

LYMPHOMA  
RESEARCH • FOUNDATION

# Understanding Hodgkin Lymphoma



A Guide for Patients,  
Survivors, and  
Loved Ones

September 2015

# LYMPHOMA

RESEARCH • FOUNDATION

**Lymphoma Research Foundation  
(LRF) Helpline and Clinical Trials  
Information Service**

## **CONTACT THE LRF HELPLINE**

Trained staff are available to answer questions and provide support to patients, caregivers and healthcare professionals in any language.

Our support services include:

- Information on lymphoma, treatment options, side effect management and current research findings
- Financial assistance for eligible patients and referrals for additional financial, legal and insurance help
- Clinical trial searches based on patient's diagnosis and treatment history
- Support through LRF's Lymphoma Support Network, a national one-to one volunteer patient peer program

Monday through Friday, Toll-Free (800) 500-9976  
or email [helpline@lymphoma.org](mailto:helpline@lymphoma.org)



# Understanding Hodgkin Lymphoma

A Guide for Patients, Survivors, and Loved Ones

September 2015

This guide is an educational resource compiled by the Lymphoma Research Foundation to provide general information on adult Hodgkin lymphoma. Publication of this information is not intended to replace individualized medical care or the advice of a patient's doctor. Patients are strongly encouraged to talk to their doctors for complete information on how their disease should be diagnosed, treated, and followed. Before starting treatment, patients should discuss the potential benefits and side effects of cancer therapies.

## **National Headquarters**

115 Broadway, Suite 1301

New York, NY 10006

(212) 349-2910 phone

(212) 349-2886 fax

Helpline: (800) 500-9976; [helpline@lymphoma.org](mailto:helpline@lymphoma.org)

Website: [www.lymphoma.org](http://www.lymphoma.org)

Email: [LRF@lymphoma.org](mailto:LRF@lymphoma.org)

This patient guide is supported through unrestricted educational grants from:



© 2015 Lymphoma Research Foundation.

Information contained herein is the property of the Lymphoma Research Foundation (LRF). Any portion may be reprinted or reproduced provided that LRF is acknowledged to be the source.

## ACKNOWLEDGMENTS

---

The Lymphoma Research Foundation wishes to acknowledge those individuals listed below who have given generously of their time and expertise. We thank them for their contributions, editorial input, and advice, which have truly enhanced this publication. The review committee guided the content and development of this publication. Without their dedication and efforts, this publication would not have been possible. We hope those in the lymphoma community will now be better informed and have a better understanding of their illness because of the gracious efforts of those involved in the planning and execution of this comprehensive disease guide.

### Review Committee

#### Editorial Board Steering Committee

##### *Editorial Chairman*

**Morton Coleman, MD**, NewYork-Presbyterian Hospital/Weill Cornell Medical College

##### *Senior Advisors*

**George P. Canellos, MD**, Dana-Farber Cancer Institute, Harvard Medical School

**Bruce D. Cheson, MD, FACP, FAAAS**, Lombardi Comprehensive Cancer Center, Georgetown University Hospital

**Leo I. Gordon, MD, FACP**, Robert H. Lurie Comprehensive Cancer Center of Northwestern University

**John P. Leonard, MD**, NewYork-Presbyterian Hospital/ Weill Cornell Medical College

##### *Review Committee*

**Ranjana Advani, MD**, Stanford University School of Medicine

**Nancy L. Bartlett, MD**, Washington University Medical School

**Jorge J. Castillo, MD**, Dana-Farber Cancer Institute, Harvard Medical School

**Joseph M. Connors, MD, FRCPC**, British Columbia Cancer Agency

**Catherine S. Diefenbach, MD**, NYU Langone School of Medicine

**Christopher R. Flowers, MD, MS**, Winship Cancer Institute of Emory University

**Meghan Gutierrez**, Lymphoma Research Foundation

**Fredrick B. Hagemeister, MD**, The University of Texas MD Anderson Cancer Center

**Eric D. Hsi, MD**, Cleveland Clinic

**Brad S. Kahl, MD**, Washington University in St. Louis

**Alison J. Moskowitz, MD**, Memorial Sloan Kettering Cancer Center

**Craig H. Moskowitz, MD**, Memorial Sloan Kettering Cancer Center

**Izumi Nakano**, Lymphoma Research Foundation

**Carol S. Portlock, MD**, Memorial Sloan Kettering Cancer Center

**Oliver W. Press, MD, PhD**, Fred Hutchinson Cancer Research Center

**Mark Roschewski, MD**, Center for Cancer Research, National Cancer Institute

**Sonali M. Smith, MD**, The University of Chicago

**David J. Straus, MD**, Memorial Sloan Kettering Cancer Center

**Francisco Vega, MD, PhD**, University of Miami/Sylvester Comprehensive Cancer Center

**Sven de Vos, MD, PhD**, UCLA Jonsson Comprehensive Cancer Center

**Anita E. Welborn, LMSW**, Lymphoma Research Foundation

**Michael E. Williams, MD, ScM**, University of Virginia Cancer Center

# TABLE OF CONTENTS

---

- List of Abbreviations . . . . . 4
- Introduction . . . . . 6
- Part 1 — Learning the Basics** . . . . . 7
  - Chapter 1: Understanding the Disease** . . . . . 7
    - Table 1.1. Subtypes of Classical Hodgkin Lymphoma** . . . . 18
    - Table 1.2. Known Risk Factors For Hodgkin Lymphoma** . . 20
  - Chapter 2: Seeking Medical Attention** . . . . . 21
    - Table 2.1. Symptoms That Might Be Associated With Hodgkin Lymphoma** . . . . . 22
  - Chapter 3: Receiving a Diagnosis** . . . . . 24
    - Table 3.1. The Three Main Types of Biopsies** . . . . . 27
    - Table 3.2. Immunohistochemistry and Flow Cytometry Tests** . . . . . 32
  - Chapter 4: Work-Up Before Treatment Can Begin** . . . . . 34
    - Table 4.1. Types of Imaging Tests** . . . . . 36

<b>Part 2 — Treatment of Hodgkin Lymphoma</b> . . . . .	44
<b>Chapter 5: What to Know Before Starting Treatment</b> . . . . .	44
<b>Table 5.1. Poor Prognostic Risk Factors</b> . . . . .	47
<b>Table 5.2. The Eastern Cooperative Oncology Group PS Scale</b> . . . . .	48
<b>Chapter 6: Treatments for Hodgkin Lymphoma</b> . . . . .	60
<b>Table 6.1. Catheters Used to Administer Chemotherapy</b> . . . . .	62
<b>Table 6.2. Terms Used to Describe Treatment and Its Outcomes</b> . . . . .	71
<b>Table 6.3. Forms of Complementary Therapy</b> . . . . .	73
<b>Chapter 7: Treatments for Classical Hodgkin Lymphoma</b> . . . . .	75
<b>Table 7.1. Common First-Line Treatments for CHL</b> . . . . .	77
<b>Table 7.2. Common Second-Line Treatments For CHL</b> . . . . .	78
<b>Chapter 8: Treatment of Nodular Lymphocyte-Predominant Hodgkin Lymphoma</b> . . . . .	82
<b>Table 8.1. Treatment For Various Stages of NLPHL</b> . . . . .	82

**Part 3 — Living With the Side Effects of Treatment** ..... 86

**Chapter 9: Common Treatment Side Effects** ..... 86

**Table 9.1 The Four Main Conditions Caused by Decreased Blood Cell Production** ..... 91

**Chapter 10: Managing Life During and After Treatment** ... 112

**Table 10.1. Coping Strategies** ..... 112

**Part 4 — Hospital Admission** ..... 118

**Chapter 11: Preparing to Go to the Hospital** ..... 118

**Part 5 — Clinical Trials and Advances in Treatment** ..... 125

**Chapter 12: Overview of Clinical Trials** ..... 125

**Table 12.1. The Four Main Types (or Phases) of Clinical Trials** ..... 126

**Chapter 13: Advances in Treatment of Patients With Hodgkin Lymphoma** ..... 133

**About The Lymphoma Research Foundation** ..... 137

## LIST OF ABBREVIATIONS

ABMS	American Board of Medical Specialties	FNA	fine needle aspirate
ACA	Affordable Care Act	GVHD	graft-versus-host disease
AIDS	acquired immunodeficiency syndrome	HBV	hepatitis B virus
ANC	absolute neutrophil count	HIV	human immunodeficiency virus
ASCO	American Society of Clinical Oncology	HL	Hodgkin lymphoma
ASCT	autologous stem cell transplant	IFRT	involved field radiation therapy
ASH	American Society of Hematology	IHC	immunohistochemistry
CBC	complete blood count	IMRT	intensity modulated radiotherapy
CHL	classical Hodgkin lymphoma	IRB	institutional review board
CLL	chronic lymphocytic leukemia	ISRT	involved site radiation therapy
CNS	central nervous system	IV	intravenous
CPR	cardiopulmonary resuscitation	LDH	lactate dehydrogenase
CR	complete remission	LP	lymphocyte predominant (cell)
CT	computed tomography	LRF	Lymphoma Research Foundation
DNA	deoxyribonucleic acid; genetic material	MMAE	monomethyl auristatin E
DNR	do not resuscitate	MR	minor response
EBV	Epstein-Barr virus	MRI	magnetic resonance imaging
ECHO	echocardiogram	mTOR	mammalian target of rapamycin
ECOG	Eastern Cooperative Oncology Group	MUGA	multi-gated acquisition
ESR	erythrocyte sedimentation rate	NCI	National Cancer Institute
FDA	U.S. Food and Drug Administration	NCCN	National Comprehensive Cancer Network
		NHL	non-Hodgkin lymphoma
		NIH	National Institutes of Health
		NK	natural killer (cell)

NLPHL	nodular lymphocyte- predominant Hodgkin lymphoma
PD-1	programmed cell death-1
PET	positron emission tomography
PFT	pulmonary function test
PICC	peripherally inserted central catheter
PR	partial remission
PS	performance status
RIT	radioimmunotherapy
RS	Reed-Sternberg
SAB	Scientific Advisory Board
SCT	stem cell transplant

## INTRODUCTION

---

The purpose of this booklet is to help patients with Hodgkin lymphoma (HL) and their caregivers. It is designed to allow them to become familiar with their illness and to become active participants in their healthcare decisions. Chapters in this book address different issues faced by these patients, including what to expect during diagnosis, work-up, and treatment; how to cope with treatment side effects; and what questions to ask doctors. In addition to this booklet, information is available online at the Lymphoma Research Foundation's (LRF's) website at [www.lymphoma.org](http://www.lymphoma.org), and the Foundation's HL-specific website at [www.FocusOnHL.org](http://www.FocusOnHL.org). The Helpline can also provide additional information and copies of LRF educational and support publications. For Helpline assistance, call (800) 500-9976 or email [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

# Part 1 — Learning the Basics

## Chapter 1: Understanding the Disease

Hodgkin lymphoma (HL) is a type of cancer that affects specialized white blood cells called lymphocytes. Lymphocytes work together with other cells in the immune system to defend the body against invasion by bacteria, viruses, parasites, and other foreign substances.

Lymphocytes travel in the bloodstream and in another network of vessels called the lymphatic system. Lymphocytes are also found in specialized structures called lymph nodes. Lymph nodes are bean-shaped structures that act as sentinels (ie, soldiers or guards who keep watch) because they are often the first defense against invading organisms, such as viruses and bacterial infections.

This chapter explains these and other terms that will help you understand HL and how it affects a person's health. A better understanding of the disease will help patients take a more active role in deciding the course of their treatment.

### What Is Cancer?

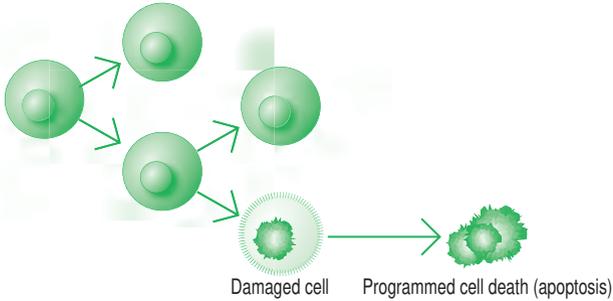
The body is made up of many different types of specialized cells that are organized into tissues and organs that perform the many different tasks needed to function. To keep it running smoothly, there are cells in the body that grow, work, and divide in a very controlled fashion.

All of these cells also have a limited lifespan. Normally, a self-destruct mechanism is triggered when a cell becomes *senescent* (too old) or when it gets damaged; this process is called *apoptosis* or programmed cell death. However, sometimes damage to the genetic material (DNA) of a cell gives it the ability to override this self-destruct mechanism and allows the cell to continue to live and grow, making the cell “immortal” in many ways; this means that the cells that would normally be unable to divide and grow continue to grow indefinitely. Unless the body's immune system gets rid of these abnormal cells, they can become cancerous.

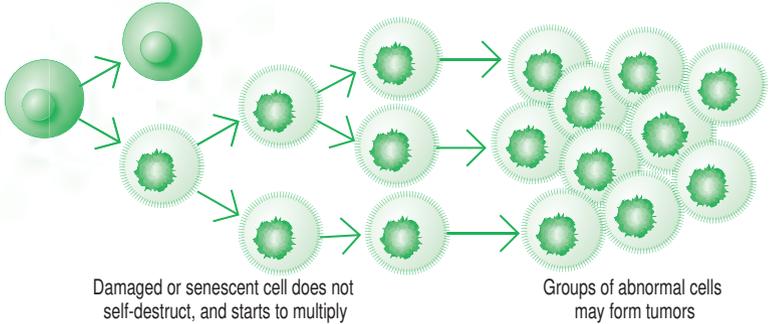
*Cancer*, or malignancy, is defined as a disease whereby abnormal cells gain the ability to divide uncontrollably and without stopping. When these cells accumulate, they form a mass called a *tumor*, which can then interfere with normal organ function.

## HOW CANCER FORMS INSIDE THE BODY

### Normal cell division



### Cancer cell division



Most cancers are named after the organ or cell type of their origin. For example:

- A cancer that started in the pancreas is called *pancreatic cancer*.
- A cancer of the lymphocyte is called a *lymphoma* or *lymphatic leukemia* depending on whether the cancer started in tissue/lymph nodes (lymphoma) or in the bone marrow and circulation (leukemia).

## What Are Red Blood Cells, Platelets, and White Blood Cells?

Red blood cells carry oxygen from the lungs to all the tissues in the body. Red blood cells also sweep up the carbon dioxide waste produced by cells and bring it to the lungs. In the lungs, the carbon dioxide is released into the air each time you exhale.

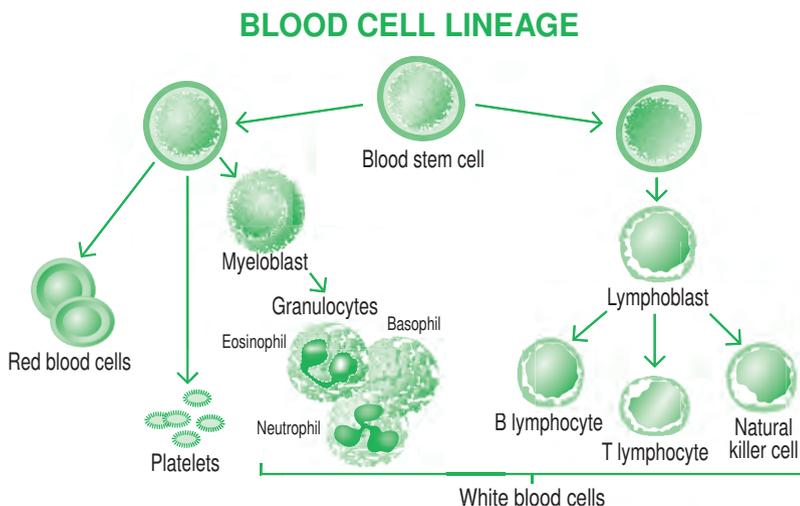
Unlike red and white blood cells, platelets are actually cell fragments that help enable blood clotting (*coagulation*) when a blood vessel is damaged. Platelets become drawn to the point of injury in the vessel and collectively form a foundation upon which the blood clots.

White blood cells work as part of the immune system to help the body fight off infections. The main types of white blood cells are lymphocytes, granulocytes, and monocytes. There are also three types of granulocytes (neutrophils, basophils, and eosinophils) and at least three types of lymphocytes (B cells, T cells, and natural killer [NK] cells).

Because red and white blood cells have a limited lifespan, the body needs to constantly replenish its supply of these cells. Red blood cells live for about 120 days; most white blood cells have an even shorter life, ranging from a few hours to a few weeks.

Both red and white blood cells are made by *hematopoietic* (blood) stem cells, which are specialized blood cells found in the *bone marrow* (the spongy, fatty material inside large bones, such as the pelvis, vertebrae, and ribs). Healthy bone marrow produces hematopoietic stem cells, which are immature (non-specialized) blood cells that can

take on various roles. The hematopoietic stem cells in the bone marrow divide and differentiate, becoming either a “myeloid” stem cell (myeloblast or precursor of myeloid cells) or a “lymphoid” stem cell (lymphoblast or precursor of lymphocytes) as shown in the figure below.



Note: Details of the steps in the lineage diagram above, especially between stem cells and blast cells, are still under investigation. Source: [CLL PDQ NCI Patient version].

Hematopoietic stem cells become mature cells that travel in the blood, such as:

- Red blood cells (also known as erythrocytes) — These cells carry oxygen and other materials to tissues in the body. A low number of red blood cells causes *anemia*. A person with anemia may feel tired, weak, and short of breath.
- Neutrophils, basophils, and eosinophils — Neutrophils are a type of white blood cell that helps fight off bacterial infections. A low number of neutrophils causes *neutropenia*. People with neutropenia are more likely to get infections than people with healthy numbers of neutrophils. Basophils are part of inflammatory reactions, like allergies. Eosinophils also help fight infections and are involved in allergic reactions.

- Platelets — These cells are fragments of cells called megakaryocytes. Platelets help stop bleeding by assisting in the formation of blood clots. A low number of platelets is called *thrombocytopenia*. People with thrombocytopenia are more likely to bruise and bleed. They are also more likely to have severe and recurring nosebleeds and bleeding gums.

Lymphoblasts are the cell precursors of mature lymphocytes that circulate in the blood. There are three main types of lymphocytes:

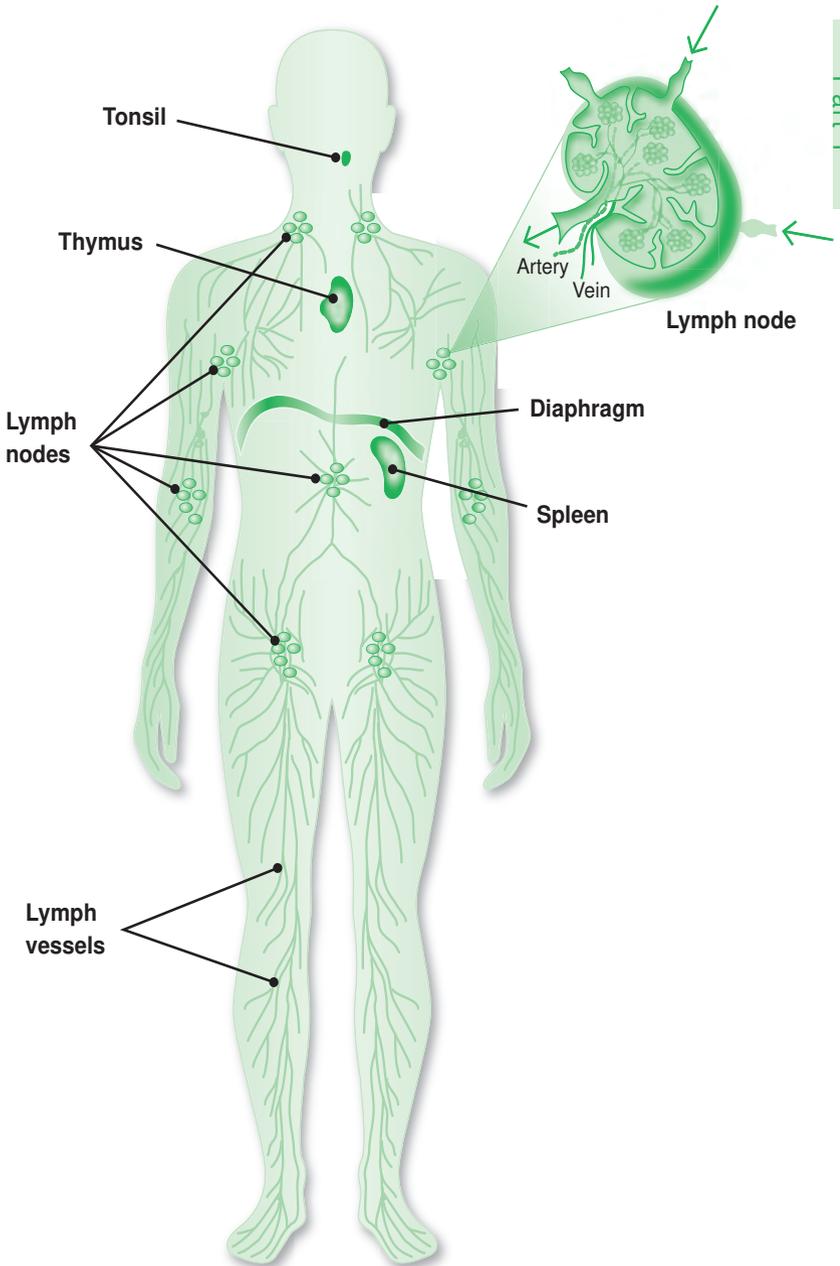
- B lymphocytes (B cells; make antibodies found in gamma globulin)
- T lymphocytes (T cells)
- Natural killer (NK) cells

To learn more about these types of cells, see page 13.

## What Is the Lymphatic System?

As shown in the image on the following page, the *lymphatic system* is a circulatory system that is made up of a spidery network of thin tubes called *lymph vessels* or *lymphatic vessels*. Similar to blood vessels, lymph vessels branch out into all tissues of the body. While people can clearly see blood vessels, especially at their wrists and on the tops of their hands, most lymph vessels are not visible to the naked eye. However, there is one large vessel of the lymphatic system; it is called the *thoracic duct*.

# THE LYMPHATIC SYSTEM



Lymph vessels carry *lymph*, a type of liquid rich in lymphocytes to help fight infection. Within this huge network of vessels are groups of small, bean-shaped organs called *lymph nodes*, which are also commonly known as “glands.” Thousands of lymph nodes are found at locations throughout the body, including the neck, underarms, elbows, and groin. Lymphocytes can mostly be found in lymph nodes, where they monitor for signs of infection in the body. The lymph nodes can change in size, becoming bigger or smaller depending on the number of lymphocytes inside them.

Lymph fluid flows through lymph nodes and specialized lymph tissues, such as the spleen, tonsils, bone marrow, and thymus gland. Lymph nodes filter lymph fluid, removing bacteria, viruses, and other foreign substances from the body. The liquid in lymph vessels usually drains into a large lymphatic vessel near the heart.

If a large number of foreign substances are filtered through a lymph node or series of lymph nodes, swelling may occur and the nodes may become tender to the touch. Most swollen lymph nodes are a reaction to infection and are not cancerous. Lymph cells can also multiply (and lymph nodes can be enlarged) in states of inflammation, such as autoimmune diseases like rheumatoid arthritis.

## What Are Lymphocytes?

Lymphocytes are one type of white blood cell. There are three main types of lymphocytes:

- B lymphocytes (B cells) — B cells make antibodies or immunoglobulins (which are also found in gamma globulins) to fight infections. They are called “B” cells because they were first discovered in the “Bursa of Fabricius” in birds. Later, similar cells were found in humans.
- T lymphocytes (T cells) — There are many types of T cells. Some help B cells make antibodies, some attack and kill infected cells, and others help control the way other parts of the immune system fight

infections. They are called “T” cells because they may spend part of their lifespan in the thymus gland, a small organ in the front part of the chest.

- Natural Killer (NK) cells — NK cells attack and kill cancer cells and virus-infected cells. They also make chemicals called cytokines that help the body get rid of viruses and tumor cells.

## How Does the Immune System Work?

The immune system is the body’s defense against things that might cause it harm. The immune system is made up of a network of cells, tissues, and organs that work together to detect and destroy invaders, such as bacteria, viruses, and parasites that can make people sick.

The immune system provides two different types of immunity:

- Innate immunity — This type of immunity is provided by natural barriers in the body, substances in the blood, and specific types of cells that attack and kill foreign cells that invade the body. Examples of natural barriers include skin, mucous membranes (in the nose, mouth, eyelids, windpipe, lungs, stomach, intestine, and bladder), stomach acid, and the cough reflex. These barriers keep germs and other harmful substances from entering the body. Inflammation (redness and swelling) is also a type of innate immunity. Blood cells that are also part of the innate immune system include neutrophils, macrophages, eosinophils, and basophils among others.
- Adaptive immunity — This type of immunity is provided by the thymus gland, spleen, tonsils, bone marrow, circulatory system, and lymphatic system. These systems work together to make, store, and move specialized cells (such as B cells and T cells) and molecules (such as antibodies) that recognize specific parts (antigens) of invading organisms, ridding the body of viruses, bacteria, or parasites that have these antigens. This process can be tricky because, in order for the immune system to destroy foreign invaders, it has to be able to recognize what is a part of the body (“self” or “auto”) and what is not part of the body (“non-self”). Through a complicated process, the body’s adaptive immune

system “remembers” the identity of the invader, so the next time the body is infected by the same virus, for example, the immune response will be even stronger. Vaccinations prevent disease by turning on the adaptive immune response before the body is exposed to the disease, ensuring that it is prepared to recognize and fight the disease.

## What Is Lymphoma?

A *lymphoma* is a type of cancer that affects lymphocytes. There are two major categories of lymphomas: HL and non-Hodgkin lymphoma (NHL). Both of these major categories of lymphoma are further subdivided into multiple types, which are different in the way they develop and spread and how affected patients are treated. The particular type of lymphoma a patient has may need its own plan of treatment. Unlike other cancers, therapy and prognosis are not based on the stage at which the disease is diagnosed but is rather determined by the lymphoma subtype in addition to a variety of other factors (age, other medical issues, etc.).

## What Is Hodgkin Lymphoma?

HL (previously called Hodgkin or Hodgkin’s disease) is a type of cancer that starts in the lymphocytes. HL is named after Dr. Thomas Hodgkin, a British physician who first described the disease in 1832. In the United States, approximately 9,000 people a year are diagnosed with HL. Although both children and adults can develop HL, the disease is most common in adults aged 20 to 34.

As a result of advances in the diagnosis and treatment of the disease, many patients with HL can be cured.

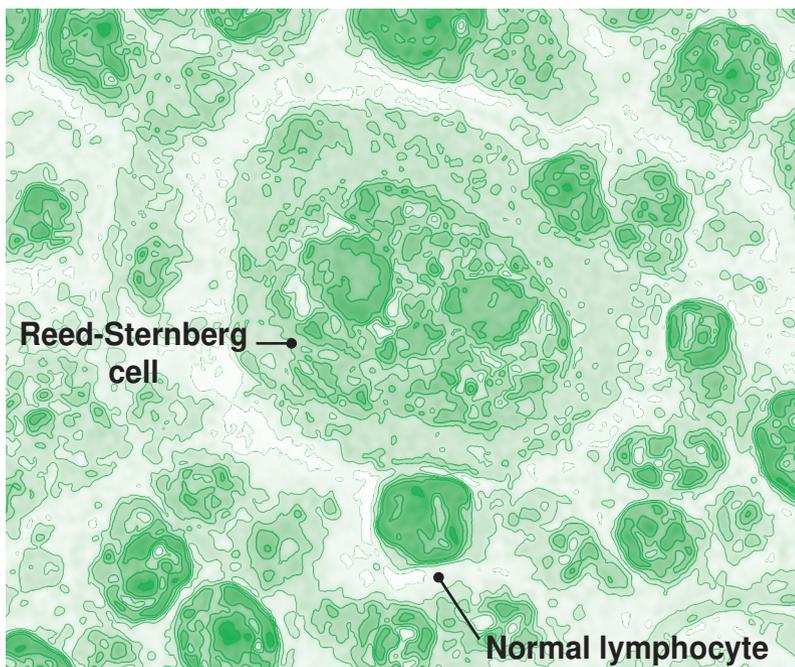
## How Does HL Develop?

HL develops when a B-cell lymphocyte becomes abnormal (cancerous).

These abnormal cells are called Reed-Sternberg (RS) cells, named after the two scientists, Dorothy Reed and Carl Sternberg, who

provided the first definitive microscopic descriptions of HL. Most patients with HL have RS cells or RS-cell variants (“Hodgkin” cells), which are characteristic cells of HL, although they usually constitute only a small fraction (one to two percent) of the overall tumor mass. RS cells produce factors that attract many inflammatory cells that usually comprise most of the overall tumor. Because of this, HL was not initially recognized as a cancer but thought of as an infection.

### A REED-STERNBERG CELL



The mere presence of cells that have the microscopic features of RS cells does not necessarily mean that a person has HL. Such RS-like cells can be seen in many conditions, some of which are benign (not malignant). To confirm a diagnosis, the lymphatic tissue sample must also contain other cells and features that are characteristic of HL. To help make the diagnosis, a *hematopathologist* (doctor specialized in recognizing blood cancers by examining tissues under a microscope) will use tests that look for specific molecules or markers (antigens), which help to identify RS and Hodgkin cells and establish the diagnosis of HL. The hematopathologist might also use more sophisticated molecular tests to help secure a confident diagnosis. HL usually starts in the lymph nodes and may be noticed first in the neck, above or below the collarbone, under the arms, or in the chest (mediastinum). Because lymph tissues are connected all over the body, abnormal (cancerous) lymphocytes can circulate in the lymph vessels, causing the lymphoma to spread from one lymph node to another throughout the body. HL may also spread to other areas and organs outside of the lymphatic system.

### What Distinguishes HL From NHL?

While the presence of cells with RS features is not exclusively diagnostic for HL, their presence is an integral component of the HL diagnosis. RS cells are not present in NHL. Also unlike the more common NHL, HL tends to spread sequentially from one group of lymph nodes to the next, rarely skipping lymph nodes, which is a characteristic of NHL.

The different types and subtypes of HL are distinguished according to how they look when examined under a microscope. The type of tumor a patient has may affect his or her treatment options. The two main types of HL are classical HL (CHL) and nodular lymphocyte-predominant HL (NLPHL).

## Classical Hodgkin Lymphoma and Its Subtypes

CHL affects 95 percent of patients diagnosed with HL in developed countries. CHL can be subclassified in four pathologic subtypes. Table 1.1 describes the four subtypes of CHL.

**Table 1.1. Subtypes of Classical Hodgkin Lymphoma**

<b>Nodular Sclerosis HL</b>	<ul style="list-style-type: none"> <li>■ The most common subtype of CHL, affecting between 60 to 80 percent of patients.</li> <li>■ Involved lymph nodes often become divided into nodules by broad bands of fibrosis tissue.</li> <li>■ Typically affects young adults and is more common in women.</li> <li>■ Lymph nodes in the chest (mediastinum) are most often affected.</li> </ul>
<b>Mixed Cellularity HL</b>	<ul style="list-style-type: none"> <li>■ Affects 15 to 30 percent of patients with CHL.</li> <li>■ Under the microscope, the lymph nodes contain many classic RS cells mixed with various other types of inflammatory cells.</li> <li>■ Primarily affects older adults.</li> <li>■ Lymph nodes in the abdomen are most often affected.</li> </ul>
<b>Lymphocyte-Rich HL</b>	<ul style="list-style-type: none"> <li>■ Occurs in about five percent of patients.</li> <li>■ Under the microscope, this subtype shows many normal lymphocytes and a few RS cells.</li> <li>■ Usually diagnosed in men.</li> </ul>
<b>Lymphocyte-Depleted HL</b>	<ul style="list-style-type: none"> <li>■ The least common form of CHL, accounting for less than one percent of patients.</li> <li>■ Under the microscope, there are very few normal lymphocytes and many RS cells.</li> <li>■ More common in older adults.</li> <li>■ More likely to be advanced when first diagnosed.</li> </ul>

## Nodular Lymphocyte-Predominant Hodgkin Lymphoma

While academically still categorized as a form of HL, clinically NLPHL is not considered among the CHL subtypes but rather as a distinct clinical entity completely unto itself. Only about five percent of patients diagnosed with HL are diagnosed with NLPHL. In NLPHL, the abnormal B cells are called lymphocyte predominant cells (LP cells) – formerly called L&H cells for lymphocytic and/or histiocytic. These abnormal cells are also called “popcorn cells” (the nuclei of the cells resemble an exploded kernel of corn) and are different from the typical RS cells seen in CHL. Unlike RS cells seen in HL, these cells are positive for B-cell antigens like CD20 and negative for CD15 and CD30 antigens often seen in CHL. This form of HL is often found in the lymph nodes of the neck, groin, or underarms and is slow-growing (*indolent*). Because treatment for NLPHL differs from treatment for CHL, treatments for NLPHL are discussed in Chapter 8.

## Why Do Some People Develop HL?

The reasons why some people develop HL are not understood. Scientists, however, have found that people with certain characteristics have a slightly higher risk of developing HL compared with people who do not have these characteristics.

The characteristics that make a person possibly more susceptible to developing any type of disease are called *risk factors*.

Having one or more risk factors for HL does not mean a person will develop the disease. In fact, most people with the known risk factors never develop HL, and many people diagnosed with HL do not have any of these risk factors. However, there does seem to be a connection between these risk factors and the development of HL.

**Table 1.2. Known Risk Factors For Hodgkin Lymphoma**

<b>Age</b>	<ul style="list-style-type: none"> <li>■ People who are aged 15 to 40 years or older than the age of 55 have a higher risk of developing HL than people in other age groups.</li> </ul>
<b>Family History</b>	<ul style="list-style-type: none"> <li>■ People with a family history of the disease, especially among first-degree relatives (parent, brother, or sister), have a higher risk of developing HL compared with people who do not have first-degree relatives with the disease; siblings of patients with HL have a three- to seven-fold increased risk of developing this disease, and the risk is higher in identical twins. Even with this increased risk, the chance of a patient's family member developing HL is still very small.</li> <li>■ Only one percent of patients with HL have a family history of the disease.</li> </ul>
<b>Gender</b>	<ul style="list-style-type: none"> <li>■ Men have a slightly higher risk of developing HL than women, but more women than men tend to develop the nodular sclerosis subtype.</li> </ul>
<b>Infection by Certain Viruses</b>	<ul style="list-style-type: none"> <li>■ People infected with Epstein-Barr virus (EBV; the virus that can cause infectious mononucleosis) or the human immunodeficiency virus (HIV; the virus that can cause acquired immunodeficiency syndrome [AIDS]) have a higher risk of developing HL compared with people who do not have these infections.</li> </ul>

Like other types of cancer, HL cannot be caused by injury and cannot be caught from someone who has the disease. Children and siblings of patients with HL have a slightly increased risk of developing this disease compared with the general population. However, there are no clearly identifiable genetic or hereditary factors to predict this slightly increased risk, and routine screening for HL is not recommended.

# Part 1 — Learning the Basics

## Chapter 2: Seeking Medical Attention

This chapter explains the signs and symptoms of Hodgkin lymphoma (HL) and discusses how a doctor determines whether a person has the disease.

A *sign* is anything unusual that doctors or nurses notice when they examine their patients.

A *symptom* is anything unusual in a normal body function, appearance, or sensation that a patient experiences. During a visit with a healthcare practitioner, patients should report all of their symptoms to their doctor or nurse. Symptoms may indicate the presence of HL or another disease.

In patients who do not have any symptoms, doctors might discover HL after a test is given for another reason, such as a chest x-ray or routine physical examination.

### What Are the Signs and Symptoms of HL?

Some patients with HL do not have any obvious signs or symptoms of the disease. Their doctors might detect the disease during routine tests and/or a physical examination. For others, the disease is detected when symptoms occur and the patient goes to the doctor because he or she is worried, uncomfortable, or does not feel well. Table 2.1 lists some examples of HL symptoms. Keep in mind that, because these signs and symptoms are not specific to HL, they may be due to various other conditions.

**Table 2.1. Symptoms That Might Be Associated With Hodgkin Lymphoma**

Symptoms	Possible Reasons
Lumps under the skin in the neck above the shoulder, under the arm, or sometimes in the groin, which are usually not tender or painful.	Lymph nodes, or “glands,” that swell when the lymphocytes inside them sense that something is wrong, like an infection, or because of an increased number of lymphocytes.
“B symptoms” including fever and/or chills for no known reason, unexplained weight loss, and drenching night sweats that soak clothing and sheets.	Increased levels of inflammatory chemicals in the blood.
Unexplained itching that may be severe.	Unknown cause, but often associated with B symptoms or reactivation of viruses.
Coughing, trouble breathing, chest pain, or pressure.	Lymphoma in the chest, which may press on the windpipe ( <i>trachea</i> ).
Feeling tired ( <i>fatigued</i> ).	Low red blood cell count ( <i>anemia</i> ).
Increased sensitivity to alcohol or pain in certain areas where lymph nodes are present after drinking alcohol.	Poorly understood cause, but thought to be due to increased blood flow through the lymph nodes in response to alcohol.

Having one or more of these symptoms does not mean that a person has HL. Infections, anxiety, or other conditions (including other cancers) may also cause some of these symptoms.

### When Should a Patient Seek Medical Attention?

Anyone who has an enlarged lymph node that does not go away within a few weeks, and/or persistent symptoms, should see a doctor to make sure that lymphoma or another serious condition is not present. A good rule of thumb is to seek medical attention if any of the symptoms listed in Table 2.1 last longer than two weeks, or sooner if the symptoms are harsh enough to impact daily life. Most patients with these symptoms do not have lymphoma, as diseases or conditions not related to lymphoma can also cause many of these symptoms and are more likely to occur.

## What Does the Doctor Look For During the Visit?

There are no specific tests that doctors can use to routinely screen patients for HL.

During the visit with the doctor, patients should describe all of their symptoms. The doctor will ask detailed questions about medical history and perform a complete physical examination. During the physical examination, the doctor is likely to:

- Measure blood pressure and pulse
- Look for any physical signs of infection or any other cancers, especially on the skin
- Check for swollen lymph nodes under the chin, in the neck and tonsil area, above the shoulders, on the elbows, in the underarms, and in the groin
- Examine other parts of the body to see if there is swelling or fluid in the chest and/or abdomen that may be caused by swollen lymph nodes
- Examine the abdomen to see if the liver and/or spleen are enlarged
- Listen to the heart and lungs
- Ask about any pain the patient is experiencing
- Ask about B symptoms (unexplained fever/chills/weight loss or night sweats) or itching or pain in a lymph node after drinking alcohol

If the doctor suspects HL after reviewing the symptoms reported and signs they have uncovered during the examination, he or she will order other tests that can confirm the diagnosis.

These tests should include a complete blood count (CBC) with differential (a study that counts the different kinds of blood cells present) and biopsy; they may also include specific laboratory tests, chest X-rays, and other imaging tests, scans, and a bone marrow evaluation. These tests and procedures are discussed in more detail in Chapters 3 and 4.

# Part 1 — Learning the Basics

## Chapter 3: Receiving a Diagnosis

Doctors need the results of various diagnostic tests to accurately determine if a patient has Hodgkin lymphoma (HL). This chapter explains the purpose of these different tests and describes what to expect during and after these procedures.

### How Is HL Diagnosed?

To be sure of a diagnosis of HL or any cancer, a biopsy is required. An excisional biopsy to remove an entire lymph node is preferred in helping to diagnose HL. Sometimes, however, a core needle or an incisional biopsy to remove a portion of the diseased tissue is performed (see “What Is a Biopsy?” on page 26). A pathologist examines slides containing portions from the biopsy sample under a microscope to see if they contain the characteristic cells of HL (Reed-Sternberg [RS] and Hodgkin cells) and to see if the cells are arranged in ways typical of HL.

The following tests may be used to confirm the HL diagnosis:

- Bone marrow biopsy and/or bone marrow aspiration for advanced stage HL
- Complete blood count (CBC) with differential
- Erythrocyte (red blood cell) sedimentation rate (ESR)
- Comprehensive metabolic panel to check liver and kidney function
- Pathology examination of the lymph node biopsy (a detailed review of the biopsy by a pathologist or hematopathologist)
- Testing for human immunodeficiency virus (HIV) and the hepatitis B and C virus infections
- Positron emission tomography (PET) and computed tomography (CT) scans

Patients diagnosed with HL will be asked to undergo a variety of procedures for the initial diagnosis and work-up before treatment begins, during the course of treatment, and during the follow-up period. Before patients agree to a procedure, they should make sure they understand the reasons for the procedure and what will be involved. Here is a list of questions patients may want to ask their doctor.

**PATIENT TIP**

### Questions to Ask Before Having a Diagnostic Procedure

- Why is this procedure necessary?
- What will the procedure tell us about my condition?
- Can the same information be obtained in another way?
- What is involved in doing this procedure?
- What are the possible risks, complications, and side effects?
- Where will I have the procedure done?
- Will I have to do anything to prepare for the procedure?
- How long will the procedure take? Will I be awake? Will I feel pain?
- How long will it take for me to recover from the procedure?
- Should anyone else be present when I have the procedure?
- Will I need someone to take me home afterward?
- When will I know the results? When will we discuss the results?
- Will my insurance cover the procedure?
- What will my out-of-pocket costs be?

## What Is a Biopsy?

A *biopsy* is a procedure in which a piece of tissue from an area of suspected disease is removed from the body and examined under a microscope. The information provided by this tissue sample is crucial to correctly diagnose the disease and decide on the best course of treatment.

A *pathologist* is a doctor who specializes in the diagnosis of diseases by studying the cells from a patient's body fluids and tissue samples. A *hematopathologist* (a pathologist who has undergone additional training in the diagnosis of blood diseases by studying lymph nodes, blood, and bone marrow samples) examines the biopsy sample under a microscope to see if it contains any lymphoma cells and, if so, to identify the specific type of HL. A *lymphoma hematopathologist* specializes in the diagnosis and classification of HL. These pathologists are trained to recognize different cell types by looking at the shape and size of cells and how they are grouped in tissue samples.

In addition to routine pathology analyses, portions of biopsy samples will be used for other tests to confirm the diagnosis and to more accurately identify the specific subtype of lymphoma. Table 3.1 on the following page shows the three main types of biopsies used for the initial diagnosis of patients with HL and other types of lymphoma.

**Table 3.1. The Three Main Types of Biopsies**

<b>Excisional or Incisional Biopsy</b>	<ul style="list-style-type: none"><li>■ This type of biopsy is generally considered the best to establish an initial diagnosis of lymphoma because it allows the removal of bigger samples than other biopsy procedures. The larger the sample, the more tissue the pathologist can examine, which improves the accuracy of the diagnosis.</li><li>■ A surgeon cuts through the skin to remove an entire lymph node (<i>excisional biopsy</i>) or a large portion of a lymph node or other tissue (<i>incisional biopsy</i>).</li><li>■ If the lymph node is close to the skin surface, the procedure can be done under local anesthesia to numb the area. If the lymph node is in the chest or abdomen, the patient is sedated and the surgeon removes the tissue either <i>laparoscopically</i> (through a tube inserted in the body) or by performing more extensive surgery.</li></ul>
<b>Core Needle Biopsy</b>	<ul style="list-style-type: none"><li>■ This procedure is used when the lymph nodes are deep in the chest or abdomen or in other locations that are difficult to reach with excisional biopsy, or when there are medical reasons for avoiding an excisional or incisional biopsy.</li><li>■ A large needle is inserted into a lymph node suspected to be cancerous and a small tissue sample is withdrawn using a syringe attached to the needle.</li><li>■ A needle biopsy can be done under local anesthesia and stitches are usually not required.</li><li>■ It is important to realize that the size of the tissue obtained via core needle biopsy is often not large enough for the pathologist to diagnose some types of lymphoma like nodular lymphocyte-predominant HL. In some cases, an excisional biopsy may be necessary later on.</li></ul>

**Table 3.1. The Three Main Types of Biopsies** (*continued*)

<b>Fine Needle Aspirate (FNA) Biopsy</b>	<ul style="list-style-type: none"> <li>■ As its name implies, this procedure is performed with a very thin needle (smaller than that used for a core needle biopsy).</li> <li>■ Because of the small needle size, the sample will only contain scattered cells without preserving how the cells are actually arranged in the lymph node. An FNA is rarely adequate for the diagnosis of HL because the RS cells make up only a few of the cells in the sample. Observation of RS cells is essential for the diagnosis.</li> <li>■ When supported by immunohistochemistry or flow cytometry, FNA is sometimes helpful in evaluating lymph nodes.</li> <li>■ An FNA biopsy is most often used to check for return of disease (<i>relapse</i>).</li> </ul>
--	---

After a tissue sample has been removed, it is examined by a pathologist who develops a pathology report. An *oncologist* (doctor specialized in treating patients with cancer) or *hematologist* (doctor specialized in treating patients with blood cancers and other blood disorders) then uses this report, along with results of other diagnostic tests, to confirm a diagnosis. A pathologic diagnosis and accurate classification of specific lymphoma types can sometimes be difficult to make. If the pathologist's interpretation of the biopsy is uncertain, the biopsy should be reviewed by a hematopathologist.

### What Are a Bone Marrow Biopsy and a Bone Marrow Aspiration?

*Bone marrow* is the spongy, fatty material inside large bones where blood cells are generated. Patients with advanced HL may undergo a bone marrow biopsy because HL can involve the bone marrow. A *bone marrow biopsy* involves removing a small amount of bone marrow from inside a bone. The bone marrow is then examined for the presence of lymphoma cells. A *bone marrow aspiration* is similar to a bone marrow biopsy except it involves removing only the liquid portion of the marrow, using a fine needle inserted into a bone. A bone marrow biopsy or aspiration is not typically used for initial diagnosis but is commonly used to see if the HL has spread to the

bone marrow. The most recent guidelines suggest that fewer patients with HL will need a bone marrow biopsy and aspiration.

### **What Is the Purpose of Blood Tests?**

Doctors will test a patient's blood to measure the quantity of the different types of cells (red blood cells, white blood cells, and platelets). Although HL cells are not found in the blood, blood tests can help doctors determine how advanced the disease is and whether a patient will be able to tolerate certain kinds of treatments. The blood tests will most likely include a CBC with differential (to measure the relative amounts of different types of white blood cells), platelets, ESR, alkaline phosphatase and other liver enzymes, and serum lactate dehydrogenase (also known as lactic acid dehydrogenase).

Patients with risk factors for HIV will also be tested for the virus. Prior to therapy, the blood will also be tested for exposure to the hepatitis B and C viruses. This type of testing is important because some kinds of chemotherapy can reactivate these viruses.

If the patient is a woman of childbearing age, the doctor will also obtain a pregnancy test because some of the possible tests and treatments may potentially harm a fetus.

The results from these tests will help patients and their doctors decide between different types of treatments. Many of these blood tests will be repeated during the course of treatment to check how the treatment is affecting the patient's body functions.

## What Is a Complete Blood Count With Differential Test?

For a CBC with differential test, samples of blood are examined to determine:

- The number of red blood cells
- The amount of hemoglobin (the oxygen-carrying protein) in red blood cells
- The number of total white blood cells and the different subtypes of white blood cells (neutrophils, eosinophils, basophils, lymphocytes, and monocytes)
- The number of platelets

The results from the CBC with differential test will be used to check for low red (*anemia*) and white (*leukopenia*) blood cell counts.

## What Is Erythrocyte Sedimentation Rate?

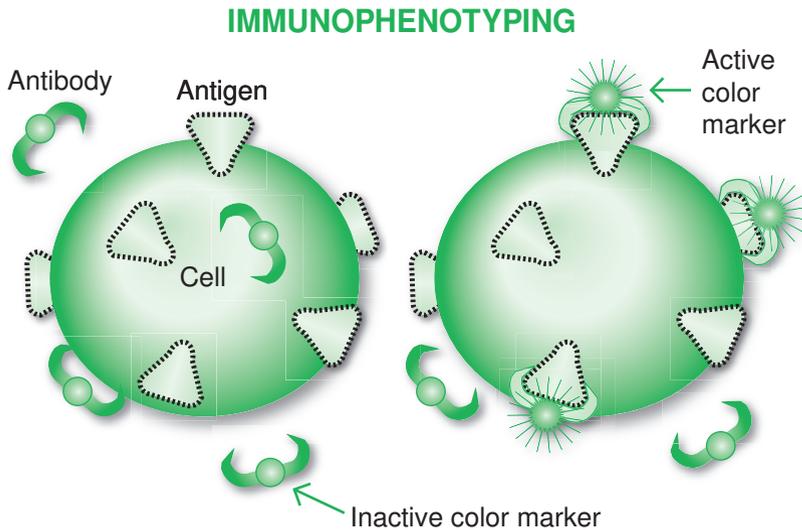
The rate at which red blood cells (*erythrocytes*) settle to the bottom of a tube of blood is an indicator of the amount of inflammation in the blood. A higher ESR is a risk factor for disease that may be more difficult to treat.

## What Is Hematopathology?

*Hematopathology* is the study of blood, lymph node, and bone marrow samples to identify disease. Doctors who have undergone special training in this area (hematopathologists) interpret these studies. These specialists identify and classify the cancer cells by looking at their shape and size and how they are grouped in samples from lymph nodes and bone marrow in conjunction with additional tests, such as immunophenotyping, cytogenetic analysis, and/or molecular studies.

## What Is Immunophenotyping?

*Immunophenotyping* is a process used to distinguish between different types of cells (for example, between normal lymphocytes and lymphoma cells) by detecting small identifying substances, cell “markers” or “antigens,” expressed in or on the cells. These cell markers are antigens that are detected using special antibodies, which lock onto the antigens like a key and lock, made and chemically modified in the laboratory so they will show color or emit light when they stick to their corresponding markers.



Upon binding to specific antigens inside the cells or on the cell surface, the antibodies can be stained with chemicals so the markers appear as different colors and are studied under a microscope using immunohistochemistry (IHC) analysis. Alternatively, a fluorescent molecule can be attached to the antibody so that it can be made to emit light when it binds to the antigen, allowing the cells to be sorted and counted using a process called flow cytometry. Sometimes, both IHC and flow cytometry are necessary for accurate immunophenotyping (see Table 3.2).

**Table 3.2. Immunohistochemistry and Flow Cytometry Tests**

<b>Immunohistochemistry (IHC)</b>	<ul style="list-style-type: none"><li>■ IHC refers to the process of detecting antigens in cells present in a tissue section by exploiting the principle of specific antibody-antigen binding.</li><li>■ Thin slices of the biopsy sample (or thin layers of fluid or blood) are placed on slides and treated with sets of antibodies that recognize different markers found in different types of lymphoma cells and normal lymphocytes.</li><li>■ The pathologist examines the slides under a microscope to look for the visible color change that happens when the antibody sticks to the marker.</li><li>■ The pathologist identifies and counts the number of cells that change color (meaning that they are positive for the marker) with each of the different antibodies and uses that information to identify the specific type of lymphoma.</li></ul>
<b>Flow Cytometry</b>	<ul style="list-style-type: none"><li>■ Cells from the biopsy sample are placed in a liquid solution and treated with sets of antibodies that recognize different antigens found in different types of lymphoma cells.</li><li>■ The cell-antibody mixture is injected into an instrument called a flow cytometer. This machine uses laser beams to sense the different colors the cells emit from the different antibodies attached to them. This information is measured and analyzed by a computer and interpreted by a hematopathologist.</li><li>■ The results from the flow cytometry analysis can help distinguish between different types of lymphoma, other cancers, or some other diseases.</li></ul>

Below is a list of cautions that patients should be aware of about interpreting diagnostic reports.

PATIENT TIP

### Cautions About Interpreting Diagnostic Reports

- A biopsy is the only definitive test for HL.
- Some tests can be reported as “normal” even though HL may be present.
- Some tests may be reported as “abnormal” even though HL is not present.
- Other conditions can produce signs and symptoms similar to HL.
- The interpretation of tests, such as imaging studies and scans, can be lengthy and difficult in some situations.
- Follow-up tests are often needed to determine the significance of previous results; additional biopsies may be needed to clarify the results.
- Some patients like to review their written reports; when doing so, it is important for the patient to carefully review the findings with his or her doctor.

## Part 1 — Learning the Basics

### Chapter 4: Work-Up Before Treatment Can Begin

After the initial diagnosis of Hodgkin lymphoma (HL), the doctor may order other tests, such as blood tests, imaging studies, heart and lung function tests, a bone marrow biopsy and aspiration, and, less frequently, additional biopsies. This process is often called the *work-up* or *staging studies*. Some of these work-up studies are needed to see if and how much the disease has spread to other parts of the body. Doctors will use these test results to determine the state of advancement, or *stage*, of a patient's disease. Other tests will check how the disease has affected a patient's overall health and major organ functions.

Together, all of these tests will provide the information needed to help patients and their doctors decide on the best course of treatment. This chapter will help you understand the reason for the various tests, how these tests work, what to expect, and how HL is staged.

#### What Tests Are Used in the Work-Up For HL?

Patients with HL may undergo some or all of the following work-up tests before starting treatment, and many of these tests may also be repeated during the course of treatment.

- Physical examination with special attention to the size of the lymph nodes in the neck, underarms, and groin, and the size of the liver and spleen
- A determination of general health status (also called *performance status*) to see how well a patient feels and how well he or she can carry out his or her normal daily activities (such as getting washed and dressed, going to work, and doing chores). This is discussed in Chapter 5
- Presence or absence of fever, night sweats, and weight loss (these are also called “B symptoms”)
- Complete blood count (CBC) with differential and platelets

- Erythrocyte sedimentation rate (ESR)
- Comprehensive metabolic panel
- Testing for signs of infection with hepatitis viruses
- Chest X-ray
- Positron emission tomography (PET) and computed tomography (CT) scans of the neck, chest, abdomen, and pelvis
- Excisional or core needle lymph node biopsy
- Bone marrow aspiration and/or biopsy
- Cardiac and pulmonary studies

### **What Is the Purpose of a Complete Blood Count Test?**

Doctors will test a patient's blood to measure the quantity of the different types of cells (red blood cells, white blood cells, and platelets). This information can help determine how advanced the lymphoma is. These blood tests will most likely include a CBC with differential (to measure the relative amounts of different types of white blood cells), platelets, and serum lactate dehydrogenase (LDH). Fast-growing lymphoma can cause very high LDH levels in the blood.

Depending on the type of lymphoma, the blood may also be tested for signs of infection with hepatitis B virus, hepatitis C virus, or human immunodeficiency virus (HIV).

### **What Is a Comprehensive Metabolic Panel?**

A comprehensive metabolic panel measures the amount of different chemicals in the blood that will show if the HL is affecting any of the main organs in the body. The comprehensive metabolic panel usually includes 14 specific tests that measure liver and kidney function, electrolyte, acid/base balance, and the levels of blood sugar and different blood proteins. Calcium, magnesium, potassium, and sodium are some of the electrolytes found in the body; abnormal levels of electrolytes can make a person sick.

The results from these tests will help patients and their doctors decide between different types of treatments. Many of these blood tests will be repeated during the course of treatment to check if and how the treatment and the cancer are affecting body functions.

### What Types of Imaging Tests May Be Used?

A doctor will most likely order imaging tests to help find areas of the body where there may be cancer, to learn how far the cancer has spread, and to determine how well the treatment is working later on. Most of these tests are painless and require no anesthetic. Several types of the following imaging procedures may be needed to thoroughly evaluate the extent of disease.

The imaging tests usually recommended for a patient with HL are a chest X-ray and PET/CT scan of the neck, chest, abdomen, and pelvis. The PET/CT scan is very important. Common procedures described in Table 4.1 may be needed to thoroughly evaluate the extent of disease.

**Table 4.1. Types of Imaging Tests**

<b>Chest X-Ray</b>	<ul style="list-style-type: none"> <li>■ X-rays use radiation to take pictures of areas inside the body. The amount of radiation used in most diagnostic tests is so small that it generally poses little risk to the patient.</li> <li>■ Findings on a chest X-ray may indicate whether the disease is “bulky” (tumor greater than 10 centimeters) or more than one-third of the diameter of the chest wall.</li> </ul>
--------------------	--

**Table 4.1. Types of Imaging Tests** (*continued*)

<b>Computed Tomography (CT) Scan</b>	<ul style="list-style-type: none"><li>■ A CT scan takes X-rays from many different angles around the body. A computer combines the pictures obtained from these different angles to give a detailed image of organs inside the body.</li><li>■ Patients with HL often have CT scans of the neck, chest, abdomen, and pelvis to find out how many nodes are involved, how large they are, and whether internal organs are affected by the disease.</li><li>■ Before a CT scan, the patient may be asked to drink a contrast liquid and/or get an intravenous injection of a contrast dye that will more clearly outline abnormal areas that may be present in the body.</li></ul>
<b>Echocardiogram</b>	<ul style="list-style-type: none"><li>■ During an echocardiogram (ECHO), an instrument called a transducer is placed on the patient's ribs near the breast bone and directed toward the heart.</li><li>■ The transducer releases high-frequency sound waves then picks up the echoes of sound waves and transmits them as electrical impulses. The echocardiography machine converts these impulses into moving pictures of the heart. Still pictures are also taken.</li></ul>
<b>Magnetic Resonance Imaging (MRI)</b>	<ul style="list-style-type: none"><li>■ Like a CT scan, magnetic resonance imaging (MRI) takes images from different angles around the body, but an MRI does not use radiation (X-rays) like a CT scan; instead, it uses magnets and radiofrequency waves.</li><li>■ Although not commonly used in helping to diagnose HL, an MRI can provide important information about tissues and organs, particularly the nervous system, which is not available from other imaging techniques.</li><li>■ Because this testing technique works well to obtain images of the bones, brain, and spinal cord, an MRI may be ordered if a doctor wants to see whether the lymphoma has spread to these areas.</li></ul>

**Table 4.1. Types of Imaging Tests** (*continued*)

<b>Multi-Gated Acquisition (MUGA) Scan</b>	<ul style="list-style-type: none"> <li>■ A multi-gated acquisition (MUGA) scan creates video images of the ventricles (lower chambers of the heart that hold blood) to check whether they are pumping blood properly. Other names for this test include cardiac blood pooling imaging, nuclear heart scan, nuclear ventriculography, and radionuclide ventriculography.</li> <li>■ During the procedure, stickers called electrodes are placed on the chest to monitor the heart's electrical activity during the test.</li> <li>■ A small amount of a radioactive material, called a tracer, is injected into a vein in the arm. The radioactive material binds to red blood cells. A special camera that uses gamma rays to track the tracer is placed over the chest. As the tracer moves through your bloodstream, the camera takes pictures to see how well the blood is pumping through the body.</li> </ul>
<b>Positron Emission Tomography (PET) Scan</b>	<ul style="list-style-type: none"> <li>■ A PET scan evaluates HL activity in all parts of the body. Radioactive fluorodeoxyglucose (a type of sugar) is injected into the body. A positron camera is then used to detect the radioactivity and produce cross-sectional images of the body.</li> <li>■ PET scans help distinguish active tumors from scar tissue and may be used to assess a patient's response to treatment.</li> <li>■ At the end of treatment a PET scan evaluation is considered the "gold standard" test for complete remission (CR).</li> <li>■ While CT scans show the size of a lymph node, PET scans show if the lymph node is active (still has disease). PET and CT scans are now combined into one test (PET/CT).</li> </ul>

## What Is a Bone Marrow Biopsy and Aspiration?

Once the diagnosis of HL is made, the doctor may order a bone marrow biopsy and aspiration. The procedure is not performed often; however, it is done to see if the lymphoma has spread to the bone marrow. The *bone marrow* is the spongy, fatty material found inside large bones where blood cells are generated. A bone marrow biopsy involves removing a small amount of bone marrow from inside a bone. The bone marrow is then examined for the presence of lymphoma cells. A bone marrow aspiration is similar to a bone marrow biopsy except it involves removing only the liquid portion of the marrow, using a fine needle inserted into a bone.

A bone marrow biopsy is recommended for patients with symptoms of Stage III or IV disease or radiological evidence (PET scan) of bone marrow disease. The information from this procedure will help the doctor determine the stage of the disease.

## What Happens During a Bone Marrow Aspiration and Biopsy?

- The patient lies on the examination table, either on his or her side or on his or her stomach.
- For the aspiration part of this procedure, the doctor cleans and numbs the skin over the hip and inserts a thin, hollow needle through the skin and into the bone.
- The doctor uses a syringe to remove a small amount of liquid from the bone marrow. Even with the numbing local anesthetic, this procedure can briefly cause pain when the marrow is withdrawn.
- For the biopsy part of this procedure (which is usually done right after the aspiration), the doctor inserts a slightly larger needle to withdraw a small piece of bone and marrow. This procedure can also briefly cause pain. The procedure does not require any stitches.
- A pathologist examines the samples under a microscope to see if there are lymphoma cells (Reed-Sternberg [RS] and/or Hodgkin cells) of HL.

Patients who are anxious about the test should talk with their doctor and nurse to see whether taking a calming medication before the procedure would be helpful.

### Why Evaluate Heart Function?

Some treatments, like doxorubicin (Adriamycin), can impact heart function. It is important, however, for the doctor to establish baseline heart function for a number of treatments in lymphoma to make sure that the patient's body can withstand treatment.

Heart function is typically evaluated by one of two tests. A *MUGA* (multi-gated acquisition) scan is an imaging test that looks at how well the heart muscle is working. MUGA scans may be done when patients are resting or exercising, depending on what their doctor wants to assess.

Alternatively, the doctor may order a two-dimensional echocardiogram (ECHO). This test can also evaluate the function of the cardiac muscle and may be done while the patient is resting or after exercise. It has the additional benefit of providing information about the heart valves.

### Why Might a Lung Function Test Be Needed?

Lung or pulmonary function tests are done to make sure that the body can withstand treatment with certain lymphoma drugs that may stress a patient's lung function (for example, bleomycin and cyclophosphamide). A doctor may order breathing tests (pulmonary function tests [PFTs]) before beginning treatment and at other times during treatment to make sure a patient's lungs are still working properly.

One type of PFT is *spirometry*, which measures the amount of air a patient breathes in and out. For this test, the patient sits in front of a machine and is fitted with a mouthpiece. Patients will also be given a nose clip to wear so that they cannot exhale any air through their nose. Patients may be asked to breathe normally, and may also be

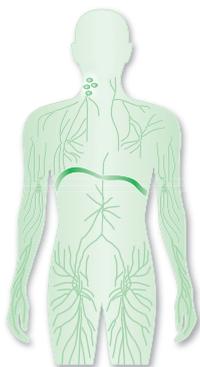
told to inhale and exhale as deeply and/or as rapidly as they can for several seconds.

A *plethysmography test* measures the volume of gas in your lungs. For this test, the patient sits or stands in a small booth and breathes into a mouthpiece. The pressure in the booth will be measured to gain information about lung volume.

## How Is HL Staged?

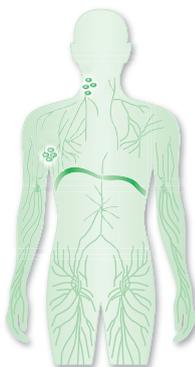
Staging is used to describe how widely the lymphoma has spread in patients with HL and other types of cancer. The Ann Arbor staging system has been used for staging HL, originally described in 1966. Although the older staging system is still in use, a modification of the Ann Arbor staging system—the Lugano Classification—was proposed in 2014, which is shown in the figure on the following page. There are two main classifications (limited and advanced disease) and four stages of lymphoma designated by the Roman numerals I through IV. Stages I and II are considered limited disease, although Stage II can be considered advanced in some cases. Stages III and IV are considered advanced disease. Staging is not to be confused with grade. These are not the same. Grade is the number of large cells seen under the microscope.

## STAGING OF HL (Lugano Classification)



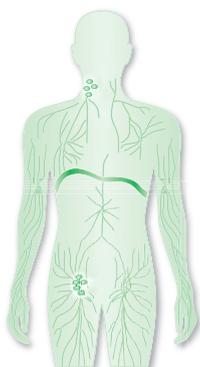
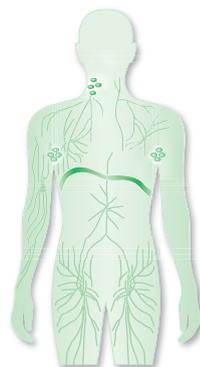
### Stage I:

- Single lymph node or group of adjacent nodes



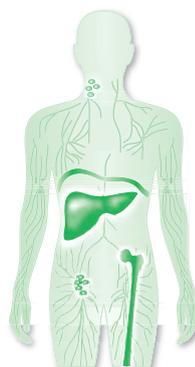
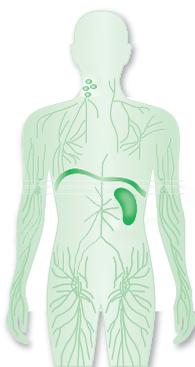
### Stage II:

- Two or more groups of lymph nodes on the same side of the diaphragm



### Stage III:

- Lymph nodes on both sides of the diaphragm
- Lymph nodes above the diaphragm with spleen involvement



### Stage IV:

- Widespread disease in lymph nodes and organ involvement

Stage II disease that is also *bulky*, meaning that the patient has a tumor greater than 10 centimeters (4 inches) wide or that is one-third of the chest wall can sometimes be considered advanced disease.

The newer staging system is similar to the previous Ann Arbor system, except that the “A” and “B” designations are no longer used for non-Hodgkin lymphoma but are still used for patients with HL. The “A” designation means that the patient does not have B symptoms, while the “B” designation means that the patient does have B symptoms. Examples of B symptoms include presence or absence of fever, night sweats, and weight loss.

Doctors use the stage of disease, test results, and/or other prognostic information to help decide the best time to begin treatment and what treatments are likely to be the most effective for each patient.

Being diagnosed with advanced (some Stage II, Stage III, or Stage IV) HL is common. Keep in mind that these advanced stages can be successfully treated.

## Part 2 — Treatment of Hodgkin Lymphoma

### Chapter 5: What to Know Before Starting Treatment

Receiving a cancer diagnosis can be an overwhelming experience. It is perfectly normal to be shocked by the diagnosis, anxious about the future, and confused about the medical information and decisions that need to be made. This chapter will help patients and caregivers prepare for the start of treatment by explaining the next steps and providing tips for talking with a patient's doctor about any questions and concerns.

#### PATIENT TIP

#### First Steps to Take After Receiving a Diagnosis

- Take care of yourself (eat, sleep, rest, and exercise).
- Seek the support of family, friends, and others you trust and rely on.
- Learn about the disease and treatment options.
- Find medical care that meets your needs.
- Find emotional and social support.
- Understand the cost of care, what your insurance will cover, and what financial assistance programs may be available to you.
- Maintain a copy of your medical records (paperwork, test results, and your own notes).

## Who Will Plan and Carry Out the Treatment?

The treatment is usually overseen by a medical oncologist or hematologist who specializes in the treatment of patients with Hodgkin lymphoma (HL). Depending on the patient's healthcare needs, the doctor may refer him or her to work with specialists, such as a surgical oncologist and a radiation oncologist.

The healthcare team will also include other healthcare professionals, such as an oncology nurse, nurse practitioner, physician's assistant, clinical research associate, social worker, and registered dietitian. The healthcare team will work together and consult with the patient to plan, carry out, and monitor the treatment and plan the patient's cancer care.

## What Is a Prognosis?

*Prognosis* is the medical term that doctors use for predicting how the disease will progress and the likelihood for recovery, which is often one of the first questions that patients ask their doctor. Keep in mind that HL is highly curable. At least 80 percent of all patients with HL will be cured of their disease; that number rises to more than 90 percent in patients with early stage disease.

A prognosis is usually based on information gathered from hundreds or thousands of other patients who have had the same disease. This statistical information provides doctors with a general idea of what to expect when a patient is diagnosed with a specific type of HL, and it also gives guidance on the kinds of treatments that have been most successful in treating that HL type.

While doctors and scientists have learned a lot about HL, it is not always possible to predict which specific treatments are most likely to work in an individual patient.

**Keep in mind that statistics from large groups of people cannot accurately predict what will happen to a specific patient.** The doctor most familiar with the patient's situation is in the best position to help interpret these statistics and understand if and how they may apply to a patient's particular situation.

### What Are Prognostic Factors?

The characteristics that help predict a patient's prognosis are called *prognostic factors*. Some prognostic factors tend to be associated with a better outcome, while others tend to be associated with a worse outcome.

Keep in mind that prognostic factors are generated by studying the outcomes of large groups of patients. **Since no two patients are alike, it is impossible to accurately predict what will happen to a specific patient. A patient should talk with their doctor to understand if and how prognostic factors might apply to his or her specific situation.**

Patients with classical HL are grouped in prognostic categories reflective of their risk factors. Some of the poor prognostic risk factors are grouped in Table 5.1 on the following page to help doctors determine the best course of treatment.

**Table 5.1. Poor Prognostic Risk Factors**

Stage	Risk Factors
Not Advanced	<ul style="list-style-type: none"> <li>■ A tumor in the chest larger than one-third of the width of the chest according to a chest X-ray or at least 10 centimeters constitutes <i>bulky disease</i>.</li> <li>■ Cancer has spread outside the lymph node to an adjacent site.</li> <li>■ A high sedimentation rate—also called erythrocyte sedimentation rate (ESR), which refers to the distance red blood cells travel in one hour in a sample of blood as they settle to the bottom of a test tube; inflammation, infection, cancer, rheumatic disease, and diseases of the blood and bone marrow increase the ESR.</li> <li>■ Cancer in three or more nodal areas.</li> <li>■ The presence of B symptoms (fever, weight loss, or night sweats).</li> </ul>
Advanced (≥4 Risk Factors)	<ul style="list-style-type: none"> <li>■ Male.</li> <li>■ Age 45 years or older.</li> <li>■ Stage IV disease.</li> <li>■ Low blood albumin (protein) level (below four grams per deciliter).</li> <li>■ Low hemoglobin level (below 10.5 grams per deciliter).</li> <li>■ High white blood cell count (15,000 per microliter or higher).</li> <li>■ Low lymphocyte count (below 600 per liter or less than eight percent of the white blood cell count).</li> </ul>

## What Is Performance Status?

*Performance status* (PS) is a numerical way to describe a patient's general health, presence or absence of chronic health problems, and ability to carry out normal daily activities (such as getting washed and dressed, going to work, and doing chores). As shown in Table 5.2, which depicts the Eastern Cooperative Oncology Group (ECOG) PS scale, PS is graded on a zero to four scale, with the lower numbers indicating a better PS. Doctors do not generally use PS values unless the patient is part of a clinical study. Many clinical studies of new drugs restrict participation to more physically fit patients (those with lower PS grades).

**Table 5.2. The Eastern Cooperative Oncology Group PS Scale**

Grade	Description
0	<ul style="list-style-type: none"> <li>Fully active; able to carry on all pre-disease activities without restriction.</li> </ul>
1	<ul style="list-style-type: none"> <li>Cannot perform taxing physical activities, but can move around (ambulatory) and carry out light work (such as light house work) or do things that can be done while sitting (such as office work).</li> </ul>
2	<ul style="list-style-type: none"> <li>Can move around and take care of oneself, but unable to do any work. Up and about for more than half of awake hours.</li> </ul>
3	<ul style="list-style-type: none"> <li>Can only partially take care of oneself. Confined to a bed or chair for more than half of awake hours.</li> </ul>
4	<ul style="list-style-type: none"> <li>Completely disabled. Cannot take care of oneself. Completely confined to a bed or chair.</li> </ul>

## How Does a Bulky Tumor Affect a Patient's Prognosis?

A bulky or high-bulk tumor means that the patient has a tumor in the chest at least one-third as wide as the chest according to a chest X-ray, or a single mass of tumor tissue greater than 10 centimeters (4 inches) located anywhere. If the patient has a bulky tumor, he or she will need to be treated more aggressively than a patient with the same stage of disease but no bulky tumor. Sometimes, but not always since the advent of PET/CT scans, radiation therapy is incorporated into the treatment of patients with bulky tumors.

While smaller tumors are usually easier to treat than larger tumors, patients with bulky HL also have a high chance of being cured.

## How to Decide What Treatment Is Best

There are many effective treatment options for patients with HL. To identify which treatments may work best, doctors may consider the following factors:

- The type of HL
- The stage, location, and bulkiness of the lymphoma
- The presence or absence of B symptoms in the presence or absence of other factors
- Results of blood tests and other laboratory tests
- A patient's overall health and age
- A patient's prognostic factors
- A patient's preferences and goals for treatment
- Whether the treatment is the first the patient has received or if the disease has returned after prior therapy (*relapsed*)

A doctor will discuss the risks, benefits, and side effects associated with the different treatment choices applicable to the patient's particular situation. Patients and caregivers should share questions and concerns with the doctor so that, together, they can decide which option is best. The following questions can be used before treatment begins to guide the conversation and help patients make an informed decision.

## Questions to Ask Before Treatment Begins

- What is my exact diagnosis? May I have a copy of the report from the pathologist?
- What is the stage of my disease? Where is the disease located?
- What are my prognostic factors?
- What are my treatment choices? Which do you recommend for me? Why?
- Are clinical trials available that are studying new treatments? Would a clinical trial be appropriate for me? How would I benefit?
- Do I need more than one type of treatment?
- What is the goal of treatment?
- What are the expected benefits of each type of treatment? How will we know if the treatment is working? What tests will I need to determine if treatment is working? How often will I need to be tested?
- What are the risks and possible side effects of each treatment? Can these side effects be prevented or controlled?
- What should I do to take care of myself during treatment?
- Are there any late or long-term side effects I should be aware of? Will treatment impact my ability to have children?
- How long will the treatment last?
- What are the chances the treatment will be successful?
- How will the treatment affect my normal activities (for example, work, school, childcare, driving, sexual activity, and exercise)?
- Is there anything my caregiver needs to do to prepare while I undergo treatment?

## Questions to Ask Before Treatment Begins

*(continued)*

- Will I be able to drive or take public transportation?
- Should I take care of other medical or dental issues before I start treatment?
- Will I be able to work during treatment?
- How often will I need a checkup?
- How much will the treatment cost? Will my insurance cover it?

### When to Get a Second Opinion

Before starting any type of treatment, the patient may want to consider getting a second opinion—especially if some characteristics of the diagnosis are complicated or uncertain. The purpose of the second opinion is not to question the doctor's expertise but to make sure the suggested treatment plan is reasonable and optimal for the patient's particular case.

Most doctors will be supportive and helpful if patients tell them they would like to get a second opinion. Patients should ask the doctor if it would be okay to briefly delay the start of treatment to provide the time needed to get a second opinion. Keep in mind that some insurance programs require second opinions; others may provide coverage if a patient or doctor requests it. The following page contains a list of tips for patients getting a second opinion.

## Getting a Second Opinion

- Some hematologists/oncologists/lymphoma specialists associated with medical schools or cancer centers may provide a consultation and be willing to work together with a local oncologist to provide treatment and follow-up care.
- As part of the second opinion, another pathologist must review the tissue and blood samples to confirm the diagnosis. Please request a pathologist with a lot of experience diagnosing patients with lymphoma. Consider an experienced lymphoma pathologist/hematopathologist among the criteria you require of the highly experienced team of lymphoma specialists who will provide you with a second opinion.
- To get a second opinion, you will have to provide the consulting doctor with a complete copy of all medical records, original X-rays, pathology materials, scans, and reports. When you set up the appointment, ask their office for a list of all the materials they will need. It may be useful to keep your own copy of all these records in case you have questions or concerns later on.

### **To identify lymphoma specialists to contact for a second opinion:**

- Ask your current doctors, family members, other patients, friends, and coworkers.
- Contact the patient referral service at your local hospital and at the nearest hospital associated with a medical school; many hospitals have online directories that can be searched to find a specialist in your area.
- Visit the Lymphoma Research Foundation's (LRF's) website at [www.lymphoma.org](http://www.lymphoma.org) or contact LRF directly by phone (800-500-9976) or email ([helpline@lymphoma.org](mailto:helpline@lymphoma.org)).

## Getting a Second Opinion (*continued*)

- Visit the American Society of Clinical Oncology (ASCO) website at [www.cancer.net](http://www.cancer.net) to search their oncologist database.
- Visit the American Society of Hematology (ASH) web page at [www.hematology.org/patients](http://www.hematology.org/patients) to search for hematologists with an interest in lymphoma.
- Visit the National Cancer Institute (NCI) web page at <http://www.cancer.gov/researchandfunding/extramural/cancercenters/find-a-cancer-center> to identify the nearest NCI-designated cancer center, call (800-4-CANCER or 800-422-6237), or visit their website to find out about their lymphoma specialists.

## How to Find an Oncologist and Treatment Center

A patient's primary care doctor will probably make a referral to a specialist—likely a medical oncologist, hematologist, or hematologist/oncologist. *Oncologists* are physicians who specialize in diagnosing and treating patients with cancer. *Hematologists* are physicians who specialize in diagnosing and treating patients with disorders of the blood and lymphatic system.

Before agreeing to treatment by a specific specialist and treatment center, make sure they will be able to meet all of the patient's medical and personal needs. Patients and caregivers should feel comfortable with the healthcare team and the quality of care they provide. The following questions can be used by patients to select the best medical team.

## Questions to Ask to Select the Best Medical Team

- What are the credentials of the doctor, the other members of the medical team, and the hospital or cancer center?
- Is the doctor board certified as a medical oncologist or hematologist? Has he or she passed qualifying examinations by the American Board of Internal Medicine to certify competency in these specialties?
- How much experience do the doctor and treatment center have in treating patients with cancer in general, and HL in particular?
- How many patients with HL are being treated here now?
- Does the doctor and/or center participate in clinical trials?
- Does the clinic or center have modern surgical facilities and diagnostic equipment?
- Is the doctor or clinic affiliated with any major medical center or medical school?
- What arrangements are made for medical assistance after hours and on weekends, in case of an emergency?
- Is my health insurance accepted at this center? Will the treatment center file claims for reimbursement and process the paperwork?
- What kind of patient resources does the clinic or cancer center have for patients with HL?
- If I see other specialists (cardiologist, endocrinologist, etc.), will you coordinate my cancer care with my other doctors?

Patients enrolled in a managed care program may have limited choices. However, patients have the right to choose another healthcare team if they are not entirely satisfied with their first consultation visit. They should talk with other patients and caregivers about their experience and ask them if they would recommend their doctor and healthcare team. Also, patients and caregivers who are not satisfied with their healthcare team should share their concerns with their primary doctor and ask for a referral to a different doctor.

## **How to Communicate With the Healthcare Team**

Patients and caregivers can ease some of their anxieties by establishing open, honest communication with their healthcare team regarding their diagnosis. Open communication with the healthcare team can help patients and caregivers better learn about what the prescribed treatment regimen is, how it works, what tests are involved, and what side effects and complications may be associated with it.

A good first step for patients is to write down all questions that come to mind. Before meeting with a doctor or nurse, for the first time or for follow-up visits, patients should consider organizing questions into a list to bring to the visit. Since time with doctors or nurses may be limited, patients should put the two or three most important questions at the top of the list. However, patients should make sure a member of the medical team reads all of the questions because he or she may see some that are more important than the patient realizes.

Patients should consider having a family member or close friend accompany them to the doctor's office or clinic to help ask questions and understand and remember answers. A companion could also help by taking notes during the visit. Some patients bring a recording device to record the answers. Patients should ask the doctor or nurse for permission before recording any conversations.

Most oncology nurses are also very well informed about cancer treatments and are a good source of information on a wide range of topics. Additionally, oncology social workers are available to assist with

practical and emotional needs from the time diagnosis is received and onward.

Although family members are often very concerned about their loved one and want information concerning his or her care, confidentiality rules prohibit doctors from giving out information to anyone without the patient's expressed permission. For efficiency, designate one family member as the family contact. The patient must remember to specifically tell the doctor the identity of the primary family contact.

Open communication between patients and doctors is paramount. The following tips can be used to help patients better communicate with their healthcare team.

PATIENT TIP

## Communicating With Your Doctors

### At home

- Keep a journal of your symptoms to help you remember the details you want to discuss with your doctor during your next office visit.
- Ask your doctor or nurse which symptoms need to be communicated immediately to them and which can wait for your next visit.
- Make a list of questions you want to ask your doctor. However, if the questions are urgent, do not wait for the next visit; call the doctor's office to discuss your concerns.
- Review patient portals for contacting your healthcare team. They may provide secure email contact, educational materials, allow patients to check benefits and coverage, schedule non-urgent appointments, and order prescription refills.
- Download the free *Focus on Lymphoma* mobile application (app) from LRF to help you plan appointments, keep track of medications and blood work, and document treatment side effects ([www.FocusOnLymphoma.org](http://www.FocusOnLymphoma.org)).

## Communicating With Your Doctors *(continued)*

### At your next doctor's visit

- Bring your symptom journal and list of questions to discuss with your doctor or nurse.
- Ask a family member or friend to come with you to provide emotional support and take notes.
- Do not be afraid to ask questions if you do not understand something. Your doctor will want to know if you are uncertain or confused and will be happy to address your concerns.
- Inquire about whom should be contacted for specific questions or weekend support and how you can reach them.
- Inquire whether members of your healthcare team communicate electronically (by email, patient portals, etc.). Please note that there could be privacy issues.
- Make sure you understand the next steps in your care before leaving the doctor's office.
- Request written information that you can take home to help you.

### How to Be a Self-Advocate

Being a self-advocate and an active participant in healthcare decisions can be a positive experience and may help restore a sense of control that may have been lost following the diagnosis. Patients and caregivers should remember they are partners in their treatment plan. Many patients feel better when they actively participate in their own care. Ask questions, learn about options, and work closely with the doctor.

It is important for patients to be comfortable with the doctors and the approaches they take. If patients or caregivers are not comfortable, they should openly discuss their concerns. Confidence in the medical team often leads to confidence in treatment. If the patient feels that the team is not a good match, he or she should ask for a referral for a new healthcare team.

Questions will likely vary depending on the purpose of the meeting with the doctor (such as the initial visit to discuss the diagnosis or a routine visit to monitor a remission). Patients should inquire about the timing of office visits, treatments, and tests. The doctor can help explain what the tests will look for and define the possible responses and options for further care depending on the patient's response to treatment.

Although each patient is different and each response to therapy is unique, knowing someone who has been through the same situation and who may have had similar concerns can be a source of great comfort. If patients or caregivers are interested in talking to and learning from people who have had similar experiences, they can ask the oncologist, hematologist, oncology nurse, or the oncology social worker about any support groups in the area.

Before agreeing to any tests, patients need to check with the healthcare team to determine which costs are covered by insurance and which are not. It's important that patients not be afraid to talk with the healthcare team about nonmedical issues, such as transportation, finances, insurance, working through treatment or taking time off, and childcare. The tips on the following page offer self-advocacy strategies for patients.

## Self-Advocacy

- Do not be afraid to ask your doctors or nurses questions about your care.
- Learn more about HL by asking your doctor for information and visiting reliable websites, such as LRF at [www.lymphoma.org](http://www.lymphoma.org) or [www.FocusOnHL.org](http://www.FocusOnHL.org).
- Take advantage of counseling, support groups, nutritional counseling, fitness classes, expressive arts, and other services offered at your doctor's office, cancer center, or hospital.
- Consider joining the Lymphoma Support Network, a nationwide buddy program that matches patients and caregivers with people who have had similar experiences. For information about the program, call (800) 500-9976 or email [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

## Part 2 — Treatment of Hodgkin Lymphoma

### Chapter 6: Treatments for Hodgkin Lymphoma

Numerous treatments and medications are available to treat Hodgkin lymphoma (HL) including chemotherapeutic agents, steroids, monoclonal antibodies, radiation, and stem cell transplantation. This chapter discusses various therapeutic approaches to treating HL. Keep in mind new therapies may have been approved by the U.S. Food and Drug Administration (FDA) since this booklet went to print. Read Chapter 13 to learn more about new treatments under investigation.

Cancer refers to a large group of very complicated diseases. There are many different ways for a cell to become abnormal enough to cause cancer. Because of this, the path taken by a healthy liver cell to become a cancerous liver cell can be quite different from the path taken by a lymphocyte to become lymphoma. This is why a treatment that works against one type of cancer may not necessarily work against another.

There are also small but important differences in the cancer cells found in different patients diagnosed with the same type of cancer. Because of these differences, a treatment that may work very well in one patient may not have the same positive effect in another.

## What Is Chemotherapy?

Chemotherapy drugs work against general characteristics of cancer cells such as their tendency to grow and multiply very quickly. Depending on the drug, patients may have to swallow a pill or receive a liquid infused directly into a vein (*intravenous infusion* or *IV*).

During chemotherapy, patients receive the drug(s) at certain intervals, such as once every two weeks, followed by a rest period. This regular treatment schedule is called a *cycle*. The length of the rest period and the number of cycles vary depending on the patient's disease and the types of drugs used.

Most patients with HL are treated with combination chemotherapy, meaning two or more drugs, instead of a single drug. These chemotherapy drugs are given in a specific order (*schedule*) during certain days of each treatment cycle—this is called a *treatment regimen*. The purpose of combining drugs is to increase how effectively they damage or kill the cancer cells while minimizing the side effects of the treatment.

Oncology nurses are usually responsible for administering the chemotherapy prescribed by the doctor. Most patients receive their chemotherapy in an outpatient clinic, hospital outpatient department, or doctor's office, but sometimes patients have to stay in the hospital for their treatment.

## How Is Chemotherapy Given?

Patients will be given chemotherapy in a pill form, as an injection, or as an IV drip through a vein. To make it easier to give and receive multiple cycles of chemotherapy by IV, the doctor may insert an IV catheter that will stay in place for a few weeks or for the duration of the chemotherapy treatment. There are several types of catheters, which are described in Table 6.1. Patients and caregivers should discuss with the doctor which catheter, if any, would be best for their particular situation.

**Table 6.1. Catheters Used to Administer Chemotherapy**

Type of Catheter	Description	Advantages	Disadvantages
<b>Peripheral Venous Catheter</b>	A needle is used to insert a small, flexible tube (the catheter or cannula) into a vein in the hand or arm. Drugs and other fluids are given through the various types of attachments.	No need for surgical insertion.  A good option for patients who require few infusions spaced wide apart.	Sterile dressing needs to be kept clean and dry and replaced daily; the line needs to be injected periodically with a blood thinner (heparin) to prevent blockage.  To minimize the risk of infections, the catheter needs to be replaced at least every three days or sooner if it becomes blocked.  Cannot be used to draw blood for blood tests.
<b>Hickman and Broviac</b>	Consists of one to three tubes surgically inserted through the subclavian vein (the vein that runs underneath the collar bone) in the chest wall into a vein. Six to 12 inches of tubing remain outside the skin.	It makes it easy to draw blood and give drugs using standard needles and without having to pierce the skin.	Requires proper care to reduce the risk of infection and blockage.  The tubes on the outside of the body make it more obvious that a catheter is in place.  Patients need training and instructions to learn how to clean and take care of the external tubes.
<b>Infusaport or Portacath</b>	A catheter is surgically inserted through the subclavian vein and attached to a small reservoir (port) that lies under the skin. Nothing is visible on the outside except for a bump on the chest.	Patients do not have to do anything to care for it; a nurse keeps the line open by “flushing” once a month with a small amount of injected liquid.	The patient must be injected through the skin with a special needle each time it needs to be used.  Sometimes it is hard to use it to draw blood samples because of clogging (due to a blood clot).  If an infection occurs, the catheter may need to be removed through a minor surgical procedure.

**Table 6.1. Catheters Used to Administer Chemotherapy**

(continued)

Type of Catheter	Description	Advantages	Disadvantages
Peripherally Inserted Central Catheter (PICC line)	A thin, soft plastic tube is inserted in a large vein in the arm.	A good option for patients who only need to have many short infusions or continuous infusions given in a hospital or at home with a portable pump.	This is more temporary than the other types of catheters.

### Why Is It Important to Adhere to the Chemotherapy Treatment Schedule?

Patients should adhere to their chemotherapy treatment schedule because a full course of chemotherapy given on time works best in the treatment of their disease. In clinical studies, doctors have found that reducing the dose or delaying chemotherapy may decrease the chance of complete remission and long-term survival for patients with certain types of lymphomas. Changing the regimen to reduce short-term side effects may actually be harmful in the long run.

Some treatment-related side effects may be unpleasant but are tolerable. Other side effects may be serious, but they can often be anticipated and prevented. It is very important that chemotherapy treatment schedules be maintained to the greatest extent possible.

### What Other Types of Therapies Are Used to Treat Patients With HL?

In addition to chemotherapy, steroids, monoclonal antibodies, radiation therapy, and stem cell transplantation are also used to treat HL. Some of these drugs and therapies have been developed relatively recently, and others may have been approved by the FDA since the time this booklet was printed.

## What Are Steroids?

Steroids are hormones made naturally by the body. Steroids may be given to help chemotherapy agents work more effectively.

## What Are Monoclonal Antibodies?

As part of our immune system, specialized white blood cells (plasma cells) make proteins called antibodies. Antibodies help fight infection by recognizing and sticking to anything the body considers “foreign.” Each antibody our body makes is naturally designed to recognize one specific type of molecule (antigen).

*Monoclonal antibodies* are molecules engineered in the laboratory that are designed to recognize and stick to a specific part of a particular molecule (called an *antigen*) on, for example, the surface of cancer cells. When a monoclonal antibody attaches itself to a cancer cell, it can stop or slow down its growth or it can make it easier for the immune system to recognize and destroy it. Once injected in the patient, the monoclonal antibodies travel through the blood and stick to the cells that have the antigen they recognize. Most of these will be HL cells. Once they stick, the antibodies trigger an alarm that draws cells from the immune system to help destroy and kill the cancer cells.

Monoclonal antibody therapies are given to patients as IV infusions during visits at the doctor's office or clinic. To prevent serious allergic reactions, patients are given oral antihistamines (Benadryl), acetaminophen (Tylenol), and sometimes steroids before the antibody infusion. Single-agent monoclonal antibodies are not widely used to treat HL. A conjugate chemotherapy monoclonal antibody agent is used to treat classical Hodgkin lymphoma (CHL) patients. The following sections provide additional information about each of these therapeutic approaches.

## What Is Radiation Therapy?

*Radiation therapy* (also called *radiotherapy*) uses high-energy X-rays or other types of radiation to kill cancer cells and shrink tumors. The term is used to describe *external beam radiotherapy*, in which radiation is delivered using an external radiation beam. Radiation therapy is limited to patients who require it because of the potential long-term toxicities of this treatment.

A radiation oncologist will be in charge of the radiation therapy. The part of the body selected to receive the radiation therapy is called the *radiation field*. Doctors usually limit the radiation field to affected lymph nodes, the areas immediately surrounding lymph nodes, or other non-lymph node areas where the lymphoma started. Doctors will decide on the type and size of the radiation field depending on the type of tumor and the extent of disease. In HL, the common areas of the body that receive radiation include lymph nodes in the neck, chest, and underarms (mantle field); lymph nodes in the abdomen and possibly spleen; lymph nodes in the pelvis and groin; and in certain circumstances, extended field radiation to both the mantle and upper abdominal fields.

To prepare for radiation therapy, the healthcare team will precisely mark the patient's body with tiny ink dots (called *tattoos*) to make sure that only the targeted areas receive radiation. During the day of treatment, they will use lead shields to protect a patient's normal tissues around the radiation field. They use plastic forms, pillows, and rolled blankets to make the patient comfortable and keep him or her in the proper position. Patients need to lie still on a table beneath a large machine that delivers the radiation painlessly. Once the preparations have been made, it takes only a few minutes to deliver the prescribed dose. The total dose of radiation is usually divided and given over two to six weeks. During and after the radiation treatment, patients will have to carefully protect the radiation site from the sun.

*External beam radiation therapy* is a type of radiation therapy used to treat patients with HL. This form of radiation therapy uses a machine

outside the body to send electrons, or negatively charged particles, directly to the area where the lymphoma is found and, potentially, to nearby lymph nodes. The main type of external beam radiation therapy used for HL is *involved field radiation therapy (IFRT)*. In IFRT, the radiation field includes the lymph node regions that are known to contain HL. IFRT is the preferred form of radiation therapy for patients with HL and is usually given after chemotherapy. IFRT is used alone only to treat certain patients with NLPHL.

Whenever possible, radiation therapy is now directed only at the affected area to reduce the exposure of the surrounding healthy tissues. *Involved site radiation therapy (ISRT)* is a modified involved field that is smaller than that used in IFRT, and spares nearby tissues and organs from receiving radiation. ISRT uses newer radiation techniques like *intensity modulated radiotherapy (IMRT)*, which varies the strength of the radiation to spare surrounding healthy tissues. Proton therapy, which utilizes positively charged particles called protons rather than X-rays, may also be an option for patients with HL.

*Total body irradiation* may be given to patients who are preparing for a stem cell transplant. In this circumstance, the whole body is exposed to radiation along with high-dose chemotherapy in an attempt to kill the lymphoma cells throughout the body.

Patients can use the questions on the following page to ask their doctors about what happens before they start radiation therapy.

## Questions to Ask Before Starting Radiation Therapy

- What is the goal of my radiation therapy?
- How will the radiation be given?
- When will treatment begin? When will it end?
- How will I feel during the therapy?
- What are the side effects of radiation therapy? Is there anything that can be done to prevent them?
- Are there any lasting effects?
- What can I do to take care of myself during and after therapy?
- How will we know if the radiation therapy is working?
- How will the radiation treatment affect my normal activities (for example, work, school, childcare, driving, sexual activity, and exercise)?

## What Is Stem Cell Transplantation?

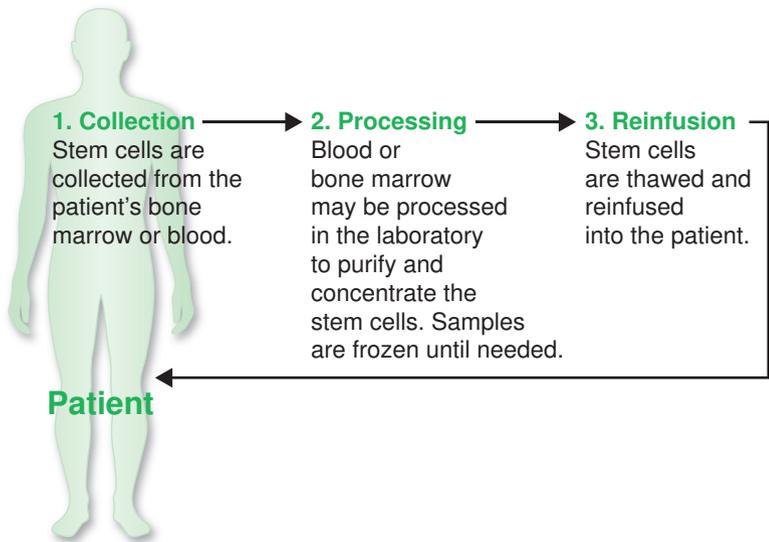
There are different types of stem cell transplantation, depending on who donates the stem cells. In an *autologous stem cell transplant*, the patient is his or her own donor. In an *allogeneic stem cell transplant*, the donor is another person who is genetically similar to the patient; this person is typically a brother or sister, but the donor can also be an unrelated person.

The purpose of autologous or full-intensity (“myeloablative”) allogeneic stem cell transplantation is to allow patients to receive high-dose chemotherapy. Such high doses effectively kill cancer cells but can also severely damage the bone marrow as a side effect, destroying the body’s source of blood cells responsible for fighting infection, preventing bleeding, and carrying oxygen. Stem cell transplantation re-populates the stem cells responsible for making these blood cells.

Because high-dose chemotherapy and stem cell transplantation place great strain on a patient's body, they are not options for everyone. In deciding if transplantation is a good option, doctors will consider the patient's health status, age, medical history, cancer stage, and response to previous therapy. For more information, view the *Transplant in Lymphoma* fact sheet on the Lymphoma Research Foundation's (LRF's) website at [www.lymphoma.org](http://www.lymphoma.org).

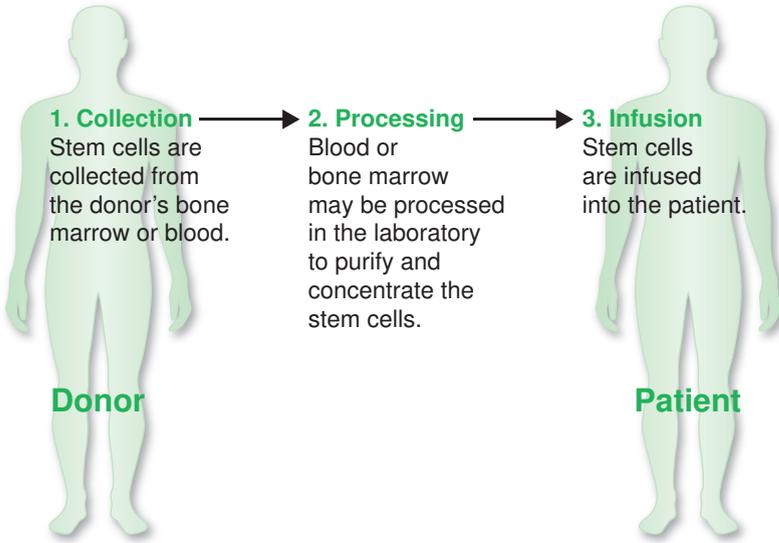
## AUTOLOGOUS STEM CELL COLLECTION

A patient's own stem cells



## ALLOGENEIC STEM CELL COLLECTION

Stem cells from a donor who is genetically similar to the patient



*Reduced-intensity transplantation* (also called non-myeloablative or mini-allogeneic stem cell transplantation) uses lower doses of chemotherapy and/or radiation prior to allogeneic transplantation. This option is available only for allogeneic transplantation and cannot be used for autologous transplantation. This approach takes advantage of the graft-versus-host disease (GVHD) effect, in which the transplanted cells (the “graft”) recognize the cancerous cells in the patient’s body as foreign and destroy them. Patients receiving reduced-intensity transplants may avoid some of the side effects seen with higher-dose chemotherapy, although they still have increased risks of serious side effects as compared with autologous stem cell transplantation due to the potential for GVHD.

Suggested questions for patients to ask their healthcare team before deciding to undergo stem cell transplantation are listed on the following page.

## Questions to Ask Before Deciding to Undergo Stem Cell Transplantation

- What type of transplantation is most appropriate for me?
- Why do you think this is a good idea?
- Why do you recommend this particular type of transplantation?
- What are the risks versus benefits associated with this procedure?
- If I need a donor, how will I find one?
- How long will I need to be in the hospital?
- Will my insurance cover this procedure?
- What type of special care will I receive?
- How sick will this treatment make me?
- What will you do to lessen the side effects?
- How will we know if the treatment is working?
- How and for how long will the treatment affect my normal activities (for example, work, school, childcare, driving, sexual activity, and exercise)?
- Once I'm back home, will I need special care? Will I need someone to care for me immediately after the transplant?
- What is my chance of making a full recovery?

## What Terms Do Doctors Use to Describe Treatment and Its Outcomes?

Once a patient has completed a course of treatment, doctors will test to see if the treatment worked. Table 6.2 on the following page defines the terms doctors use to describe a patient's treatment or response to treatment.

**Table 6.2. Terms Used to Describe Treatment and Its Outcomes**

<b>Complete Remission (CR)</b>	While complete remission (CR) is a first step for cure, it is not a guarantee that the disease will not return. This term is used when all signs of the lymphoma have disappeared after treatment. This does not necessarily mean that the lymphoma is cured; it means that the symptoms have disappeared and the lymphoma cannot be detected using current tests. If this response is maintained for a long period, it is called a <i>durable remission</i> . Relapses can occur for patients in CR.
<b>Cure</b>	This word is cautiously used by doctors when there are no signs of the lymphoma reappearing after many years of continuous CR. The term is most often applied to diffuse large B-cell lymphoma or HL.
<b>Disease Progression</b>	This term means the disease has worsened or the tumor has grown during therapy or observation. Other terms used to describe disease progression are treatment resistance or resistant disease.
<b>Minor Response (MR) or Improvement</b>	This term is used if the tumor has shrunk following therapy but is still more than one-half of its original size.
<b>Partial Remission (PR)</b>	This term is used if the lymphoma has responded to treatment and shrunk to less than one-half of its original size.
<b>Primary Therapy</b>	This is the first (also called <i>initial</i> or <i>front-line</i> ) therapy that a patient receives. The choice of primary therapy depends on the type of HL and the pathologic characteristics of the disease, including the factors described previously in this booklet.
<b>Refractory Disease</b>	This term is used when the lymphoma does not respond to treatment (meaning that the cancer cells continue to grow) or when the response to treatment does not last very long.
<b>Relapse</b>	This term refers to disease that reappears or grows again after a period of remission.
<b>Stable Disease</b>	This term means the disease has not gotten worse or better following therapy (the tumor has not grown or shrunk) but has stayed about the same.

## What Is Relapsed or Refractory HL?

*Relapsed HL* means that the disease has returned after responding to treatment, which is sometimes also called a *recurrence*. *Refractory HL* means that the patient's disease no longer responds to a specific treatment or that the response to treatment does not last very long. There are many treatment options for patients with relapsed or refractory HL. Exactly what type of treatment is optimal for individual patients with relapsed or refractory HL depends on such factors as the type of lymphoma, the patient's age and overall health, extent and location of disease, type of previous therapies received, and length of response to previous therapies. For more information, view the *Hodgkin Lymphoma: Relapsed/Refractory* fact sheet on LRF's website at [www.lymphoma.org](http://www.lymphoma.org).

## When Should a Clinical Trial Be Considered?

Clinical trials are appropriate for patients at all phases of disease (see Chapter 12 "Overview of Clinical Trials"). The purpose of a clinical trial is to safely monitor the effects of a drug on patients over time and to identify more effective therapies for specific diseases. By participating in a randomized clinical trial, patients may or may not get access to the newest therapies but will, at a minimum, receive quality care and the standard treatment in a very carefully controlled and supportive environment.

Participation in clinical trials is especially important for patients with HL because it is a rare disease, which makes it very hard to find enough patients to enroll in studies that are critical for improving treatment. If patients are interested in participating in a clinical trial, they should ask their doctor if there is an appropriate trial for them and what the potential risks and benefits may be. For more information about clinical trials, please refer to LRF's "Clinical Trial Information Service" available at [www.lymphoma.org/clinicaltrials\\_forpatients](http://www.lymphoma.org/clinicaltrials_forpatients).

## What Are Alternative and Complementary Therapies?

*Alternative therapy* refers to treatments that are used instead of standard therapy recognized as effective by the medical profession.

**Currently, there are no proven alternative therapies to conventional cancer care for patients with HL. Patients should not use alternative remedies to replace the care suggested by their doctors.**

*Complementary therapy* is used in addition to standard medicine to help improve a patient's quality of life and to relieve the effects of drug therapy, radiation, and surgery. Patients and caregivers should talk to their doctor and healthcare team before starting any form of complementary therapy because some of these practices can make their cancer treatment less effective.

Table 6.3 outlines some forms of complementary therapy, also known as integrative medicine or integrative oncology.

**Table 6.3. Forms of Complementary Therapy**

<b>Acupuncture</b>	<ul style="list-style-type: none"><li>■ Some studies show that acupuncture may relieve pain, nausea, fatigue, hot flashes, and <i>neuropathy</i> (numbness or tingling in the hands and feet) associated with chemotherapy and may help decrease mild depression.</li><li>■ Using ultra-thin needles applied to specific points on the body, acupuncture is safe and painless. Needles should only be used once and disposed of after use.</li></ul>
<b>Mind/Body Therapies</b>	<ul style="list-style-type: none"><li>■ Examples of mind/body therapies include meditation, guided imagery, self-hypnosis, Tai Chi, and yoga.<ul style="list-style-type: none"><li>– Meditation, guided imagery, and self-hypnosis can help manage stress.</li><li>– Yoga and Tai Chi have been shown to minimize stress and improve balance and flexibility.</li></ul></li></ul>

**Table 6.3. Forms of Complementary Therapy** (*continued*)

<b>Nutrition</b>	<ul style="list-style-type: none"> <li>■ Patients undergoing lymphoma treatment should eat a healthy, well-balanced diet that contains five to seven servings of fruits and vegetables a day, fish or poultry, and whole grains.</li> </ul>
<b>Touch Therapies</b>	<ul style="list-style-type: none"> <li>■ Examples of touch therapies include massage, reflexology (foot massage), and Reiki.             <ul style="list-style-type: none"> <li>- These techniques apply therapeutic pressure to the body to help restore a sense of harmony, relaxation, and well-being.</li> <li>- Studies suggest that massage may lessen pain.</li> </ul> </li> </ul>

### Drug Costs: What to Do if Insurance Will Not Pay

Many patients today face the problem of how to pay for rising healthcare costs. Cancer organizations like LRF ([www.lymphoma.org](http://www.lymphoma.org)) offer limited financial assistance to patients who qualify. Most pharmaceutical companies have patient assistance programs in place that help provide drugs to qualifying patients.

Patients in need of financial assistance should talk with their doctor and social worker about available options and how to enroll in an appropriate program. Before undergoing a medical procedure, patients should check with the insurance carrier to ensure that it is covered. If there is a dispute about coverage or if coverage is denied, patients should ask the insurance carrier about their appeals process. If a claim is repeatedly denied, the patient should contact their state's insurance agency. For more information on financial aid, view the *Resources for Financial Assistance* fact sheet on LRF's website at [www.lymphoma.org](http://www.lymphoma.org). You may also call LRF's Helpline at (800) 500-9976 or email [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

# Part 2 — Treatment of Hodgkin Lymphoma

## Chapter 7. Treatments For Classical Hodgkin Lymphoma

In this chapter, you will learn about the most common therapies currently used in the treatment of patients with classical Hodgkin lymphoma (CHL). Keep in mind that new therapies may have been approved by the U.S. Food and Drug Administration (FDA) since this booklet went to print. Read Chapter 13 to learn about new agents under investigation.

### What Types of Treatments Are Used in Patients With Classical HL?

There are three general types of treatments for patients with CHL:

- Drug therapy, which includes one or more of the following types of drugs:
  - Chemotherapy, which affects general cell growth and division
  - A monoclonal antibody, such as brentuximab vedotin (Adcetris), attached to a drug that can specifically target and kill lymphoma cells
- Radiation therapy, which uses high-energy radiation to kill lymphoma cells
- High-dose chemotherapy and stem cell transplantation

These types of therapies are described in detail throughout this chapter and in Chapter 6.

Most patients treated for HL receive some form of chemotherapy and sometimes also receive radiation therapy as their *front-line* (initial) treatment. In North America, the standard of care for all stages is varying numbers of cycles of the chemotherapy regimen, ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine; see Table 7.1). Radiation therapy is rarely added except for Stages IA/B and IIA/B

bulky, and many medical oncologists will not do radiation therapy if the posttreatment positron emission tomography/computed tomography (PET/CT) scan is negative.

PET/CT scans are often used to evaluate and stage disease before starting treatment, and to evaluate whether the lymphoma is responding to the treatment after one or several cycles of therapy. Often scans are used during treatment to confirm that the lymphoma is shrinking, and at the end of treatment to confirm that the lymphoma is in remission.

If cancer cells can still be detected after treatment, most experts believe continuation of the same treatment is not effective. Therefore, a different approach is likely to be taken. Stem cell transplantation is typically used for patients with *relapsed* (disease returns after treatment) or *refractory* (disease does not respond to treatment) disease. Brentuximab vedotin, which is FDA approved for the treatment of patients with CHL in some situations (as described on page 79), may be used. Patients with resistant, recurrent, and/or relapsed disease may also consider entering a clinical trial.

A variety of treatments can be used for CHL. The choice of which regimen to use is based on many factors including the stage, favorable or unfavorable status, and the patient's age and health. Table 7.1 on the following page lists the common first-line chemotherapy regimens given for patients with CHL. This list is subject to change as new approvals are made by the FDA.

**Table 7.1. Common First-Line Treatments for CHL**

Drug or Regimen Abbreviation	Generic Name of Drugs (Brand Name)
ABVD	Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex) Bleomycin (Blenoxane) Vinblastine (Velban, Velsar) Dacarbazine (DTIC-Dome)
BEACOPP	Bleomycin (Blenoxane) Etoposide (Etopophos, Toposar, Vepesid) Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex) Cyclophosphamide (Clafen, Cytoxan, Neosar) Vincristine (Oncovin, Vincasar PFS) Procarbazine (Matulane) Prednisone (Deltasone)
C-MOPP	Cyclophosphamide (Clafen, Cytoxan, Neosar) Vincristine (Oncovin, Vincasar PFS) Procarbazine (Matulane) Prednisone (Deltasone)
Stanford V	Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex) Vinblastine (Velban, Velsar) Mechlorethamine (Mustargen) Vincristine (Oncovin, Vincasar PFS) Bleomycin (Blenoxane) Etoposide (Etopophos, Toposar, Vepesid) Prednisone (Deltasone)

**Treatment of Patients Who Do Not Achieve a Complete Response**

Patients with HL whose disease does not go into complete remission (CR) after initial therapy or who relapse after achieving CR are often treated with second-line chemotherapy regimens (treatment given after the disease relapses or does not respond to initial treatment).

The preferred treatment for transplant-eligible patients with relapsed HL is a chemotherapy regimen that is typically different from the therapy used initially, followed by high-dose chemotherapy with autologous stem cell transplantation (using the patient's own stem cells). Alternately, patients may be treated with radiation therapy, chemotherapy given with or without radiation therapy, or treatment with the immunoconjugate brentuximab vedotin (Adcetris) as described on the following page.

Table 7.2 shows examples of second-line chemotherapy regimens used in patients whose disease has relapsed or recurred after the initial treatment.

**Table 7.2. Common Second-Line Treatments For CHL**

Drug or Regimen Abbreviation	Generic Name of Drugs (Brand Name)
Brentuximab vedotin	Brentuximab vedotin (Adcetris)
ChIVPP	Chlorambucil (Leukeran) Vinblastine (Velban, Velsar) Procarbazine (Matulane) Prednisone (Deltasone)
DHAP	Dexamethasone (Decadron) Cisplatin (Platinol, Platinol-AQ) High-dose Cytarabine (Cytosar, Depocyt, Tarabine PFS)
DICE	Dexamethasone (Decadron) Ifosfamide (Ifex) Cisplatin (Platinol, Platinol-AQ) Etoposide (Etopophos, Toposar, Vepesid)
ESHAP	Etoposide (Etopophos, Toposar, Vepesid) Methylprednisolone (Medrol) High-dose Cytarabine (Cytosar, Depocyt, Tarabine PFS) Cisplatin (Platinol, Platinol-AQ)

**Table 7.2. Common Second-Line Treatments For CHL** (continued)

Drug or Regimen Abbreviation	Generic Name of Drugs (Brand Name)
GCD	Gemcitabine (Gemzar) Carboplatin (Paraplatin) Dexamethasone (Decadron)
GDP	Gemcitabine (Gemzar) Dexamethasone (Decadron) Cisplatin (Platinol, Platinol-AQ)
Gem-Ox	Gemcitabine (Gemzar) Oxaliplatin (Eloxatin)
GVD	Gemcitabine (Gemzar) Vinorelbine (Navelbine) Liposomal doxorubicin (Doxil)
ICE	Ifosfamide (Ifex) Carboplatin (Paraplatin) Etoposide (Etopophos, Toposar, Vepesid)

*Brentuximab Vedotin (Adcetris)*

Brentuximab vedotin is an antibody drug conjugate. It is a monoclonal antibody (brentuximab) that recognizes CD30, a specific molecule found on the surface of certain lymphoma cells including Reed-Sternberg cells, combined with a toxin called monomethyl auristatin E (MMAE) or vedotin. When brentuximab vedotin molecules bind to the surface of lymphoma cells, the drug is transported to the inside of the cell. Once inside cells, the MMAE drug is separated from the antibody molecule. The MMAE attacks and breaks up an internal support skeleton (called the *microtubule network*) of the cells, causing them to stop dividing and die.

Brentuximab vedotin received approval by the FDA for the treatment of patients with the following:

- CHL after failure of autologous stem cell transplantation (SCT) or after failure of at least two previous multiagent chemotherapy regimens in patients who are not candidates for autologous SCT
- CHL after autologous stem cell transplantation as consolidation treatment in patients who are at high risk of disease relapse or progression
- Systemic anaplastic large cell lymphoma after failure of at least one previous multiagent chemotherapy regimen

Brentuximab is given as an intravenous infusion once every three weeks.

As an investigational treatment (not FDA approved), some patients with relapsed or refractory CHL who have undergone an autologous SCT may receive brentuximab vedotin maintenance therapy. This means that treatment is continued for a long period of time to keep the disease from returning.

Patients who do not go into CR following treatment or who do not respond to treatment should not lose hope. Lasting responses to therapy may be achieved after a diagnosis of relapsed or refractory disease. Many patients seek second opinions at any point from diagnosis onward and often choose to do so if their disease relapses or is considered refractory. Clinical trials are a good option for patients at all stages of disease.

## *Clinical Trials*

Many of the novel therapeutic agents being investigated in clinical trials are used specifically for patients with relapsed or refractory disease. Lymphoma research continually evolves as doctors and scientists discover new therapies and more effective ways of giving existing treatments. Chapter 13 describes some of the options currently under investigation. The Lymphoma Research Foundation (LRF) provides a Clinical Trials Information Service to increase awareness and education around clinical trials and assist patients and caregivers to find trials that may offer access to new lymphoma therapies.

## Part 2 — Treatment of Hodgkin Lymphoma

### Chapter 8: Treatment of Nodular Lymphocyte-Predominant Hodgkin Lymphoma

As discussed in Chapter 1, although nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is still considered as a form of Hodgkin lymphoma (HL), it is different from classical Hodgkin lymphoma (CHL) in both the absence of Reed-Sternberg cells and the presence of “popcorn cells.” It is treated more like non-Hodgkin lymphoma (NHL) than like CHL. Therefore, treatment for NLPHL is presented separately in this chapter.

#### What Types of Treatments Are Used in Patients With NLPHL?

NLPHL tends to grow slowly and sometimes causes a late relapse. Because of this, treatment approaches for NLPHL can differ from CHL treatments. Patients with early stage favorable NLPHL tend to have a better prognosis than those with CHL. Watchful waiting (observation) is also an option for patients who have early stage disease that is not bulky (no tumor greater than 10 centimeters). Table 8.1 shows treatments used for various stages of NLPHL.

**Table 8.1. Treatment For Various Stages of NLPHL**

Stage	Commonly Used Treatment(s)
Early Stage Disease	<ul style="list-style-type: none"><li>■ Observation; watchful waiting.</li><li>■ Involved field radiation therapy (IFRT).</li><li>■ Single-agent monoclonal antibody rituximab (Rituxan).</li><li>■ IFRT with chemotherapy and with or without rituximab.</li></ul>

**Table 8.1. Treatment For Various Stages of NLPHL** (*continued*)

Stage	Commonly Used Treatment(s)
Advanced Disease	<ul style="list-style-type: none"><li>■ IFRT with or without chemotherapy with or without rituximab.</li><li>■ Radiation therapy.</li><li>■ RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy.</li><li>■ Radioimmunotherapy (RIT).</li></ul>
Recurrent or Relapsed Disease	<ul style="list-style-type: none"><li>■ Clinical trial.</li><li>■ Observation (watchful waiting) if recurrence is limited and there are no symptoms.</li><li>■ Chemotherapy, rituximab, or IFRT alone or in any combination.</li><li>■ If aggressive relapsed disease, chemotherapies for aggressive NHL may be considered.</li><li>■ RIT.</li></ul>

In some cases, NLPHL can transform into a more aggressive type of NHL. Rapid growth of one or more lymph nodes is a clear indication for a biopsy to see if such a transformation has occurred. If transformation occurs, treatment of the resulting NHL will be necessary.

### What Is Watchful Waiting?

With the *watchful waiting*, or *watch and wait*, approach, patients do not receive any anti-lymphoma treatments, but their health and disease are monitored through regular checkup visits and follow-up evaluation procedures, such as laboratory and imaging tests. These patients continue to remain untreated as long as they do not show any signs or symptoms and there is no evidence that the lymphoma is growing or spreading.

Doctors recommend watchful waiting for selected patients with early stage NLPHL. This approach may be started after the initial diagnosis

or after *relapse* (disease returns after responding to treatment), depending on the situation. Active treatment is started if the patient begins to develop lymphoma-related symptoms or if there are signs that the disease is progressing.

Watchful waiting is not a treatment option for patients with symptomatic NLPHL. Here is a list of questions that patients can ask before starting the watchful waiting approach.

### Questions to Ask Before Starting Watchful Waiting

- What happens if I choose watchful waiting and then change my mind?
- Will the disease be harder to treat later?
- How often will I have checkups?
- Between checkups, what symptoms and other problems should I report?

PATIENT TIP

Part 2

### *Rituximab (Rituxan)*

Rituximab is a monoclonal antibody that recognizes CD20, a specific molecule found on the surface of almost all B cells. In 1997, rituximab became the first monoclonal antibody approved by the U.S. Food and Drug Administration (FDA) for the treatment of patients with cancer—specifically for patients with relapsed or *refractory* (disease does not respond to treatment) low-grade or follicular B-cell NHL. As of 2015, rituximab is approved by the FDA for the treatment of patients with NHL, chronic lymphocytic leukemia, rheumatoid arthritis, and Wegener granulomatosis and microscopic polyangiitis.

While it is not explicitly approved by the FDA to treat HL, it may sometimes be given along with chemotherapy treatment or on its own to patients with NLPHL.

Rituximab is used as *monotherapy* (alone, not in combination with other drugs) or in various combinations with chemotherapy drugs. Rituximab treatment is given as an intravenous (IV) infusion usually once weekly for a certain number of cycles, but the schedule varies depending on the type of combination regimen used. When combined with chemotherapy, rituximab is usually given during the first day of each chemotherapy cycle.

### What Is Maintenance Therapy?

*Maintenance therapy* refers to the ongoing treatment of patients whose disease has responded well to *first-line* (initial) treatment. The purpose of maintenance therapy is to help prevent the cancer from returning and to help keep a more aggressive cancer that has stopped growing from beginning to grow again and spread to other parts of the body.

As an investigational therapy (not FDA approved), some patients with relapsed or refractory NLPHL who are treated with rituximab alone may receive rituximab maintenance for up to two years.

## Part 3 — Living With the Side Effects of Treatment

### Chapter 9: Common Treatment Side Effects

Patients being treated for Hodgkin lymphoma (HL) may experience various side effects or toxicities caused by their cancer treatment. All treatments (including chemotherapy, biologic/targeted therapies, and radiation therapy) can cause side effects. Fortunately, medications and lifestyle changes can effectively prevent or lessen the severities of most side effects. Patients should ask their healthcare team about possible treatment side effects and how to prevent and manage them and tell their doctor or nurse if they experience any side effects. This chapter explains the causes of these side effects, the types of side effects caused by different treatments, and steps to take to minimize these side effects.

#### Why Does Chemotherapy Cause Side Effects or Toxicities?

Chemotherapy drugs cause side effects because of the non-specific way these drugs attack cancer cells. Most chemotherapy drugs are designed to kill cells that multiply quickly like cancer cells. Most normal cells in the body do not multiply as quickly as cancer cells. However, healthy cells in hair roots and cells in the mouth, gastrointestinal tract, and bone marrow do multiply more rapidly. As a result, these tissues are more commonly damaged by chemotherapy. Some chemotherapy drugs can also damage cells in the heart or other organs and tissues.

The number and severity of side effects caused by chemotherapy vary widely across individual patients. Even with the same drug, one patient may experience very few side effects during therapy, while other patients may experience relatively severe ones.

## What Is the Difference Between Short-Term, Long-Term and Late Side Effects?

*Short-term side effects* are toxicities that occur during or shortly after cancer treatment. These side effects usually go away within several weeks after completing treatment, but some may continue for months or several years.

*Long-term side effects* of treatment typically become apparent during cancer treatment and continue for months or several years. Fatigue, effects on concentration and memory, menopausal symptoms, neuropathy, and pulmonary problems are examples of *persistent side effects*.

*Late effects* of treatment become apparent only after treatment has ended and may arise months, years, or even decades after treatment is complete. Infertility, osteoporosis, heart problems, and secondary cancers (such as melanoma) are examples of late effects.

The likelihood of late secondary cancers and cardiovascular toxicities, such as heart attacks and strokes for example, can be increased with the use of radiation therapy, particularly if it is extensive and/or delivered to the chest region. For this reason, the dose and duration of radiation therapy have been reduced in current treatment regimens compared with past treatments. In some cases, it is omitted altogether.

As another example, the combination of the chemotherapy drug doxorubicin (Adriamycin) and radiation, especially when the radiation is directed to the chest area, can lead to late effects on the heart, causing a decrease in heart function and accelerated atherosclerosis (heart disease) in which plaque builds up on the inside of the arteries. These late effects can lead to congestive heart failure or coronary artery disease. These and other types of side effects need to be discussed and looked for after the treatment is over. Because some of these late effects may occur many years after therapy is over, they may require coordination between the cancer treatment team and a primary care doctor and/or clinic.

## What Side Effects Are Caused by Chemotherapy?

Side effects vary depending on the type of chemotherapy. Additionally, these adverse effects can be caused by factors other than chemotherapy.

Some of the most common side effects caused by chemotherapy used to treat patients with HL include:

- Cardiotoxicity (heart toxicity)
- Changes in taste
- Cognitive problems (trouble concentrating, impaired memory)
- Decreased blood cell production leading to anemia; increased risk of infection (due to decreased white blood cells); or bleeding (due to decreased platelets)
- Diarrhea or constipation
- Fatigue
- Hair loss
- Increased chance of infections
- Loss of appetite
- Lung (pulmonary) toxicity
- Mouth sores
- Nausea or vomiting
- Peripheral neuropathy (changes in the sensation, strength in hands or feet)
- Problems with sexual function
- Sterility

Chemotherapy can also cause other side effects, such as cough, skin rashes, general weakness, sore throat, and loss of balance or coordination. Many of these side effects are temporary, but some could last for an extended period.

### *Cardiotoxicity*

*Cardiotoxicity* refers to damage to cells in the heart or heart muscle. Use of certain chemotherapy drugs can cause long-term heart damage in some patients. Doxorubicin is an example of a drug that is possibly cardiotoxic in some patients.

In general, most patients with HL who are treated with potentially cardiotoxic chemotherapy receive these drugs at dose levels and numbers of cycles where cardiac toxicity does not become a problem.

A patient's history of heart disease, high cholesterol, and high blood pressure as well as obesity and lifestyle choices (such as smoking and lack of exercise), may increase the chance of developing chemotherapy-related or radiation-related cardiotoxicity.

Careful monitoring of patients by the healthcare team can reduce the chances of developing cardiotoxicity. Before deciding to treat patients with a potentially cardiotoxic drug, most doctors will have the patient undergo either an echocardiogram (ECHO) or a multi-gated acquisition (MUGA) scan to measure the cardiac function; a cardiac function study may be repeated during therapy (typically after the third or fourth chemotherapy cycle). This treatment will ensure that patients are prescribed a safe chemotherapy dose given their current heart function and that they are monitored more intensively if needed.

### *Changes in Taste*

Some patients will experience a change in the way foods or beverages taste. Familiar foods may taste differently (*dysgeusia*), or the flavors of foods may not be as strong (*hypogeusia*). Some patients commonly find that foods have a metallic taste. These side effects are temporary and usually disappear after the end of chemotherapy. Sometimes this side effect can be helped by dietary changes.

### *Cognitive Problems*

Chemotherapy can result in mild cognitive impairment, such as trouble concentrating, impaired memory, or issues with motor control. Although these side effects can be stressful, they typically disappear over time. If they do not improve with time, it may be helpful for the patient to see a neurologist or undergo neuropsychiatric testing.

### *Decreased Blood Cell Production*

The bone marrow constantly produces red blood cells, white blood cells, and platelets. Some types of chemotherapy and immunotherapy temporarily interfere with the ability of the bone marrow to produce enough of one or more of these different types of blood cells. This is called *myelosuppression*.

To detect myelosuppression, samples of a patient's blood are tested for complete blood count (CBC; which measures the numbers of white blood cells, red blood cells, and platelets) and the differential (which measures the numbers of the different types of white blood cells). These tests are usually done before and sometimes during each chemotherapy cycle. Table 9.1 on the following page describes the four main conditions caused by a decrease in blood cell production.

**Table 9.1 The Four Main Conditions Caused by Decreased Blood Cell Production**

<b>Anemia</b>	<ul style="list-style-type: none"><li>■ This condition is caused by a decrease in the number of red blood cells.</li><li>■ Many chemotherapy drugs cause mild or moderate anemia.</li><li>■ Anemia can make people feel tired and short of breath, especially when it is severe. Although seldom needed, anemia can be treated with red blood cell transfusions.</li></ul>
<b>Lymphopenia</b>	<ul style="list-style-type: none"><li>■ Lymphopenia, also called lymphocytopenia, refers to a decrease in the number of lymphocytes. Lymphocytes produce antibodies that fight bacterial and viral infections.</li><li>■ Patients with low levels of lymphocytes are at risk of new infections and reactivation of old infections. For example, if the patient had chicken pox as a child, which is an infection caused by the varicella virus, he or she could get shingles, which is caused by the latent varicella virus becoming active again, if the patient had low levels of lymphocytes.</li></ul>

**Table 9.1 The Four Main Conditions Caused by Decreased Blood Cell Production** (*continued*)

<b>Neutropenia</b>	<ul style="list-style-type: none"><li>■ Neutropenia refers to a decrease in neutrophils—the primary type of white blood cells that fight bacterial or other infections.</li><li>■ Patients with low neutrophil counts are at risk of serious and even life-threatening infections. Symptoms of infection include fever, chills, and night sweats. A normal white blood cell count ranges from 4,000 to 10,000 cells per microliter. Doctors regularly monitor the <i>absolute neutrophil count</i> (ANC), the number of neutrophils in the peripheral blood. Because patients with an ANC below 500 are at high risk for infection, their doctors may decrease their chemotherapy dosage, delay the next treatment, or add a neutrophil boosting medication, such as filgrastim (Neupogen and Granix) or pegfilgrastim (Neulasta), in order to boost the ANC. Some patients require treatment with antibiotics and hospitalization to prevent or treat infections if it occurs when ANC is low.</li><li>■ For patients with HL, pegfilgrastim (Neulasta) and filgrastim (Neupogen and Granix) or other white blood cell growth factors <b>SHOULD ALMOST NEVER BE GIVEN</b> for patients receiving their first-line chemotherapy treatment (usually ABVD). Although the use of white blood cell growth factors can help to raise the ANC, white blood cell growth factors can also increase the chances that one of the chemotherapy drugs (eg, bleomycin) produces lung problems.</li></ul>
<b>Thrombocytopenia</b>	<ul style="list-style-type: none"><li>■ Thrombocytopenia refers to a decrease in the number of platelets in the blood; platelets help start the clotting process when bleeding occurs.</li><li>■ Patients with low platelet counts may bruise easily; have cuts that bleed for too long or too much; have nosebleeds or bleeding gums or pass blood in their urine; or may bleed from places that have not been injured. Although seldom needed, thrombocytopenia can be treated with platelet transfusions.</li></ul>

## *Diarrhea or Constipation*

Some types of chemotherapy may cause diarrhea or constipation. While most patients do not experience severe diarrhea or constipation, the most important point to remember is to avoid dehydration, which is a loss of body fluids. The doctor should be contacted if the patient has bloody diarrhea or fever with diarrhea. Patients may follow the tips below that outline how to avoid dehydration from diarrhea or vomiting.

**PATIENT TIP**

### **Avoiding Dehydration From Diarrhea or Vomiting**

- Drink plenty of liquids (8 glasses a day), such as water or electrolyte replacement drinks like Gatorade, Pedialyte, and Powerade. Sometimes it helps to drink small amounts very frequently rather than too much at once. Soup, especially broth, is a rich source of nutrients.
- Look for the following signs of dehydration: dry mouth or skin, decreased urine, or feeling dizzy or lightheaded when you stand up.
- Do not drink or eat dairy products when diarrhea occurs because they can worsen the diarrhea. However, dairy products are a good source of calcium and should be included in the diet at other times.
- Do not eat high-fiber and other hard-to-digest foods because they can worsen diarrhea.
- Eat plenty of bananas and other high-potassium foods (check with your doctor or dietitian to make sure these foods will not interfere with your chemotherapy or other medications you are taking).
- Include fresh fruits and vegetables in your diet to prevent constipation and provide a good supply of vitamins and minerals.
- Take the medicines that your doctor recommends to control diarrhea or vomiting (call your doctor if symptoms persist).

## *Fatigue*

Fatigue is a common side effect of many types of chemotherapy. Fatigue should decrease after patients have completed their lymphoma treatment, but it could take weeks or months until they return to their normal energy levels. Patients may use the tips below to help them cope with fatigue.

**PATIENT TIP**

### **Coping With Fatigue**

- Keep a diary to help keep track of when you have the most energy and which activities make you feel tired or give you energy. Use this information to plan your activities for the times when you have the most energy.
- Ask for help.
- Exercise if your doctor says it is okay to do so, but do not overdo it. Try simple stretching and range-of-motion exercises or a short walk; these activities may energize you without tiring you out. Start slowly and build up to the level that is right for you. Ask your doctor, nurse, or physical therapist to help you create a personalized exercise plan.
- Rest and sleep during therapy are very important, but do not rest more than you need because it may decrease your energy levels. An afternoon nap helps many patients feel less tired for the rest of the day. Other patients cannot sleep at night if they nap during the day. If you have trouble sleeping, talk to your healthcare team to find out why and what you can do about it.
- Be patient. These symptoms usually improve once treatment is completed.

## Hair Loss

Certain chemotherapy drugs can cause thinning or loss of hair (*alopecia*) anywhere in the body including the scalp, eyebrows, eyelashes, arms, legs, and pelvis. The amount of hair loss varies, but most chemotherapy results in alopecia.

If hair loss occurs, it often starts two or three weeks after the first chemotherapy treatment. Remember that hair loss caused by chemotherapy is usually temporary. Hair will probably grow back after the end of chemotherapy treatments. When the hair first grows back, it may have a slightly different texture or color than it had before treatment. Over time, the texture and color often return to normal. Patients may follow the tips below for managing chemotherapy-induced hair loss.

### Managing Chemotherapy-Induced Hair Loss

- After washing your hair, pat it dry instead of rubbing it with a towel.
- Brush your hair with a soft-bristle brush or a wide-tooth comb.
- Do not use curlers or hair dryers.
- Do not color or perm your hair, or treat it with other chemicals.
- Many patients choose to use a wig, scarf, turban, soft cotton hat, or head wrap. Some health insurance companies cover the cost of wigs if you have a doctor's prescription. Check your policy to see if it covers this cost.
- Use a hat or scarf to protect your scalp when you are out in the sun and to help keep you warm when you are indoors.

PATIENT TIP

## *Infections*

Some types of treatments can lower a patient's ability to prevent infections. Patients are at increased risk for viral infections, particularly shingles (herpes zoster), characterized by blisters on the skin. Sometimes the doctor will prescribe medication to prevent a shingles outbreak during therapy. Most outbreaks of shingles are short-lived, but the residual pain could last for an extended period.

Patients with a fever of 100.5°F or greater should call a healthcare provider or go to the emergency room. They should ask their provider what to do if they have a sore throat, rash, diarrhea, cough, or redness, swelling, or pain around a wound. The doctor should be contacted if the patient experiences any painful local rash with or without blisters.

To reduce or prevent the risk of infections, patients may be prescribed antibiotic medications. Other ways to reduce the risk of infections are included below.

### PATIENT TIP

#### **Reducing Your Risk of Serious Infection During Chemotherapy**

- Check with your doctor to ensure your vaccinations are up to date before starting treatment.
- Wash your hands diligently and regularly.
- Avoid crowds, especially during times in which influenza is prevalent in the community.
- Cook all food; avoid raw foods that may carry germs, as your body is more sensitive to them.
- Avoid fresh flowers (the water they're in may harbor bacterial overgrowth).
- Avoid swimming.
- Do not sleep with pets.

### *Loss of Appetite*

Loss of appetite is sometimes a symptom of the lymphoma or may be a side effect of chemotherapy. Patients may eat less than normal, not feel hungry, or feel full after eating only a small amount of food. Ongoing loss of appetite can lead to weight loss and poor nutrition, which can become serious. Side effects from chemotherapy, such as nausea and vomiting, mouth sores or pain, fatigue, depression, or dry mouth and difficulty swallowing, can all contribute to a patient's loss of appetite. The patient's healthcare team should be notified about lack of appetite to determine the underlying cause. Loss of appetite can be managed by changing eating habits, such as eating several small meals each day and making nutritious food choices. Despite these effects on appetite, weight gain is a common occurrence with many chemotherapy regimens, likely because of less healthy food choices or less physical activity than one is typically used to pursuing. For more information on nutrition, please view the *Nutrition* fact sheet on the Lymphoma Research Foundation's (LRF's) website at [www.lymphoma.org](http://www.lymphoma.org).

### *Lung (Pulmonary) Toxicity*

Damage to the lungs is a serious side effect that can be caused by bleomycin-containing chemotherapy regimens. Patients should report any changes in lung function, such as cough, chest pain, or shortness of breath to their doctor, who may decide to monitor their lung health by regularly performing pulmonary function tests (PFT) during the course of chemotherapy.

## Mouth Sores

Some chemotherapy drugs can cause a patient's mouth to become red, sore, or irritated, which is called *mucositis*. Additionally, some patients undergoing chemotherapy become more susceptible to viral or fungal infections of the mouth and throat.

The doctor should be informed if the patient develops a sore throat. The doctor will examine the patient's throat and may take a swab that will be sent to the laboratory to check for infection. Several medications are available to treat different types of infections. To help decrease chances of infection, patients should have a complete dental checkup and cleaning before starting chemotherapy. Patients may use the tips below for preventing and caring for mouth sores caused by treatment.

### PATIENT TIP

#### Preventing and Caring for Mouth Sores

- Clean your mouth and teeth. Use a soft-bristle toothbrush, nonabrasive toothpaste, and lip moisturizer.
- Do not use mouthwashes that contain alcohol. Your doctor or nurse may recommend a mouth rinse.
- Do not eat citrus fruits (such as oranges, grapefruit, lemons, or clementines) or drink citrus juices, and be cautious with other acidic foods such as products that include tomatoes.
- Do not eat spicy foods.
- Eat soft foods while you are receiving chemotherapy to avoid bruising your gums and other soft tissues in your mouth.
- Do not floss your teeth if your blood counts are low, as it may cause your gums to bleed.

## *Nausea or Vomiting*

Many chemotherapy drugs can cause nausea or vomiting, which can occur during chemotherapy infusion or even days later. The doctor usually prescribes a drug that prevents nausea and vomiting (*antiemetic*) before chemotherapy and often after therapy is complete. Examples of antiemetics include: aprepitant (Emend), ondansetron (Zofran), granisetron (Kytril), metoclopramide (Reglan), prochlorperazine (Compazine), and dolasetron (Anzemet), and a variety of corticosteroids, such as prednisone (Deltasone) or dexamethasone (Decadron). In most cases, these antiemetics are able to partially or completely prevent nausea and vomiting. Patients may follow the tips below for controlling or minimizing nausea and vomiting.

**PATIENT TIP**

### **Controlling or Minimizing Nausea and Vomiting**

- Before chemotherapy, drink a liquid diet, such as broth, consommé, or water. Do not drink milk or have a meal in which the main ingredients are dairy products.
- Do not eat foods that are too hot or too cold, greasy or fatty, or sweet or spicy.
- Eat smaller and more frequent meals instead of fewer large meals each day.
- Avoid strong or offensive smells. Get plenty of fresh air.
- Take prescribed antiemetics before chemotherapy to prevent nausea.
- If you vomit, make sure to avoid becoming dehydrated.
- Finding the best approach is often a process of trial and error. Try different approaches to determine what works best for you.

### *Peripheral Neuropathy*

Some chemotherapy drugs may damage the nervous system by affecting signaling between the central nervous system (CNS; the brain and spinal cord) and the rest of the body through all the nerves that make up the peripheral nervous system. This damage may cause *peripheral neuropathy* symptoms, such as numbness, a tingling or prickling sensation in the fingers and/or toes, sensitivity to touch, pain, and muscle weakness. Other signs of neuropathy can include change in voice or constipation and should be reported to the healthcare team.

### *Problems With Sexual Function*

Psychological factors, such as fear about illness, altered body image due to hair loss and depression, and the physical side effects of treatment can cause a drop in sex drive (*libido*). However, a normal libido usually returns after treatment is finished. Patients should not be embarrassed to talk with their doctor about any problems or concerns they have about changes in their libido or sexual function. The doctor might order tests to track hormone levels, recommend seeing a specialist, or prescribe medications to restore erectile function in men or hormone therapy to alleviate vaginal dryness and other menopausal symptoms in women.

### *Sterility*

Because chemotherapy and radiation may damage sperm and egg cells, these treatments can sometimes cause temporary or permanent *sterility* (the inability to have children) in both men and women. The potential for developing sterility depends on the treatment type and specific dose, the number of therapies given, and the patient's age at the time of treatment. There are options available to help preserve fertility including possible protection of the ovaries, cryopreservation of sperm cells and egg cells, or in vitro-fertilized embryos. Patients should speak with their doctor about fertility preservation as early as possible before beginning treatment. Even though a patient may just be starting to learn about the diagnosis of HL, it is okay to talk about fertility at the first visit with the cancer team. For more information and

resources about sterility, visit LRF's web page on "Fertility" available at [www.lymphoma.org/fertility](http://www.lymphoma.org/fertility).

Patients receiving chemotherapy and/or radiation should always use birth control because these treatments may harm the fetus or cause birth defects.

### **What Side Effects Are Caused by Steroids?**

Corticosteroids, such as prednisone and dexamethasone, are sometimes given with chemotherapy for their anti-lymphoma effects or for other reasons, such as for nausea or before a monoclonal antibody infusion. Dexamethasone, prednisone, and other corticosteroid drugs can cause side effects, such as *insomnia* (the inability to fall asleep), increased appetite, mood or personality changes, anxiety, high blood pressure, fluid retention, and weight gain.

Prednisone can also trigger diabetes in patients prone to that disease or worsen diabetes in patients who already have the disease. High doses of steroids can also cause osteoporosis in at-risk patients. Patients should alert their family and friends that personality changes may occur during their treatment. Patients should avoid making hasty decisions. If personality changes do occur, the doctor should be informed, as the dose may need to be reduced.

### **What Side Effects Are Caused by Monoclonal Antibody Therapies?**

The monoclonal antibodies used to treat patients with HL may cause side effects similar to other forms of chemotherapy, such as low blood cell counts and infusion reactions, which are usually mild but could become life threatening. Other rare, but potentially very serious, side effects include unusual infections.

### *Infusion Reactions*

When infusion reactions occur, they typically happen during or within 24 hours after the infusion and are most likely to happen in association with the first infusion. Symptoms of infusion reactions include dizziness, fainting, headache, feeling warm or flushed, fever or chills, hives, itching, shortness of breath, changes in heart rate and blood pressure, pain in the back or abdomen, and swelling of the face, tongue, or throat.

To prevent infusion reactions, patients are given antihistamines (Benadryl) and acetaminophen (Tylenol) and sometimes corticosteroids, before the antibody infusion. Nurses should closely monitor patients during the infusions. Patients should report any new symptom they experience during or after an infusion as soon as it occurs.

### *Hepatitis*

Reactivation of hepatitis B virus (HBV) infection is a rare but very serious side effect of rituximab (Rituxan) therapy, which is used in patients with NLPHL. People may not know they have HBV because a healthy immune system can force the virus to hide without causing noticeable symptoms. Treatment with the CD20-directed monoclonal antibodies or chemotherapy can wake up the virus. If unchecked, this reinitiation of HBV infection can cause acute liver failure and possibly death. To prevent HBV from reinitiating, patients may be screened for HBV before chemotherapy or monoclonal antibody treatment. Patients who have the virus are closely monitored during and after treatment or may need to take medication to prevent reactivation of the hepatitis virus. Patients should be mindful of signs of an active HBV infection, such as increasing fatigue and yellowing of the skin or eyes.

## What Side Effects Are Caused by Brentuximab Vedotin (Adcetris)?

The most common side effects reported in patients treated with brentuximab vedotin include depressed immune system, low blood counts, *peripheral neuropathy* (numbing or tingling in the hands and/or feet), fatigue, nausea, anemia, upper respiratory tract infection, diarrhea, fever, rash, thrombocytopenia, cough, and vomiting. Patients may also experience reactions at the site of the treatment infusion.

## What Side Effects Are Caused by Radiation Therapy?

Radiation therapy itself is painless, but it can cause short-term and long-term side effects, which vary depending on the type and location treated with the radiation, the radiation dose used, and the area of the body treated. Side effects are usually worse when radiation therapy and chemotherapy are given at the same time.

Some of the short-term side effects caused by radiation therapy used to treat patients with HL include:

- Cardiovascular damage
- Dry mouth
- Fatigue
- Loss of appetite and taste
- Nausea
- Skin reactions
- Throat irritation
- Mouth or throat pain secondary to *mucositis* (tissue swelling in your mouth)

Examples of some of these potential short-term side effects of radiation therapy are shown in the box on the following page.

## Examples of Potential Short-Term Side Effects of Radiation Therapy

- Nausea, vomiting, and diarrhea due to radiation to the stomach area.
- A dry, sore throat, mouth sores, and trouble swallowing due to radiation to the chest and neck.
- Hair loss in the area, and red, dry, tender skin may occur due to radiation to any area of the body.
- Decreased levels of red blood cells and white blood cells may occur due to radiation to the pelvis, legs, and torso (the large areas of your body that contain most of your blood-producing bone marrow).
- Fatigue, which may progressively worsen during the later weeks of the treatment cycle, may occur due to radiation to any part of the body.

### *Dry Mouth*

Patients who receive radiation therapy to the mouth may experience a temporary decrease in saliva production, or dry mouth (*xerostomia*). Dry mouth may result in difficulty swallowing foods or thick liquids. Dry mouth can also cause food particles to stick to the teeth and gums. Because saliva helps prevent cavities, doctors may advise patients to visit the dentist for fluoride treatments before they start radiation therapy. In some cases, dry mouth may be a more permanent toxicity.

### *Fatigue*

The likelihood that patients will experience fatigue depends on their disease and their specific radiation plan. Techniques for coping with fatigue are included on page 94.

### *Loss of Appetite and Taste*

During radiation treatment, patients might lose their appetite for foods they normally enjoy. The loss of appetite and taste are usually short-term problems. Patients should remember to eat well because their body needs energy and good nutrition to heal. Eating four or five small meals a day may be more comfortable than eating two or three larger meals. Patients should ask their healthcare team for information on how to maintain a healthy diet during treatment.

### *Nausea*

Radiation treatment can cause nausea, especially in patients who receive radiation to the abdomen. Not eating (especially sweet, spicy, or fatty foods) a few hours before radiation therapy may help avoid nausea. The doctor may prescribe an anti-nausea (*antiemetic*) medication to be taken before each radiation therapy session. Techniques for coping with nausea are included on page 99.

### *Throat Irritation*

Radiation therapy to the neck, throat, or chest may cause sore throat, dry mouth, nausea, and/or cough. Patients may have difficulty eating or swallowing, especially toward the end of their treatment regimen. Patients should tell their doctor if swallowing becomes difficult, as there are treatments for the discomfort. Difficulty swallowing will usually go away a few weeks after treatment is completed. Patients may follow the tips on the following page to help ease throat irritation during radiation therapy.

## Easing Throat Irritation During Radiation Therapy

- Eat bland foods that are soft, smooth, and easy to digest, such as pudding, yogurt, and milkshakes.
- Take small bites and swallow each bite completely before taking another bite.
- Try drinking thicker liquids, such as fruit that has been pureed in a blender, which are easier to swallow than thin liquids.
- Avoid citrus fruits, especially juices.

### *Skin Reactions*

Radiation therapy can cause skin changes to the affected area, such as redness, itchiness, dry and peeling skin, sores or ulcers, swelling, and puffiness. These skin changes usually decrease and disappear over a few weeks after the radiation therapy ends. Some skin changes may last much longer or be permanent. These changes include darker and blotchy skin, very dry skin, or thicker skin. The radiated area will sunburn more easily than other parts of the body. Avoid tanning beds and protect skin from the sun with a hat, long sleeves, long pants, and sunscreen with an SPF of at least 30. Moist areas, such as around the mouth, may be more prone to irritation; the doctor may recommend zinc oxide ointment for these areas. The patient's skin could look and feel as if it was sunburned, and it may eventually peel.

Patients should speak with the doctor or nurse if they experience any skin changes. They can also use the list of tips on the following page to care for their skin during and after radiation therapy.

## Skin Care During and After Radiation Therapy

- Be gentle with your skin; do not rub, scrub, or scratch.
- Use lotions and other skin products your doctor prescribes or your nurse suggests.
- Do not put anything on your skin that is very hot or cold (such as heating pads or ice packs).
- Take a shower or bathe in lukewarm water; if you bathe, do it every other day and soak for less than 30 minutes; always use a mild, unscented soap; pat your skin dry; do not wash off the ink markings needed for radiation therapy.
- Check with your doctor or nurse before using bubble bath, cornstarch, cream, deodorant, hair removers, makeup, oil, ointment, perfume, powder, and sunscreen.
- Wear soft clothes and use soft sheets, such as those made with cotton.
- Do not wear tight clothes because they do not allow your skin to breathe.
- Add moisture (humidity) to the rooms in your home by placing a bowl of water on the radiator or using a properly cleaned and maintained humidifier.
- Do not sunbathe; protect your skin from the sun every day (use a wide-brimmed hat, long-sleeved shirt, and long pants or skirt outside).
- Do not use tanning beds.
- Do not put adhesive tape or bandages on your skin. Ask your nurse about ways to bandage without tape.
- Ask your doctor or nurse if you may shave the affected area; shave with an electric razor and do not use pre-shave lotion.
- Report any skin changes you notice to your doctor or nurse.

## Will Radiation Treatment Make the Body Radioactive?

External beam radiation does not cause a patient's tissues to become radioactive. In some cases, the patient will remain in the hospital and shielded from others during short exposures to internal radiation therapy. With permanent internal radiation and systemic radiation treatment, patients will be sent home emitting low levels of radiation, especially through bodily fluids. In these cases, patients should avoid contact with pregnant women and young children. The healthcare team will provide more information to patients, family members, and caregivers about special precautions that should be taken. The radioactivity will break down over time to the point where no radiation can be measured outside the patient's body.

## What Long-term and Late Side Effects Are Caused by Treatment For HL?

In addition to the short-term side effects caused by chemotherapy or radiation, these treatments can cause long-term and late side effects that may not show up for years or even decades after the initial treatments.

### *Cardiovascular Damage (sometimes called cardiotoxicity)*

Some types of chemotherapy such as doxorubicin (Adriamycin) or radiation therapy to the chest area can cause damage to the muscle tissue in the heart or to the arteries, most commonly those in the neck (carotid arteries) and in the heart (coronary arteries), which could increase the risk of heart attack and stroke. Patients treated with doxorubicin or radiation to the chest should speak with their doctors about whether they should have regular evaluations to check for heart damage.

In general, most patients with HL treated with potentially cardiotoxic chemotherapy receive these drugs at dose levels and numbers of cycles where cardiac toxicity is usually not a problem.

The presence of high blood cholesterol, high blood pressure, obesity, and lifestyle choices (such as smoking and lack of exercise) may increase the chance of developing chemotherapy-related or radiation-related cardiotoxicity.

Careful monitoring of the patient by the healthcare team can reduce the chances of developing cardiotoxicity. Before deciding to treat patients with a cardiotoxic drug, most doctors will have the patient undergo either an ECHO or a MUGA scan to measure their cardiac function. The results from this scan will ensure that patients are prescribed a safe chemotherapy dose given their current heart function and that they are monitored more intensively if needed.

### *Secondary Cancers*

The risk of developing secondary cancers from chemotherapy or radiation therapy depends on factors such as the type of chemotherapy or the amount of radiation given (the dose), the age of the patient, and the part of the body treated (the field). Most information currently available is from studies when higher doses of radiation were used and larger areas of the body were treated within the radiation fields. Newer methods of radiation therapy limit the amount of healthy tissue exposed to radiation; while these approaches appear to decrease the risk of secondary cancers, the absolute risk after reduced-dose and reduced-field treatments is unknown.

Most secondary cancers can develop more than 10 years after the completion of treatment, and the risk may be higher when radiation therapy is used as part of *first-line* (initial) treatment. Lung cancer and breast cancer are the most common secondary cancers in patients with HL. Recommendations include:

- Low-dose computed tomography (CT) for patients at increased risk for lung cancer should be performed for high-risk individuals following the recommendations of evidence-based guidelines.

- Annual breast screening should be performed for standard-risk women following the recommendations of evidence-based guidelines. Annual breast screening with or without magnetic resonance imaging (MRI) for women at higher risk for breast cancer (eg, those who had radiation to the chest) should generally start at a younger age and be discussed with the care team. Regular follow-up and monitoring in a high-risk breast clinic is appropriate for many women.

### What Side Effects Are Caused by Stem Cell Transplantation?

Patients treated with high doses of chemotherapy and/or radiation before undergoing a stem cell transplant are at increased risk for developing infection, bleeding, and other side effects as described previously (see the previous sections “What Side Effects Are Caused by Chemotherapy?” on page 88 and “What Side Effects Are Caused by Radiation Therapy?” on page 103).

Patients receiving high-dose chemotherapy with autologous stem cell transplantation are followed carefully for the first three to four weeks because of the risks of mouth sores (mucositis), infection, anemia, and bleeding. Transfusions and antibiotics may be necessary, which are often administered in the hospital.

Patients receiving stem cells from a relative or unrelated donor (allogeneic transplantation) are also at risk of developing graft-versus-host disease (GVHD), a condition where the donated bone marrow attacks the patient’s tissues. GVHD can occur at any time after the transplant. Drugs can be used to reduce the risk of developing GVHD or to treat the condition once it develops.

## When Should a Patient's Doctor Be Contacted?

As a general rule, a patient's doctor should be contacted if:

- The patient experiences a side effect that is unexpected or lasts longer than expected.
- The patient experiences a medical problem—such as high fever, shortness of breath, prolonged or constant nausea and vomiting, chest pains, and/or dizziness—that cannot wait for a regularly scheduled appointment.

# Part 3 — Living With the Side Effects of Treatment

## Chapter 10: Managing Life During and After Treatment

This chapter discusses some general issues that patients may encounter while they live their life during and after treatment.

### Coping Strategies

Each person's experience with cancer is different, and how he or she copes with the physical and emotional impacts of having Hodgkin lymphoma (HL) is unique to a patient's personality and situation. Table 10.1 lists some suggestions for how to cope with some issues that patients may face.

**Table 10.1. Coping Strategies**

<b>Maintain a Strong Support System</b>	<ul style="list-style-type: none"><li>■ Communicate your fears and concerns about your disease by talking to your family, friends, doctors, and counselors.</li><li>■ Writing down your concerns in a journal may also help.</li><li>■ Find a support group or other individuals who are also coping with cancer.</li></ul>
<b>Get Help For Depression</b>	<ul style="list-style-type: none"><li>■ Feeling sad or depressed is not unusual in patients living with cancer.</li><li>■ Watch out for signs of depression: sleeping more or less than usual; feeling a lack of energy; crying; inability to concentrate.</li><li>■ Ask for a referral to a psychiatrist, social worker, psychologist, or counselor who can help you cope with your feelings through talk therapy, medications, or both.</li><li>■ Find a support group of people who have had similar experiences.</li></ul>

**Table 10.1. Coping Strategies** (*continued*)

<b>Deal With Physical Changes</b>	<ul style="list-style-type: none"><li>■ Some patients with cancer may feel unattractive because of hair loss and other changes in appearance caused by their treatment.</li><li>■ Ask your doctor what changes you should expect; plan ahead and buy a wig or head covering if hair loss is a possibility.</li><li>■ Seek advice from a beautician about makeup for the areas that you consider a problem.</li><li>■ Ask your healthcare team for advice on how to manage temporary changes, such as dry skin, brittle nails, and a blotchy complexion.</li></ul>
<b>Maintain a Healthy Lifestyle</b>	<ul style="list-style-type: none"><li>■ Eat a healthy diet that includes fruits, vegetables, proteins, and whole grains.</li><li>■ Engage in regular physical exercise, which can help reduce anxiety, depression, and fatigue, and improve mood.</li><li>■ Get sufficient rest to help combat the stress and fatigue of your disease and its treatment.</li><li>■ Quit smoking and reduce alcohol consumption.</li></ul>
<b>Set Reasonable Goals</b>	<ul style="list-style-type: none"><li>■ Having goals for how you want to live your life during and after treatment can help you maintain a sense of purpose.</li><li>■ Avoid setting unreasonable goals, such as deciding to work full-time when part-time would be much better for your health.</li><li>■ Stay as active and involved as you can in work and other activities that interest you.</li></ul>

## The Importance of Pain Control

In some situations, patients may experience pain from the cancer itself or from treatments and procedures. Cancer pain is very treatable, and there is no reason for a patient to endure this pain without help. Patients should tell their doctors and nurses if they have any pain because they can offer advice regarding medications and other ways to relieve the pain, as some medications may not be appropriate for their disease.

Different types of pain are best controlled by different types of pain relievers. Patients should ask their healthcare team which options are best to help manage their pain. They can follow the tips below for managing their pain.

PATIENT TIP

### Managing Pain

- Tell your doctor or nurse about your pain. Be specific when you describe it.
  - Where do you feel the pain?
  - When did the pain start?
  - What type of pain is it (sharp, dull, throbbing)?
  - Does it come and go, or is it steady?
  - How strong is it? How long does it last?
  - Does anything make the pain feel better or worse?
  - Which drugs have you taken for the pain? Do they help? If so, for how long?
- Take your pain medication on a regular schedule even if the pain seems to be better. Do not skip doses.
- Tell your family and friends about your pain so they can help you and understand why you may be acting differently.
- Try deep breathing, yoga, or other ways to relax.
- Ask to meet with a pain specialist or palliative care specialist to help you find better ways to control your pain.
- Tell your doctor or nurse of any changes in your pain.

## Maintain a Healthy Lifestyle

Regular physical activity helps keep the cardiovascular system strong and body muscles flexible. Exercise can also help patients to alleviate breathing problems, constipation, and mild depression. Additionally, it may help them to reduce stress and fatigue. Patients should talk to their doctor before starting an exercise program and consider visiting a physical therapist for advice.

Several types of exercise are particularly helpful, including:

- General physical activity, such as swimming, dancing, household chores, and yard work
- Aerobic activity to improve cardiovascular fitness, such as walking, jogging, and bicycling
- Resistance training to strengthen muscles, protect joints, and help remedy osteoporosis by building bone mass
- Flexibility exercises, such as stretching and yoga, to improve range of motion, balance, and stability

Eating a healthy diet is especially important during treatment for HL because it will help patients keep up their strength and energy, tolerate treatment-related side effects, decrease their risk of infections, and heal and recover more quickly. Patients should aim for a diet high in fruits and vegetables, protein (poultry, fish, and eggs), and whole grains. During chemotherapy and after a stem cell transplant, a patient may be asked to temporarily avoid raw fruits and vegetables that may increase the risk of infection if they have a low white blood cell count (“neutropenic diet”). The healthcare team can help develop an eating plan that is appropriate. Patients should talk to their doctor before taking any dietary supplements such as multivitamins or individual vitamin supplements, as well as any herbal or “natural” supplements, because they may interfere with treatments or have unexpected side effects.

## The Importance of Follow-up Care

At the first visit following the completion of treatment, patients should discuss their follow-up schedule with the doctor. This schedule will be different for each patient depending on his or her disease type and stage, age, and overall health. Patients should adhere to their schedule of follow-up visits—these are very important for monitoring disease recurrence and detecting and treating any new health problems that might have been caused by the treatment.

During these follow-up visits, the doctor will ask about any medical changes since the last appointment and give a physical examination. The doctor may also prescribe blood, molecular diagnostic, imaging, or other laboratory tests.

## Be Proactive in Healthcare Decisions

To stay proactive in healthcare decisions, patients should write out their questions and bring them to their appointments, take notes during their visit, and obtain the following information from their medical team:

- Copies of all medical records and a written summary of their treatment(s) in case the patient switches doctors or needs to see a primary care physician for routine medical care
- A list of signs of disease recurrence and late side effects from treatment

At the follow-up care appointments, patients should inform their doctor of:

- Any new symptoms
- Pain
- Physical problems that disrupt their daily life, such as fatigue, insomnia, sexual dysfunction, and weight gain or loss
- Any new health problems such as heart disease, diabetes, and high blood pressure
- Any new medications and vitamins they are taking
- Emotional problems, such as anxiety and depression
- Any other questions or concerns

## Part 4 — Hospital Admission

### Chapter 11: Preparing to Go to the Hospital

#### What Are Some Reasons That Patients May Be Admitted to the Hospital?

Hospital admission usually occurs either in the emergency room or through direct admission by the patient's doctor for diagnostic testing or for treatment, if needed. In the case of a direct admission, the patient has seen their doctor and he/she feels that the patient should be admitted to the hospital. The doctor will call ahead and reserve a bed for the patient.

Most doctors make daily visitation rounds at about the same time each day. The nurse can tell you when the patient's doctor usually makes rounds. It is a good idea for family members to know when the doctor is likely to be making visitation rounds so they can be there to ask questions.

Whether admitted through the emergency room or a direct admission, patients will probably first be evaluated by a hospitalist. Hospitalists are employed by the hospital, or are private doctors consulting for the hospital. Their specialty is typically internal medicine. Patients will also be assigned a case manager (usually a nurse) who will work with the patient's healthcare team.

#### What Should Patients Bring With Them When Being Admitted to the Hospital?

When being admitted to the hospital, being prepared can ease the process of admission and positively impact patients' care. The following page provides a brief list of items for patients to take with them.

## What to Bring if You Are Being Admitted to the Hospital

- Identification (driver's license, student ID) and emergency contacts (relatives and friends names and phone numbers).
- List of all allergies and the reaction that occurs in response to allergen exposure (especially important for latex and pharmaceutical allergies).
- List of all current medications (name, strength, frequency) and "treatments" (include over-the-counter medications, such as Tylenol, vitamins, herbals, and any other items such as energy enhancers) If you do not have a list, place all medications in a bag and bring them with you.
- List of **all** medical conditions (name all conditions, not just cancer, for example: hypertension, epilepsy, active ulcer).
- List **all** surgeries (even elective plastic surgeries) regardless of how long ago they occurred.
- Name all physicians currently treating you.
- Copy of any completed advance directives (for more information see the following section describing Advance Healthcare Directives).
- All insurance cards, a checkbook and/or a credit card.

**Do not bring valuables. Leave money and jewelry at home.**

If the patient has access to an up-to-date and complete medical record through a patient portal, flash drive, or phone app, bring the security code for these medical records and the name of the website, or the flash drive or phone app or device that contains the health information.

## What Is the Purpose of an Advance Healthcare Directive and Appointing a Healthcare Proxy?

Having an *Advance Healthcare Directive* (a living will) and appointing a healthcare proxy is important for all adults to consider, not just people with cancer, because accidents and other unforeseen circumstances can happen at any time.

Writing down wishes for critical medical care in an Advance Healthcare Directive is a way to formally tell the doctor, family members, and friends about healthcare preferences and what special treatments someone does or does not want if they become critically ill or injured and are unable to make and communicate their decisions.

Besides stating medical care instructions, people may also consider naming a *healthcare proxy*, or a decision maker, in an Advance Healthcare Directive. This person should be someone who will carry out their wishes, including any do-not-resuscitate (DNR) instructions. It is best to have both an Advance Healthcare Directive and a healthcare proxy.

Before writing an Advance Healthcare Directive, it is important to understand patients' rights and laws regarding Advance Healthcare Directives in each state. Consulting an attorney can provide legal information, but an attorney is not required to write an advance directive. An Advance Healthcare Directive may include:

- Specific instructions on medical care, including the type of special treatment that is or is not desired, such as cardiopulmonary resuscitation (CPR), artificial respiration, drugs to make the heart function, kidney dialysis, artificial feeding, and certain surgical procedures
- A choice of a healthcare proxy

For more information about Advance Healthcare Directive laws for your state, please visit the “Planning Ahead” section of the National Hospice and Palliative Care Organization website at [www.caringinfo.org](http://www.caringinfo.org).

## What Are Patient’s Rights?

A patient’s rights are listed in the hospital’s Patient’s Bill of Rights. See the tips below for more information about these rights.

PATIENT TIP

### Your Rights As a Patient

- You must be given a medical screening examination and be evaluated for care whenever you are admitted to a hospital.
- You have the right to considerate and respectful care.
- You have the right to complete information regarding all aspects of your current condition.
- You have the right to know the names of all doctors and healthcare personnel providing your care.
- Sufficient information about the benefits and risks for all treatments or procedures to enable you to provide informed consent.
- You have the right to refuse any treatment.
- You have the right to privacy—none of your healthcare team can talk about your condition.
- If you must be transferred to another facility, the information on why you require transfer must be provided and the institution that you are being transferred to must have accepted you prior to transfer.
- You also have a right to know whether the hospital has any relationship to other healthcare or educational institutions and if/how this relationship impacts your care.

## Your Rights As a Patient (*continued*)

- You have the right to be informed about your continuing healthcare requirements after you are discharged.
- You have the right to examine and receive an explanation of your bill.
- You have a right to know what hospital rules and regulations apply to your conduct.

## What Do Patients Need to Know About Informed Consent Documents When in the Hospital?

If the patient is admitted to a teaching hospital, he/she may receive informed consent documents. These documents should enable patients to decide which treatments/procedures they are willing to receive. Signing these documents indicates that the patient understands the risks and benefits of the treatments/procedures being performed. The tips below will help patients know what to look for in informed consent.

### What to Look For On the Hospital Informed Consent Document

- Read the informed consent documents carefully.
- Request an explanation of anything you do not completely understand.
- Be sure to determine whether you are being enrolled in research.
- Treatment alternatives should be covered as well so you are aware of all options.
- Names of the physician(s) performing your treatments and/or procedures and the risks and benefits of the treatments/procedures you are agreeing to.
- Identify what will be done with any tissue/fluid samples and photos or videos (if taken).

**PATIENT TIP**

Part 4

## What Do Patients Need to Know at Discharge?

When the patient is to be discharged, make sure the case manager addresses the issues identified in the following Patient Tip.

PATIENT TIP

### Issues For the Case Manager to Resolve Before Discharge

- Are there any new limitations to what you can do at work or at home? If so, your doctor can provide a note for your employer if needed.
- Will you need physical therapy to maintain functions?
- If you need any new medical equipment, where can it be obtained? Who will order it? Obtain a phone number to ensure you can follow up if there are any problems with equipment delivery.
- Will you need home nursing care or other arrangements?
- What new medication will you need to take, and for how long?
- Does your insurance cover the new medication as an outpatient? If not, or if you don't have insurance, what will the cost be?
- If you don't have insurance, does the hospital have a sliding-scale fee or charity care?
- Are there alternative medications if the cost is beyond your capacity to pay?
- What are the side effects of the new medications?
- Will they interact with any medications you currently are on?
- Are there other instructions from your doctor or the hospital physician?
- Whom should you follow up with and when?
- If you are to schedule your own follow-up, whom do you call?
- Who is responsible for paying for your care?

For itemized bills, make sure no mistakes were made. If there are discrepancies in the bill and the care patients receive, bring it to the attention of both the hospital and the insurance company.

### **Should Patients Look For An Opportunity to Provide Feedback on Their Stay?**

Hospitals may send patient satisfaction surveys to patients after discharge. This survey is an opportunity for patients to share issues they had with their care during their stay and/or to recognize those staff members whose care and support they felt were exceptional. Believe it or not, hospitals and their administrators pay close attention to these surveys so it is worth the time to complete and return the survey so issues can be addressed and staff members providing excellent care can be acknowledged. If no survey is sent and you still want to report problems or satisfaction with the patient's care, you can write a letter to the hospital administrator or appropriate department director.

## Part 5 — Clinical Trials and Advances in Treatment

### Chapter 12: Overview of Clinical Trials

Although the cure rate in Hodgkin lymphoma (HL) is already high, researchers continue to look for ways to treat the minority of patients whose disease is resistant (*refractory*) to treatment. Ongoing research also continues to find ways to refine currently available treatments by limiting their toxicity and potential for causing secondary illnesses. Researchers are also trying to develop improved targeted drugs that cause less damaging side effects.

There are hundreds of HL clinical trials now underway in hospitals, cancer centers, and doctors' offices around the country. The government, pharmaceutical and biotechnology companies, universities, and doctor groups often sponsor clinical trials.

#### What Is a Clinical Trial?

A *clinical trial* is a carefully designed research study that involves people who volunteer to participate. Clinical trials are also sometimes referred to as clinical studies. However, the term “clinical study” is broadly used to describe many different types of studies in addition to those described in this chapter.

The purpose of clinical trials in cancer is to answer specific questions about new ways to prevent, diagnose, treat, or manage a disease or the side effects caused by a new or existing treatment. The investigators in clinical trials want to determine the safety and effectiveness of the treatment being investigated by making specific assessments before, during, and after the trial. Strict rules and oversight procedures make sure that clinical trials are designed and run in a way that protects the rights and safety of the people who volunteer to participate. It can sometimes take years for a clinical trial to be completed and for the results to be compiled and published.

In the United States, a new drug must pass through a strict approval process governed by the U.S. Food and Drug Administration (FDA) before it can become a standard therapy for use in people. The FDA-regulated approval process for drugs includes preclinical studies (done in laboratories) and clinical trials (done in hospitals and clinics). In addition to the FDA, all trials must be approved by an institutional review board (IRB) consisting of experts and lay persons to determine the correctness of the study.

As shown in Table 12.1, there are four main types (or phases) of clinical trials. The first three (Phase I, Phase II, and Phase III) are usually required before a drug is considered for approval by the FDA. Phase IV trials are conducted after a drug has received FDA approval; these trials are sometimes called postmarketing studies. Each phase is designed to find out certain information, building upon the information learned from the previous phase. Patients may be eligible to participate in different types of clinical trials depending on their health status, type and stage of HL, and type of treatment, if any, they previously received.

**Table 12.1. The Four Main Types (or Phases) of Clinical Trials**

Phase	Purpose	Number of Volunteer Patients
Phase I	<ul style="list-style-type: none"> <li>■ To find a safe dose.</li> <li>■ To decide on a schedule.</li> <li>■ To see what side effects are related to the therapy.</li> </ul>	<ul style="list-style-type: none"> <li>■ 15–30 patients with one or more different types of cancer.</li> </ul>
Phase II	<ul style="list-style-type: none"> <li>■ To find out if a new treatment is effective against a certain type of cancer.</li> <li>■ To see if the treatment causes side effects.</li> </ul>	<ul style="list-style-type: none"> <li>■ Usually less than 100 patients with the same type of cancer.</li> </ul>

**Table 12.1. The Four Main Types (or Phases) of Clinical Trials**  
(continued)

Phase	Purpose	Number of Volunteer Patients
Phase III	<ul style="list-style-type: none"> <li>To compare a new treatment or new uses of existing treatments with current standard treatments.</li> <li>The main comparisons are usually how well the treatment works and what types of side effects it causes.</li> </ul>	<ul style="list-style-type: none"> <li>From 100 to several thousand patients with the same type of cancer.</li> <li>Patients are randomly assigned to a treatment group; one group receives the standard therapy and the other group receives the experimental treatment.</li> </ul>
Phase IV	<ul style="list-style-type: none"> <li>To find more information about the long-term safety and effectiveness of a new treatment.</li> <li>These trials take place after the drug has been marketed.</li> </ul>	<ul style="list-style-type: none"> <li>Several hundred to several thousand patients with the same type of cancer.</li> </ul>

### Why Is a Placebo Sometimes Used in Phase III Trials?

**In cancer clinical trials, patients are never given a placebo in place of an effective standard therapy.** Patients would be given a placebo only if there were no standard therapies available. Placebo-controlled trials are NEVER DONE in a manner that would deny patients an effective therapy.

A *placebo*, or sugar pill, is an inactive ingredient that is used as a comparator in some clinical trials. The placebo is made to look and taste the same as the experimental pill. The patients and the doctors and nurses treating them may not know what type of treatment is being given. In Phase III trials, patients are usually selected at random for either the experimental group receiving the study drug or the control group receiving the current standard treatment(s) for their particular lymphoma. Many patients who are in the control group will still benefit from the standard of care.

## Should a Patient Participate in a Clinical Trial?

Clinical trials are not a “last resort” for patients. Patients with all stages of HL can participate in clinical trials, whether at the time of initial diagnosis or at *relapse* (disease returns after treatment). Clinical trials may offer benefits but also include risks. Patients in clinical trials may be able to try a new treatment that is not otherwise available. This treatment may involve the use of a new drug for patients with relapsed HL. Or it may make a drug that is already FDA approved for relapsed HL available for the *first-line* (initial) treatment of patients with newly diagnosed HL.

Being part of a randomized trial means that a group of patients receive the standard therapy. The new treatment may or may not be more effective than the standard therapy. However, an advantage of clinical trials in general is that the health of enrolled patients is monitored very closely, often closer than in standard practice. The healthcare team studying the new treatment will explain the possible benefits and risks of a specific clinical trial in detail.

Every clinical trial is led by a principal investigator who is a medical doctor. Members of the research team may include doctors, nurses, social workers, and other healthcare professionals. Patients usually continue regular visits with their current healthcare provider who may work with the research team to ensure that any investigational treatment would not interfere with current medication or treatments.

Some professional organizations, like the National Comprehensive Cancer Network (NCCN, which develops guidelines for doctors to use in treating patients with all types of cancers), actively encourage the participation of patients with cancer in clinical trials because they often provide the best management option for patients with cancer.

## What Is Informed Consent in a Clinical Trial?

*Informed consent* is a process in which patients learn all about the clinical trials they are interested in joining. During this process, members of the clinical trial research team will explain:

- The purpose of the study
- The factors used to decide if a patient is allowed to participate in the study
- The tests, procedures, and visits participants will be expected to agree to
- The type of treatment provided in the study
- The possible risks, benefits, and alternatives
- The rights of patients to decide whether or not to participate and to leave the study at any time

The research team will answer questions and provide written information about the trial. After the team explains all of the details and the patient does not have any more questions, he or she will be asked to read and sign an informed consent document before entering the study that details all the trial information discussed, describes how his or her records will be kept private, and shows that he or she was given information on the risks, potential benefits, and alternatives.

Remember that even after signing the consent form, patients can leave the study at any time. If a patient leaves the study or decides not to take part in the study, the doctor will discuss other treatment options available to him or her. Patients may use the list of questions on the following page when asking their doctor about a clinical trial.

## Questions to Ask About a Clinical Trial

- What is the purpose of this clinical trial?
- Why are you recommending this clinical trial for me?
- Who is sponsoring this trial (the National Cancer Institute [NCI], a cancer center, an international study group, other state or national study group, or a pharmaceutical/biotechnology company)?
- Who has reviewed and approved this clinical trial?
- Does this clinical trial include the use of a placebo (no active ingredient/no intervention)?
- How long will the study last? Where will it take place?
- What are the risks involved?
- What are the possible benefits? If I benefit from the intervention, will I be allowed to continue receiving it after the trial ends?
- What are my responsibilities during the clinical trial?
- What kinds of tests, procedures, or treatments will be performed? How many and how often?
- Will I be in any discomfort or pain?
- Will I be able to see my own doctor during the clinical trial?
- What type of long-term follow-up care is part of this trial?
- What costs will I be responsible for? Who will pay for my participation? Will I be reimbursed for other expenses?
- What happens if my health gets worse during the clinical trial?

## What Is the Cost of Participating in a Clinical Trial?

Clinical trials are very expensive undertakings for the study sponsor. However, the cost to the patient varies depending on the trial, who is sponsoring the trial, what portion of the trial-related expenses the sponsor will cover, and the patient's health insurance coverage.

The March 2010 Affordable Care Act (ACA) states that all healthcare plans (offered through an employer or purchased through an ACA exchange) that were newly issued or renewed on or after January 1, 2014, are not allowed to limit or deny coverage to people who decide to participate in an approved clinical trial. However, this patient protection provision does not apply to healthcare plans that existed before January 1, 2014. Some of these “grandfathered” plans do pay for the basic medical procedures associated with the trial, such as laboratory tests, scans, and hospitalization when required, while others may define clinical trials as “experimental” or “investigational” and not cover some of the routine costs, such as doctor visits, tests, or treatments. Medicare provides coverage for patient care associated with most clinical trials.

If a patient is taking part in a National Cancer Institute (NCI) trial being conducted at the National Institutes of Health (NIH) campus located in Bethesda, Maryland, the NCI will pay for the study drug and the costs related to the study. Additional funding to assist with travel, food, and lodging expenses is also provided. Some cancer centers provide financial assistance or discounted rates for lodging and meals and have special research units that will pay for study-related costs. Some organizations, including the Lymphoma Research Foundation (LRF), provide financial assistance for treatment-related expenses. For more information on financial aid, please view the *Resources for Financial Assistance* fact sheet on LRF's website at [www.lymphoma.org](http://www.lymphoma.org).

Patients should ask their doctor what clinical trials may be most appropriate for them. Here are some additional sources of clinical trial information:

- The LRF Helpline at (800) 500-9976
- The NCI's Cancer Information Center at (888) NCI-1937 or the NCI's Clinical Trials Referral Office at (800) 4-CANCER
- The NIH websites at [www.cancer.gov](http://www.cancer.gov) and [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
- Cancer centers in the area

## Part 5 — Clinical Trials and Advances in Treatment

### Chapter 13: Advances in Treatment of Patients With Hodgkin Lymphoma

Over 90 percent of patients with early stage classical Hodgkin lymphoma (CHL) and 80 percent of those with advanced stage disease will be cured. Because of this high cure rate, minimizing the long-term effects of therapy is a very important issue and an active area of investigation.

Doctors and scientists around the world are working very hard to improve currently available treatment options and find better and safer drugs to treat patients with Hodgkin lymphoma (HL). Advances are being made in different areas including genetics, molecular biology, immunology, treatments, and supportive care. In particular, recent developments have provided a better understanding of the biology of the disease.

Drugs that are not yet approved for sale by the U.S. Food and Drug Administration (FDA) are said to be investigational. Some of these investigational drugs are being studied in laboratory experiments using tissue culture cells and laboratory animals. This stage is often referred to as the preclinical phase. The drugs in more advanced stages of research are being studied in patients in clinical trials and are then referred to as being in the clinical phase of development.

The most common way for a patient to receive an investigational drug is through a clinical trial. To find out more about getting access to investigational drugs, visit the National Cancer Institute's (NCI's) website at [www.cancer.gov](http://www.cancer.gov) and search for "access to investigational drugs." Alternatively, visit the website at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) to search for trials using a particular drug or to find clinical trials nearby.

Remember that today's science is moving quickly. Please check with your doctor or the Lymphoma Research Foundation (LRF) for additional information and recent updates.

For a detailed discussion of currently approved treatment options, please see the "Treatments for Hodgkin Lymphoma" chapter of this booklet.

### Interim Positron Emission Tomography Scans

Six cycles represents the current standard of care for HL patients with disseminated disease. Early in therapy, after one, two, or three cycles, interim positron emission tomography (PET) scans are now being performed in order to determine how much and what form of therapy should be given to individual patients. These tests are given to eliminate needless cycles of chemotherapy or radiation in patients with limited disease (ie, HL Stages I-II) and are designed to reduce toxicity while maintaining high cure rates.

### Chemotherapy

Researchers are trying to develop new chemotherapy drugs, improve versions of existing drugs, and find better ways to combine different doses and sequences of existing drugs. The goal is to develop drugs and regimens that are better at killing HL cells while leaving healthy cells alone (decreasing the chance of side effects). Some drugs being studied in patients with HL are already FDA approved and being used for patients with other types of cancer. For example, bendamustine (Treanda), a form of nitrogen mustard that interferes with the DNA (deoxyribonucleic acid; genetic material) of cells and inhibits cell division and growth, is being investigated for treatment in patients with relapsed or refractory HL in combination with the chemotherapy drug gemcitabine (Gemzar), brentuximab vedotin (Adcetris), or lenalidomide (Revlimid).

## Stem Cell Transplantation

Ongoing research in stem cell transplantation is focused on finding better ways to collect stem cells from the bone marrow or peripheral blood; eliminating graft-versus-host disease in allogeneic (donor) transplantations; improving ways to remove all lymphoma cells from stem cell collections used for autologous (self) transplants; and developing more effective non-myeloablative (reduced-intensity) stem cell transplants.

## Monoclonal Antibodies

Monoclonal antibodies are drugs that mimic our own immune proteins and are designed to recognize and stick to specific target molecules. Novel monoclonal antibodies help the immune system to fight cancer, including HL.

Some cancer cells, such as melanoma or HL, express a protein called programmed cell death ligand 1 (PD-L1) that helps the cell escape attacks from the immune system by switching on programmed cell death-1 (PD-1) on T cells. Switching on PD-1 puts the T cell “to sleep.” A new class of agents, called PD-1 inhibitors is being tested in HL. When PD-L1 on the surface of tumor cells binds to PD-1 on T cells, the T cells become inactive. When a PD-1 antibody blocks PD-1 on T cells and keeps it from binding to PD-L1 on tumor cells, the T cell becomes activated and can kill the tumor cell.

Nivolumab (Opdivo) and pembrolizumab (Keytruda) are monoclonal antibodies against PD-1 that disable this switch, and “wake up” T cells so they can fight against Hodgkin cells. Nivolumab and pembrolizumab are both being studied in patients with relapsed/refractory CHL and have shown significant clinical activity. There are several PD-1 inhibitors in development, and most are now available through clinical trials. Investigators believe that immunotherapy holds huge promise for the future treatment of HL.

Another type of antibody-based treatment is bispecific antibodies.

Bispecific antibodies are made up of two different monoclonal antibodies so that they can bind to two different *antigens* (targets) and bring together cells that harbor these two targets. For example, AFM13 is a bispecific antibody that binds to both natural killer cells (cells of the immune system) and cells that express CD30 such as HL. It is in clinical trials for treatment of patients with relapsed/refractory HL.

### Other Targeted or Novel Therapies

In addition to monoclonal antibodies that target molecules (antigens) on the surface of cancer cells, many drugs are in development that target molecules inside cancer cells. A better understanding of the biology and genetics of HL is helping researchers identify specific molecules in lymphoma cells that may be good targets for new drugs. These specific molecules usually have important roles in controlling the growth and survival of lymphoma cells. The drugs that target these molecules are broadly called targeted or novel therapies. These drugs may kill the lymphoma cells or slow down or stop their growth. Targeted therapies attack cancer cells in a more specific way than chemotherapy drugs and are less likely to kill or damage healthy cells. This factor makes it less likely that these agents will cause serious side effects.

Other targeted therapies for HL are also being studied in the laboratory and in clinical trials. For example, the mammalian target of rapamycin (mTOR) inhibitors everolimus (Afinitor) and temsirolimus (Torisel) have shown activity in HL. The histone deacetylase inhibitors panobinostat (Farydak), entinostat, and resminostat are also being studied in clinical trials. An AKT kinase inhibitor, MK-2206, has shown activity in patients with relapsed/refractory HL.

Lenalidomide, an immunomodulatory agent that interacts with the immune system to encourage the destruction of cancer cells, is another drug being explored for the treatment of HL.

In summary, the availability of novel, active, and non-chemotherapeutic agents may lead to the development of more

effective treatment for both newly diagnosed and relapsed/refractory patients with HL and further improve survival. That prospect is yet another argument for considering participation in clinical trials at all stages of HL treatment.

## **ABOUT THE LYMPHOMA RESEARCH FOUNDATION**

At the Lymphoma Research Foundation (LRF), our goal is to change the future for everyone whose life has been affected by a lymphoma diagnosis. We are dedicated to funding biomedical research; training the next generation of lymphoma investigators; raising public awareness of the disease; and providing education and support to people with lymphoma, their families and caregivers.

### **Advocacy Program**

LRF supports public policies which seek to increase federal funding for lymphoma research and ensure access to high quality cancer care. The LRF Advocacy Program provides volunteer advocates with the resources necessary to garner attention and support for those public policies most important to the lymphoma community. There are currently more than 5,000 LRF advocates in all 50 states and the District of Columbia.

### **Outreach and Awareness**

LRF offers numerous fundraising and awareness programs – including the signature Lymphoma Walk program and Team LRF – which allow members of the lymphoma community to become involved with the organization and support the LRF mission.

## Patient Education and Services

LRF provides a comprehensive series of programs and services for members of the lymphoma community, including: Clinical Trials Information Service; Disease-Specific e-Newsletters, Publications, Videos, and Websites; Financial Assistance Programs; In-Person Education Conferences; Lymphoma Helpline; Lymphoma Support Network; Mobile App ([www.focusonlylymphoma.org](http://www.focusonlylymphoma.org)); Teleconferences; and Webcasts/Podcasts.

## Professional Education

LRF is committed to educating healthcare professionals on the latest developments in lymphoma diagnosis and treatment. The Foundation offers a wide range of lymphoma-focused continuing education activities for nurses, physicians, and social workers, including workshops, conference symposia, and webcasts.

## Research

LRF remains dedicated to finding a cure for lymphoma through an aggressively-funded research program and by supporting the next generation of lymphoma investigators. LRF supports these goals through Clinical Investigator Career Development Awards, Fellowships and several disease-specific research initiatives. These efforts are led by the Foundation's Scientific Advisory Board (SAB), comprised of 45 world-renowned lymphoma experts.

## Contact Information

### *LRF National Headquarters*

115 Broadway, Suite 1301

New York, NY 10006

Phone: (212) 349-2910

Fax: (212) 349-2886

Email: [LRF@lymphoma.org](mailto:LRF@lymphoma.org)

Website: [www.lymphoma.org](http://www.lymphoma.org)

### *LRF Helpline*

Phone: (800) 500-9976

Email: [helpline@lymphoma.org](mailto:helpline@lymphoma.org)



# FOCUS ON LYMPHOMA MOBILE APP

The Lymphoma Research Foundation's mobile app, *Focus on Lymphoma*, is a great tool and resource for lymphoma patients to manage their disease.

*Focus on Lymphoma* is the first mobile app that provides patients and caregivers comprehensive content

based on their lymphoma subtype and tools to help manage their diagnosis, including a medication manager, doctor sessions tool and side effects tracker.

The *Focus on Lymphoma* mobile app was recently named Best App by PR News and is available for free download for iOS and Android devices in the Apple App Store and Google Play.

For further information on LRF's award winning mobile app or any of our programs and services, call the **LRF Helpline toll free (800) 500-9976**, **email [helpline@lymphoma.org](mailto:helpline@lymphoma.org)** or visit us at **[lymphoma.org](http://lymphoma.org)**.



# Understanding Hodgkin Lymphoma

This patient guide is supported through  
unrestricted educational grants from:

**Genentech**  
*A Member of the Roche Group*

 **Biogen**

 **SeattleGenetics**<sup>®</sup>

**National Headquarters**

115 Broadway, Suite 1301  
New York, NY 10006

(212) 349-2910 phone • (212) 349-2886 fax

Helpline: (800) 500-9976; [helpline@lymphoma.org](mailto:helpline@lymphoma.org)

Website: [www.lymphoma.org](http://www.lymphoma.org) • Email: [LRF@lymphoma.org](mailto:LRF@lymphoma.org)