LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

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Hodgkin Lymphoma

Erica, Hodgkin lymphoma survivor

Revised **2016**

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Publication Update
Hodgkin Lymphoma

The Leukemia & Lymphoma Society wants you to have the most up-to-date information about blood cancer treatment. See below for important new information that was not available at the time this publication was printed.

- In May 2017, the Food and Drug Administration (FDA) approved nivolumab (Opdivo®) for the treatment of adult patients with classical Hodgkin lymphoma (HL) that has relapsed or progressed after 3 or more lines of systemic therapy that includes autologous hematopoietic stem cell transplantation (HSCT).

  It is also approved for the treatment of adult patients with classical HL that has relapsed or progressed after autologous HSCT and brentuximab vedotin.

  These indications are approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

- In March 2017, the Food and Drug Administration (FDA) approved pembrolizumab (Keytruda®) for the treatment of adult and pediatric patients with refractory classical Hodgkin lymphoma (cHL), or who have relapsed after 3 or more prior lines of therapy.

  This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

For more information, contact an Information Specialist at (800) 955-4572 or infocenter@lls.org.

A Message from Louis J. DeGennaro, PhD

President and CEO of The Leukemia & Lymphoma Society

The Leukemia & Lymphoma Society (LLS) is the world's largest voluntary health organization dedicated to finding cures for blood cancer patients. Our research grants have funded many of today's most promising advances; we are the leading source of free blood cancer information, education and support; and we advocate for blood cancer patients and their families, helping to ensure they have access to quality, affordable and coordinated care.

Since 1954, we have been a driving force behind almost every treatment breakthrough for blood cancer patients. We have invested more than $1 billion in research to advance therapies and save lives. Thanks to research and access to better treatments, survival rates for many blood cancer patients have doubled, tripled and even quadrupled.

Yet we are far from done.

Until there is a cure for cancer, we will continue to work hard—to fund new research, to create new patient programs and services, and to share information and resources about blood cancers.

This booklet has information that can help you understand Hodgkin lymphoma, prepare your questions, find answers and resources, and communicate better with members of your healthcare team.

Our vision is that, one day, all people with Hodgkin lymphoma will either be cured or will be able to manage their disease so that they can experience a great quality of life. Today, we hope our expertise, knowledge and resources will make a difference in your journey.

Louis J. DeGennaro, PhD
President and Chief Executive Officer
The Leukemia & Lymphoma Society

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Acknowledgement

The Leukemia & Lymphoma Society gratefully acknowledges

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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. Brief descriptions of normal blood and marrow, the lymphatic system and definitions of medical terms are included in this booklet.

An estimated 8,500 people living in the US are expected to be diagnosed with HL in 2016. There are an estimated 181,967 people either living with, or in remission from, HL.

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

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, 9 a.m. to 9 p.m. EST)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org
- Visit: www.LLS.org/informationspecialists.

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.

Telephone/Web Education Programs. LLS offers free telephone/Web education programs for patients, caregivers and healthcare professionals. For more information, please visit 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.

Sign Up for an E-Newsletter. Read the latest disease-specific news, learn about research studies and clinical trials, and find support for living with blood cancer. Please visit www.LLS.org/signup.

Community Resources and Networking

Online Blood Cancer Discussion Boards and Chats. Online discussion boards and moderated online chats can provide support and help cancer patients to reach out and share information. For more information, please visit www.LLS.org/discussionboards and www.LLS.org/chat.

LLS Community. An online social network and registry for patients, caregivers, and supporters of those with blood cancer. It is a place to ask questions, get informed, share your experience, and connect with others. To join, visit www.LLS.org/community.

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.

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, locating summer camps and other needs. For more information, please visit 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.

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.

Additional Help for Specific Populations

Información en Español (LLS Information in Spanish). For more information, please visit www.LLS.org/espanol.

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 World Trade Center (WTC) Health Program. People eligible for help include

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

For more information, please

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

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 two-week period. For more information, please

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

Feedback. To give suggestions about this booklet, visit www.LLS.org/publicationfeedback.

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 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 treatment approach may be based on the subtype. See *Subtypes of Hodgkin Lymphoma* on page 10.

You can find general information about lymphoma in the free LLS booklet *The Lymphoma Guide: Information for Patients and Caregivers.*

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 evident that the disease results from an injury to the DNA of a lymphocyte (a type of white blood cell).

The altered DNA in the lymphocyte produces a malignant (cancerous) change that—if untreated—results in the uncontrolled growth of abnormal lymphocytes. The accumulation of these lymphocytes results in tumor masses that are found in the lymph nodes and other sites in the body (see *Signs and Symptoms* on page 7).

HL is distinguished from other types of lymphoma by the presence of Reed-Sternberg cells (named for the scientists who first identified them). Reed-Sternberg cells are large, abnormal lymphocytes, which have characteristics that set them apart from other cells. These differences can be observed under the microscope and identified by special pathology tests. When viewed under the microscope, patterns of Reed-Sternberg cells can be visualized and features specific to these cells can be observed. This is important information that helps doctors to determine a patient's HL subtype.

This booklet covers many HL subtypes and provides detailed information (including diagnosis, staging and treatment) about the more common ones. It also provides a brief description of normal blood and marrow and the lymphatic system. There is a list of medical terms to help readers understand information that may be new to them.

Incidence, Causes and Risk Factors

Incidence. Although HL can occur in both adults and children, it is most likely to be diagnosed among young adults in their 20s or early 30s and adults age 65 and older (see Figure 1). It is more common among men than women. HL 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 US are expected to be diagnosed with HL in 2016.

Figure 1. Hodgkin Lymphoma: Age-Specific Incidence Rates 2009-2013

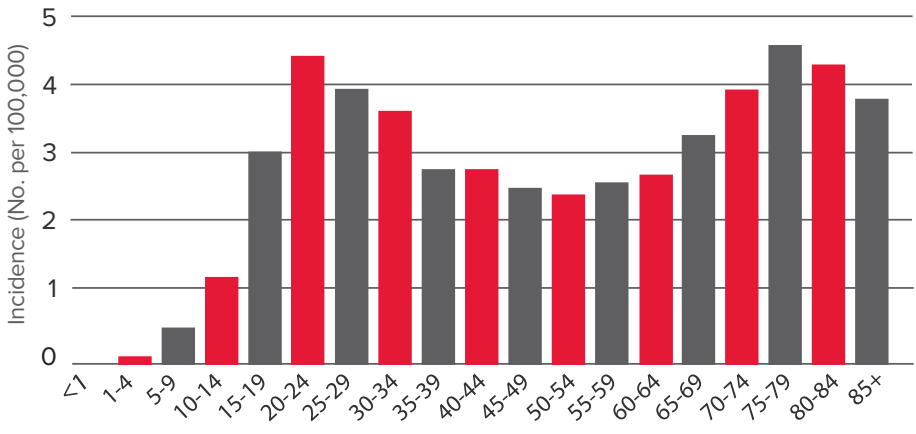


Figure 1. | The horizontal axis shows 5-year age intervals. The vertical axis shows the frequency of new cases of HL per 100,000 people, by age-group. Incidence of HL peaks between the ages of 15 and 44 and at age 65 and older. Source: Surveillance, Epidemiology and End Results (SEER) Program; National Cancer Institute; 2016.

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.
- People infected with human immunodeficiency virus (HIV) also have increased probability of developing HL.
- There are occasional cases of familial clustering; having a parent or a sibling with HL may increase the risk of developing the disease. These cases are uncommon, but 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 under the heading "Blood Cancer - General Information" or contact our Information Specialists at (800) 955-4572.

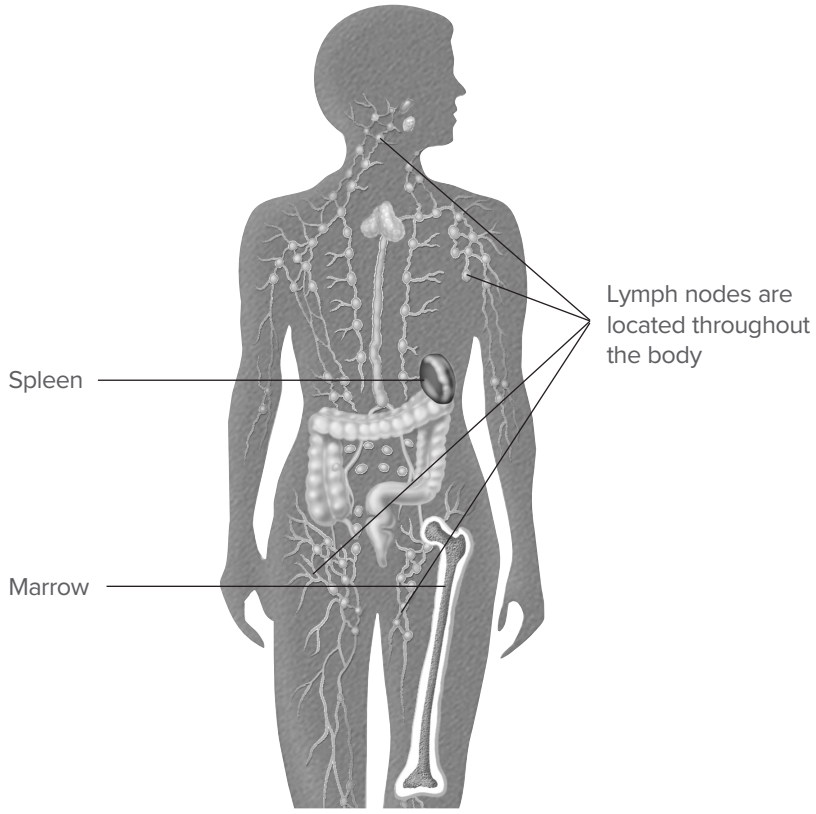
Signs and Symptoms

A person who has signs or symptoms that suggest the possibility of lymphoma is usually referred to a specialist in hematology-oncology. Typically, this specialist is a member of a team that consists of the hematologist-oncologist and a nurse practitioner, physician assistant and registered nurse. This healthcare provider will order additional tests to make a diagnosis (see *Diagnosis* on page 9). The signs and symptoms of HL are also associated with a number of other, less serious diseases.

The most common early sign of HL is painless swelling of one or more lymph nodes.

- There are about 600 lymph nodes in the body (see Figure 2 on page 8).
- Most patients with HL 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.

Figure 2. 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 some of the parts of the immune system. There are about 600 lymph nodes throughout the body.

Figure 2. | 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.

Other HL signs and symptoms may include

- Unexplained fever
- Persistent fatigue
- Persistent cough and shortness of breath (if HL is located in the chest)
- Drenching night sweats
- Unexplained weight loss
- Decreased appetite

- Abdominal pain or swelling and feeling of fullness (due to an enlarged spleen)
- Itching.

Individuals with HL may experience pain in the lymph nodes after drinking alcohol—this is an uncommon but specific symptom. Many patients have no symptoms at all.

B Symptoms. Fever, drenching night sweats and loss of more than 10 percent of body weight over six months are sometimes termed "B symptoms." These symptoms are significant to the prognosis and staging of the disease. Other HL symptoms such as itching, fatigue and alcohol-related pain do not have the same prognostic importance and are not considered B symptoms.

Diagnosis

An accurate diagnosis of the subtype of HL is important. Obtaining a precise diagnosis will help the doctor to

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

Patient Evaluation. The healthcare provider will take a comprehensive medical history and ask questions regarding symptoms, including the absence or presence of B symptoms. Physical examination will include measurement of all accessible lymph node groups (neck, underarms and groin) as well as the size of palpable 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 of the lymph node is usually not sufficient to make a firm diagnosis. The entire lymph node or part of the lymph node is surgically removed so that the hematopathologist (a doctor who specializes in diagnosing diseases of the blood and marrow) has enough tissue to make a firm diagnosis. HL may be difficult to diagnose as the Reed-Sternberg cells may be less clear, comprising only 0.1 to 10 percent of the biopsy specimen. It is important that a specialist with experience in diagnosing HL analyze 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 categorize the patient's HL into one of several subtypes (see Table 1 on page 11).

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 Reed-Sternberg cells to confirm a diagnosis of HL.

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

Subtypes of Hodgkin Lymphoma

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

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

cHL is characterized by the presence of Reed-Sternberg cells. NLPHL is characterized by the presence of lymphocyte-predominant cells, sometimes termed "popcorn cells," and Reed-Sternberg cells are not found. About 95 percent of HL patients have the classical subtype. cHL is further classified into four subtypes (see Table 1 on page 11), each with different characteristics. Knowing the patient's HL subtype is a very important consideration when the doctor is making treatment decisions.

Table 1. Subtypes of Hodgkin Lymphoma

Hodgkin Lymphoma Subtype	Features
Classical Hodgkin Lymphoma (cHL)	
Nodular Sclerosis	• Accounts for 70% of cHL cases • Most common type in young adults • Involved lymph nodes contain scar tissue (sclerosis) • Incidence similar in males and females • Highly curable • B symptoms in approximately 40% of cHL cases
Mixed Cellularity	• Accounts for 20%-25% of cHL cases • Most common in older adults • Most common in males • Prevalent in patients with HIV infection • Involved lymph nodes contain RS cells and several other cell types • B symptoms common
Lymphocyte-rich	• Accounts for about 5% of cHL cases • Involved lymph nodes contain numerous normal-appearing lymphocytes and RS cells • Usually diagnosed at an early stage • More common in males • B symptoms are rare
Lymphocyte-depleted	• Rarest cHL subtype, <1% of cHL cases • Involved lymph nodes contain few normal lymphocytes and numerous RS cells • Median age range 30-37 years • Prevalent in patients with HIV infection • Usually diagnosed at an advanced stage • B symptoms common
Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL)	• Accounts for 5% of all HL cases • Most common in 30 to 50-year-old age-group • More common in male than in female patients • Slow growing and highly curable • Small risk of transformation to aggressive NHL (3%-5% of cases)

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; WHO, World Health Organization.

Table 1. | Subtypes of Hodgkin Lymphoma as designated by World Health Organization (WHO) classification.

Staging and Prognostic Factors

Doctors use physical examinations, imaging tests, blood tests and, sometimes, bone marrow biopsy findings to determine the extent of the disease. This determination is called "staging." Staging provides important information for treatment planning.

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
- Whether there are very large masses of tumors in one site or another.

Imaging is a very important part of the staging and management of 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 is a noninvasive 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 and it may document a mediastinal (the area between the lungs) mass.
- A CT (computed tomography) scan—A CT 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 have CT scans of the neck, chest, abdomen and pelvis—all the areas where lymph nodes are present—to identify areas of disease. A CT scan can also show whether there is involvement of the lungs, liver and other organs. This information is helpful in staging HL.
- An FDG-PET (fluorodeoxyglucose [FDG] positron emission tomography) scan—A PET scan is an imaging technique that produces a 3D image of functional processes in the body. This type of scan uses a small amount of FDG, the radioactive glucose, which is injected into the patient. The FDG is then absorbed by tissue cells. 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. In an FDG-PET scan, 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. These images frequently help to guide to an appropriate biopsy site.

- A combination PET-CT scan is an essential tool that is used to stage the disease precisely, to determine the margins of radiotherapy (when needed) and to provide a baseline to assess future treatment response. PET-CT scans are increasingly being used for assessment of response during 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—MRIs use a powerful magnet and radio waves 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, if a doctor is concerned about the disease involving the spinal cord or the brain, MRI is useful for looking at 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. In addition, the ratio of white blood cells, known as "lymphocytes" and "monocytes," has been shown to have prognostic significance.
- Determine whether lymphoma cells are present in the blood and whether the immunoglobulins made by lymphocytes are 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 an erythrocyte sedimentation rate (ESR).
- Assess kidney and liver functions.

Bone Marrow Tests. Some patients who have been diagnosed with HL may undergo a bone marrow biopsy. Your doctor will decide if this procedure is necessary. That determination will be based on certain features, such as the location of the disease in your body (see Figure 3 on page 15). A bone marrow biopsy may not be required for patients with early-stage disease and 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 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 effects of treatment.

Staging. Staging for HL is based on the Ann Arbor staging system. Each stage is subdivided and assigned to category A, B or E. (see Table 2).

- Category A indicates no symptoms are present
- Category B indicates the presence of "B symptoms"
  - Unexplained fevers
  - Drenching night sweats
  - Unexplained weight loss of more than 10 percent of body weight
- Category E indicates involvement of organs or tissues beyond the lymph system.

Table 2. Stages of Hodgkin Lymphoma

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.

Modifying Features

A—No symptoms

B—Presence of fever, drenching sweats, unexplained loss of more than 10% of body weight over 6 months

E—Involvement of organs or tissues beyond the lymph system

Table 2. | The stage and modifying features direct the treatment approach.

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.

Figure 3. Hodgkin Lymphoma Stages

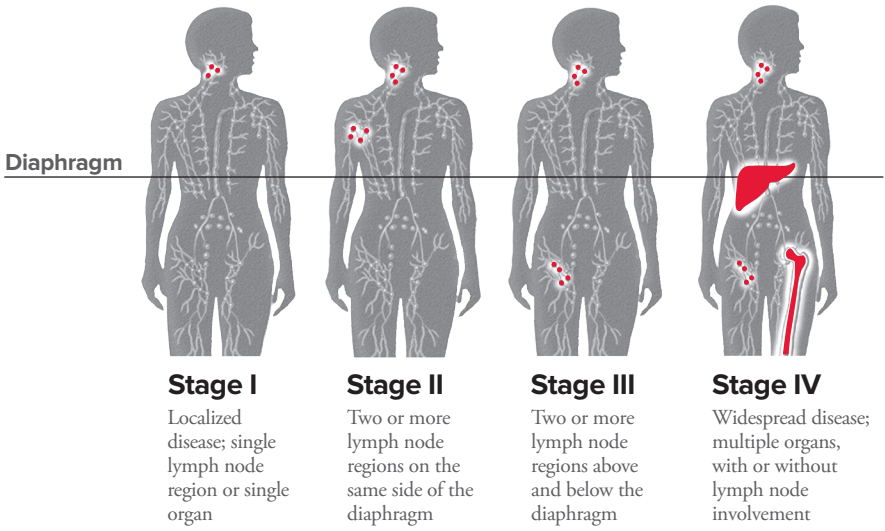


Figure 3. | This illustration shows the location of Hodgkin lymphoma in the body for each stage. The stages are described in Table 2, page 14.

Treatment Planning

Prognostic Factors. Hodgkin lymphoma 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-II with no unfavorable risk factors
- Early-stage unfavorable
  Disease is stage I-II with unfavorable risk factors
- Advanced-stage
  Disease is stage III-IV.

Prognostic Factors for Early-Stage Hodgkin Lymphoma. Patients are designated as having early-stage favorable HL if they have stage I or stage II disease and no adverse or unfavorable risk factors. Sometimes, early-stage favorable patients are treated with less intensive treatment regimens. However, the use of staging information to modify therapy is variable.

Unfavorable early-stage HL risk factors include

- B symptoms—fever, drenching night sweats, unexplained weight loss greater than 10 percent of body weight over six months
- Extranodal disease—masses located beyond the lymph system
- Bulky disease—a chest mass greater than one third of the chest diameter 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 (ESR) greater than 50 mm/h.

International Prognostic Score Factors for Advanced-Stage Hodgkin Lymphoma. An international collaboration among several cancer research groups in North America and Europe evaluated thousands of patients with advanced disease (stages III and IV) and identified seven unfavorable prognostic factors (see Table 3 on page 17).

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

Table 3. International Prognostic Score Factors for Advanced-Stage Hodgkin Lymphoma

Higher risk is associated with these seven factors—the more factors present, the greater the risk.

The patient is

- Male
- 45 years or older.

The patient has

- Stage IV disease
- Hemoglobin of less than 10.5 g/dL
- A white blood cell (WBC) count of 15,000/µL or higher
- A lymphocyte count less than 600/µL and/or less than 8 percent of the total WBC count
- An albumin level of less than 4 g/dL.

Clinical trials to identify other prognostic indications for HL patients are under way. See *Research and Clinical Trials* on page 29. Use of this information to modify therapy is variable.

Treatment for HL is changing due to new drugs and research findings from clinical trials. Therefore, before treatment begins, it is important to consider getting a second opinion at a 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 disease. Even if the disease recurs, many patients can be cured with further treatment.

Most patients become long-term survivors of the disease. Thus, treatment goals aim 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.

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

Many (but not all) treatments for HL have no or little adverse effect on future fertility. Adults of childbearing age and parents of children diagnosed with HL should ask their doctors for information that may lessen the risk for infertility. See the free LLS fact sheet *Fertility Facts* for more details.

Treatment

Chemotherapy alone or combined modality therapy (chemotherapy and radiotherapy) are commonly administered treatment approaches for HL.

Chemotherapy. Chemotherapy is the mainstay of treatment for HL and usually involves a combination of drugs. The drugs are dissolved in fluid and usually administered via a peripheral intravenous (IV) line. If finding an accessible vein becomes a problem, a port, a central line or a percutaneously inserted central venous catheter (a "PICC" or a "PIC line") may be used for some HL patients.

Radiotherapy. Radiotherapy, also known as "radiation therapy" (RT), consists of the use of special machines that produce high-energy rays capable of killing the HL cells. RT alone was a standard treatment option for patients with early-stage disease for many decades. However, because of the potential for long-term toxic side effects, this treatment approach has changed.

Involved field radiation therapy (IFRT) and involved site radiation therapy (ISRT) are the most common types of radiotherapy used to treat HL. The radiation targets primarily the lymph node regions involved by disease. Continuous improvements in the devices that deliver radiation therapy have led to more precise targeting of treatment areas. In addition, the uninvolved organs, such as the lungs, liver and reproductive organs, are shielded to help minimize the side effects of the treatment. IFRT and ISRT differ by the size of the area (field) that is exposed to radiation. If radiation therapy is being considered, this distinction (and pros/cons) of different approaches should be carefully reviewed with the treating doctor.

Table 4. Some Treatment Approaches for Classical Hodgkin Lymphoma (cHL)

Early-stage cHL

- Chemotherapy combinations
  - ABVD (Adriamycin® [doxorubicin], bleomycin, vinblastine and dacarbazine)
  - BEACOPP (bleomycin, etoposide, Adriamycin [doxorubicin], cyclophosphamide, Oncovin® [vincristine], procarbazine and prednisone)
  - Stanford V (mechlorethamine [Mustargen®], doxorubicin, vinblastine, vincristine, bleomycin, etoposide and prednisone) (this regimen is rarely used)
- Combination chemotherapy, either with or without involved field radiation

Advanced-stage cHL

- Chemotherapy combinations

Relapsed/Refractory cHL

- Stem cell transplantation
- Brentuximab vedotin (Adcetris®)
- Nivolumab (Opdivo®)

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 combination chemotherapy either alone or with reduced amounts of radiation. This approach has resulted in less toxicity and improved outcome.

ABVD (Adriamycin® [doxorubicin], bleomycin, vinblastine, dacarbazine) is the most effective and least toxic regimen available to date. It poses less of a risk for later development of leukemia or infertility than many other adult chemotherapy combinations.

The Stanford V regimen (see Table 4) is a brief but dose-intensive regimen that is rarely used. It is associated with a lower risk for chemotherapy-related infertility, secondary cancers and toxicity to the heart and lungs. Radiation therapy is an important part of the Stanford V regimen.

Current practice guidelines for treatment of early-stage, low-risk HL suggest that at least 90 percent of patients can be cured with as few as two courses of ABVD, followed by involved field radiation with a reduced dose of radiation.

Other treatment regimens omit radiotherapy altogether and treat with chemotherapy alone. Sometimes the use of PET-CT scan results, either during or after treatment, can guide whether or not radiation therapy is included. Concerns about the late effects of radiotherapy (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. Examples of patients who meet these criteria may be women younger than 35 years or those who have a family history of breast cancer and for whom the radiation therapy would involve breast tissue.

Early-Stage Unfavorable Hodgkin Lymphoma Treatment. Patients in this category (stages I and II with unfavorable risk factors) are considered to have higher-risk disease and 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 involved field 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 (preferred regimen)
  Adriamycin [doxorubicin], bleomycin, vinblastine, dacarbazine
- Dose-escalated BEACOPP
  bleomycin, etoposide, Adriamycin [doxorubicin], cyclophosphamide, vincristine, procarbazine, prednisone.

Advanced-Stage Hodgkin Lymphoma. Hodgkin lymphoma is potentially curable 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 (preferred regimen)
  Adriamycin [doxorubicin], bleomycin, vinblastine, dacarbazine
- Dose-escalated BEACOPP (in selected patients who are younger than 60 years and who have an IPS [International Prognostic Score, see page 17] of 4 or higher) bleomycin, etoposide, Adriamycin [doxorubicin], cyclophosphamide, vincristine, procarbazine, prednisone
- Stanford V (this regimen is rarely used)
  mechlorethamine [Mustargen®], doxorubicin, vinblastine, vincristine, bleomycin, etoposide, prednisone.

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. For this reason it is a less commonly used treatment in the United States and Canada. It may be used for patients who have advanced HL.

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

Relapsed or Refractory Hodgkin Lymphoma. ABVD results in shrinkage of disease in most patients. 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." For these patients, HL is still potentially curable.

A small percentage of patients have disease that does not respond to initial treatment (this is called "refractory HL"). Approximately 10 percent of patients with early-stage disease and 20 to 30 percent of patients who have advanced disease either respond briefly or do not respond to standard chemotherapy combinations and experience disease progression. These patients often require treatment consisting of high-dose chemotherapy followed by autologous (using the patient's own cells) stem cell transplantation.

Brentuximab vedotin (Adcetris®), a monoclonal antibody-drug combination, given intravenously (IV), has been approved by the FDA for treatment of relapsed or refractory HL. Adcetris is also approved for the treatment of HL after failure of autologous stem cell transplant and in HL patients who are not autologous stem cell transplant candidates after failure of at least two multiagent chemotherapy regimens. See www.LLS.org/drugs for more information. It is also sometimes administered in selected patients as consolidation treatment after autologous stem cell transplantation (see below).

Nivolumab (Opdivo®), a PD-1 checkpoint inhibitor, given IV, has been FDA approved for treatment of cHL that has either relapsed or progressed after autologous stem cell transplantation, hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin. See 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 stem cell transplantation is used routinely for many patients who relapse. This treatment can provide better than 50 percent long-term survival for patients, although specific outcomes can vary depending on patient-specific risk factors.

Allogeneic Stem Cell Transplantation. Some patients who have relapsed several times have been treated successfully with allogeneic (using another person's cells) stem cell transplantation. However, this treatment has a significant risk of mortality. 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 (NLPHL) Treatment. NLPHL accounts for about 5 percent of all HL diagnoses. In some ways, the characteristics of NLPHL are more similar to those of indolent non-Hodgkin lymphoma than they are to those of cHL. Treatment plans for patients with this HL subtype are different from those prescribed for patients with cHL. About 75 percent of patients with NLPHL are diagnosed with stage I disease.

This subtype is an indolent (slow-growing) form of HL and it is associated with an excellent long-term survival; however, to avoid unnecessary side effects, it is important not to over-treat these patients.

At present, the usual treatment for patients with early-stage NLPHL is involved field radiation alone. For more advanced disease, combination chemotherapy may be needed.

Transformation to diffuse large B-cell lymphoma (DLBCL) is reported in 8 to 14 percent of patients from four to eight years after an initial NLPHL diagnosis. NLPHL patients with suspected relapse 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 (a monoclonal antibody treatment), either with or without chemotherapy or radiotherapy. Some patients may develop chronic indolent disease and may not require aggressive treatment unless they present with symptoms.

Childhood Hodgkin Lymphoma. Hodgkin lymphoma comprises about 6 percent of childhood cancers. In the United States, the incidence of HL is age related and is highest among adolescents of ages 15 to 19 years (29 cases per 1

million per year), with children ages 10 to 14 years, 5 to 9 years, and 0 to 4 years having approximately threefold, eightfold, and 30-fold lower rates, respectively.

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 10)
- Stage of the disease (see *Staging and Prognostic Factors* on page 12)
- Fertility concerns (see *Fertility* on page 27)
- Other potential risk factors
- The response to treatment—doctors measure the response rate by using imaging techniques such as PET-CT scans.

Doctors make use of all this information about the patient's disease to determine the most effective therapy. In this way, they are able to develop treatment plans that limit the amount of therapy required to bring about remission. It is important 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.

Some of the following drug combinations may be used:

- ABVD (Adriamycin® [doxorubicin], bleomycin, vinblastine and dacarbazine)
- AV-PC (doxorubicin, vincristine, prednisone and cyclophosphamide)
- ABVE: (doxorubicin (Adriamycin), bleomycin, vincristine, and etoposide)
- ABVE-PC: (doxorubicin (Adriamycin), bleomycin, vincristine, etoposide, prednisone, and cyclophosphamide)
- BEACOPP (bleomycin, etoposide, Adriamycin [doxorubicin], cyclophosphamide, Oncovin® [vincristine], procarbazine and prednisone)
- OEPA (Oncovin [vincristine], etoposide, prednisone and Adriamycin [doxorubicin])

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
- Minimize the risk of long-term and late effects associated with treatment (for example, infertility, impaired cardiac function and secondary cancers).

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

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

Radiotherapy should generally be avoided because of the risk of toxic effects to the fetus. 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 vinblastine alone until delivery. Treatment choice must be individualized taking into consideration the mother's wishes, the stage of the HL and the length of time until delivery can occur safely.

One study showed that there was no evidence that pregnancy increased relapse rate in women with a history of HL that is in remission.

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 three weeks after the last chemotherapy treatment to avoid treatment-related inflammation being detected on PET. A 5-point scale (the Deauville criteria) has been developed as an objective measure of response. A score of 1 or 2 is considered to be a complete metabolic response, while a score of 3, 4, or 5 suggests either residual, active or progressive disease. Patients with either residual, active or progressive disease should undergo repeat biopsy.

Periodic examination for recurrence in HL patients is necessary for years after treatment. Most patients who relapse will do so within the first two years after completion of therapy. Therefore, follow-up visits during this time period will be more frequent, typically every three to six months. After two years, follow-up visits are generally scheduled every six to 12 months for the next three years (until five 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 26. 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 three to six months for one to two years and then every 6 to 12 months for the next three years. After that, they can be done annually. CT scans of the chest, abdomen and pelvis may be used to detect relapsed disease at 6, 12 and 24 months after treatment is completed. PET-CT scans are not recommended for ongoing monitoring for disease recurrence due to a high false-positive rate. The decision whether to perform imaging should be made on an individual basis and after the implications have been discussed by the patient and healthcare professional.

Treatment Side Effects

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

If the white blood cell count (particularly neutrophils) drops severely and for extended periods of time, patients may develop infections and require antibiotic treatment and possible hospitalization. In some types of cancer, it is necessary to either allow patients' blood counts to recover from the effects of treatment or to adjust their chemotherapy doses or the time between chemotherapy cycles. However, because HL has a high potential for cure, a low white blood cell count is not a reason to delay treatment or reduce the treatment dose.

Treatment with drugs such as granulocyte-colony stimulating factor (G-CSF), 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 routinely recommended because there is an increased potential for lung toxicity 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 since these treatments lower blood cell counts and weaken immune system cell function. Removal of the spleen, now performed less often, 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.

HL patients are advised to get certain vaccinations once they have finished their treatment, including vaccinations for pneumococcal pneumonia and influenza. There are two types of pneumococcal vaccines available for adults: a pneumococcal polysaccharide vaccine (PPSV23) and a pneumococcal conjugate vaccine (PCV13). Immunizations using live organisms or with high viral loads, such as the herpes zoster (shingles) vaccine, should not be administered. Your healthcare professional will give you more information.

Other Effects. Treatment may cause nausea, vomiting, reflux, bloating, constipation, diarrhea, extreme fatigue, neuropathy, fever, cough, or hair loss. These and other potential effects depend on the drugs and dosages used and on the individual patient's susceptibility. Most side effects are temporary and resolve when therapy is completed. Certain drugs have a specific tendency to affect certain tissues (for example, vincristine tends to affect nerve tissue and bleomycin may affect the lungs).

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 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 seems to increase over a longer follow-up time. However, the risk may be less with current treatments compared to the risk associated with those 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. ABVD has been used extensively for more than 20 years and, compared to prior therapies, it does not pose a significant risk for leukemia or infertility. However, there are not as much data on the long-term effects of chemotherapy as there are for the long-term effects of radiation, and further assessment is needed.

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 develop more than 10 years after the end of treatment.

Girls or women below the age of 30 years who have radiation to the breast to treat their HL are at risk for developing breast cancer 15 to 20 years later. Male survivors of childhood cancers may also be at risk for developing secondary cancers. However, they do not appear to have the same risk for developing breast cancer as female childhood cancer survivors.

Radiation therapy can also injure the lungs, especially when given with bleomycin (the B in ABVD). Survivors who have had chest radiation are also at risk for lung cancer. Smoking further increases their risk. HL 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 10 to 20 years ago have a risk of lung cancer that is about four times 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.

Heart Disease. Radiation therapy to the chest and treatment with chemotherapy containing anthracyclines (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).

Thyroid Dysfunction. Radiation therapy can injure the thyroid gland, causing decreased thyroid function (hypothyroidism).

Fertility. Patients may be less fertile after treatment. The risk of infertility varies according to the nature of the treatment—the type and amount of chemotherapy, the location of radiation therapy and the patient's age. With some regimens, however, fertility appears to be minimally affected or not at all affected. There are fertility options for both men and women. Speak to your healthcare team and see the free LLS fact sheet *Fertility Facts* for more information.

In couples of childbearing age where 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. Exercise has been shown to improve fatigue related to chemotherapy. For more information, see the free LLS fact sheet *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 professional who monitors them for potential health problems after treatment ends.
- Get blood tests every five years to measure their cholesterol levels if they were treated with chest radiation.
- Have regular screening for heart disease and annual blood pressure 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 five years after initial therapy.
- Practice monthly breast self-examination, have yearly breast examination by a healthcare professional and have early baseline mammograms (within eight to 10 years after therapy or by age 40, whichever occurs earlier). It is recommended that breast MRI is added to mammography screening for women who received irradiation of the chest when they were between 10 and 30 years of age. Although some women may develop breast cancer after HL treatment, it can be detected early and treated, providing 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 regular thyroid function checkups (at least annually) 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 publications *Long-Term and Late Effects of Treatment in Adults Facts* and *Long-Term and Late Effects of Treatment for Childhood Leukemia or Lymphoma Facts*.

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 all HL patients. The proportion of patients with HL who enter remission, stay in remission for years or are cured has increased dramatically during the last 30 years.

Clinical Trials. Every new drug or treatment regimen goes through a series of studies called "clinical trials" before it becomes part of standard therapy. Clinical trials are carefully designed and rigorously reviewed by expert clinicians and researchers to ensure as much safety and scientific accuracy as possible. 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, available 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 will conduct individualized clinical-trials searches for patients, family members and healthcare professionals.

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

Biomarkers and Genetic Causes. Studies are under way to identify biological markers, or "biomarkers," which are high levels of substances released by cancer cells. Biomarkers can be used to get information about the presence and level of cancer cells. Biomarkers under investigation in HL include interleukin (IL) 10, an immune factor, and CD30 antigen. High levels of IL10 may indicate a relatively poor outlook and high levels of CD30, paired with advanced-stage disease, are associated with an unfavorable prognosis.

Studies of familial HL are under way to obtain a better understanding of the genetic causes of HL. The goal is to identify genetic changes. This information may help doctors predict a person's risk of developing HL.

Interim PET-CT as Decision Tool for Chemotherapy Adjustment. Recent studies comparing different chemotherapy regimens such as ABVD and BEACOPP have led to new challenges to identify clinical or biological prognostic factors that may help doctors recognize those patients who will benefit most from more intensive treatment. Further studies are under way to address the challenges of using PET and combined PET-CT scans to assess the benefits of specific (risk-adapted) therapies for individual patients.

Long-Term and Late Effects of 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 been conducted with results suggesting chemotherapy alone is a viable approach. 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
- Comparing outcomes between the uses of involved field radiation therapy and involved site radiation therapy (which targets a smaller area for radiation treatment).

Relapsed or Refractory Hodgkin Lymphoma. Several chemotherapy regimens, with and without targeted therapies, are being studied for effectiveness and safety in advanced, relapsed or refractory disease. Examples of studies include comparisons of outcomes between various combinations of chemotherapy with or without new drugs and antibodies. Adding new agents to chemotherapy regimens may mean that patients can receive reduced amounts of chemotherapy, thereby reducing side effects. The following includes drugs and regimens being studied.

- Brentuximab vedotin (Adcetris®) was FDA approved for relapsed and refractory HL but continues to be studied both alone and in combination with traditional chemotherapy drugs. Brentuximab vedotin is also being studied as a consolidation treatment option to be administered after an autologous stem cell transplant.
- Other agents being studied as either single agents, or in combination, in relapsed and refractory HL include histone deacetylase inhibitors, such as entinostat, panobinostat, and mocetinostat. Blockage of important pathways involved in HL cell growth is another area of active study. These drugs include PI3-kinase/Akt/mTOR pathway inhibitors, such as everolimus (Afinitor®); immune system modulators such as lenalidomide (Revlimid®); and chemotherapy drugs such as bendamustine (Treanda®).
- Some of the drug combination regimens currently being studied in clinical trials for relapsed and refractory HL include
  - Panobinostat and lenalidomide
  - Gemcitabine and bendamustine
  - Brentuximab vedotin and bendamustine
  - Everolimus and brentuximab vedotin.

Programmed Death (PD-1) Checkpoint Inhibitors. A vital part of the immune system is its ability to tell between healthy cells in the body and those that it recognizes as foreign or harmful. The immune system depends on multiple checkpoints—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.

PD-1 is a checkpoint protein that 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 normal cells and also in some cancer cells. When PD1 binds to PD-L1, a message is sent to the T cell to leave the other cell alone. Some cancer cells have large amounts of PD-L1 receptors, which helps them avoid an immune attack. Checkpoint inhibitors are drugs created to target the PD1 or PD-L1, blocking their actions, and allowing the immune system to recognize and eliminate cancer cells. Two checkpoint inhibitor drugs nivolumab (now FDA approved) and pembrolizumab that have shown great results in other cancers, such as melanoma, are now being studied (as single agents and in combination with other drugs) in clinical trials for the treatment of advanced HL. Pembrolizumab is currently being studied as a treatment for patients with relapsed or refractory classical Hodgkin lymphoma.

Quality-of-Life Studies. Several studies have described long-term effects of therapy, including secondary cancers, heart disease and depression, among HL survivors. A great deal is known about the late effects of HL that was diagnosed and treated before the late 1980s. In part, as a result of that knowledge, treatment was changed to decrease the risk of long-term effects. Investigators are now gathering information on long-term or late effects among survivors who were treated over the past 30 years. The goal is to provide less toxic treatments for people who are diagnosed in the future, while maintaining or improving the cure rates of standard therapy. This information will also be used to propose guidelines for long-term follow-up care for survivors. Study participants may be asked to complete questionnaires about their health and quality of life (such as energy level, outlook on life and any long-term physical effects of the disease).

We encourage you to contact our Information Specialists and visit www.LLS.org for more information about specific treatments under study in clinical trials.

Normal Blood and Marrow and the Lymphatic System

Blood and Marrow. Blood is composed of plasma and cells suspended in plasma. Plasma is largely made up of water in which many chemicals are dissolved. These chemicals include

- Proteins
  - Albumin, the most common protein in blood
  - Blood-clotting proteins, made by the liver
  - Erythropoietin, a protein made by the kidneys that stimulates red blood cell production
  - Immunoglobulins, antibodies made by plasma cells in response to infections, including those that develop after vaccinations (such as poliovirus antibodies, which are made by normal plasma cells in the bone marrow)
- Hormones (such as thyroid hormone and cortisol)
- Minerals (such as iron and magnesium)
- Vitamins (such as folate and vitamin B_{12})
- Electrolytes (such as calcium, potassium and sodium)
- Antibodies, which are made by plasma cells.

The cells suspended in plasma include red blood cells, platelets and white blood cells (neutrophils, monocytes, eosinophils, basophils, and lymphocytes).

- The red blood cells make up a little less than half the volume of the blood. They are filled with hemoglobin, the protein that picks up oxygen in the lungs and delivers it to the cells all around the body; hemoglobin then picks up carbon dioxide from the body's cells and delivers it back to the lungs, where it is removed when we exhale.
- The platelets are small cells (one-tenth the size of red blood cells) that help stop bleeding at the site of an injury. For example, when a person has a cut, the vessels that carry blood are torn open. Platelets stick to the torn surface of the vessel, clump together, and plug up the bleeding site with the help of blood-clotting proteins such as fibrin, and electrolytes such as calcium. Later, a firm clot forms. The vessel wall then heals at the site of the clot and returns to its normal state.
- The neutrophils and monocytes are white blood cells. They are called "phagocytes" (eating cells) because they can ingest bacteria or fungi and kill them. Unlike the red blood cells and platelets, the monocytes can leave the

blood and enter the tissue, where they can attack the invading organisms and help combat infection. Eosinophils and basophils are types of white blood cells that respond to allergens or parasites.

- Most lymphocytes, another type of white blood cell, are found in the lymph nodes, the spleen and the lymphatic channels, but some enter the blood. There are three major types of lymphocytes: T lymphocytes (T cells), B lymphocytes (B cells) and natural killer (NK) cells. These cells are a key part of the immune system.

Marrow is a spongy tissue where blood cell development takes place. It occupies the central cavity of bones. In newborns, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms and legs no longer have functioning marrow. In adults, the spine (vertebrae), hip and shoulder bones, ribs, breastbone and skull contain the marrow that makes blood cells. The process of blood cell formation is called "hematopoiesis." A small group of cells, the stem cells, develop into all the blood cells in the marrow by the process of differentiation (see Figure 4).

Figure 4. Blood Cell & Lymphocyte Development

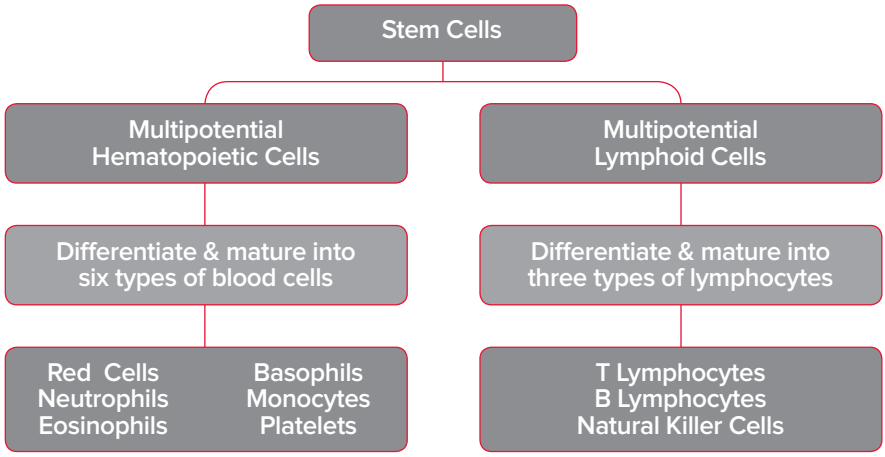


Figure 4. | **Stem cells** develop into blood cells (hematopoiesis) and lymphoid cells.

In healthy individuals, there are enough stem cells to keep producing new blood cells continuously. Blood passes through the marrow and picks up the fully developed and functional red and white blood cells and platelets for circulation in the bloodstream.

Some stem cells also enter the bloodstream and circulate. They are present in such small numbers that they cannot be counted or identified by standard blood count tests. Their presence in the blood is important because they can be collected by a

special technique. There are also methods to induce more stem cells to leave their home in the marrow and circulate in the bloodstream. Greater numbers of stem cells are then available for collection. If enough stem cells are harvested from a compatible donor, they can be transplanted into a recipient.

Stem cell circulation, from marrow to blood and back, also occurs in the fetus. After birth, placental and umbilical cord blood can be collected, stored and used as a source of stem cells for transplantation.

The Lymphatic System. The marrow is really two organs in one. The first is the blood cell-forming organ. The second is the lymphocyte-forming organ and is a part of the immune system.

The marrow produces three main types of lymphocytes. They are

- B lymphocytes (B cells), which make antibodies in response to foreign 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 other white blood cells to recognize the antibody and pull it into the cell along with its attached microbe (ingest it). 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.

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

Medical Terms

Allogeneic Stem Cell Transplantation. A treatment that uses donor stem cells to restore a patient's marrow and blood cells. A type of allogeneic transplant called a "reduced-intensity" or "nonmyeloablative" transplant is under study. It uses lower doses of conditioning therapy and may be safer, especially for older patients. For more information, see the free LLS booklet *Blood and Marrow Stem Cell 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, mark for destruction or inactivate foreign particles such as bacteria, viruses or harmful toxins.

Antigen. A foreign substance, usually a protein, that stimulates an immune response when it is ingested, inhaled or comes into contact with the skin or mucous membranes. Examples of antigens are bacteria, viruses or allergens. Antigens stimulate plasma cells to produce antibodies.

Antioncogene. See Tumor Suppressor Gene.

Apheresis. The process of removing certain components of a donor's blood and returning the unneeded parts to the donor. The process, also called "hemapheresis," uses continuous circulation of blood from a donor through a specialized machine and then back to the donor. Apheresis makes it possible to remove desired elements from large volumes of blood. Platelets, red blood cells, white blood cells and plasma can be removed separately. See Platelet Transfusion.

Autologous Stem Cell Transplantation. A treatment that uses a patient's own stem cells to delay the progression of certain blood cancers. The autologous transplantation process takes place after the patient achieves a complete response (remission), or a good partial response, to induction drug therapy. For more information, see the free LLS booklet *Blood and Marrow Stem Cell Transplantation.*

Biopsy. A procedure to obtain tissue for diagnosis. In many cases, a special needle can be used to obtain the tissue. In some cases, a larger piece of tissue may be surgically removed. Since the appearance of a lymph node 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. A spongy tissue in the hollow central cavity of the bones that is the site of blood cell formation. By puberty, the marrow in the spine, ribs, breastbone, hips, shoulders and skull is most active in blood cell formation. In these sites, the marrow is filled with fat cells. When marrow cells have matured into blood cells, they enter the blood that passes through the marrow and are carried throughout the body.

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 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). A special tubing inserted into a large vein in the upper chest. The central line, sometimes referred to as an "indwelling catheter," is tunneled under the skin of the chest to keep it firmly in place. The external end of the catheter can be used to administer medications, fluids or blood products or to withdraw blood samples. See Port.

Chemotherapy. The use of chemicals (drugs or medications) to kill malignant cells. Numerous chemicals have been developed for this purpose, and most act to injure the DNA of the cancer cells. When the DNA is injured, the cells cannot grow or survive.

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 (X for females and Y 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 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 is a combined modality therapy for patients with HL.

Computed Tomography (CT) 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 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 during and after treatment.

CT Scan. See Computed Tomography (CT) Scan.

Cycle of Treatment. An intensive, clustered period of chemotherapy and/or radiation therapy. The therapy may be given for several days or weeks, and this time period 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 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. The process by which stem cells develop or mature to possess a specific function. Differentiation of stem cells forms the red blood cells, platelets and white blood cells (neutrophils, monocytes, eosinophils, basophils and lymphocytes). 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. 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 Cells.

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 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. 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. The 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 fact sheet *Immunotherapy Facts*.

Indwelling Catheter. See Central Line.

Leukocytes. See White Blood Cells.

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

Lymphadenopathy. Enlargement of lymph nodes.

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, the skin and the spleen, along with the T, B and natural killer (NK) lymphocytes contained in these sites.

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 enlargement of lymph nodes can be seen, felt or measured by computed tomography (CT) scan or magnetic resonance imaging (MRI), depending on the degree of enlargement and the location.

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 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 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. The neutrophil is the main cell that combats infections. 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 pediatricians, who treat 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 such as HL. 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 upon the diagnosis.

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

Phagocytes. Cells that protect the body from infection by eating and killing microorganisms such as bacteria and fungi. 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 phagocytic cells.

PICC or PIC line. See Percutaneously Inserted Central Venous Catheter.

Platelets. Small blood cells (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. "Thrombocyte" is a synonym for platelet and is often used as the prefix in terms describing disorders of platelets, such as thrombocytopenia (too few) or thrombocythemia (too many).

Platelet Transfusion. Transfusion of donor platelets that may be needed to support some patients treated for HL. 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. HLA-matched platelet transfusion can be given from 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 or any special home care is required. 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.

Positron Emission Tomography (PET) Scan. A procedure used to image lymphoma masses. In this technique, 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. PET is always combined with CT to establish the precise location of lymphoma masses. In some cases, successfully treated lymphoma may convert to fibrous tissue that looks like a mass in imaging studies, 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.

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 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 Cells. Blood cells (erythrocytes) that carry 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.

Reduced-Intensity Stem Cell Transplantation. A form of allogeneic transplantation. In reduced-intensity transplantation (also called "nonmyeloablative stem cell transplantation"), patients receive lower doses of chemotherapy drugs and/or radiation in preparation for the transplant. For more information about all types of stem cell transplantation, see the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.

Refractory. Cancer that does not respond to treatment.

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 markedly improved by treatment, but residual evidence of the disease is present. 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 "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. It is often affected in lymphocytic leukemias and lymphomas. 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 marrow, but some leave the marrow and circulate in the bloodstream. 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 concentration of platelets in the blood.

Toxin. A naturally derived substance that is poisonous to cells. A toxin can be attached to antibodies that then attach to cancer cells. The toxin may kill the cancer 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 blood cells in the blood: neutrophils, eosinophils, basophils, monocytes and lymphocytes. White blood cells are also called "leukocytes."

More Information

Free LLS booklets include

Blood and Marrow Stem Cell Transplantation

Blood Transfusion

Cancer-Related Fatigue Facts

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Understanding Clinical Trials for Blood Cancers

Understanding Side Effects of Drug Therapy

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Notes

Notes

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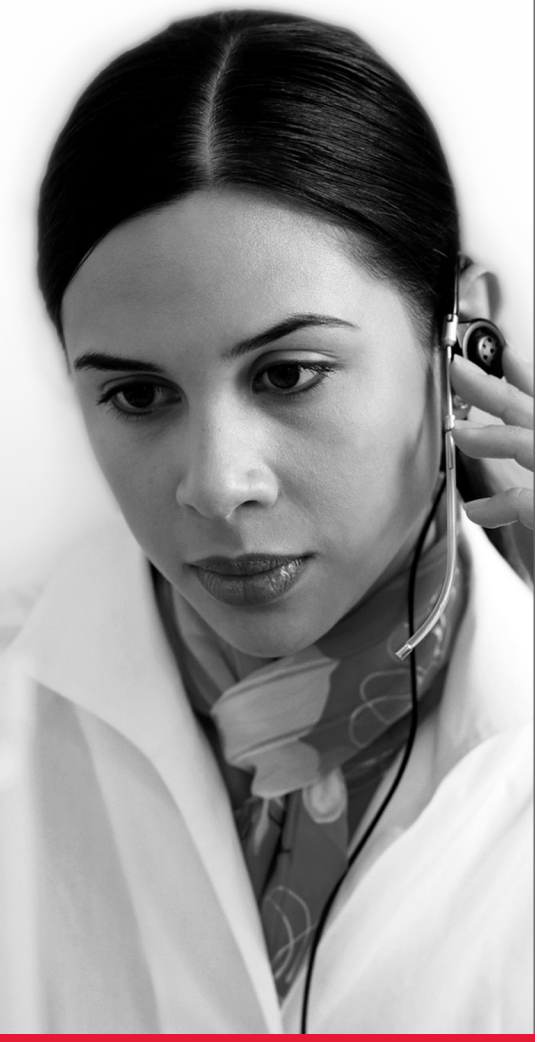

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