Antibodies.** Monoclonal antibodies are immunotherapy drugs especially designed to target specific proteins (antigens) in cancer cells. Once the antibody finds and attaches to its target cell, it can recruit other parts of the immune system to destroy the cell that contains the antigen. Some monoclonal antibodies are coupled with a chemotherapy drug or attached to a radioactive particle. They circulate throughout the body until they attach to a target antigen and then deliver the toxic substance to the cancer cell. **Brentuximab vedotin (Adcetris®)**, which targets CD30 (cluster of differentiation 30) and releases a chemotherapy drug into the cell causing its death, is FDA-approved for treatment of relapsed or refractory HL after failure of an autologous stem cell transplant. Various clinical trials are studying the use of this agent

- In combination with standard chemotherapy (**AVD**: Adriamycin [doxorubicin], vinblastine, dacarbazine as initial treatment for advanced HL [bleomycin was omitted in order to avoid pulmonary toxicity])
- As a consolidation treatment option to be administered after an autologous stem cell transplant

**Programmed Death (PD-1) Checkpoint Inhibitors.** A vital part of the immune system is its ability to distinguish between healthy cells in the body and those that are foreign or harmful. The immune system depends on multiple programmed death (PD-1 checkpoints). Checkpoints are molecules on certain immune cells that need to be activated (or turned off) in order to start an immune response. Cancer cells sometimes take advantage of these checkpoints to escape the detection of active immune cells. A checkpoint protein, PD-1 is found on the surface of T cells. It normally acts as a type of “off switch” that helps keep immune cells from attacking healthy cells in the body. It accomplishes this when it attaches to a PD-L1, a protein found on some other normal cells, as well as in some cancer cells. When PD-1 binds to PD-L1, a message is sent to the T cell to leave the other cell alone and not attack it. But some cancer cells also have large amounts of PD-L1 receptors, which help them avoid a normal immune attack. Checkpoint inhibitors are monoclonal antibodies created to target PD-1 or PD-L1, blocking their actions,

and allowing the immune system to recognize and eliminate cancer cells. Two checkpoint inhibitor drugs **nivolumab (Opdivo®)** and **pembrolizumab (Keytruda®)**, both now approved for refractory and relapsed cHL, are being studied with various other agents.

**Standard Chemotherapy vs Combined Modality Treatment.** There is considerable interest in studying the use of chemotherapy alone (without radiation therapy) for the treatment of patients with early-stage HL. Several studies have results suggesting that this may be a very reasonable approach for many patients. Studies in this area include

- Comparing outcomes between the use of chemotherapy alone and the use of combined modality therapy (chemotherapy with involved-field radiation therapy)
- Collecting and analyzing data on the long-term side effects of **ABVD** and involved-field radiation therapy (IFRT)
- Comparing outcomes between the uses of involved field-radiation therapy (IFRT) and involved-site radiation therapy (ISRT) or involved-node radiation therapy (INRT), which target smaller areas for radiation

Contact our Information Specialists for more information about specific treatments under study in clinical trials.

## Treatment Side Effects

**Suppressed Blood Cell Formation.** Blood cell counts are often low in patients who are treated with chemotherapy. If the red blood cell count drops and the patient becomes significantly anemic, a blood transfusion may be recommended. If the platelet count drops severely, a platelet transfusion may be required. See the free LLS booklet *Blood Transfusion* for more information.

If the number of white blood cells (particularly white blood cells called “neutrophils”) drops severely and for an extended time, patients may develop infections and require antibiotic treatment and possible hospitalization. In some types of cancer, it is necessary to allow a patient’s blood counts to recover from the effects of treatment. Sometimes the patient’s chemotherapy dosages or the time between chemotherapy cycles needs to be adjusted. However, because Hodgkin lymphoma (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 low blood cell counts to continue for a very long time beyond the completion of treatment. However, patients who undergo stem cell transplantation may continue to be at risk for infection.

Treatment with drugs such as granulocyte-colony stimulating factor (G-CSF) that are designed to improve white blood cell counts, may be considered in some types of cancer. However, in HL regimens that include bleomycin, G-CSF is not

typically recommended or necessary, because there is an increased potential for complications in the lungs due to the use of G-CSF.

**Infections.** 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 infection, because these treatments lower blood cell counts and weaken immune system cell function. Removal of the spleen, even though it is now performed less often than it once was, also contributes to the risk of severe infections. When patients are cured, their immune function generally improves. In addition, improved treatment of HL patients, increased awareness of the risk of infectious diseases and better antimicrobial therapy have made infectious complications less of a medical problem for patients.

Hodgkin lymphoma 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 vaccine, should not be administered. Your healthcare professional will give you more information.

**Other Effects.** Reactions to chemotherapy and radiation treatment vary from person to person. Most side effects appear shortly after the initiation of treatment but should stop 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 may cause low blood cell counts, mouth sores, nausea, vomiting, 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 [Oncovin®]** tends to affect nerve tissue, and **bleomycin** may affect the lungs).
- Radiation side effects depend on the type of treatment and the area treated. Many people experience fatigue. There are often changes in the skin after treatment; 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 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. There are ways to prevent some side effects, and there are medications available to help patients feel better.

For specific side-effect information, see the free LLS booklet *Understanding Side Effects of Drug Therapy*.

## 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. Secondary cancers, cardiovascular disease, hypothyroidism and fertility issues are the most serious late effects experienced by long-term survivors of HL. The incidence of these late effects has seemed to increase over a longer follow-up time. However, the risk of late side effects may be lower with current treatments compared to the risk associated with treatments used more than 10 years ago.

**Secondary Cancers.** The treatment of HL has changed over the past several years and continues to evolve. Early-stage HL patients are no longer exposed to extended-field radiation, reducing the risk of recurrence.

The degree of risk for developing a second cancer is related to both the extent and the dosage of radiation treatment. Lung and breast cancer are the most common secondary cancers in HL patients, and most of these cancers develop more than 10 years after the end of treatment. The risk of developing secondary cancer is highest when radiation therapy is used as a component of first-line treatment.

Girls or women younger than age 30 who have radiation to the breast to treat HL are at risk for developing breast cancer 15 to 20 years after radiation. Male survivors of childhood cancers may also be at risk for developing secondary cancers (however, men 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 when given with bleomycin (the “B” in **ABVD** [Adriamycin® (doxorubicin), bleomycin, vinblastine, dacarbazine]). Survivors who have had chest radiation are also at risk for lung cancer. Smoking further increases their risk. Hodgkin lymphoma survivors are advised not to start smoking or, if they do smoke, to stop smoking. There is strong scientific evidence that people who do not smoke but received chest radiation for HL have a risk of lung cancer 10 to 20 years after treatment that is about four times greater than that of the general population. Smokers who were treated for HL with chest radiation may have as much as 25 to 40 times the increased risk of lung cancer, depending on whether they had radiation therapy alone or also had chemotherapy.

Chemotherapy with alkylating agents increases the risk of developing acute myeloid leukemia and 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 chemotherapy (containing anthracyclines such as doxorubicin and some alkylating agents) have been linked to heart disease, including cardiomyopathy (damage to the heart muscle), pericarditis (inflammation of the sac surrounding the heart), valve dysfunction or myocardial infarction (classic heart attack). Radiation may 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 Dysfunction.** Both radiation to the chest area and treatment with bleomycin-containing chemotherapy regimens are associated with acute lung toxicity and can also lead to reduced lung function. Some reports suggest that the use of growth factors with chemotherapy significantly increases the incidence of long-term pulmonary (lung) issues. 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 survivors who received neck or upper chest radiation therapy.

**Fertility.** Patients may be less fertile after treatment. The risk of infertility varies according to the type and amount of chemotherapy, the location of radiation therapy and the patient's age. With some regimens, fertility appears to be either minimally or not at all affected. Other regimens, such as **BEACOPP** (bleomycin, etoposide, Adriamycin [doxorubicin], cyclophosphamide, Oncovin [vincristine], procarbazine, prednisone), may cause immediate and permanent infertility in both men and women. In addition, women who have received chemotherapy with alkylating agents may experience premature menopause, and this should be taken into consideration with respect to family planning before the start of treatment. There are fertility options for both men and women. Speak to your healthcare team. See *Fertility Concerns* on page 14 and see the free LLS booklet *Fertility Facts* 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 treated for cancer with chemotherapy, radiation therapy or combined modality therapy. 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 Facts*.

**Follow-Up Care.** Survivors of HL are advised to

- Keep a record of the treatments they received. These will be helpful for the healthcare professionals who monitor them for potential health problems after treatment ends.
- Have regular screening for heart disease and annual blood pressure and lipids monitoring. A baseline stress test, echocardiogram and carotid ultrasound (for patients treated with radiation to the neck) should be considered at 10-year intervals after completion of therapy.
- Have regular screening 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 early baseline mammograms (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 women who received radiation in the chest area when they were between the ages of 10 and 30. Although some women 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 screening if treated with chest radiation. Smoking further increases the risk of lung cancer and several other types of cancer including acute myeloid leukemia and myelodysplastic syndromes.
- 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.

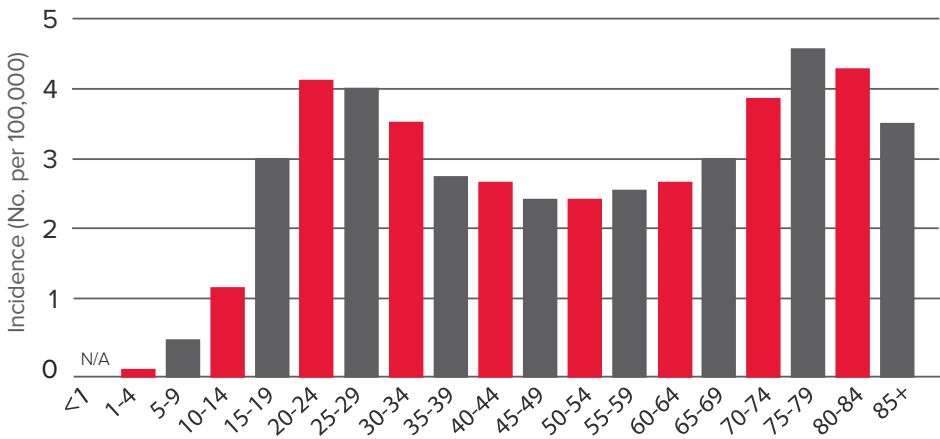
For additional information, including risks of specific chemotherapy agents, see the free LLS booklets *Long-Term and Late Effects of Treatment in Adults Facts* and *Long-Term and Late Effects of Treatment for Childhood Leukemia or Lymphoma Facts*.

# Incidence, Causes and Risk Factors

**Incidence.** Although Hodgkin lymphoma (HL) can occur in both adults and children, most patients are diagnosed between the ages of 15 and 35. There is another incidence peak in adults age 65 years and older (see **Table 4**, below). Hodgkin lymphoma is more common among men than women. It may also occur in people who have acquired immunodeficiency syndrome (AIDS)—these patients may require special treatment.

An estimated 8,500 people living in the United States are expected to be diagnosed with HL in 2018.

## Hodgkin Lymphoma: Age-Specific Incidence Rates 2010-2014



**Table 4.** The horizontal axis shows 5-year age intervals. The vertical axis shows the frequency of new cases of Hodgkin lymphoma per 100,000 people, by age-group. The incidence of Hodgkin lymphoma peaks between the ages of 15 and 44 and at age 65 and older. Source: Surveillance, Epidemiology and End Results (SEER) Program; National Cancer Institute; 2017.

**Causes and Risk Factors.** The exact cause of HL is not known but the following risk factors may increase a person’s likelihood of developing HL:

- The Epstein-Barr virus (EBV) known for causing mononucleosis is associated with the development of some cancers, including HL. Approximately 30 percent of Hodgkin and Reed-Sternberg (RS) cells carry the EBV virus in Western populations.
- People infected with human immunodeficiency virus (HIV) also have increased probability of developing HL.
- 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



by three to four times compared with the general population. Although these cases are uncommon, the concept of genetic predisposition is under study to determine its role in the sporadic occurrence of HL in otherwise healthy individuals.

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 Marrow and the Lymphatic System

**Blood.** Blood is the liquid that flows through a person’s arteries and veins. It carries oxygen and nutrients to living cells and carries away the cells’ waste products. It also contains immune cells to fight infections and platelets that can stop bleeding in damaged blood vessels.

Blood is composed of plasma and blood cells.

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

- Proteins
  - Albumin, the most common blood protein
  - Blood-clotting proteins (coagulation factors) that are made by the liver.
  - Erythropoietin, a protein made by the kidneys that stimulates red blood cell production
  - Immunoglobulins, proteins that help the body fight infection
- Hormones, such as insulin and corticosteroids
- 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.** There are three types of blood cells suspended in the plasma. They are

- Red blood cells (that carry oxygen to and from the cells). They
  - Make up a little less than half of the body’s total blood volume
  - Are filled with hemoglobin, a protein that picks up oxygen from the lungs and delivers it to cells throughout the body

- Hemoglobin then picks up carbon dioxide from the cells and delivers it to the lungs
- The lungs push out the carbon dioxide when a person exhales.
- Platelets
  - Are fragments of cells (one-tenth the size of red blood cells)
  - Help stop bleeding from an injury
  - When a person has a cut and blood vessels are torn, platelets stick to the tear, clump together and plug up the bleeding site.
- White blood cells fight infections, and are an important part of the immune system. There are several types of white blood cells, including
  - Neutrophils. Called “phagocytes” (eating cells); help fight infection by ingesting microorganisms and releasing enzymes that kill the microorganisms
  - Eosinophils. Play an important role in the body’s response to allergic reactions and parasite infection
  - Basophils. Fight off allergic reactions and asthma
  - Monocytes. Phagocytes that can leave the bloodstream and enter tissues to attack invading organisms and fight off infection by surrounding and killing microorganisms, ingesting foreign material and removing dead cells
  - Lymphocytes. Found mostly in the lymph nodes, spleen and lymphatic channels; three major types of lymphocytes are
    - T lymphocytes (T cells)
    - B lymphocytes (B cells)
    - Natural killer (NK) cells.

New red blood cells, platelets and most white blood cells are formed in the bone marrow, a spongy tissue found in the central cavity of bones. The creation of new blood cells is controlled by the body’s needs. The human body generates billions of new blood cells every day to replace old and worn-out cells. Certain events also may prompt the body to produce additional blood cells. For example, the bone marrow produces and releases extra white blood cells in response to an infection.

Red blood cells, white blood cells and platelets vary in appearance and function, but they all originate from a single type of unspecialized cell called a “hematopoietic stem cell.” Hematopoietic, or blood-forming, stem cells are found in the bone marrow of the femurs (thigh bones), hips, vertebrae (back bones) and the ribs. An unspecialized hematopoietic stem cell can give rise to specialized cells that have specific functions. For example, a hematopoietic stem cell can give rise to a red blood cell that carries oxygen throughout the body, or it can give rise to a neutrophil,

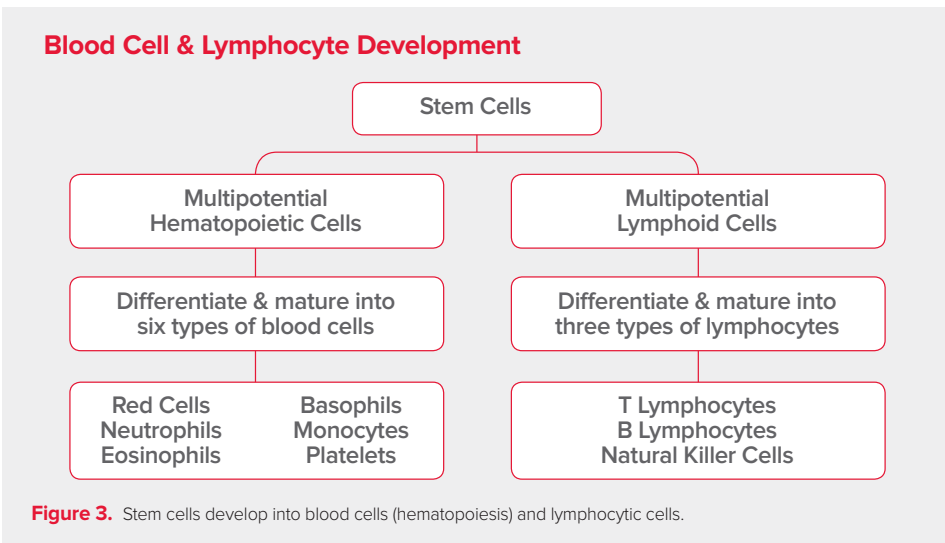
a white blood cell, that helps fight infections. The process by which an immature cell becomes a mature cell with specific functions is called “differentiation.”

The process of creating new blood cells through differentiation is called “hematopoiesis.” Differentiation occurs while the stem cells are still in the bone marrow (see **Figure 3 below**). When a stem cell divides, each “daughter” cell has the potential to either remain a stem cell or to become a specialized cell such as a red blood cell, a white blood cell or a platelet. For those cells “committed” to specialize, the stem cell generates an intermediate cell. The intermediate cell is called a “precursor” or “progenitor” cell. While the stem cell remains in an immature, unspecialized state, the progenitor cell divides and undergoes multiple stages of development, becoming more specialized at each stage, until it becomes a particular type of mature blood cell.

The hematopoietic stem cell can give rise to lymphoid stem cells and myeloid stem cells. The lymphoid stem cells create lymphoid progenitor cells. Different types of progenitor or precursor cells can then develop into different types of mature blood cells. Through the process of differentiation, lymphoid progenitor or precursor cells can mature into T cells, B cells, or NK cells.

Myeloid stem cells create myeloid progenitor cells. These precursor or progenitor cells will develop into mature blood cells including red blood cells, platelets and certain types of white blood cells (eosinophils, basophils, neutrophils and monocytes.) For example, a myeloid progenitor cell will go through various stages of development to become a neutrophil: myeloid progenitor → promyelocyte → myelocyte → metamyelocyte → band → neutrophil.

In healthy people, stem cells in the bone marrow produce new blood cells continuously. Once the blood cells have matured, they leave the bone marrow and enter the bloodstream.



**The Lymphatic System.** The lymphatic system comprises the tissues and organs, including bone marrow, spleen, thymus, and lymph nodes, that produce and store cells to fight infection and disease. The channels that carry lymph are also part of this system.

Bone marrow produces three main types of lymphocytes (white blood cells). They are

- B lymphocytes (B cells), which make antibodies in response to foreign substances (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 another white blood cell to recognize the antibody and “ingest it,” that is, pull it into the cell along with its attached microbe. The white cell then kills and digests the microbe.
- Natural killer (NK) cells, which attack virus-infected cells without requiring 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.

Throughout the body are “lymph nodes,” an important part of the immune system. These bean-shaped nodes are connected by channels called “lymphatics.” The lymphatic channels collect into large ducts that empty into blood vessels. The lymphocytes (white blood cells) 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 (special lymph nodes), intestinal lining, and in young people, the thymus.

## Resources and Information

LLS offers free information and services to patients and families affected by blood cancers. This section of the booklet 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 master’s level 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, from 9 am to 9 pm EST)
- Email: [infocenter@LLS.org](mailto:infocenter@LLS.org)
- Live chat: [www.LLS.org/information specialists](http://www.LLS.org/information specialists)
- Visit: [www.LLS.org/information specialists](http://www.LLS.org/information specialists).

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

**Some of the free LLS Booklets include**

*Blood and Marrow Stem Cell Transplantation*

*Blood Transfusion*

*Cancer-Related Fatigue Facts*

*Choosing a Blood-Cancer Specialist or Treatment Center*

*Fertility Facts*

*Long-Term and Late Effects of Treatment for*

*Childhood Leukemia or Lymphoma Facts*

*Long-Term and Late Effects of Treatment in Adults Facts*

*Understanding Clinical Trials for Blood Cancers*

*Understanding Lab and Imaging Tests*

*Understanding Side Effects of Drug Therapy*

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

**Co-Pay Assistance Program.** LLS offers insurance premium and medication co-pay assistance for eligible patients. For more information, please

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

**One-on-One Nutrition Consultations.** Access free one-on-one nutrition consultations by a registered dietitian with experience in oncology nutrition. Assistance with healthy eating strategies, side effect management, and survivorship nutrition as well as provide additional nutrition resources. For more information, please visit [www.LLS.org/nutrition](http://www.LLS.org/nutrition).

**Podcast.** Listen in as experts and patients guide listeners in understanding diagnosis, treatment, and resources available to blood cancer patients. *The Bloodline with LLS* is here to remind you that after a diagnosis comes hope. For more information and to subscribe, visit [www.LLS.org/TheBloodline](http://www.LLS.org/TheBloodline).

**Suggested Reading.** A listing of selected books that are recommended for patients, caregivers, children and teens. To find out more, visit [www.LLS.org/SuggestedReading](http://www.LLS.org/SuggestedReading).

**Continuing Education.** LLS offers free continuing education programs for healthcare professionals. For more information, please visit [www.LLS.org/ProfessionalEd](http://www.LLS.org/ProfessionalEd).

## Community Resources and Networking

**LLS Community.** The one-stop virtual meeting place for talking with other patients and receiving the latest diagnosis and treatment news. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. To join, visit [www.LLS.org/community](http://www.LLS.org/community).

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

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

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

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

**Clinical Trials (Research Studies).** New treatments for patients are under way. Patients can learn about clinical trials and how to access them. For more information, please call (800) 955-4572 to speak with an LLS Information Specialist who can help conduct clinical-trial searches. When appropriate, personalized clinical-trial navigation by trained nurses is also available.

**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, please

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

## Additional Help for Specific Populations

**Información en Español (LLS information in Spanish).** For more information, please visit [www.LLS.org/especialistas](http://www.LLS.org/especialistas).

**Language Services.** Let a member of your healthcare team know if you need a language interpreter or some other resource, such as a sign language interpreter. Often, these services are free.

**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 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. Seek medical advice if your mood does not improve over time—for example, if you feel depressed every day for a 2-week period. For more information, please

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

**Feedback.** To give suggestions about this booklet, visit [www.LLS.org/publicationfeedback](http://www.LLS.org/publicationfeedback).

## Health Terms

**Allogeneic Stem Cell Transplantation.** A treatment that uses donor stem cells to restore a patient's marrow and blood cells. First, the patient is given conditioning therapy (high-dose chemotherapy or high-dose chemotherapy with total body radiation) to treat the blood cancer and to "turn off" the patient's immune system so that the donor stem cells will not be rejected. For more information, see the free LLS booklet *Blood and Marrow Stem Cell Transplantation*. See also Reduced-Intensity Allogeneic Transplantation.

**Anemia.** A decrease in the number of red blood cells and, therefore, the hemoglobin concentration of the blood. 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 on exertion.

**Antibodies.** Proteins released by plasma cells (derived from B lymphocytes) that recognize and bind to specific foreign substances called "antigens." Antibodies coat and mark for destruction or inactivate foreign particles such as bacteria, viruses or harmful toxins.

**Antigen.** Any substance that causes the body to make an immune response against that substance. Antigens include toxins, chemicals, bacteria, viruses or other substances that come from outside the body.

**Apheresis.** The process of removing certain components of a donor's blood and separating out various parts of blood. Platelets, red blood cells, white blood cells and plasma can be removed separately. The term encompasses returning the unneeded parts to the donor. This procedure is also used to remove circulating blood stem cells, which can be frozen, stored and used later for transplantation instead of bone marrow stem cells.

**Autologous Stem Cell Transplantation.** A procedure in which stem cells are removed from a cancer patient, stored, and then given back to the patient after the patient undergoes intensive chemotherapy with or without radiation therapy. For more information, see the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.

**Biopsy.** A procedure used to obtain tissue for diagnosis. In many cases, a special needle can be used to extract the tissue. In some cases, a larger piece of tissue may be surgically removed. Because the way a lymph node looks on a PET-CT scan is important in categorizing the type of lymphoma that may be present, surgical removal of an entire, swollen lymph node or nodes may be necessary (lymph node biopsy).



**Bone Marrow.** The spongy tissue in the hollow central cavity of the bones that is the site of blood cell formation. After puberty, the 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 marrow is filled with fat cells.

**Bone Marrow Aspiration.** A test to examine marrow cells to detect cell abnormalities. A marrow sample is usually taken from the patient's hip (pelvic) bone. After medication is given to numb the skin, the liquid sample is removed using a special needle inserted through the bone into the bone marrow.

**Bone Marrow Biopsy.** A test to examine marrow cells to detect cell abnormalities. This test differs from a bone marrow aspiration in that a small amount of actual bone filled with marrow is removed, usually from the hip (pelvic) bone. After medication is given to numb the skin, a special hollow biopsy needle is used to remove a core of bone containing marrow. Bone marrow aspiration and bone marrow biopsy may be done in the doctor's office or in a hospital. The two tests are almost always done together.

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

**Central Line (Indwelling Catheter) also Called "Central Venous Catheter."** A catheter that is a venous access device used when drawing blood samples and administering therapies, medications, and other treatments. A catheter (thin tube) is inserted and guided into a large vein, usually below the collarbone. A central venous catheter may stay in place for weeks or months to avoid the need for repeated needle-sticks. Also known as a central line; the two most common types are the port and PICC (percutaneously inserted central venous catheter or PIC) line. See Port.

**Chemotherapy.** The use of chemicals (drugs or medications) to stop the growth of cancer cells by either killing the cancer cells or by stopping them from dividing.

**Chromosome.** Threadlike structures within cells that carry genes in a linear order. Human cells have 23 pairs of chromosomes: chromosome pairs 1 to 22 and one pair of sex chromosomes (XX for females and XY for males).

**Clonal.** The designation for a population of cells derived from a single transformed parent cell. Virtually all cancers are derived from a single cell with an injury (mutation) to its DNA (deoxyribonucleic acid) and thus are monoclonal. Leukemia, lymphoma and myeloma are examples of clonal cancers; that is, cancers derived from a single abnormal cell.

**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 patient's disease. For example, chemotherapy with involved-field radiation therapy (IFRT) is a combined modality therapy for patients with Hodgkin lymphoma.

**Computed Tomography Scan.** A technique for imaging body tissues and organs. X-ray transmissions are converted to detailed images using a computer to synthesize x-ray data. The images are displayed as a cross section of the body at any level from the head to the feet. A computed tomography (CT) scan of the chest, abdomen or pelvis permits detection of an enlarged lymph node, liver or spleen. A CT scan can be used to measure the size of these and other structures both during and after treatment. See PET-CT Scan.

**Cycle of Treatment.** An intensive, clustered period of chemotherapy and/or radiation therapy. The therapy may be given for several days or several weeks; the treatment team determines a particular time period and that represents one cycle of treatment. The treatment plan may call for two, three or more cycles of treatment.

**Cytogenetic Analysis.** The process of analyzing the number and size of the chromosomes of cells. It detects chromosome alterations and, in some cases, may identify the actual genes that have been affected. These findings help healthcare professionals diagnose specific types of blood cancers in order to determine treatment approaches and monitor the response to treatment. The individual who prepares and examines the chromosomes and interprets the results is called a "cytogeneticist."

**Differentiation.** See Hematopoiesis.

**DNA.** The genetic material in the cell. Deoxyribonucleic acid is the scientific name for DNA, which is made up of a sugar-phosphate backbone with ladderlike "steps" composed of purines and pyrimidines (building blocks of nucleic acids). The sequence of the purines and pyrimidines in the DNA is responsible for passing genetic information to new cells during the process of cell division; for passing genetic

information from one generation to the next during reproduction; and for providing the instructions for building proteins, which in turn carry out the major functions of a cell. A mutation is generally either a change in or a loss of the sequence of the purines or pyrimidines of the DNA (deoxyribonucleic acid). Mutations can lead to cell death, to changes in the way a cell functions or, in some cases, to cancer.

**DNA-Gene Chip.** See Microarray.

**Eosinophil.** A type of white blood cell that participates in allergic reactions and helps fight certain parasitic infections.

**Erythrocytes.** See Red Blood Cell.

**Extranodal Lymphoma.** Lymphoma that has spread outside the lymph nodes to the organs—the thyroid, lungs, liver, bones, stomach or central nervous system. Doctors adjust their therapeutic approach if organs outside of lymph nodes are involved. If the brain, liver or bones are involved, for example, the treatment approach is likely to target these areas. If lymphoma is found in any of the organs but not in lymph nodes or multiple lymphatic sites, the disease is called a “solitary extranodal lymphoma.”

**Flow Cytometry.** A test that permits the identification of specific cell types within a sample of cells. The test helps healthcare professionals examine blood cells, marrow cells or cells from a biopsy. One use of flow cytometry is to determine whether a sample of cells is composed of T cells or B cells. This permits the doctor to determine if the leukemia or lymphoma is of the B- or T-cell type.

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

**Gene Expression Profiling.** A research method that uses microarray analysis to identify a combination of genes that are either turned off or turned on in response to a specific condition. A set of genes in a blood or tissue sample can be used to monitor the levels of thousands of genes at once.

**Germ-Cell Mutation.** See Mutation.

**GM-CSF (Granulocyte-Macrophage 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 chemical used to stimulate the production of neutrophils and shorten the period of low neutrophil counts in the blood after chemotherapy. Granulocyte-colony stimulating factor (G-CSF) and granulocyte-macrophage colony stimulating factor (GM-CSF) are examples of growth factors that are made commercially. GM-CSF can also stimulate monocytes.

**Hemapheresis.** See Apheresis.

**Hematologist.** A doctor who specializes in the treatment of blood cell diseases. This person is either an internist who treats adults or a pediatrician who treats children.

**Hematopathologist.** See Pathologist.

**Hematopoiesis.** The process of blood cell development in the bone marrow. The most undeveloped cells in the marrow are stem cells. They start the process of blood cell development. The stem cells begin to develop into young or immature blood cells such as red blood cells or white blood cells of various types. This process is called “differentiation.” The young or immature blood cells then further develop into fully functional blood cells. This process is called “maturation.” The mature cells leave the marrow, enter the bloodstream and circulate throughout the body. Hematopoiesis is a continuous process that is active normally throughout life. The reason for this activity is that most blood cells live for short periods and must be steadily replaced. About 200 billion blood cells are made each day. When the marrow is invaded with cancer cells, the constant demand for new blood cells cannot be met, resulting in a severe deficiency in blood cell counts.

**HLA.** The abbreviation for “human leukocyte antigen(s).” These antigens are proteins on the surface of most tissue cells, and they give an individual his or her unique tissue type. HLA factors are inherited from mother and father, and the greatest chance of having the same HLA type is between siblings. On average, one in four siblings is expected to share the same HLA type. HLA tests are done before a donor stem cell or organ transplant, to find out if tissues match between the donor and the person receiving the transplant. This testing for HLA antigens is referred to as “tissue typing.”

**Immunophenotyping.** A method that uses the reaction of antibodies with cell antigens to determine a specific type of cell in a sample of blood cells, marrow cells or lymph node cells. The antibodies react with

specific antigens on the cell. A tag is attached to an antibody so that it can be detected. The tag can be identified by the laboratory equipment used for the test. As cells carrying their array of antigens are tagged with specific antibodies, they can be identified. Normal lymphocytes may be distinguished from Reed-Sternberg and Hodgkin cells.

**Immunotherapy.** The term for several treatment approaches used by doctors to harness the body's immune system to treat lymphoma and other diseases. These therapies include monoclonal antibody therapy, radioimmunotherapy and vaccine therapy. Monoclonal antibodies are proteins made in the laboratory that either react with or attach to antigens on the target cells. The antibodies are used therapeutically in three ways: as “naked” antibodies (monoclonal antibodies), as antibodies to which radioactive isotopes are attached (radioimmunotherapy), and as antibodies to which toxins are attached (immunotoxins). For more information, see the free LLS booklet *Immunotherapy Facts*.

**Indwelling Catheter.** See Central Line (Indwelling Catheter) also called “Central Venous Catheter (CVC).”

**Leukocyte.** See White Blood Cells.

**Leukopenia.** A decrease below normal in the concentration of blood leukocytes (white blood cells).

**Lymphadenopathy.** Enlargement of lymph nodes.

**Lymph Nodes.** Bean-sized structures that contain large numbers of lymphocytes and are connected with each other by small channels called “lymphatics.” These nodes are distributed throughout the body. In patients with lymphoma and some types of lymphocytic leukemia, the malignant lymphocytes grow and the lymph nodes may become enlarged. This can be seen, felt or measured by imaging techniques including PET-CT scan and magnetic resonance imaging (MRI). See PET-CT Scan (Positron Emission Tomography-Computed Tomography) and Magnetic Resonance Imaging (MRI).

**Lymphatic System.** The system comprising the lymph nodes, the thymus gland (in the first several decades of life), the lymphatic channels, the lymphatic tissue of the marrow, the gastrointestinal tract, and the skin and spleen, along with the T, B and natural killer (NK) lymphocytes contained in these sites.

**Lymphocyte.** A type of white blood cell that is the essential cell type in the body's immune system. There are three major types of lymphocytes: B lymphocytes, which produce antibodies to help combat infectious agents like bacteria, viruses and fungi; T lymphocytes, which have several functions, including assisting B lymphocytes to make antibodies; and natural killer (NK) cells, which can attack virus-infected cells or tumor cells.

**Macrophage.** See Monocyte/Macrophage.

**Magnetic Resonance Imaging (MRI).** A testing technique that provides detailed images of body structures. It differs from the CT scan in that the patient is not exposed to x-rays. Signals are generated in the tissues in response to a magnetic field produced by a specialized instrument and are converted by computer into images of body structures. Healthcare professionals use MRI to measure the size, or a change in size, of organs such as the lymph nodes, liver and spleen or tumor masses.

**Marrow.** See Bone Marrow.

**Maturation.** See Hematopoiesis.

**Microarray.** A two-dimensional grid of molecules (often but not always DNA [deoxyribonucleic acid] genes or gene fragment spots), usually arranged on a glass slide or silicone wafer. A typical microarray (also called "DNA-gene chip") contains 10,000 to 200,000 microscopic DNA spots. Scientists use a microarray to study gene expression and to learn which genes are expressed or not expressed under given circumstances. See Gene Expression Profiling.

**Monoclonal.** See Clonal.

**Monoclonal Antibody Therapy.** See Immunotherapy.

**Monocyte/Macrophage.** A type of white blood cell that represents about 5 to 10 percent of the cells in normal human blood. The monocyte and the neutrophil are the two major microbe-eating and microbe-killing cells in the blood. When monocytes leave the blood and enter the tissue, they are converted to macrophages. The macrophage is the monocyte-in-action: it can combat infection in the tissues, ingest dead cells (in this function it is called a "scavenger cell") and assist lymphocytes in their immune functions.

**MRI.** See Magnetic Resonance Imaging.

**Mutation.** An alteration in a gene that results from a change to a part of the stretch of DNA (deoxyribonucleic acid) that represents the gene. A “germ cell mutation” is present in the egg or the sperm and can be transmitted from parent to offspring. A “somatic mutation” occurs in a specific tissue cell and can result in the growth of that cell into a tumor. Most cancers start after a somatic mutation. In leukemia, lymphoma or myeloma, a primitive marrow (blood-forming) or lymph node cell undergoes a somatic mutation or mutations that lead to the formation of a tumor. If a mutation results from a major abnormality of chromosomes such as a translocation, it can be detected by cytogenetic examination. Sometimes the alteration in the gene is more subtle and requires more sensitive tests to identify the oncogene. See Oncogene.

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

**Neutrophil.** The principal phagocyte (microbe-eating cell) in the blood. This white blood cell is the main cell that combats infection. Patients with certain blood cancers or patients who have undergone chemotherapy often do not have sufficient quantities of neutrophils circulating in their bloodstream. A severe deficiency of neutrophils increases the patient’s susceptibility to infection.

**Nonmyeloablative Stem Cell Transplantation.** See Reduced-Intensity Stem Cell Transplantation.

**Oncogene.** A mutated gene that is the cause of a cancer. Several subtypes of acute myeloid leukemia, acute lymphoblastic leukemia, lymphoma and nearly all cases of chronic myeloid leukemia are associated with an oncogene.

**Oncologist.** A doctor who diagnoses and treats patients with cancer. Oncologists are usually internists who undergo additional specialized training to treat adults who have cancer (or pediatric oncologists, who treat cancer in children). Radiation oncologists specialize in the use of radiation to treat cancer, and surgical oncologists specialize in the use of surgical procedures to diagnose and treat cancer. These doctors cooperate and collaborate to provide the best treatment plan (surgery, radiation therapy, chemotherapy or immunotherapy) for the patient.

**Pathologist.** A doctor who identifies disease by studying tissues under a microscope. A hematopathologist is a type of pathologist who studies diseases of blood cells by looking at peripheral blood smears, bone

marrow aspirates and biopsies, lymph nodes and other tissues and uses his or her expertise to identify diseases. In addition to the microscope, a hematopathologist also uses laboratory values, flow cytometry and molecular diagnostic tests to make the most accurate diagnosis. The hematopathologist works closely with the hematologist or oncologist who sees the patient and decides on the best treatment based on the diagnosis. See Hematologist.

**Percutaneously Inserted Central Venous Catheter (PICC or PIC).**

A long, thin, flexible tube that is inserted into a vein. It can be left in place for weeks, or even months, for administration of medications, fluids and nutrition. It can also be used to obtain blood samples. The PICC eliminates the need for standard intravenous (IV) administration.

**PET-CT Scan (Positron Emission Tomography [PET] Scan and Computed Tomography [CT] Scan).** A combination of two powerful imaging tool is used to make “pictures,” better known as “images”, of lymphoma masses. In the PET scan, glucose, a type of sugar, is labeled with a positron particle emitting a radioisotope such as fluorine-18. The utilization of sugar is greater in lymphoma cells than in normal tissue, and the isotope thus becomes concentrated in areas of lymphoma. The location of the lymphoma sites in the body can be identified by scanning for intense positron particle emission. A PET-CT scan can identify the precise location of lymphoma masses. In some cases, successfully treated lymphoma may convert to fibrous tissue that looks like a mass in these images, perhaps leading the doctor to think that the mass was not successfully treated. Since lymphoma tissue is not fibrous and scars (primarily fibrous) do not take up the fluorine-18-labeled sugar, PET-CT can distinguish residual lymphoma from healed scar tissue. PET-CT is used for both staging of lymphoma and assessing response.

**Phagocyte.** A cell that eats (ingests) microorganisms such as bacteria and fungi and kills them as a means of protecting the body against infection. The two principal phagocytes are neutrophils and monocytes. They leave the bloodstream and enter tissues in which an infection has developed. Chemotherapy and radiation can cause a severe decrease in the concentrations of these cells, which makes patients more susceptible to infection. Treatment may suppress blood cell production in the marrow, resulting in deficiencies of these protective cells.

**PICC or PIC.** See Percutaneously Inserted Central Venous Catheter (PICC or PIC).



**Platelets.** Small blood cells that are actually fragments (about one-tenth the volume of red blood cells) that stick to the site of blood vessel injury, cluster and then seal off the injured blood vessel to stop bleeding. A synonym for platelet is “thrombocyte,” which forms the beginning of words describing disorders of platelets, such as thrombocytopenia (too few platelets) or thrombocythemia (too many platelets).

**Platelet Transfusion.** Transfusion of donor platelets may be needed to support some patients treated for Hodgkin lymphoma. The platelets can be collected from several unrelated donors and given as pooled, random-donor platelets. The platelets from about six single-unit blood donors are required to significantly raise the platelet count in a recipient. Sufficient platelets can be obtained from one donor by a procedure known as “apheresis.” Platelets are skimmed from large volumes of blood passing through a specialized machine. The red blood cells and plasma are returned to the donor. The advantage of single-donor platelets is that the patient is not exposed to the different antigens on platelets from many different people and is thus less likely to develop antibodies against donor platelets. A human leukocyte antigen (HLA)-matched platelet transfusion can be given if the patient has a related donor who has an identical or very similar HLA tissue type. See the free LLS booklet *Blood Transfusion*.

**Port.** A small device used with a central line (indwelling catheter) to access a vein. The port is placed under the skin of the chest. After the site heals, no dressings are needed. To give medicines or nutrition or to take blood samples, the doctor or nurse inserts a needle through the skin into the port. A numbing cream can be put on the skin before the port is used. Ports must be flushed periodically. Patients and/or caregivers are given instructions about caring for the port. See Central Line.

**Radiation Therapy.** The use of x-rays and other forms of radiation in treatment. Radiation therapy may be useful in the treatment of localized lymphomas. Radiation therapy can also be an important adjunct to therapy when there are particularly large masses of lymphoma in a localized area or when local large lymph nodes are either compressing or invading normal organs or structures and chemotherapy cannot control the problem.

**Recurrence/Relapse.** The return of a disease after it has been in remission following treatment.

**Red Blood Cell.** A blood cell that carries the red-colored protein hemoglobin, which binds oxygen and carries it to the tissues of the body. The red blood cells make up about 40 to 45 percent of the volume of the blood in healthy individuals. Another term for red cell is “erythrocyte.”

**Reduced-Intensity Allogeneic Stem Cell Transplantation.** A form of allogeneic transplantation in which patients receive lower doses of chemotherapy drugs and/or radiation in preparation for the transplant. Immunosuppressive drugs are used to prevent rejection of the graft (donor tissue). The engraftment of donor immune cells may allow these cells to attack the disease (graft-versus-disease effect). Reduced-intensity allogeneic stem cell transplant is also called “nonmyeloablative stem cell transplantation.” For more information about all types of stem cell transplantation, see the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.

**Refractory Disease.** Disease that is either resistant to or does not go into remission or improve substantially after initial therapy.

**Remission.** A disappearance of evidence of a disease, usually as a result of treatment. The terms “complete” and “partial” are used to modify the term 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. Long-term benefit usually requires a complete remission, especially in progressive lymphomas.

**Scavenger Cell.** See Monocyte/Macrophage.

**Sedimentation Rate.** A blood test that measures how quickly red blood cells (erythrocytes) settle in a test tube in one hour. A sedimentation rate test is done to find out if inflammation is present in the body, to check on the progress of a disease or to see how well a treatment is working. This test is also called a “sed rate” or an “erythrocyte sedimentation rate (ESR).”

**Somatic Mutation.** See Mutation.

**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, enabling the spleen to remove debris such as bacteria and old blood cells. The spleen is often affected in lymphocytic leukemia and lymphoma. Enlargement of the spleen is called “splenomegaly.” Surgical removal of the spleen is known as “splenectomy.”

**Stem Cells.** Primitive cells in marrow that are essential to the formation of red blood cells, white blood cells and platelets. Stem cells are largely found in the bone marrow, but some leave the bone marrow and circulate in the blood. They are also found in the umbilical cord of a newborn. Using special techniques, the stem cells in blood can be collected, preserved by freezing and later thawed and used for stem cell therapy. See Hematopoiesis.

**Thrombocyte.** See Platelets.

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

**Toxic.** Used to describe a substance that is poisonous to cells.

**Translocation.** An abnormality of chromosomes in marrow or lymph node cells that occurs when a piece of one chromosome breaks off and attaches to the end of another chromosome. In a balanced translocation, genetic material is exchanged between two different chromosomes with no gain or loss of genetic information. When a translocation takes place, the gene at which the break occurs is altered. This is one form of somatic mutation that may transform the gene into an oncogene (cancer-causing gene). See Mutation.

**Tumor Suppressor Gene.** A gene that acts to prevent cell growth. If a mutation occurs that “turns off” this gene and causes loss of function, it may make the individual more susceptible to the development of cancer in the tissue in which the mutation occurred. Another term for tumor suppressor gene is “antioncogene.”

**White Blood Cells.** Any of the five major types of infection-fighting white cells in the blood: neutrophils, eosinophils, basophils, monocytes and lymphocytes. White blood cells are also called “leukocytes.”

## References

- Allen PB, Gordon LI. Frontline therapy for classical Hodgkin lymphoma by stage and prognostic factors. *Clinical Medical Insights: Oncology*. 2017;11:1-10.
- Arulogun S, Hertzberg M, Gandhi MK. Recent treatment advances in Hodgkin lymphoma: a concise review. *Internal Medicine Journal*. 2016;46(12):1364-1369.
- Bachanova V, Connors JM. Hodgkin lymphoma in pregnancy. *Current Hematologic Malignancy Reports*. 2013;8:211-217.
- Benekou K, Montoto S. Role of stem cell transplant in lymphoma in the era of new drugs. *Current Opinion in Oncology*. 2017;29(6):455-459.
- Borchman S, Engert A. The genetics of Hodgkin lymphoma: an overview and clinical implications. *Current Opinion in Oncology*. 2017;29:307-314.
- Broadfoot J, Johnson PWM. Response-adapted therapy in Hodgkin lymphoma. *Hematological Oncology*. 2017;35(suppl 1):33-36.
- Carbone A, Gloghini A. Hodgkin lymphoma classification: are we at a crossroads? *Cancer*. 2017;123(19):3654-3655. doi:10.1002/cncr.30824.
- Connors JM, Jurczak W, Straus DJ, et al. Brentuximab vedotin with chemotherapy for stage III or IV Hodgkin's lymphoma. *New England Journal of Medicine*. 2018;378:331-344.
- Fernandez KS, Schwartz L, Chen L, Constine LS, Chauvenet A, de Alarcon PA. Outcome of adolescents and young adults compared to children with Hodgkin lymphoma treated with response-based chemotherapy on pediatric protocols: A Children's Oncology Group report. *Pediatric Blood and Cancer*. 2017;64(12). doi:10.1002/pbc.26681.
- Ghosh A, Politikos I, Perales MA. Stop and go: hematopoietic cell transplantation in the era of chimeric antigen receptor cells and checkpoint inhibitors. *Current Opinion in Oncology*. 2017;29(6):474-483.
- Glimelius I, Diepstra A. Novel treatment concepts in Hodgkin lymphoma. *Journal of Internal Medicine*. 2017;281(3):247-260. doi:10.1111/joim.12582.
- Hsi ED. 2016 WHO Classification update—What's new in lymphoid neoplasms. *International Journal of Laboratory Hematology*. 2017;39(suppl 1):14-22.
- Jelinek T, Mihalyova J, Kascak M, et al. PD-1/PD-L2 inhibitors in haematological malignancies: update 2017. *Immunology*. 2017;152(3): 357-371.
- Marron TU, Kalac M, Brody J. An update on the use of immunotherapy in the treatment of lymphoma. *Current Hematologic Malignancy Reports*. 2017;12(4):282-289.

Matsuki E, Younes A. Checkpoint inhibitors and other immune therapies for Hodgkin and non-Hodgkin lymphoma. *Current Treatment Options in Oncology*. 2016;17(6):31.

National Comprehensive Cancer Network. Hodgkin lymphoma, 2015. In: *NCCN Guidelines for Patients*. <https://www.nccn.org/patients/guidelines/hodgkin/index.html>. Accessed June 4, 2018.

National Comprehensive Cancer Network. Hodgkin lymphoma. In: *Practice Guidelines in Oncology—v.1.2017*. [https://www.nccn.org/professionals/physician\\_gls/pdf/hodgkins.pdf](https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf). Accessed October 25, 2017.

PDQ® Adult Treatment Editorial Board. *PDQ Adult Hodgkin Lymphoma Treatment*. Bethesda, MD: National Cancer Institute; updated April 20, 2017. <https://www.cancer.gov/types/lymphoma/patient/adult-hodgkin-treatment-pdq>. Accessed June 4, 2018. [PMID: 26389245]

PDQ® Pediatric Treatment Editorial Board. *PDQ Childhood Hodgkin Lymphoma Treatment*. Bethesda, MD: National Cancer Institute; updated September 1, 2017. <https://www.cancer.gov/types/lymphoma/patient/child-hodgkin-treatment-pdq>. Accessed June 4, 2018. [PMID: 26389224]

The Leukemia & Lymphoma Society. *Facts 2017-2018*. Available at [www.LLS.org/booklets](http://www.LLS.org/booklets). Accessed on June 4, 2018.

Townsend W, Linch D. Hodgkin's lymphoma in adults (seminar). *Lancet*. 2012;380(9844):836-847.

Younes A, Ansell S. Novel agents in the treatment of Hodgkin lymphoma: biological basis and clinical results. *Seminars in Hematology*. 2016;53:186-189.

## NOTES

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