



PROVIDING THE LATEST INFORMATION FOR
PATIENTS & CAREGIVERS

Hodgkin Lymphoma



Revised **2020**

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

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



Discover what thousands already have at
www.LLS.org/Community

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

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

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

John P. Leonard, MD

Professor of Medicine, Weill Cornell Medical College

Richard T. Silver Distinguished Professor of Hematology and Medical Oncology,

Weill Cornell Medical College

Attending Physician, NewYork-Presbyterian Hospital

New York, NY

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Introduction

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

There are two major types of lymphoma: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Both types are further classified into subtypes. Knowing your subtype is important because your treatment is based on the subtype. A discussion of HL subtypes begins on page 6.

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

Approximately 8,110 new cases of HL were expected to be diagnosed in 2019. As of 2015, the latest year for which statistics are available, an estimated 196,508 people are either living with or in remission from HL.¹

Advances in the treatment of HL are resulting in improved remission and cure rates. The 5-year relative survival rate for people with HL is 88.4 percent for all races from 2008 to 2014.¹ New treatment approaches are being studied in clinical trials for patients of all ages and at all stages of the disease.

All LLS publications mentioned in this booklet are free and can be viewed, downloaded or ordered online at www.LLS.org/Booklets.

¹Source: *Facts 2018-2019*. The Leukemia and Lymphoma Society. April 2019.

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Hodgkin Lymphoma Basics

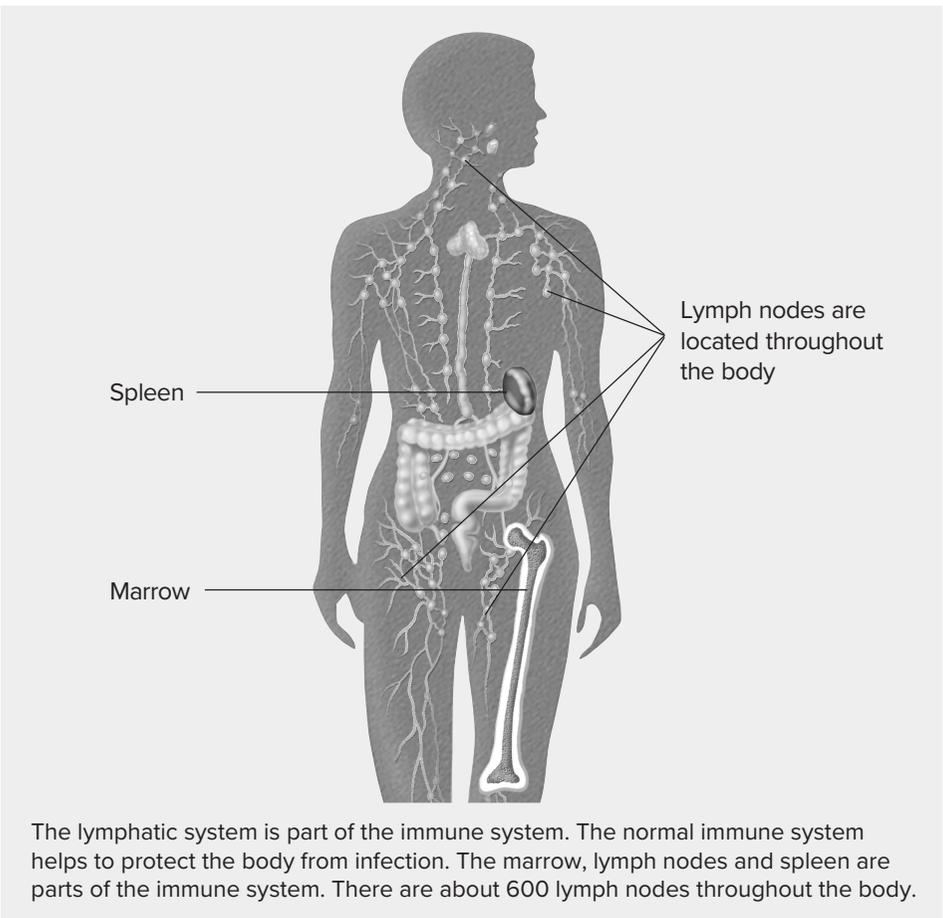
Hodgkin lymphoma (HL) was named after Dr. Thomas Hodgkin, a British pathologist who, in 1832, described several cases of people with symptoms of a cancer involving the lymph nodes. The disease was called “Hodgkin’s disease” until it was officially renamed “Hodgkin lymphoma,” when it became clear that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

When a normal lymphocyte, a type of white blood cell, undergoes a change (mutation) in a lymph node or other lymphatic structure, the abnormal cell (referred to as a “lymphoma cell” or “HL cell”) begins to multiply. Lymphoma cells may then build up in one or more lymph nodes or in other lymphoid tissues and organs, such as the spleen. They may form a mass (tumor), invade neighboring tissues, or travel from one group of lymph nodes to the next. Over time, the lymphoma cells can

spread to tissues and organs outside the lymphatic system. In HL, the accumulation of malignant lymphocytes results in masses that are typically found in the lymph nodes and other sites in the body.

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

Figure 1. Hodgkin Lymphoma and the Lymphatic System



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

Signs and Symptoms

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

A person who has signs or symptoms that suggest the possibility of lymphoma is usually referred to a specialist called a “hematologist-oncologist.” This is a doctor who has special training in diagnosing and treating blood cancers such as leukemia, lymphoma and myeloma.

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

- Painless, swollen lymph nodes in the neck, underarm or groin
- Unexplained fever*
- Drenching night sweats*
- Unexplained weight loss*
- Itchy skin, especially after bathing or drinking alcohol
- Fatigue, extreme tiredness or lack of energy
- Loss of appetite
- Persistent cough and shortness of breath (due to enlarged lymph nodes in the chest)
- Abdominal pain or swelling and feeling of fullness (due to an enlarged spleen)
- Occasional pain in lymph nodes after drinking alcohol

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

Diagnosis

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

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

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

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

During the physical examination, the doctor may listen to your lungs and heart and carefully examine your body for signs of infection and disease. The physical examination should include measurement of all accessible lymph node groups in the neck, underarms and groin, as well as palpation (checking by feeling) of the size of organs such as the spleen and liver.

Lymph Node Biopsy. A biopsy of an enlarged lymph node is needed to diagnose HL. The preferred and most common type of biopsy is called an “excisional biopsy,” in which the whole lymph node is typically removed (excised). If the lymph node is just under the skin, the biopsy procedure is usually simple and can sometimes be done with a numbing medication (local anesthetic). If the lymph node is inside the chest or abdomen (stomach area), you may be sedated or receive general anesthesia.

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

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

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

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

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

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

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

Hodgkin Lymphoma Subtypes

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

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

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

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

Hodgkin Lymphoma Subtype	Features
Classical Hodgkin Lymphoma (cHL)	<ul style="list-style-type: none"> • Accounts for 95% of all HL cases
Nodular Sclerosis	<ul style="list-style-type: none"> • Accounts for 70% of cHL cases • Most common subtype in young adults • Involved lymph nodes contain elements of fibrous tissue (sclerosis) • Similar incidence in males and females • Highly curable • B symptoms in approximately 40% of cases
Mixed Cellularity	<ul style="list-style-type: none"> • Accounts for 20%-25% of cHL cases • Most common in older adults • Most common in males • More prevalent in patients with HIV infection • Involved lymph nodes contain RS cells and several other cell types • B symptoms common
Lymphocyte-rich	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Rarest cHL subtype • Involved lymph nodes contain few normal lymphocytes but numerous RS cells • Median age range 30-37 years • More prevalent in patients with HIV infection • Usually diagnosed at an advanced stage • B symptoms common
Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL)	<ul style="list-style-type: none"> • Accounts for 5% of all HL cases • Most common in age range 30 to 50 • More common in males • Slow growing and can relapse many years later like indolent NHL; highly curable • Small risk of transformation to aggressive NHL (7% 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.

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

Staging

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

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

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

The imaging tests may include:

- **Chest x-ray.** This test produces a black and white “picture” of the inside of the chest that shows the heart, lungs, airways and blood vessels. It is often one of the first tests performed to evaluate symptoms of cough, chest pressure, or shortness of breath. It may show a mass between the lungs (this is called the “mediastinal” area). Healthcare professionals can also see lymph nodes on an x-ray and note if there is any enlargement.
- **Computed tomography (CT) scan.** A CT scan, also referred to as a “CAT scan,” uses special x-ray equipment to take multiple images of areas inside the body from different angles. A computer then processes this information and produces one detailed picture. For certain CT procedures, a special dye (called a “contrast” dye) is used to highlight specific areas inside the body, resulting in clearer pictures. The patient may drink the contrast dye, or it may be injected into a vein.

Patients may have CT scans of all the areas where lymph nodes are present, which could include the neck, arms, chest, abdomen and pelvis, to identify areas of disease involvement. A CT scan can also show whether there is involvement in the lungs, liver and other organs.

- **Positron emission tomography-computed tomography (PET-CT) scan.** This procedure combines a PET scan with a CT scan to obtain a more detailed image of areas inside the body than either scan can produce alone. A PET scan is an imaging technique that produces a 3D image of functional processes in the body. It is sometimes referred to as an “FDG-PET scan” because a small amount of fluorodeoxyglucose (FDG), a radioactive glucose, is injected into the patient and absorbed by tissue cells. The imaging device detects the radiation given off by the FDG and produces color-coded images that show differences between normal and cancerous tissues: areas with cancerous tissue appear brighter or “light up” in the scan. The images from a PET-CT scan frequently help to identify an appropriate biopsy site. Before treatment, PET-CT scans may be used to determine the stage of HL. They may also be used after treatment to assess treatment response.
- **Magnetic resonance imaging (MRI) scan** (in select cases). The scanners for MRIs use powerful magnetic fields and radio waves that are processed by a computer to create clear and detailed cross-sectional images (slices) of the body. These “slices” can then be displayed on a video monitor and also saved on a disk for future analysis. While MRI scans are rarely used to diagnose HL, they may be used for close examination of the spinal cord or the brain if a doctor is concerned that the disease may have spread to these areas. They may also be used for pregnant women, to protect the unborn baby, since an MRI does not use radiation.

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

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

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

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

Pregnancy Test. Some cancer treatments can harm an unborn baby, so a pregnancy test should be given before women of childbearing age undergo treatment. Treatment options may depend on the results. See *Hodgkin Lymphoma in Pregnant Women* on page 26.

Bone Marrow Tests. Some patients who have been diagnosed with HL may need to undergo a bone marrow aspiration and biopsy. These tests are not typically used to diagnose HL, but they may be done after diagnosis to see if there are lymphoma cells in the bone marrow. The doctor will decide if these procedures are necessary. That determination will be based on considerations including the location of the disease in the body (see **Figure 2** on page 12). A bone marrow aspiration and biopsy may not be required for patients who have early-stage HL with low-risk (favorable) clinical features, for example, no B symptoms or “bulky” disease (large mass in the chest or lymph node mass greater than 10 centimeters). Also, the need for a bone marrow biopsy may be eliminated by the use of a PET scan to assess the disease.

Stages of HL. Staging for HL is based on the Lugano classification, which is derived from the Ann Arbor staging system (see **Table 2** below). These names come from meetings of lymphoma specialists, where the classification systems were developed and adopted for use in patients.

Table 2. Lugano Classification System for Hodgkin Lymphoma

Stage I

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

Stage II

- HL cells found in two or more lymph node regions on the same side of the diaphragm (the thin muscle below the lungs and heart that separates the chest from the abdomen), either above the diaphragm or below the diaphragm, OR
- HL cells found in a lymph node area and a nearby organ outside the lymphatic system, on the same side of the diaphragm

Stage III

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

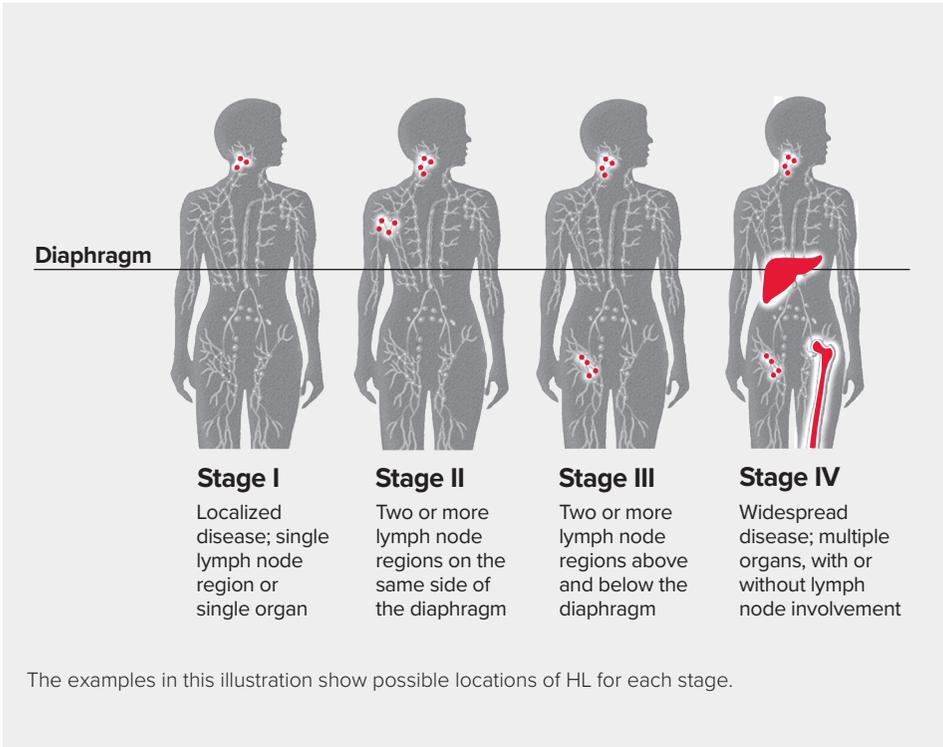
Stage IV

- HL cells have spread widely into one or more organs outside the lymphatic system

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

- **Category A:** The patient does not have B symptoms (fever, weight loss or night sweats).
- **Category B:** The patient has B symptoms.
- **Category E:** The patient has HL cells in organs or tissues outside the lymphatic system.
- **Category S:** The patient has HL cells in the spleen.

Figure 2. Hodgkin Lymphoma Stages



- Category S: The patient has HL cells in the spleen.

For example, stage IIB would indicate that the patient has

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

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

Treatment Planning

Hodgkin lymphoma (HL) cases are generally classified into the three subgroups described below.

- Early-stage favorable: stage I to II with no unfavorable risk factors
- Early-stage unfavorable: stage I to II with one or more of the following unfavorable risk factors
 - Bulky disease: a mass in the chest that is one-third the width of the chest, or any lymph node mass greater than 10 centimeters
 - Involvement of 3 or more lymph nodes
 - B symptoms: fever, drenching night sweats and/or unexplained weight loss greater than 10 percent of body weight over 6 months
 - Extranodal disease: involvement of an organ outside the lymphatic system
 - Erythrocyte sedimentation rate (ESR) of 50 or higher
- Advanced stage: stage III to IV
 - Seven factors (shown in **Table 3**, below) provide a basis for recommending either aggressive or less-intensive treatment options

Table 3. Adverse Prognostic Factors for Advanced-Stage Classical Hodgkin Lymphoma

- Being male
- Age 45 or older
- Stage IV disease
- Albumin level below 4 g/dL (grams per deciliter)
- Hemoglobin level below 10.5 g/dL
- Leukocytosis: white blood cell count greater than 15,000/mm³
- Lymphocytopenia: lymphocyte count less than 8% of the white blood cell count and/or lymphocyte count less than 600/mm³

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

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

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

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

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

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

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

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

- Sperm Banking. Men who want to conceive children after treatment may choose to store their semen in a sperm bank for later use.
- Egg or Ovarian Tissue Freezing. A woman's eggs can be removed, frozen and stored for later use. The eggs could be fertilized with sperm before freezing. Another option is for a part of the ovary that contains eggs to be removed, frozen and stored.

- Ovarian Transposition. This less commonly used method, called “oophorexy,” is an option for women who will be treated with radiation therapy. An ovary is surgically transposed (moved) out of the range of the radiation beam in order to protect it.

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

Treatment for Hodgkin Lymphoma

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

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

Treatment Overview. Most patients with newly diagnosed HL have a high likelihood of being cured with appropriate treatment. The mainstays of treatment for classical HL (CHL) are chemotherapy only or a “combined modality therapy” consisting of chemotherapy followed by radiation therapy. The treatment for nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) requires a different treatment approach. For more information on the treatment of NLPHL, see page 22.

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

Chemotherapy is usually given in treatment cycles. Each cycle is made up of a number of days of treatment followed by a rest period of a few days or weeks in between each cycle. In most cases, treatment is administered over the course of one to three days, depending on the particular combination of drugs. Then you have a rest period of a few days to a few weeks to allow your body to recover from the effects of the chemotherapy. Then another cycle begins. Generally, a treatment cycle is 3 or 4 weeks long. The number of cycles you will have depends on:

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

Some chemotherapy drugs are given by intravenous (IV) infusion, which means they are injected slowly, over a period of time, into a vein. The IV infusion, called a “continuous infusion,” may take a few hours or up to a few days to complete. These chemotherapy drugs are generally given through a thin, soft tube called a “central venous line,” “catheter,” or “central line.” The central line is often attached to a “port,” surgically placed under the skin in the patient’s upper chest that allows access to the central line.

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

Involved-site radiation therapy (ISRT) is sometimes used to treat HL. It selectively treats the lymph nodes where the cancer started and the cancerous masses near those nodes. With a special machine, carefully focused beams of radiation are directed at the cancer. This is also called “external beam therapy” (EBT). The size of the targeted area is restricted to minimize radiation exposure to adjacent, uninvolved organs, and to decrease the side effects associated with radiation therapy.

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

During radiation treatments, you will lie on a table in the same position you were in for the simulation session. You will be alone while the radiation therapist operates the machine from a nearby room. The treatment is similar to an x-ray, but the radiation is stronger. Each treatment session typically lasts only a few minutes, although the setup time usually takes longer.

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

- Four-dimensional computed tomography (4D-CT), which can adjust for movement of tumors near the breastbone (sternum), caused by the patient breathing
- Image-guided radiation therapy (IGRT), which can improve how well the radiation beam targets some tumors. The machine used for IGRT delivers radiation and, at the same time, takes images of the tumor and normal body structures.
- Three-dimensional conformal radiation therapy (3D-CRT), which uses photon beams that are adjusted to match the shape of the tumor

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

Monoclonal Antibody Therapy. This is a type of targeted therapy. When the body's immune system identifies something harmful, such as bacteria or a virus, it produces antibodies. Antibodies are proteins that help fight infection. Monoclonal antibodies are a type of protein made in the laboratory that can bind to only one substance. By design, they can only attack a specific target, typically a substance on cancer cells (though sometimes they are designed to bind to a substance on immune cells, in order to improve their function). This targeting can reduce damage to normal, healthy cells.

Brentuximab vedotin (Adcetris®). In patients with classical HL, the malignant Hodgkin and Reed-Sternberg cells typically express a protein called CD30. Brentuximab vedotin is an anti-CD30 antibody attached to a chemotherapy drug. It binds to cells that express CD30 and then enters the cancer cells. Once inside the cancer cells, it releases the chemotherapy drug. By targeting only cells that express CD30, fewer normal cells are harmed.

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

- Previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine
- Classical Hodgkin lymphoma (cHL) at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation
- Classical Hodgkin lymphoma (cHL) after failure of auto-HSCT or after failure of at least two prior multi-agent chemotherapy regimens, in patients who are not auto-HSCT candidates
- Certain other lymphomas with CD30 expression

Rituximab (Rituxan®). Rituximab is a monoclonal antibody designed to bind to cells expressing CD20. Rituximab is often combined with chemotherapy drugs. It is not used to treat cHL because, in this subtype of the disease, the lymphoma cells do not usually express CD20. However, it is sometimes used to treat NLPHL because CD20 is expressed by the lymphoma cells in this subtype of the disease. In rituximab therapy, the monoclonal antibodies attach to and kill the lymphoma cells.

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

Immune checkpoint inhibitors are a type of immunotherapy. Checkpoints are molecules found on T-cells, a type of white blood cell. T cells circulate throughout the body looking for signs of infection and diseases, including cancer. When a T cell comes across any type of cell, it probes (looks for) certain proteins on the cell's surface. If the T cell determines that it is a normal, healthy cell, it moves on to check other cells. If the proteins indicate that the cell is foreign or cancerous, the T cell attacks it. But cancer cells can sometimes send misleading signals to these checkpoints, telling the T cells that they are not harmful. Checkpoint inhibitors work by blocking the signals that cancer cells send to T cells. When the signals are blocked, it is more likely the T cells will distinguish the cancer cells from healthy cells and begin an attack.

Nivolumab (Opdivo®) and pembrolizumab (Keytruda®) are checkpoint inhibitors, both given by IV, that can be used for some patients with HL that has become refractory (come back or spread during treatment), or that has relapsed (returned) after completing other treatments. They are also used to treat certain other types of cancer in which their effects on the immune system can be helpful.

Nivolumab is FDA-approved for the treatment of adult patients with classical Hodgkin lymphoma that has relapsed or progressed after

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

Pembrolizumab is FDA-approved for the treatment of adult and pediatric patients with refractory cHL, or who have relapsed after 3 or more prior lines of therapy.

Table 4. Some Treatment Approaches for Classical Hodgkin Lymphoma

Early-stage classical Hodgkin lymphoma (cHL)

- Chemotherapy combinations
 - ABVD (Adriamycin® [doxorubicin], bleomycin, vinblastine, dacarbazine)
 - Escalated BEACOPP (bleomycin, etoposide, Adriamycin [doxorubicin], cyclophosphamide, Oncovin® [vincristine], procarbazine, prednisone)
- Combination chemotherapy, administered with or without radiation therapy

Advanced-stage cHL

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

Relapsed/Refractory cHL

- Further chemotherapy is given, such as
 - ICE (ifosfamide, carboplatin, etoposide)
 - DHAP (dexamethasone, high-dose Ara-C [cytarabine], Platinol [cisplatin])
 - ESHAP (etoposide, methylprednisolone, high dose-cytarabine, cisplatin)
 - GDP (gemcitabine, dexamethasone, Platinol [cisplatin])
 - GVD (gemcitabine, vinorelbine, liposomal doxorubicin)
 - IGEV (ifosfamide, gemcitabine, vinorelbine)
- Brentuximab vedotin (Adcetris®), either alone or in combination with chemotherapy or other agents
- Stem cell transplantation
- Nivolumab (Opdivo®)
- Pembrolizumab (Keytruda®)

This table lists treatment approaches for classical Hodgkin lymphoma.

Drugs may have been approved since this book was printed.
Check www.LLS.org/DrugUpdates or call (800) 955-4572.

Stem Cell Transplantation. Some patients may benefit from stem cell transplantation. It is not used as an initial treatment for HL, but may be recommended for people who have refractory or relapsed HL. Refractory means the disease does not respond to treatment. Relapsed means the disease returns after a remission following treatment.

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

There are two main types of stem cell transplantation:

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

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

The first step is to collect the patient's own stem cells after initial treatment is completed and the patient is in remission. The stem cells are removed from the patient's bone marrow (inside the bones), and are frozen and stored until they are needed for the transplant. The patient is then given high doses of chemotherapy to destroy any lymphoma cells not killed during the initial treatment. After the high-dose chemotherapy is completed, the stem cells are returned to the patient's bloodstream by IV infusion (similar to a blood transfusion). The goal is to "rescue" the bone marrow from the effects of the high doses of chemotherapy, reintroducing healthy stem cells into the system in order to restore normal blood cell production.

Brentuximab vedotin is sometimes also given to patients before the transplant, or, in select patients, it is administered as maintenance treatment after autologous stem cell transplantation (see page 17 for more information).

Allogeneic Stem Cell Transplantation. This type of transplantation has been successful in some patients with HL after several relapses of the disease, but it is not commonly used as a treatment for HL. It is generally only done if a patient relapses after an autologous transplant.

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.**

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

Imaging tests are used to distinguish between tumor and fibrous (scar) tissue. PET-CT scans help doctors determine if the disease is responding to treatment. PET-CT has become the standard method for assessment of treatment response in most types of lymphoma.

The Deauville score, based on a five-point scale developed in 2009, is now an internationally recognized way of using PET-CT to assess treatment response. This scale determines the “FDG uptake” (the absorption of this radioactive material by tissues) in the involved sites. The Deauville score is then used to determine if any treatment modifications are needed.

If your doctors conclude that the treatment is working, your treatment plan will likely remain the same. If the treatment does not appear to be working, your treatment plan may be changed.

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

Treatment of Early-Stage (Stage I-II) Favorable HL. The cure rate for patients in this category exceeds 90 percent. The current treatment approach is to administer chemotherapy alone (without radiation therapy) or a combined modality therapy (combination chemotherapy followed by radiation therapy to areas of the body where lymphoma was found).

For many years, **ABVD** (see **Table 4** on page 19) has been the most commonly used chemotherapy regimen for these patients. ABVD poses less of a risk for later development of leukemia or infertility than many other chemotherapy combinations used for adults. Another treatment regimen is escalated **BEACOPP** (see **Table 4** on page 19).

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

Concerns about the late effects of radiation therapy (especially an increased risk of developing a second cancer) have led some oncology groups to recommend the use of chemotherapy alone for some patients, particularly when the risk of developing a second cancer is considered to be significant. Patients who are at a

higher risk of developing a second cancer include women younger than age 30 and with a family history of breast cancer, and those who will have radiation therapy involving their breast tissue. See *Long-Term and Late Effects of Treatment* on page 31.

Treatment of Early-Stage (Stage I-II) Unfavorable HL. For patients in this category, the disease is considered to be high risk. Initial treatment usually consists of either a combined modality therapy (chemotherapy plus radiation therapy) or chemotherapy alone. Treatment is generally more intense for these patients than for those in the favorable category. Results of PET-CT scans done both during and after treatment may affect decisions about the type and duration of chemotherapy and the use of radiation therapy. Some drug combinations used for treatment of these patients (see **Table 4** on page 19) include:

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

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

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

Dose-escalated BEACOPP results in a good cure rate, but it puts patients at a slightly higher risk of developing leukemia or other second cancers. Patients are also at a much higher risk of infertility, and it is less commonly used for this reason.

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

Treatment Options for Nodular Lymphocyte-Predominant Hodgkin lymphoma (NLPHL). This is a rare subtype of HL that accounts for only about 5 percent of all HL cases. The cancer cells in NLPHL are a variant of Reed-Sternberg cells. They are larger and are sometimes called “popcorn” cells because their unique shape is similar to pieces of popcorn.

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

Because NLPHL is associated with an excellent long-term survival rate, the risk of overtreatment is an important consideration for these patients. Overtreatment may lead to problems and harmful side effects from cancer therapies that are not needed. One option for some patients is the “watch-and-wait” approach, in which the patient is closely monitored for disease progression without getting any treatment until symptoms appear or begin to change. Another option for early-stage NLPHL without any B symptoms or bulky disease is the use of radiation therapy alone.

Combination chemotherapy may be needed in more advanced stages of the disease, with **rituximab (Rituxan®)** added to the regimen in some cases. Common treatments used in NLPHL include:

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

NLPHL can sometimes recur many years (or even decades) after initial treatment. In a small percentage of patients, it can transform into diffuse large B-cell lymphoma (DLBCL), a type of non-Hodgkin lymphoma that is usually aggressive. For patients with a suspected relapse of NLPHL, another biopsy should be considered to rule out transformation to DLBCL. Patients with refractory or relapsed NLPHL can be treated with a second-line therapy that includes rituximab, either with or without chemotherapy or radiation therapy.

Treatments for Relapsed or Refractory Cases

Most patients with classical HL are cured by their initial (first-line) treatment. However, in a significant percentage of patients—especially those with advanced-stage HL—the disease relapses or is refractory. Relapse means the disease comes back after a remission following treatment. Refractory means the disease has not responded to treatment. For these patients, HL is still potentially curable.

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

- Alternate chemotherapy combinations
- Monoclonal antibody therapy with brentuximab vedotin
- Checkpoint inhibitors, nivolumab and pembrolizumab
- Autologous stem cell transplantation (see page 20)

Alternate Chemotherapy Combinations. Traditional chemotherapy-based regimens include:

- ICE (ifosfamide, carboplatin, etoposide)
- DHAP (dexamethasone, High-dose Ara-C [cytarabine], Platinol [cisplatin])
- ESHAP (etoposide, methylprednisolone, high-dose cytarabine, cisplatin)
- IGEV (ifosfamide, gemcitabine, vinorelbine)
- GDP (gemcitabine, dexamethasone, Platinol [cisplatin])
- GVD (gemcitabine, vinorelbine, liposomal doxorubicin)

Brentuximab vedotin (Adcetris®). This is a monoclonal antibody drug combination given intravenously (IV). It is approved by the FDA for the treatment of adult patients with previously untreated stage III or stage IV classical Hodgkin lymphoma (cHL), in combination with chemotherapy (doxorubicin, vinblastine and dacarbazine). It is also approved for cHL patients at high risk of relapse or progression as postautologous hematopoietic stem cell transplantation (auto-HSCT) consolidation and for cHL patients after failure of auto-HSCT or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates.

As a second-line therapy, brentuximab vedotin can be used

- Alone, as a single agent
- In combination with chemotherapy
- In combination with checkpoint inhibitors
- As maintenance therapy after an autologous stem cell transplantation

Nivolumab (Opdivo®). This checkpoint inhibitor, given by IV, is FDA-approved for the treatment of adult patients with classical HL that has relapsed or progressed after

- Autologous stem cell transplantation and brentuximab vedotin, OR
- 3 or more lines of systemic therapy that included autologous stem cell transplant

Pembrolizumab (Keytruda®). This is a checkpoint inhibitor given IV. It is approved by the FDA for the treatment of adult and pediatric patients with refractory cHL, or who have relapsed after 3 or more prior lines of therapy.

Hodgkin Lymphoma in Children and Pregnant Women

Hodgkin Lymphoma in Children. Hodgkin lymphoma (HL) accounts for about 3 percent in those under 15. It is very rare in infants.

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

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

- Specific subtype of the disease (see *Hodgkin Lymphoma Subtypes* on page 6)
- Stage of the disease (see *Staging* on page 8)
- Risk of treatment-related fertility issues (see *Fertility Concerns* on page 14)
- Other risk factors

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

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

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

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

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

- **ABVE-PC** (Adriamycin [doxorubicin], bleomycin, vincristine [Oncovin], etoposide, prednisone, cyclophosphamide)
- **BEACOPP** (bleomycin, etoposide, Adriamycin [doxorubicin], cyclophosphamide, Oncovin [vincristine], procarbazine, prednisone)
- **OEPA-COPDAC** (Oncovin [vincristine], etoposide, prednisone, Adriamycin [doxorubicin]-cyclophosphamide, Oncovin [vincristine], prednisone, dacarbazine) for males
- **OPPA/COPP** (Oncovin [vincristine], procarbazine, prednisone, Adriamycin [doxorubicin]-cyclophosphamide, Oncovin [vincristine], prednisone, procarbazine) for females
- **VAMP** (vinblastine, Adriamycin [doxorubicin], methotrexate, prednisone)

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

For more information, see the following free LLS booklets: *Coping with Childhood Leukemia and Lymphoma* and *Learning & Living with Cancer: Advocating for your child's educational needs*. Also visit www.LLS.org/FamilyWorkbook to find information for children and families.

Hodgkin Lymphoma in Pregnant Women. Because HL primarily affects young adults, it is one of the most common types of cancer diagnosed during pregnancy. If a woman is pregnant when diagnosed with HL, the treatment options depend on several factors, including: the trimester at the time of diagnosis; the stage and aggressiveness of the disease; and whether or not the patient has life-threatening symptoms.

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

Monitoring After Completion of Treatment

PET-CT scan (see page 9) is the most accurate way to evaluate treatment response and remission status after completion of treatment. This scan should occur at least 3 weeks after the last chemotherapy treatment because, if done earlier, temporary treatment-related inflammation could be mistaken for lymphoma masses.

Because of the risk of recurrence, periodic examination of HL patients is necessary for years after treatment. Most relapses occur within the first 2 years after completion of treatment, so follow-up visits during this time period will be more frequent, typically every 3 to 6 months. After 2 years, follow-up visits are generally scheduled every 6 to 12 months for the next 3 years (until 5 years after completion of treatment). There are long-term risks associated with HL therapy, so you should plan to continue your annual follow-up visits with a doctor who will monitor you for potential late complications of HL treatments, including second cancers and cardiovascular disease. See *Long-Term and Late Effects of Treatment* on page 31. Many comprehensive cancer centers now have “survivorship clinics” to provide patients with individualized recommendations and follow-up planning after treatment ends.

The patient’s history, as well as physical examination and blood tests, are effective assessment tools for follow-up purposes. Unless new symptoms or signs suggesting relapse are evident, follow-up CT or PET-CT scans are not recommended for ongoing monitoring of potential disease recurrence because of high false-positive rates. The decision about whether to perform imaging tests should be made on an individual basis, after the healthcare professional discusses the implications of their use with the patient.

Research and Clinical Trials

New approaches to HL treatment are being studied in clinical trials. Researchers are studying novel strategies to improve the cure rate and minimize the side effects and late effects associated with current treatments, such as second cancer risk, damage to the heart and lungs, and infertility. Many of these clinical trials are being supported by LLS research programs.

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 reviewed by expert clinicians, researchers and patient advocates to ensure safety and scientific accuracy. Participation in a carefully conducted clinical trial may be the best available treatment option and should be considered each time the doctor and patient discuss treatment options. The outcomes of patient participation in past clinical trials have resulted in the therapies we have today.

The Leukemia & Lymphoma Society (LLS) offers help for patients and caregivers in understanding, identifying and accessing clinical trials. LLS Information Specialists, available at (800) 955-4572, offer guidance on how patients can work with their doctors to determine if a specific clinical trial is an appropriate treatment option. When appropriate, patients and caregivers can work with LLS Clinical Trial Nurse Navigators, who will help patients find appropriate clinical trials and then personally assist them throughout the entire clinical-trial process. Please visit www.LLS.org/CTSC for more information.

Research Approaches. A number of approaches are under study in clinical trials for the treatment of patients with HL.

Genetic Studies. HL is a rare disease. However, there are cases of the disease occurring in more than one person in the same family; this is called “familial clustering.” This supports the theory that there is a genetic basis of HL susceptibility. Studies of familial HL are under way to obtain a better understanding of the genetic causes of the disease and to determine which genetic variations are responsible for the disease in these cases. This information may help doctors predict a person’s risk of developing HL, and also help scientists discover biological pathways that can be targeted with novel treatments.

Interim Use of PET-CT Scans as a Decision Tool for Risk-Adapted Therapy.

Recent studies have focused on assessing the role of interim PET-CT scans in patients with HL. Accurate mid-treatment scans are expected to further enable tailoring of treatments, allowing healthcare professionals to improve remission rates while minimizing treatment toxicity. Interim PET-CT scans may be useful in identifying a subgroup of patients with early-stage disease that can be treated with chemotherapy alone.

Monoclonal Antibodies. Monoclonal antibodies are immunotherapy drugs that are specially designed to target specific proteins (antigens) in cancer cells.

Brentuximab vedotin (Adcetris®), which is approved for untreated and relapsed/refractory cHL, targets CD30 and releases a chemotherapy drug into the cancer cell, causing its death. Various clinical trials are studying the use of this agent in combination with standard chemotherapy drugs and checkpoint inhibitors.

Programmed Death (PD-1) Checkpoint Inhibitors. Two checkpoint inhibitor drugs—**nivolumab (Opdivo®)** and **pembrolizumab (Keytruda®)**, both of which are approved for refractory and relapsed cHL—are still being studied for other potential uses and indications. While the results of checkpoint inhibitors have been encouraging, most of the responses are partial and not all patients derive benefits. Researchers are now studying approaches that may use combinations of therapies consisting of checkpoint inhibitors, chemotherapy drugs and brentuximab vedotin, along with other immune-activating agents.

CAR T-Cell Therapy. This type of immunotherapy consists of engineering a patient's own immune cells to recognize and then attack cancerous cells. This approach has shown very promising results in patients with blood cancers. A patient's T cells are genetically engineered to produce receptors, called "chimeric antigen receptors" (CARs), on their surfaces. These receptors recognize and bind to a specific target found on the cancerous cells. CAR-T cells targeting CD30 have shown promising results in relapsed/refractory cases of HL. Hodgkin and Reed-Sternberg cells overexpress the CD30 molecule, so T lymphocytes that are redirected to eliminate these cells have the potential to generate a sustained antitumor effect. Although there is limited data, CAR-T cell therapy appears to be a promising approach for treating HL.

For more information on this type of therapy, please see the free LLS booklet *Chimeric Antigen Receptor (CAR) T-Cell Therapy Facts*.

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

Side Effects and Complications

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

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

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

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

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

Treatment with drugs that are designed to improve white blood cell counts, such as granulocyte-colony stimulating factor (G-CSF), may be considered in patients with some types of cancer. However, in HL regimens that include **bleomycin**, G-CSF is not typically recommended or necessary because its use may increase the potential for lung complications. G-CSF is commonly recommended for use in regimens that combine **brentuximab vedotin** with chemotherapy drugs.

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

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

Patients at home should seek medical attention right away if any sign of infection develops. A rise in temperature to 100.4°F or higher, or the onset of chills, may be the only sign of infection in a patient with a very low white blood cell count. Other signs of infection may include persistent coughing, tenderness at a site prone to infection (such as the area surrounding the anus or the facial sinuses), sore throat, pain on urination, or frequent loose stools.

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

HL patients are advised to get certain vaccinations once they have finished their treatment, including vaccinations for pneumococcal pneumonia and influenza. There are two types of pneumococcal vaccines available for adults: a pneumococcal polysaccharide vaccine (PPSV23) and a pneumococcal conjugate vaccine (PCV13). Immunizations using live organisms or with high viral loads, such

as the herpes zoster or shingles vaccine, should not be administered. Patients who have HL can receive the shingles vaccine **Shingrix®** because it is an “inactivated” rather than a “live” vaccine. Speak to your doctor for more information.

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

- Chemotherapy side effects depend on various factors including the drug type, dose administered, length of treatment and the patient’s susceptibility. Treatment with chemotherapy drugs may cause low blood cell counts, mouth sores, nausea, vomiting, acid reflux, bloating, constipation, diarrhea, extreme fatigue, neuropathy (numbness and pain, usually in the hands or feet), fever, cough and hair loss. Certain drugs have a specific tendency to affect certain tissues—for example, **vincristine (Oncovin®)** tends to affect nerve tissue, and **bleomycin** may affect the lungs.
- Radiation therapy side effects depend on the area treated. Many people experience fatigue. The skin may look and feel as if it is mildly sunburned and it may also become dry, sore and feel painful when touched. Patients may also have short-term hair loss in the area that was treated. Treatment to the head or neck can cause mouth sores, dry mouth and changes in taste. Chest radiation can cause dry cough or a sensation of a lump in the throat when swallowing. Radiation in the abdomen may cause nausea, vomiting, diarrhea and cramps.

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

Visit www.LLS.org/booklets to view, print or order the free LLS series *Side Effect Management*.

Survivorship

Long-Term and Late Effects of Treatment. Today, much is understood about the specific types of treatment for Hodgkin lymphoma (HL) and the risk for long-term or late effects. The most serious late effects experienced by long-term survivors of HL are second cancers, cardiovascular disease, hypothyroidism and fertility issues. The incidence of these late effects appears to increase over time. However, the risk of late side effects may be lower with current treatments than it was with treatments used more than 10 years ago. Patients should be examined regularly by an oncologist and should also be seen by a primary care doctor for a general health examination at least once a year.

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

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

Girls or women younger than age 30 who have radiation therapy to the breast are at risk for developing breast cancer 15 to 20 years later. Male survivors of childhood cancer may also be at risk for developing second cancers (however, men who have had HL in childhood do not appear to have the same risk for developing cancer in the breast/chest area as female childhood cancer survivors). Radiation therapy can also injure the lungs, especially in patients who receive the chemotherapy drug **bleomycin**. Bleomycin is the “B” in the commonly used chemotherapy regimen **ABVD**, which stands for Adriamycin® (doxorubicin), bleomycin, vinblastine, and dacarbazine. Survivors who have had chest radiation therapy are also at risk for lung cancer. Smoking further increases this risk, so HL survivors are advised not to start smoking or, if they do smoke, to stop.

Use of chemotherapy with alkylating agents increases the risk of developing another type of leukemia called acute myeloid leukemia (AML). Chemotherapy treatment can also significantly increase the risk of other malignancies such as lung, stomach and pancreatic cancer.

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

Lung Damage. Radiation therapy to the chest and treatment with chemotherapy regimens that include **bleomycin** are both associated with acute lung toxicity and can also lead to reduced lung function. Some reports suggest that the use of growth factors with chemotherapy drugs significantly increases the incidence of long-term lung problems. Risk factors include older age, cumulative bleomycin dose, lung radiation and prior history of lung disease.

Thyroid Dysfunction. Radiation therapy can injure the thyroid gland, causing decreased thyroid function (hypothyroidism). This is reported in about 50 percent of long-term HL survivors who received neck or upper chest radiation therapy.

Fertility. Patients may have decreased fertility after treatment. The risk of infertility varies according to the type and amount of chemotherapy, the area of the body exposed to radiation therapy and the patient's age. With some chemotherapy regimens, fertility appears to be affected either minimally or not at all. Other regimens, such as **BEACOPP** (see page 19), may cause immediate and permanent infertility in both men and women. In addition, women who have received chemotherapy with alkylating agents may experience premature menopause, and this should be taken into consideration with respect to family planning before the start of treatment. There are fertility preservation options for both men and women, so speak to your healthcare team before starting treatment. See *Fertility Concerns* on page 14 and see the free LLS booklet *Fertility and Cancer* for more information.

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

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

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

Survivors of HL are encouraged to

- Keep records of the treatments they have received. This information can help the doctor follow up on specific late effects that may be associated with those treatments, and also help the healthcare team develop a schedule of follow-up exams.
- These records should include the following information: the patient's diagnosis; the names of all drugs taken; information about any radiation therapy, surgery or transplant received; information about any other treatments; and the names and dates of any significant complications and the treatment received for those complications.

- Have regular screenings for heart disease and annual blood pressure and lipid/cholesterol monitoring. A baseline cardiac stress test, echocardiogram and carotid ultrasound (for patients treated with radiation to the neck) should be considered after completion of therapy.
- Have regular screenings for cancer. Cancers of the breast, lung, stomach, bone and soft tissues have been reported as soon as 5 years after initial therapy for HL.
- Practice monthly breast self-examination, have yearly breast examination by a healthcare professional and have an early baseline mammogram (within 8 to 10 years after therapy or by age 40, whichever occurs earlier). It is recommended that a breast MRI be added to mammography screening for women who received radiation in the chest area when they were between the ages of 10 and 30. Although some women may develop breast cancer after HL treatment, it can be detected early and treated, which provides the best chance for a cure.
- Have regular lung cancer screenings if treated with chest radiation. Smoking further increases the risk of lung cancer and several other types of cancer, including acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS). If you smoke, ask your doctor for strategies to help you quit.
- Have a colonoscopy every 10 years. This is recommended for survivors aged 50 and older, or by age 40 for survivors at increased risk for colorectal cancer due to previous treatment.
- Have regular thyroid function checkups (at least every year) to rule out hypothyroidism, especially in patients who were treated with radiation to the neck.
- Seek medical and psychosocial support for fatigue, depression and other long-term effects, if needed.

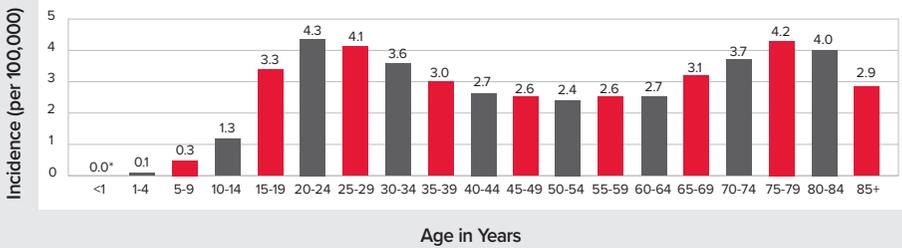
For additional information, see the free LLS booklet *Long-Term and Late Effects of Treatment in Adults Facts and Long-Term*. Also visit www.LLS.org/FamilyWorkbook to find information for children and families.

Incidence, Causes and Risk Factors

Although Hodgkin lymphoma (HL) can occur in both adults and children, in most patients the disease is diagnosed between the ages of 15 and 34. The incidence reaches a second peak in adults 75-79 years of age and older (see **Figure 3**, page 35). The disease is more common among men than women.

Approximately 8,110 new cases of HL were expected to be diagnosed in 2019.

Figure 3. Age-Specific Incidence Rates for Hodgkin Lymphoma, 2012-2016



Source: SEER (Surveillance, Epidemiology, and End Results) Cancer Statistics Review, 1975-2016. National Cancer Institute; 2019.

*<16 cases for each age and time interval, SEER 21 areas.

Causes and Risk Factors. In most cases, it is not clear what causes the genetic changes that lead to HL. There are, however, some known risk factors for HL. A “risk factor” is anything that increases a person’s chance of developing a disease. Having a risk factor, though, does not mean that a person will develop the disease. Some people with several risk factors may never develop that disease, while others with no known risk factors for a disease do. It is known with certainty that HL is not contagious.

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

- Past Epstein-Barr virus infection. The Epstein-Barr virus (EBV), known for causing mononucleosis, is associated with the development of some types of cancer, including HL. Infection with EBV in early childhood or having “mono” in the teenage years increases the risk of developing HL. But while many people are infected with EBV, very few actually develop HL.
- Age. People can develop HL at any age, but it is most common in young adults (ages 15-30) and in older adults (ages 65 years and older).
- Gender. The risk of developing HL is slightly higher in males than females.
- Family history. There are occasional cases of familial clustering: having a first-degree relative (parent or sibling) with HL may increase the risk of developing the disease by three to four times compared with the general population.
- Weakened immune system. People infected with HIV, the virus that causes AIDS, have an increased risk of developing HL. People who take medicines to suppress the immune system and people with auto-immune disease are also at a higher risk of developing HL.

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

Normal Blood and Bone Marrow

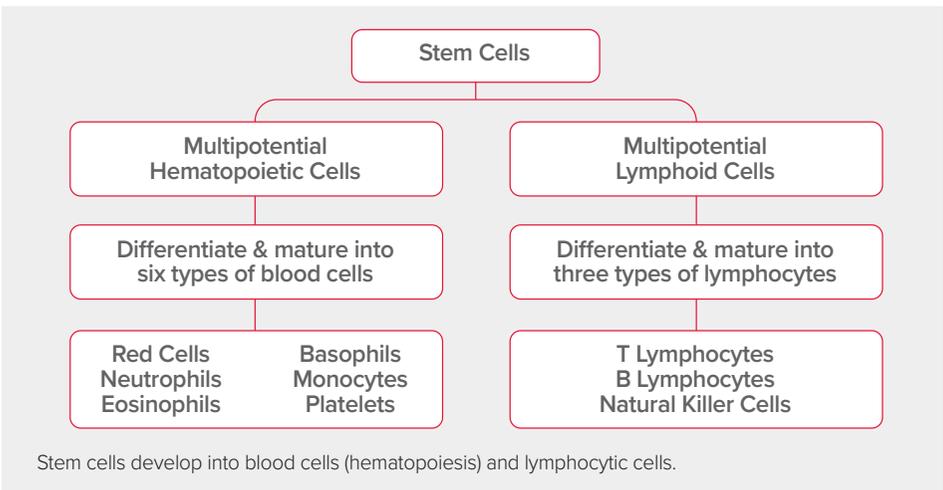
Blood. Blood is the liquid that flows through a person’s arteries and veins. It carries oxygen and nutrients throughout the body. It also carries away waste products. Blood is composed of plasma and cells.

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

- Proteins
 - Albumin. This is the most common blood protein.
 - Blood-clotting proteins (coagulation factors). They are made by the liver.
 - Erythropoietin. It is made by the kidneys and stimulates red blood cell production.
 - Immunoglobulins. These are cells that fight infection.
- Hormones, such as thyroid and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin B₁₂
- Electrolytes, such as calcium, potassium and sodium.

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

Figure 4. Blood Cell & Lymphocyte Development



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

These are

1. Red blood cells (the cells that carry oxygen); they
 - Make up a little less than half of the body's total blood volume
 - Are filled with hemoglobin, the protein that picks up oxygen from the lungs and takes it around the body. It binds with carbon dioxide (CO₂) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the CO₂ is removed from the lungs.
2. Platelets (cells that help blood clot); they
 - Are small cells (one-tenth the size of red blood cells)
 - Help stop bleeding from an injury or cut
 - Stick to the torn surface of the vessel, clump together, and plug up the bleeding site. They form a clot, with the help of proteins, such as fibrin, and electrolytes, such as calcium.
3. White blood cells (WBCs) are cells that fight infections. The several types of WBCs include
 - Neutrophils and monocytes: These are “phagocytes” (eating cells) that ingest and destroy bacteria and fungi. Unlike red cells and platelets, monocytes can leave the bloodstream and enter tissues to attack invading organisms and fight off infection.
 - Eosinophils and basophils: WBCs that respond to allergens or parasites.
 - Lymphocytes: WBCs found mostly in the lymph nodes, spleen and lymphatic channels, they are a key part of the immune system. Some enter the bloodstream. There are three major types of lymphocytes:
 - T lymphocytes (T cells)
 - B lymphocytes (B cells)
 - Natural killer (NK cells)

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

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

Hematopoietic stem cells are found in the marrow. These stem cells are important because they can be transplanted. Some stem cells enter the bloodstream and circulate; there are not enough of them to be counted in standard blood tests. Doctors know how to stimulate the growth of these cells in the marrow and have them migrate into the bloodstream. Then a special technique called “apheresis” is used to separate them from the circulating blood so they can be collected and stored. Stem cells from the placenta and the umbilical cord of a newborn infant can also be harvested and used for future transplantation.

The Lymphatic System

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

The marrow produces three main types of lymphocytes. They are

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

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

Resources and Information

LLS offers free information and services to patients and families affected by blood cancers. This section lists various resources available to you. Use this information to learn more, to ask questions, and to make the most of the knowledge and skills of the members of your healthcare team.

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 am to 9 pm EST)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org/InformationSpecialists
- Visit: www.LLS.org/InformationSpecialists

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

Free Information Booklets. LLS offers free education and support booklets that can be either read online or ordered. Please visit www.LLS.org/booklets for more information.

Telephone/Web Education Programs. LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit www.LLS.org/programs for more information.

Financial Assistance. LLS offers financial assistance to individuals with blood cancer. Please visit www.LLS.org/finances for more information.

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

LLS Health Manager™ App. This free mobile app helps you manage your health by tracking side effects, medication, food and hydration, questions for your doctor, and more. Export the information you've tracked in a calendar format and share it with your doctor. You can also set up reminders to take medications, hydrate, and eat. Please visit www.LLS.org/HealthManager to download for free.

One-on One Nutrition Consultations. Access free one-on-one nutrition consultations with a registered dietitian who has experience in oncology nutrition. Dietitians assist callers with information about healthy eating strategies, side effect management, and survivorship nutrition. They also provide additional nutrition resources. Please visit www.LLS.org/nutrition to schedule a consultation or for more information.

Podcast. The *Bloodline with LLS* is here to remind you that after a diagnosis comes hope. Listen in as patients, caregivers, advocates, doctors and other health care professionals discuss diagnosis, treatment options, quality-of-life concerns, treatment side effects, doctor-patient communication and other important survivorship topics. Please visit www.LLS.org/TheBloodline for more information and to subscribe.

Suggested Reading. LLS provides a list of selected books recommended for patients, caregivers, children and teens. Please visit www.LLS.org/SuggestedReading to find out more.

Continuing Education. LLS offers free continuing education programs for health care professionals. Please visit www.LLS.org/ProfessionalEd for more information.

Community Resources and Networking

LLS Community. The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. Please visit www.LLS.org/community to join.

Weekly Online Chats. Moderated online chats can provide support and help cancer patients to reach out and share information. Please visit www.LLS.org/chat to join.

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, patient care and other needs. For more information, please visit www.LLS.org/ResourceDirectory to obtain our directory.

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). Please visit www.LLS.org/espanol for more information.

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

Information for Veterans. Veterans who were exposed to Agent Orange while serving in Vietnam may be able to get help from the United States Department of Veterans Affairs. For more information please

- Call: the VA (800) 749-8387 (select option 4)
- Visit: www.publichealth.va.gov/exposures/AgentOrange

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 2-week period. For more information, please

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

Health Terms

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

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

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

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

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

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

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

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

Bone Marrow. The spongy tissue in the hollow central cavity of the bones, where blood cell formation occurs. It produces red blood cells, white blood cells and platelets. After puberty, the bone marrow in the spine, ribs, breastbone, hips, shoulders and skull is most active in blood cell formation. In adults, the bones of the hands, feet, legs and arms do

not contain blood-forming marrow (in these sites, the bone marrow is filled with fat cells). When bone marrow cells have matured into blood cells, they enter the blood that passes through the bone marrow and are carried throughout the body in the bloodstream.

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

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

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

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

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

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

Colony-Stimulating Factor. See Growth Factor.

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

Computed Tomography (CT) Scan. A procedure in which a series of x-ray images are processed by a computer to create 3D views of tissues and organs in the body.

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

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

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

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

Erythrocyte. See Red Blood Cell.

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

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

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

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

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

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

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

Hematopoiesis. The formation of all types of blood cells in the bone marrow. For more information on the process of blood cell development, see *Normal Blood and Bone Marrow* on page 36.

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

Immunophenotyping. A lab test that can measure the number of cells in a sample as well as certain characteristics of cells, such as their size and shape. It can also detect tumor markers on the surface of cells and identify specific types of leukemia and lymphoma cells.

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

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

Leukocyte. See White Blood Cell.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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