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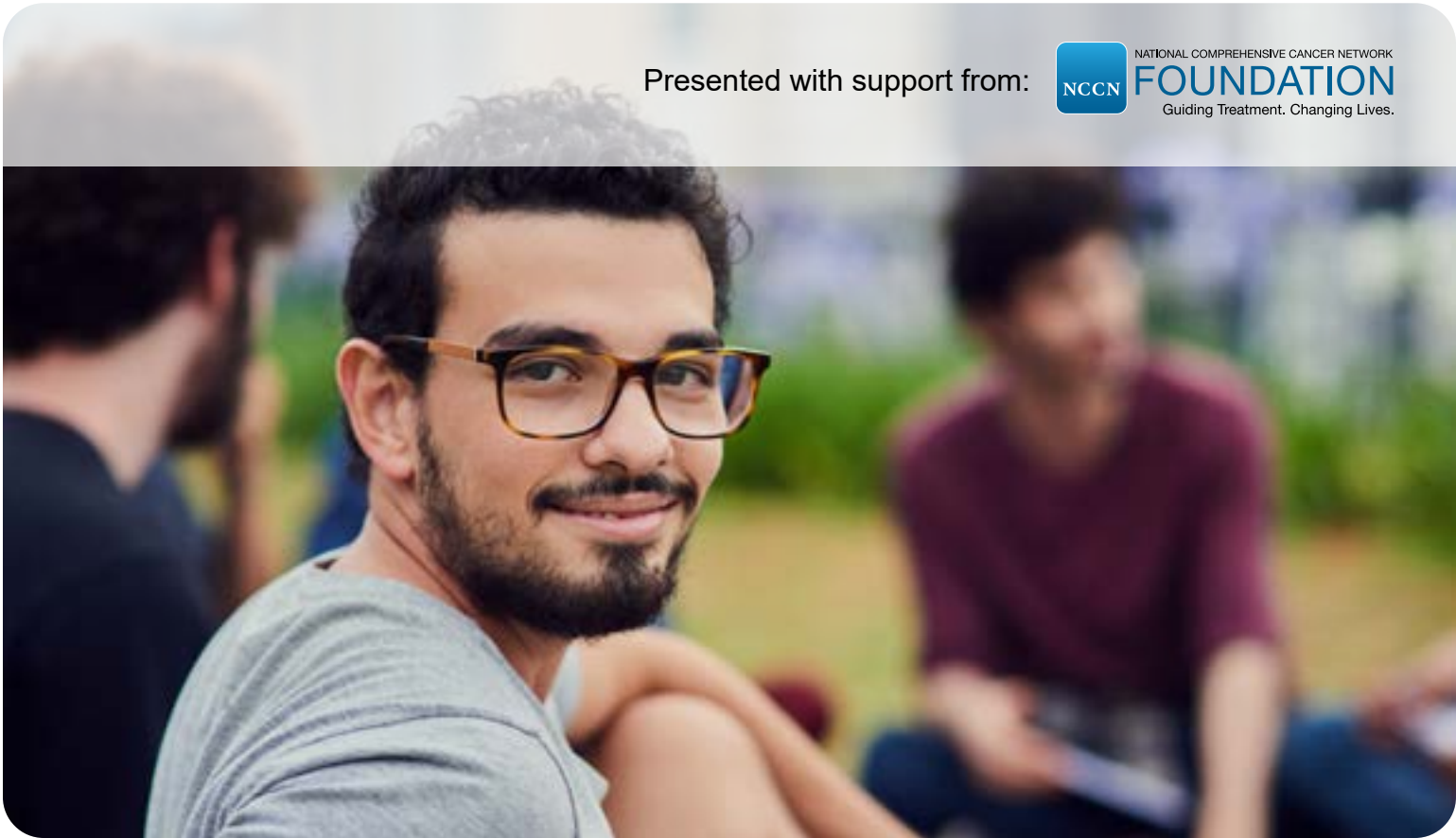
2019

Hodgkin Lymphoma

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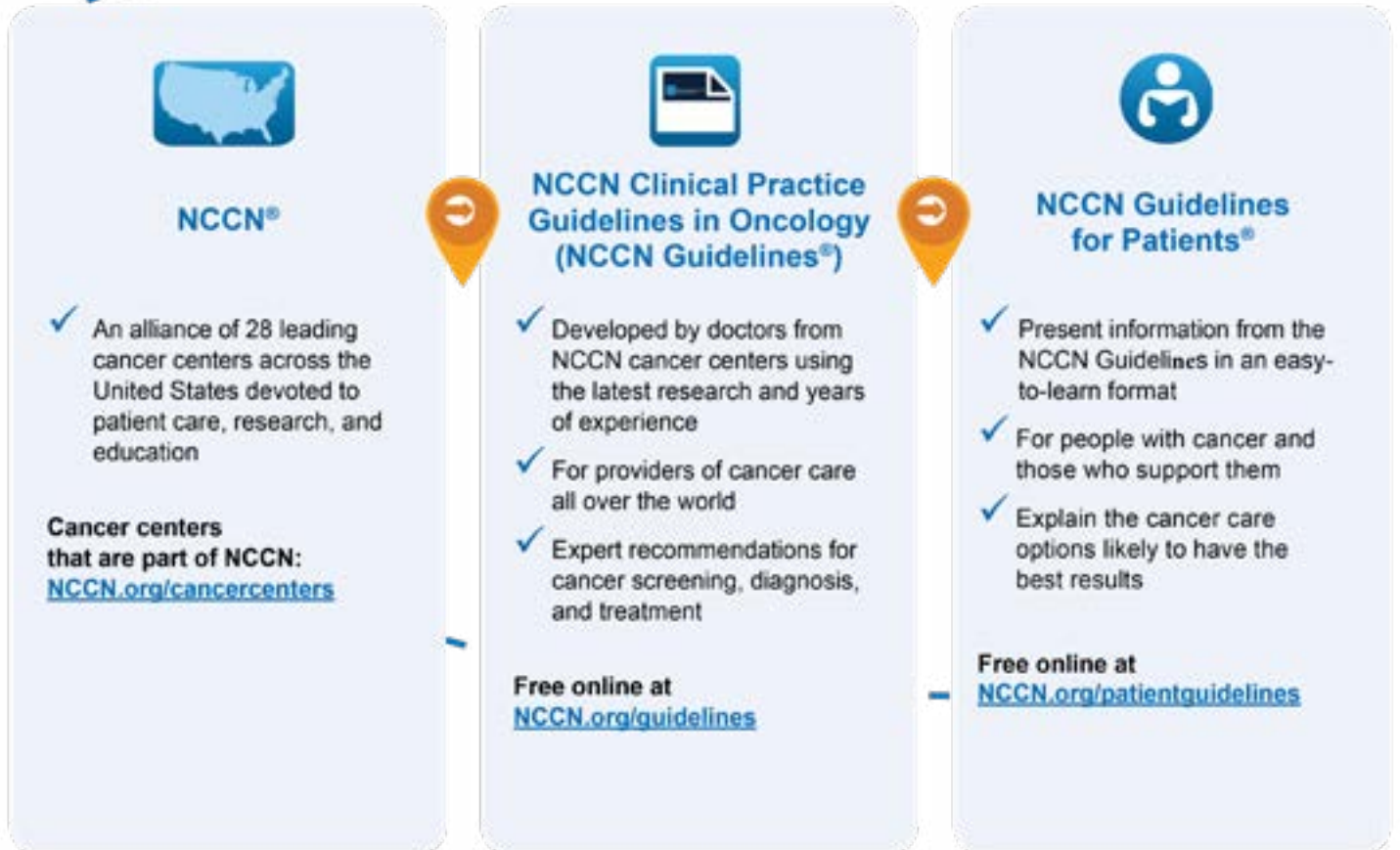
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for Patients[®]
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- ✓ Step-by-step guides to the cancer care options likely to have the best results
- ✓ Based on treatment guidelines used by health care providers worldwide
- ✓ Designed to help you discuss cancer treatment with your doctors

About



NCCN Guidelines for Patients® are developed by the National Comprehensive Cancer Network® (NCCN®)



and supported by funding from NCCN Foundation®



These NCCN Guidelines for Patients® are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hodgkin Lymphoma (Version 2.2019, July 15, 2019).

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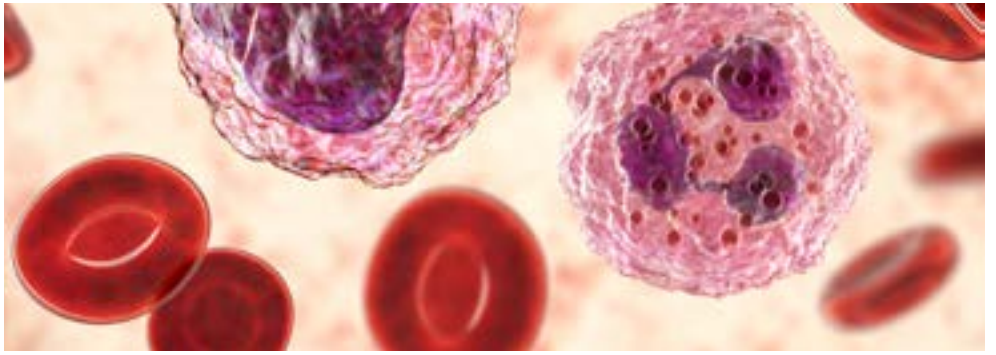
BMT InfoNet provides information and support services to patients undergoing a bone marrow, stem cell or cord blood transplant service. Our mission is to empower patients and their loved ones with reliable information and support about issues before, during and after transplant so that they may take an active, informed role in managing their healthcare choices. Visit us online at bmtinfonet.org, or contact us by email at help@bmtinfonet.org and by phone 847-433-3313.

The Leukemia & Lymphoma Society

LLS is dedicated to developing better outcomes for blood cancer patients through research, education and patient services and is happy to have this comprehensive resource available to patients. LLS.org/PatientSupport

National Bone Marrow Transplant Link (nbmtLINK)

Educating and informing people about their cancer diagnosis as well as the transplant process is an important part of the National Bone Marrow Transplant Link's mission and contributes to the psychosocial support of bone marrow/stem cell transplant patients and their caregivers. For information and resources, please visit nbmtlink.org, call toll free at 800-LINK-BMT or e-mail, info@nbmtlink.org. The LINK is supportive of resources like the NCCN Guidelines for Patients.



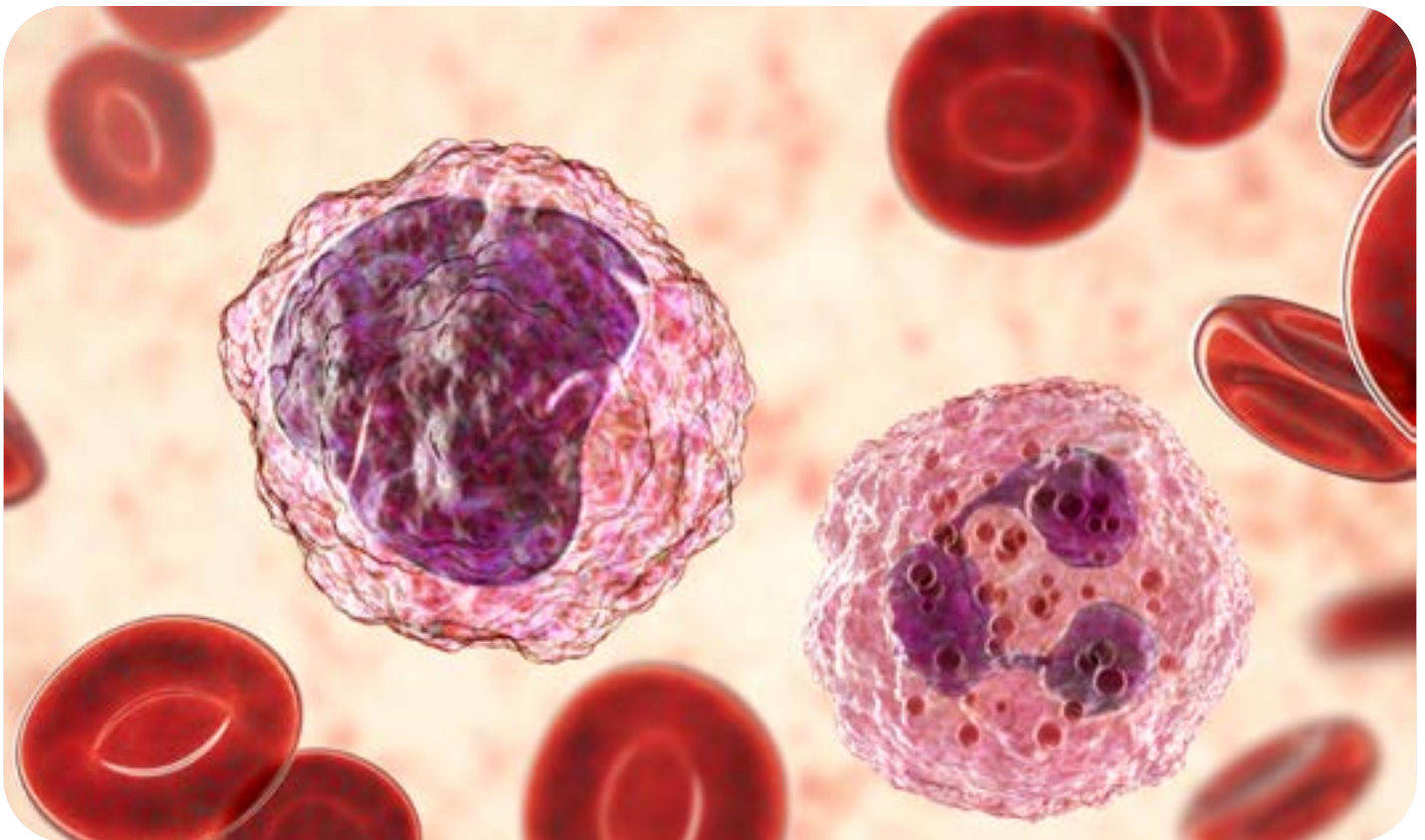
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Hodgkin lymphoma basics

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Hodgkin lymphoma is a rare but highly curable cancer of the lymph nodes and the lymphatic system. With the right treatment, at least 8 out of 10 people can be cured. More people survive Hodgkin lymphoma than any other cancer.

The lymphatic system

The lymphatic system is a network of tissues and organs that help your body fight infection and disease. It is a major part of the body's immune system. The tissues and organs that make up the lymphatic system are made mostly of white blood cells called *lymphocytes*. There are four other types of white blood cells, but lymphocytes are the most important to understanding Hodgkin lymphoma.

Lymph and lymphatic vessels

There is a “super-highway” of ducts running through your body. These ducts are called *lymphatic vessels*. Much like how blood vessels transport blood, lymphatic vessels transport *lymph*. Lymph is a clear fluid that carries important infection-fighting white blood cells (lymphocytes) throughout the body. It is also called *lymphatic fluid*.

Lymph nodes

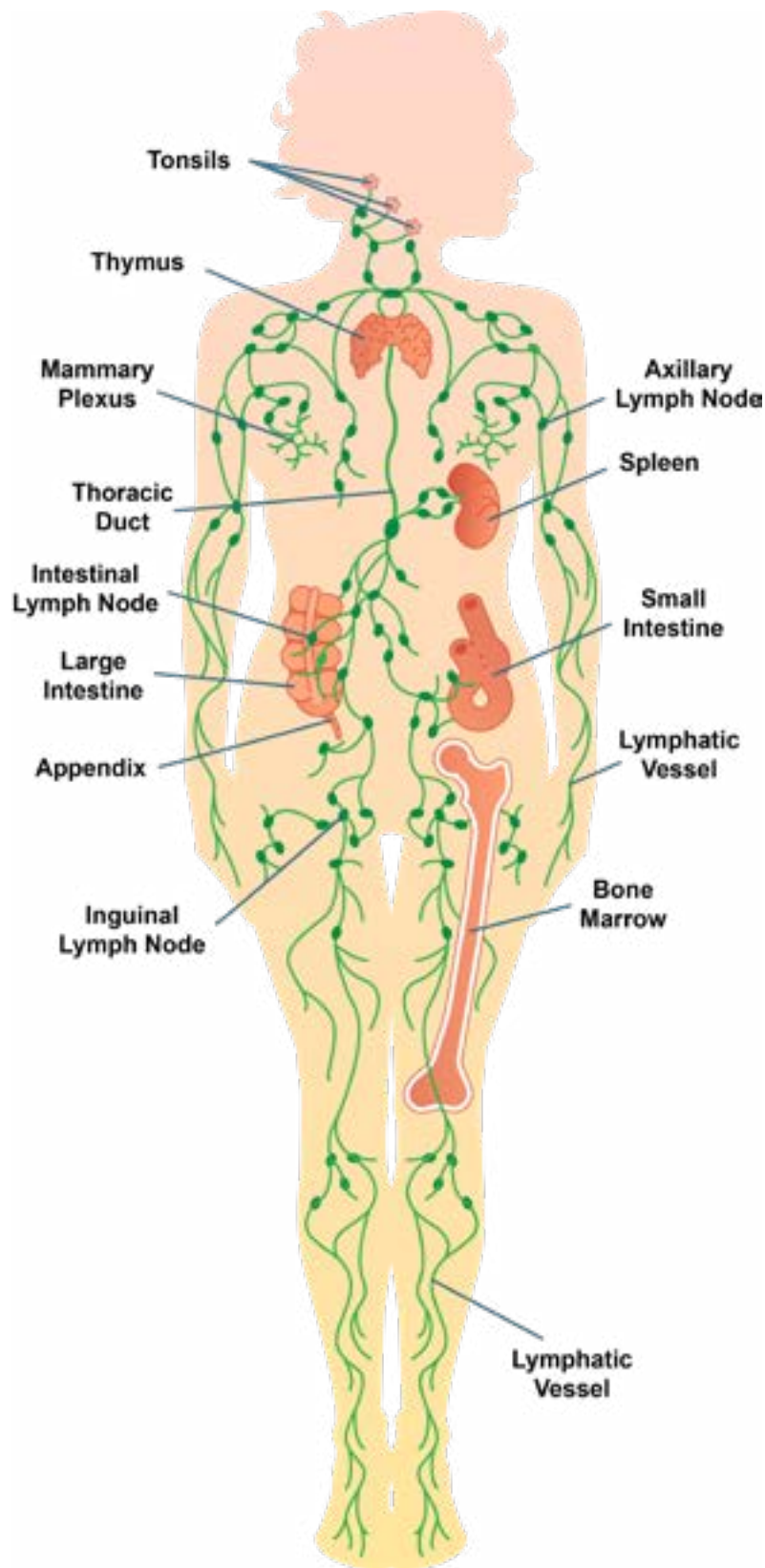
While lymph travels throughout your body in lymphatic vessels, it passes through hundreds of small bean-shaped structures called *lymph nodes*. Lymph nodes catch and filter out foreign particles and harmful cells, including cancer cells. Lymph nodes can't usually be seen or felt. Certain areas of the body contain more lymph nodes than others. The highest numbers of lymph nodes are found in the:

- Neck (*cervical lymph nodes*)
- Groin (*inguinal lymph nodes*)
- Armpits (*axillary lymph nodes*)

Lymph nodes

There are hundreds of small bean-shaped structures throughout the human body called lymph nodes. Lymph nodes catch and filter out foreign particles and harmful cells, including cancer cells.





Spleen

The spleen is the largest organ of the lymphatic system. It is about 4 inches long and shaped like a fist. It makes lymphocytes and plays an important role in blood filtration and storage.

Bone marrow

Most bones have soft, spongy tissue in the center called *bone marrow*. This is where new blood cells are made.

Thymus

After being made in bone marrow, lymphocytes travel to the thymus. The thymus is a small organ in the upper chest. Here they develop into T lymphocytes (T cells), one of the two main types of lymphocytes.

The tonsils

Tonsils are small masses of lymph tissue found at the back of the throat. They help trap disease-causing germs that enter through your nose or mouth.

How Hodgkin lymphoma starts

The human body is made of trillions of cells, which grow, divide, and die as needed. Sometimes, however, errors occur during cell division that cause cells to start growing out of control. This is cancer. Lymphoma is cancer that begins when lymphocytes grow out of control.

Types of lymphoma

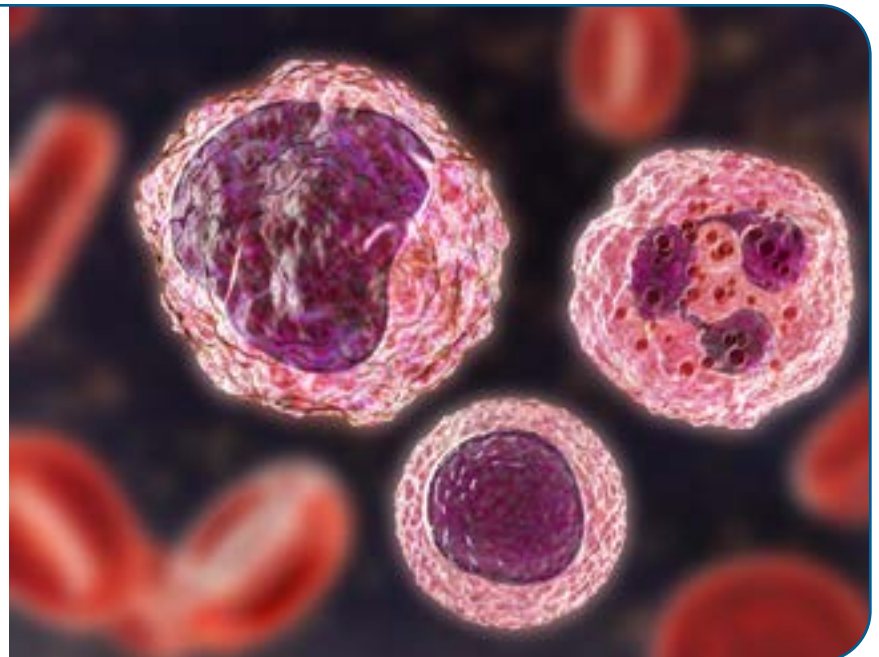
There are two main types of lymphoma:

- Non-Hodgkin's lymphoma
- Hodgkin lymphoma

Doctors can tell if a suspected lymphoma is Hodgkin lymphoma by looking at one or more lymph nodes under a microscope. If it's Hodgkin lymphoma, the lymphocytes will be abnormally large and may have

Under the microscope

Three types of white blood cells, as seen under a microscope. From left to right, there is a monocyte, a lymphocyte, and a neutrophil. You can spot the lymphocyte by its full, round nucleus.



more than one nucleus. These oversized lymphocytes are called *Reed-Sternberg cells*. Cancer researchers don't know why normal lymphocytes turn into Reed-Sternberg cells.

Non-Hodgkin's lymphomas are a large and varied group of lymphomas that do not have the distinctive Reed-Sternberg cells seen in Hodgkin lymphoma. **This book does not discuss treatment of non-Hodgkin's lymphomas.**

Hodgkin lymphoma often spreads through lymphatic vessels from one group of lymph nodes to the next. If left untreated, it will spread to tissue and organs outside the lymphatic system.

Types of Hodgkin lymphoma

There are 2 types of Hodgkin lymphoma:

- Classic Hodgkin lymphoma (CHL)
- Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL)

CHL

Most people with Hodgkin lymphoma (about 95 out of 100) have CHL. CHL can be recognized by large lymphocytes called Reed-Sternberg cells.

There are 4 subtypes of CHL:

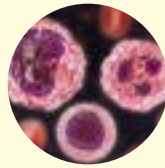
- Nodular sclerosis (most common)
- Mixed cellularity
- Lymphocyte-depleted
- Lymphocyte-rich (least common)

While they are all considered CHL, they look different under a microscope and have different characteristics. For example, some are more likely to cause symptoms than others. All of the treatment information in this chapter applies to all 4 subtypes.

NLPHL

This type of Hodgkin lymphoma is very rare. Only about 5 out of 100 people with Hodgkin lymphoma have NLPHL. While CHL is known for Reed-Sternberg cells, NLPHL is known for having "popcorn-shaped" cells.

Over time, NLPHL can transform into an aggressive (fast-growing) type of non-Hodgkin's lymphoma called diffuse large B-cell lymphoma (DLBCL).



Hodgkin lymphoma

- Rare cancer of the lymph nodes and the lymphatic system
- The 26th most common cancer in the United States
- More common in men than women
- Most people are diagnosed between the ages of 15 to 30, or after age 55
- With the right treatment, most people can be cured

CHL

- Make up 95% of all Hodgkin lymphomas
- Known for Reed-Sternberg cells
- Four main subtypes:
 - Nodular sclerosis CHL
 - Mixed cellularity CHL
 - Lymphocyte-depleted CHL
 - Lymphocyte-rich CHL

NLPHL

- Make up 5% of all Hodgkin lymphomas
- Known for “popcorn” cells made mostly of lymphocytes

Review

- CHL is a rare but highly curable cancer of the lymph nodes and the lymphatic system.
- The lymphatic system is a network of vessels and organs made of white blood cells called lymphocytes. Lymphocytes help the body fight disease and infection.
- Cancer is the uncontrolled growth of cells. When lymphocytes grow out of control, the cancer is called a lymphoma.
- Hodgkin lymphoma starts in abnormally shaped lymphocytes called Reed-Sternberg cells.
- There are 2 types of Hodgkin lymphoma—CHL and NLPHL.
- CHL is the more common of the two and has 4 subtypes: nodular sclerosis, mixed cellularity, lymphocyte-depleted, and lymphocyte-rich.
- The subtypes of CHL look different under a microscope and have different characteristics.
- NLPHL is a very rare form of Hodgkin lymphoma. It can transform into an aggressive (fast-growing) type of non-Hodgkin's lymphoma.
- Hodgkin lymphoma often spreads from one group of lymph nodes to the next. If left untreated, it will spread to tissue and organs outside the lymphatic system.

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Testing for Hodgkin lymphoma

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This chapter explains how Hodgkin lymphoma is identified (diagnosed). Other testing and care you may have before treatment is described.

Biopsy and lab testing

Excisional lymph node biopsy

The best way to diagnose Hodgkin lymphoma is to have one or more whole lymph nodes removed and tested. This is called an *excisional lymph node biopsy*. This method is the most accurate because it allows entire lymph nodes to be tested, not just samples taken from inside the lymph nodes.

Needle biopsies

While an excisional lymph node biopsy is preferred, another type of biopsy called a *core needle biopsy* may be an acceptable alternative in some cases. In a core needle biopsy, a surgeon uses a wide needle to remove a

sample of tissue from a lymph node, but does not remove the entire lymph node.

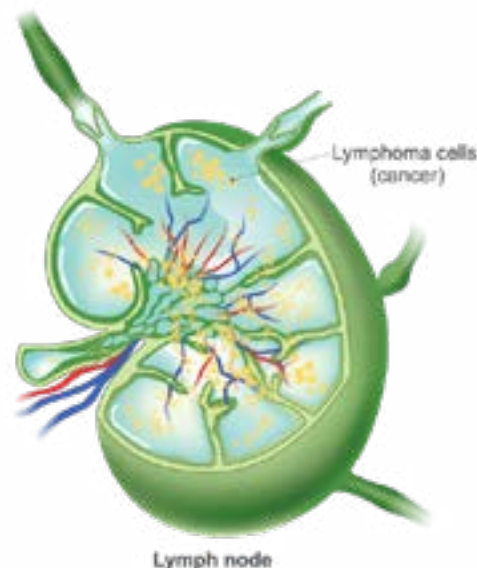
A third type of biopsy called a *fine-needle aspiration* (FNA) should not be used alone to diagnose Hodgkin lymphoma. In a FNA biopsy, a thin needle is used to remove a sample of tissue from a lymph node, but does not remove the entire lymph node. While widely used in the diagnosis of other types of cancer, it shouldn't be used by itself to diagnose Hodgkin lymphoma.

Testing the removed lymph node(s)

The removed lymph nodes are tested using a process called *immunohistochemistry* (IHC). Using a microscope, this test looks for proteins on the surface of cells. A diagnosis can be made depending on which proteins can be seen (and not seen) using this technique. For example, if you have CHL, proteins called "CD15" and "CD30" can usually be seen during immunohistochemistry, but "CD3" and "CD45" usually cannot.

Identifying Hodgkin lymphoma

The best way to diagnose Hodgkin lymphoma is to have one or more whole lymph nodes removed and tested using a process called immunohistochemistry (IHC).



Health history and physical exam

Expect your doctor to thoroughly review your health history and perform a comprehensive physical exam. These are important first steps in planning the best cancer treatment for you.

Symptoms

Hodgkin lymphoma can cause symptoms. There are three symptoms in particular that are important for your doctor to be aware of, if you have them. These are called *B symptoms* or *systemic symptoms*.

The B symptoms are:

- Unexplained high fevers (above 100.4 degrees Fahrenheit)
- Heavy, drenching night sweats
- Loss of more than 10% of your body weight without dieting

There are other symptoms that may be related to Hodgkin lymphoma. Tell your doctor if you are experiencing any of the symptoms listed below.

- Itchy skin (pruritus)
- Extreme tiredness despite sleep (fatigue)
- Having a bad reaction to alcohol

Hodgkin lymphoma B symptoms

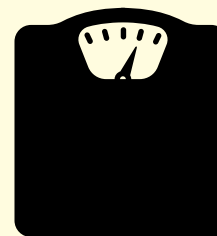
Unexplained fever



Night sweats



Weight loss



Physical exam

While lymph nodes can't usually be seen or felt, Hodgkin lymphoma can cause them to get bigger. Using his/her hands, your doctor will feel the areas of your body where there are the most lymph nodes, including the neck, armpits, and groin. In addition to examining areas where there are lots of lymph nodes, expect your doctor to feel your spleen and liver.

Performance status

Your doctor will also rate your performance status. Performance status is your ability to do day-to-day tasks and activities. It is used by doctors to decide if you are able to have certain treatments.

Guide 1**Important testing for everyone with suspected Hodgkin lymphoma****Biopsy and testing**

- Excisional lymph node biopsy
- Testing of the removed lymph node(s) for proteins related to Hodgkin lymphoma

Medical history and physical exam

- Check for B symptoms (unexplained fever, night sweats, weight loss)
- Check for other symptoms (alcohol intolerance, severe itching, fatigue)
- Performance status
- Hand examination of neck, armpits, groin, spleen, and liver

Blood tests

- Complete blood count
- Erythrocyte sedimentation rate
- Comprehensive metabolic panel
- Lactate dehydrogenase
- Liver function tests

Imaging tests

- PET/CT scan
- CT scan with contrast

Other testing and care

- Pregnancy testing (for women of childbearing age)
- Discussion of fertility and family planning
- Assessment of smoking status
- Psychosocial counseling

Blood tests

You should have a number of common blood tests as part of the workup (testing) for Hodgkin lymphoma. These common, recommended tests are described next.

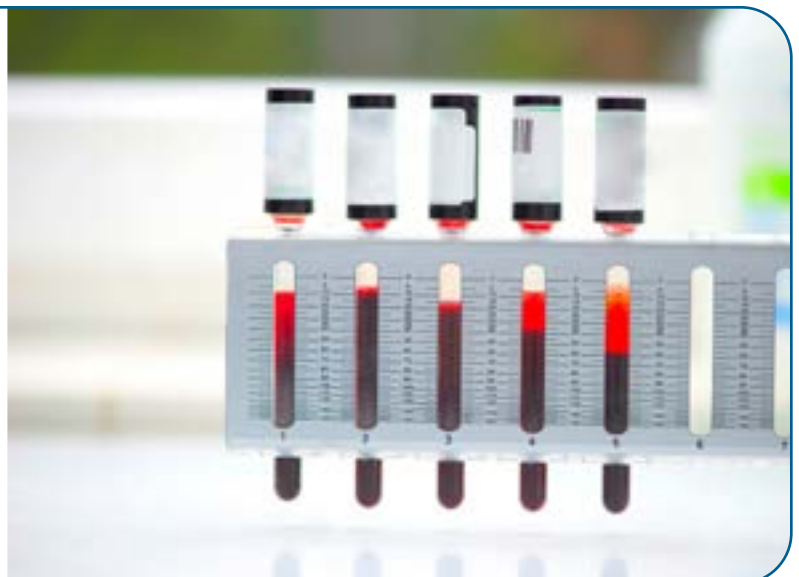
- **Complete blood count (CBC).** This common test measures the number of red blood cells, white blood cells, and platelets in a sample of blood.
- **Erythrocyte sedimentation rate (ESR).** This test measures how quickly red blood cells settle at the bottom of a test tube that contains a blood sample. A faster-than-normal ESR may be a sign of inflammation, infection, cancer, or other diseases.
- **Comprehensive metabolic panel (CMP).** This group of 14 different blood tests provides information about the health of your liver and kidneys, and other information including your blood sugar, calcium, electrolytes, and cholesterol.

- **Serum lactate dehydrogenase (LDH).** A high level of this protein can be a sign of cell damage caused by cancer or other health problems.

Your doctor may also suggest testing your blood for human immunodeficiency virus (HIV) and for hepatitis B or C. This is encouraged by NCCN experts, especially if your doctor thinks you may be at risk for these diseases.

Erythrocyte sedimentation rate

This test measures how quickly red blood cells settle at the bottom of a test tube that contains a blood sample. A faster-than-normal ESR may be a sign of inflammation, infection, cancer, or other diseases.



Imaging tests

PET/CT scan

A positron emission tomography/computed tomography (PET/CT) scan combines the use of two tests (PET and CT). Some cancer centers have one machine that does both tests. This is called an *integrated PET/CT*. Often, however, the CT part of an integrated PET/CT is not done with contrast. In this case, a CT scan with contrast (often called a *diagnostic CT scan*) should also be done. Using a contrast agent is important in order to see areas of cancer.

PET scans use a small amount of radioactive glucose (sugar), called a radiotracer. The most commonly used radiotracer is called *fluorodeoxyglucose* (FDG). The radiotracer gives off a small amount of energy that is detected by the PET/CT machine. Areas with cancer appear brighter (“hotter”) because cancer cells use sugar more quickly than

normal cells. However, these “hot spots” can be caused by health conditions other than cancer.

CT takes many pictures of a body part from different angles using x-rays. A computer combines the x-rays to make detailed pictures. A contrast dye is used for diagnostic CT. It makes the pictures clearer. The dye will be injected into your vein. You will be asked a series of questions to make sure you are not allergic to the dye. Allergic reactions to the dye include throat swelling and hives. CT of your neck is needed if your neck may be treated with radiation. Any areas that look abnormal on PET/CT should also be imaged.

PET scans play a very important role in the management of Hodgkin lymphoma. It is common to have more than one PET scan during the course of treatment. They are used to see how well the cancer is responding to treatment. Keep in mind that PET scans may be abnormal if you have an infection,

PET/CT machine

PET scans play a very important role in the management of Hodgkin lymphoma. They are used to see how well the cancer is responding to treatment.



inflammation, or other conditions, even if you don't have Hodgkin lymphoma.

Deauville scores

A scoring system is used to describe how much of the tracer is absorbed by areas with cancer compared to how much is absorbed by your liver and by the area between the lungs (but not the lungs themselves). This area is called the *mediastinum*. There are 5 possible scores (called *Deauville scores*), ranging from 1 to 5. A score of 1 or 2 is generally considered “negative”, meaning that there are no cancerous areas of concern. A score of 4 or 5 is generally considered “positive,” meaning that there are cancerous areas of concern. A score of 3 can be considered positive or negative, depending on the situation.

Chest x-ray

A chest x-ray can help spot enlarged lymph nodes in the chest. If other imaging tests show a large, suspicious mass in the area between the lungs, a chest x-ray is recommended.

Deauville scores

The Deauville score given when you are first diagnosed is not important.

Whether that score goes up or down as a result of treatment is important.

This is how doctors know how well the cancer is responding to treatment.

Chest x-ray

A chest x-ray is recommended if a large mass in the middle of your chest is seen with other imaging tests.



Heart and lung tests

Some cancer treatments can damage your heart and lungs. In order to plan your treatment, your doctors will test how well your heart and lungs work.

Ejection fraction

An echocardiogram is an imaging test of your heart. It can provide a wide range of important information, including how much blood is pumped out of the left side of your heart every time it beats. This is called the *ejection fraction*. A high or low ejection fraction may mean you can't have certain chemotherapy medicines.

Lung function tests

Bleomycin (Blenoxane®) is a chemotherapy medicine widely used in the treatment of Hodgkin lymphoma. Bleomycin can damage the lungs and cause a disease called *pulmonary fibrosis*. In order to learn if your lungs can handle treatment with bleomycin, you should have lung testing before starting treatment.

The three most common lung function tests are described below.

- **Spirometry** measures the amount of air the lungs can hold, and how fast you can empty the air out of your lungs.
- A **gas diffusion test** involves breathing in a harmless gas and measuring how much of it you breathe out. It tells how much oxygen travels from your lungs into your blood.
- **Body plethysmograph** involves sitting in a small room and breathing into a tube. This test measures how much air your lungs can hold and how much air is left in your lungs after you exhale.

Echocardiogram

An echocardiogram is one way of measuring ejection fraction, which is the amount of blood pumped out of the left side of your heart each time it beats. Measurement of ejection fraction is recommended for most people before starting chemotherapy that includes doxorubicin.



Other testing and care

Fertility and pregnancy

Some chemotherapy regimens (eg, BEACOPP) can cause immediate and permanent infertility in both men and women. Other chemotherapy regimens (eg, ABVD) rarely cause infertility. Most people will have chemotherapy with a regimen that is unlikely to cause infertility.

If you want the option of having children after treatment or are unsure, tell your doctors. There are ways for cancer patients to be able to have children after treatment. This is called *fertility preservation*. The most common methods of fertility preservation are described next. In addition, women diagnosed with Hodgkin lymphoma should expect to be tested for pregnancy before starting treatment.

Sperm banking

Men who want the option of fathering children after cancer treatment can use sperm banking. The medical term for this is *semen*

cryopreservation. Sperm banking stores semen for later use by freezing it in liquid nitrogen.

Egg freezing

Like sperm banking, a woman's eggs can be removed, frozen, and stored for later use. The medical term for this is *oocyte cryopreservation*.

Ovarian tissue banking

This method involves removing part or all of an ovary and freezing the part that contains the eggs. The frozen tissue that contains the eggs can later be unfrozen and put back in the body.

Ovarian transposition

This method is an option for women who will be treated with radiation therapy to the pelvis. This surgery moves one or both ovaries and fallopian tubes out of the range of the radiation beam to protect it from damage. This procedure is also called *oophoropexy*.

Spirometry

Spirometry is one of the most common lung function tests. It measures the amount of air the lungs can hold, and how fast you can empty the air out of your lungs.



Bone marrow biopsy

In general, bone marrow biopsies are no longer included in the initial testing for Hodgkin lymphoma. However, if you have lower-than-normal numbers of blood cells and a PET scan doesn't suggest there is cancer in the marrow, a bone marrow biopsy may be needed.

Vaccines

Your spleen is part of your lymphatic system. If your spleen is treated with radiation, your chances of getting an infection are increased. In this case, get vaccinated before treatment against pneumonia, meningitis,

and *haemophilus influenzae* type B (“Hib” or “H-flu”). Despite its name, the H-flu does not cause the common flu. It most often causes pneumonia, but can cause many different kinds of infections.

Help to quit smoking

If you smoke, it is important to quit. Smoking can limit how well cancer treatment works. If you smoke, ask your doctor about counseling and drugs to help you quit.

Guide 2**Other testing and care you may have before treatment**

Heart function testing	If chemotherapy that includes doxorubicin is planned, measuring your heart's <i>ejection fraction</i> is needed.
Bone marrow biopsy	You may need a bone marrow biopsy if you have lower-than-normal numbers of blood cells and a PET scan doesn't show cancer in bone marrow.
Lung function tests	If chemotherapy with ABVD or escalated BEACOPP is planned, lung function testing is needed.
Other imaging tests	<ul style="list-style-type: none"> • Chest x-ray if there is a mass in the area between your lungs • Neck CT if a PET/CT shows cancer in your neck, or if radiation therapy to the neck is planned • MRI or PET/MRI
Other testing and care as needed	<ul style="list-style-type: none"> • Pneumococcal, meningococcal, and <i>Haemophilus influenzae</i> type B (Hib) vaccines if radiation therapy to the spleen is planned • Testing for HIV, hepatitis B, and hepatitis C (encouraged by NCCN experts) • Fertility preservation • Help to quit smoking

Staging

Before starting treatment, it is important to know how far the cancer has spread. This process is called *staging*. The testing described earlier in this chapter is used to determine the stage (extent) of the cancer.

Hodgkin lymphoma usually starts in the upper body—often in lymph nodes in the neck, chest, or armpits. The diaphragm is a thin muscle below the lungs and heart. It can be thought of as a dividing line between the chest and the abdomen. **Hodgkin lymphoma is staged in part depending on whether cancer has spread to lymph nodes or other areas below the diaphragm.**

There are 4 stages of Hodgkin lymphoma (I, II, III, and IV). A simplified description of the stages is provided next. The individual stages are described in more detail on the following pages.

If there is cancer in only one group of lymph nodes above the diaphragm, the cancer is stage I. If the cancer spreads to more lymph nodes above the diaphragm, it is stage II. If Hodgkin lymphoma spreads to lymph nodes or other areas below the diaphragm, it is stage III. Hodgkin lymphoma that has spread to one or more areas outside of the lymphatic system is stage IV.

For the purposes of treatment, the stages are often grouped together as follows after diagnosis and initial workup:

- Stage I–II
- Stage III–IV

The letters “A” and “B” are used to indicate whether people with stage I–II disease have B symptoms (unexplained fevers, drenching night sweats, and extreme weight loss). The letter “A” after the stage means that there aren’t B symptoms. The letter “B” after the stage means that there are B symptoms.

The diaphragm

The diaphragm is a thin muscle below the lungs and heart. It separates the chest from the abdomen and is the primary muscle used for breathing.



Stage I

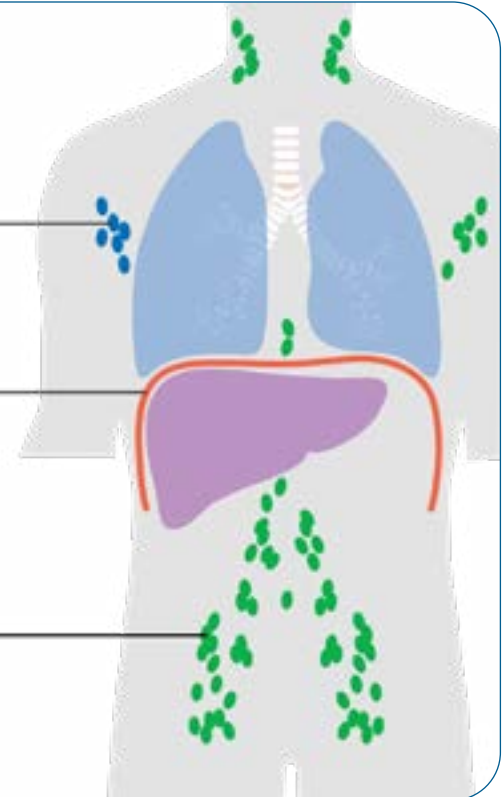
There is cancer in one group of lymph nodes above the diaphragm, and possibly in one small area or organ outside the lymphatic system.

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Hodgkin lymphoma

Diaphragm

Normal lymph nodes



Stage II

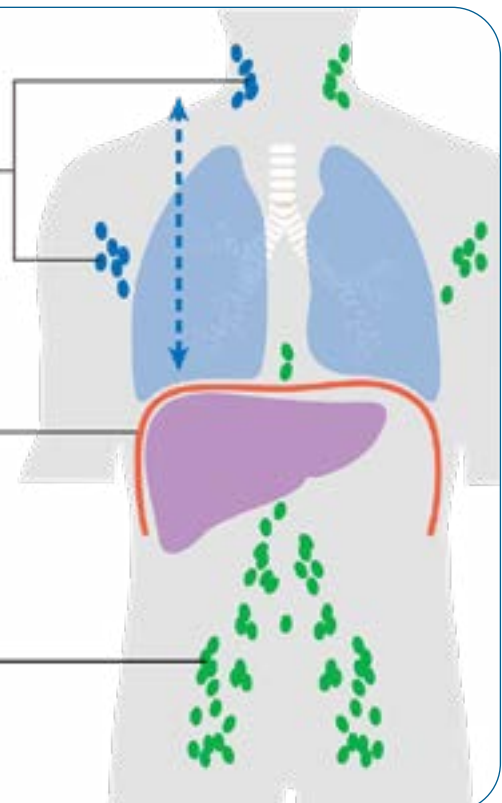
There is cancer in 2 or more groups of lymph nodes on the same side of the diaphragm, and possibly in one area or organ and its nearby lymph nodes outside the lymphatic system.

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Hodgkin lymphoma in two areas on the same side of the diaphragm

Diaphragm

Normal lymph nodes



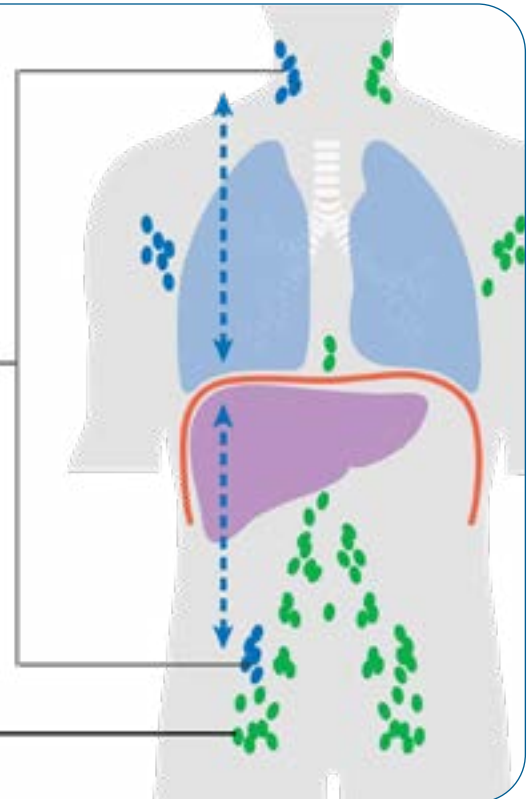
Stage III

There is cancer in lymph nodes on both sides of the diaphragm. There may also be cancer in one area or organ outside of the lymphatic system, in the spleen, or both.

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Hodgkin lymphoma on both sides of the diaphragm

Normal lymph nodes



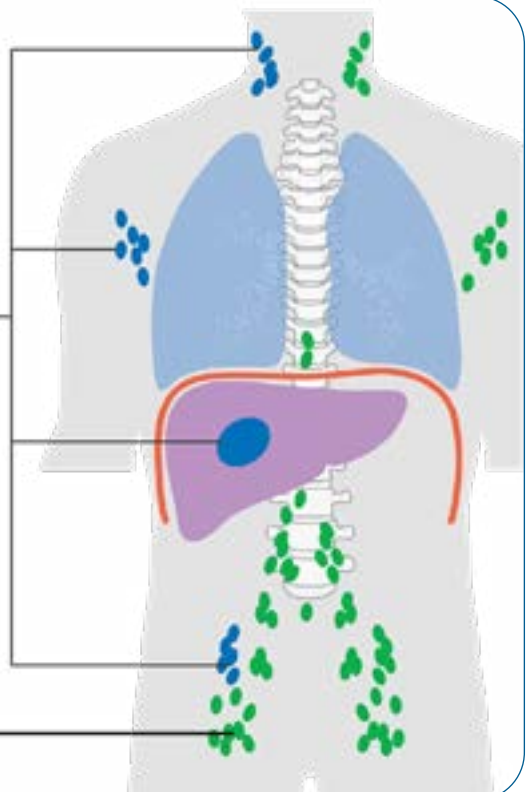
Stage IV

There are multiple areas of cancer in one or more organs outside the lymphatic system, and possibly in the neighboring lymph nodes. Or, there may be cancer in one organ outside of the lymphatic system and also in distant lymph nodes.

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Hodgkin lymphoma in lymph nodes above and below the diaphragm and in the liver

Normal lymph nodes



Review

- ▶ An excisional lymph node biopsy is the most accurate method of diagnosing Hodgkin lymphoma.
- ▶ Hodgkin lymphoma can cause unexplained high fevers, drenching night sweats, and extreme weight loss without dieting. These are called *B symptoms*.
- ▶ Other possible symptoms include itchy skin, extreme tiredness, and having a bad reaction to alcohol.
- ▶ Common blood tests for Hodgkin lymphoma include a CBC, ESR, comprehensive metabolic panel, and measurement of lactate dehydrogenase.
- ▶ PET/CT scans play an important role in the management of Hodgkin lymphoma. They are used to see how well the cancer is responding to treatment.
- ▶ Most people with Hodgkin lymphoma need testing of their heart and lungs in order to determine if they can have certain chemotherapy medicines.
- ▶ Most people are treated with chemotherapy that is unlikely to cause infertility. However, fertility preservation methods are available if treatment with a regimen that may cause infertility is planned.
- ▶ You may need to receive vaccinations to protect you from illness during cancer treatment.
- ▶ If you are a smoker, ask your doctor about ways to help you quit.
- ▶ Hodgkin lymphoma is staged in part depending on whether cancer has spread to lymph nodes or other areas below the diaphragm.
- ▶ Stage I–II (early) Hodgkin lymphoma is only in lymph nodes above the diaphragm.
- ▶ If Hodgkin lymphoma spreads below the diaphragm, it is stage III.
- ▶ Hodgkin lymphoma that has spread to organs outside of the lymphatic system is stage IV.

3

Treatments for Hodgkin lymphoma

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This chapter briefly describes the cancer treatments used for Hodgkin lymphoma. Chemotherapy is the most widely used and most effective treatment for Hodgkin lymphoma.

Chemotherapy

Chemotherapy is the use of medicine to kill cancer cells. **It is the most widely used treatment for Hodgkin lymphoma.** Most chemotherapy drugs are liquids that are slowly injected into a vein. This process is called *infusion*. The drugs travel in your bloodstream to treat cancer throughout your body. Chemotherapy also harms healthy cells, which is why it can cause very harsh side effects.

Chemotherapy is given in cycles of treatment days followed by days of rest. This allows the body to recover before the next cycle. Cycles

vary in length depending on which drugs are used. Often, a cycle is 3 or 4 weeks long.

Chemotherapy medicines may be given individually or combined. If two or more chemotherapy medicines are given together, it is called a combination regimen. Hodgkin lymphoma is usually treated with combination chemotherapy regimens.

Some chemotherapy regimens for Hodgkin lymphoma include steroids. Steroids are drugs often used to relieve inflammation, but also have anti-cancer effects. Steroids used with chemotherapy to treat Hodgkin lymphoma include:

- Dexamethasone
- Methylprednisolone (Solu-Medrol®)
- Prednisone

Guide 3

Commonly used chemotherapy regimens for classic Hodgkin lymphoma

ABVD	Doxorubicin, bleomycin (Blenoxane®), vinblastine, and dacarbazine
AVD	Doxorubicin, vinblastine, and dacarbazine
Escalated BEACOPP	Bleomycin (Blenoxane®), etoposide (Etopophos®), doxorubicin, cyclophosphamide, vincristine, procarbazine (Matulane®), and prednisone
Stanford V (Stanford "5")	Doxorubicin, vinblastine, mechlorethamine (Mustargen®), etoposide (Etopophos®), vincristine, bleomycin (Blenoxane®), and prednisone
Brentuximab vedotin	Brentuximab vedotin (Adcetris®)

Radiation therapy

Radiation therapy is often used in addition to chemotherapy to treat Hodgkin lymphoma, but is sometimes used alone. Using high-energy x-rays that damage DNA, radiation therapy kills existing cancer cells or stops new cancer cells from being made. Radiation can also harm normal cells.

Involved-site radiation therapy (ISRT)

Involved-site radiation therapy (ISRT) is recommended to treat Hodgkin lymphoma. ISRT targets the lymph nodes in which the cancer first started and nearby areas of cancer. ISRT is a type of external beam radiation therapy (EBRT). External radiation simply means that the radiation comes from a machine outside of (external to) your body.

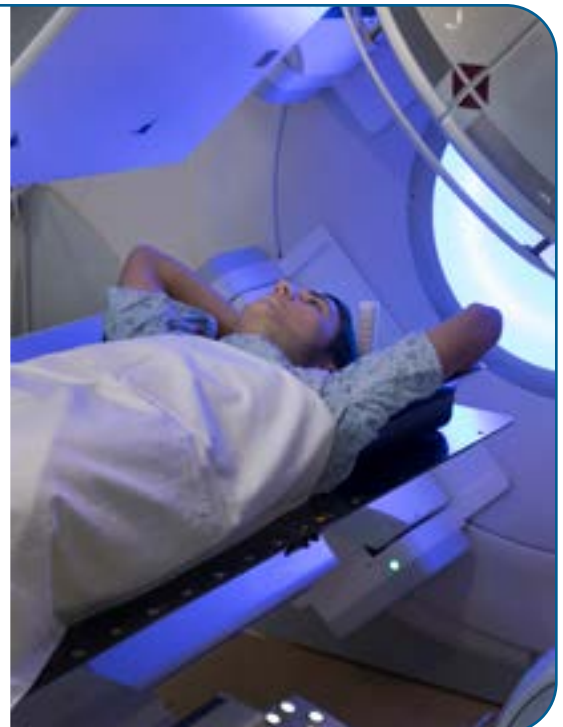
A simulation session is required if radiation therapy is planned and is done before the start

of radiation therapy. During simulation, pictures of the tumor will be taken. This is usually done using a CT scan in the radiation treatment position. The pictures are used to plan the best radiation dose, number, and shape of radiation beams, and number of treatment sessions. You may be asked to hold your breath during the simulation scan or treatment in order to limit the movement of your heart and lungs.

During treatment, you will lie on a table in the same position as done for simulation. Devices may be used to keep you from moving. These may include a mesh mask and body mold. You will be alone while the therapists operate the machine from a nearby control room.

Radiation therapy

Radiation therapy is usually used in addition to chemotherapy to treat Hodgkin lymphoma. A type of external radiation therapy called involved-site radiation therapy targets the lymph nodes where the cancer started and nearby areas of cancer.



Stem cell transplant

Blood stem cells are cells that develop into mature blood cells. Stem cells and mature blood cells are made in bone marrow. The goal of a stem cell transplant is to cure cancer by replacing unhealthy blood stem cells with healthy ones. This is done by destroying bone marrow with high doses of chemotherapy, and then transplanting healthy blood stem cells. The healthy blood stem cells form new marrow and blood cells.

The type of stem cell transplant used most often for Hodgkin lymphoma is called an *autologous* stem cell transplant.

Autologous stem cell transplant

Also called HDT/ASCR (high-dose therapy with autologous stem cell rescue), this type of transplant uses your own stem cells. You may have an autologous transplant if first-line treatment didn't work.

Collecting stem cells

The first step of a stem cell transplant is to collect, or harvest, your blood stem cells. Blood stem cells can be collected from either your blood or bone marrow.

If the stem cells are being collected from your blood, a process called *apheresis* is used. You may first be given medicine to increase the number of stem cells in your blood. Then, your blood will be removed from a large vein, most likely in your arm. It will flow through a tube and into a machine that removes stem cells. The rest of your blood will be returned to you in your other arm.

Apheresis typically takes 4 to 6 hours and does not require anesthesia. It may take two or more

sessions to obtain enough stem cells. During the procedure, you may have lightheadedness, chills, numbness around the lips, and cramping in the hands.

If the stem cells are being collected from your bone marrow, a procedure called *bone marrow aspiration* is used. For this procedure, you will be given either regional anesthesia or general anesthesia. Next, a needle will be inserted through your skin into your hip bone to draw out the bone marrow. Rarely, marrow is removed from the breastbone. The needle must be inserted many times into one or more spots to collect enough marrow. The marrow will then be processed to collect the stem cells.

After apheresis or aspiration, your harvested cells will be combined with a preservative. Then, they will be frozen and stored to keep them alive until the transplant. This process is called cryopreservation.

High-dose chemotherapy

After your stem cells have been harvested, you will receive high doses of chemotherapy. High doses are given so that your body can't make stem cells. High-dose chemotherapy also destroys normal cells in the bone marrow. This greatly weakens your immune system so that your body doesn't kill the transplanted stem cells. Not every person can tolerate high-dose chemotherapy before the transplant.

Transplanting stem cells

When chemotherapy is completed, your harvested stem cells will be put back into your body. A transfusion will be used. A transfusion is a slow injection of blood products through a central line into a large vein. A central line (or central venous catheter) is a thin tube. The tube will be inserted into your skin through one cut

then into your vein through a second cut. Local anesthesia will be used. This process can take several hours to complete.

The transplanted stem cells will travel to your bone marrow and grow. New, healthy blood cells will form. This is called *engraftment*. It usually takes about 2 to 4 weeks.

Until then, you will have little or no immune defense. You will need to stay in a very clean room at the hospital. You may be given an antibiotic to prevent or treat infection. You may also be given a blood transfusion to prevent bleeding and to treat low red blood counts (anemia). While waiting for the cells to engraft, you will likely feel tired and weak.

Allogeneic stem cell transplant

An allogeneic stem cell transplant uses stem cells from a donor. This type of stem cell transplant is not used often in the management of CHL, but may be an option for CHL that doesn't respond to treatment.

Immunotherapy

The immune system is your body's natural defense against infection and disease. Immunotherapy is a newer type of cancer treatment that increases the activity of your immune system. By doing so, it improves your body's ability to find and destroy cancer cells.

Brentuximab vedotin (Adcetris®)

Hodgkin lymphoma cells have proteins on their surface called CD30. Adcetris® attaches to CD30 and releases chemotherapy medicine into the cancer cell. By targeting only cells

with CD30 receptors, fewer normal cells are harmed.

Adcetris® is a treatment option for CHL that didn't respond well to first-line treatment, or that has returned after treatment. It is also an option for first-line treatment of advanced (stage III–IV) CHL in combination with chemotherapy. It is put directly into the bloodstream (infusion).

Rituximab (Rituxan®)

Rituxan® is an antibody therapy used to treat NLPHL. Blood cells with cancer (and some healthy blood cells) have a protein on their surface called CD20. Rituxan® targets and attaches to the CD20 protein. This helps your immune system find and attack the cancer cells. **Rituxan® may be given alone or in combination with chemotherapy to treat NLPHL.**

Checkpoint inhibitors

The following immunotherapy medicines may be used to treat Hodgkin lymphoma that doesn't respond to treatment or that comes back after treatment:

- Nivolumab (Opdivo®)
- Pembrolizumab (Keytruda®)

Clinical trials

New tests and treatments aren't offered to the public until they are deemed safe for testing and potentially effective. They first need to be studied in a way that is regulated by the FDA and other governmental agencies.

A clinical trial is a type of research that studies the safety and effectiveness of tests and treatments. They are done at all stages of a disease like Hodgkin lymphoma. When found to be safe and effective, they may become tomorrow's standard of care.

Because of clinical trials, the tests and treatments in this book are now widely used to help people with Hodgkin lymphoma. All new drugs are tested in a clinical trial before being approved for general use. Most patients will be given standard treatment first. Clinical trials are offered when standard treatment fails, or if the treatment is intolerable.

Joining a clinical trial can have both benefits and risks. You will need to weigh the potential benefits and downsides to decide what is right for you. To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial are often alike in terms of their cancer and general health. This is to ensure that any progress is because of the treatment and not because of differences between patients. To join, you'll need to review and sign a paper called an informed consent form. This form describes the study in detail, including the risks and benefits.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you're getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in the chapter, *Making treatment decisions*.

Clinical trials

A clinical trial is a type of research that studies the safety and effectiveness of tests and treatments.

Because of clinical trials, the tests and treatments in this book are now widely used to help people with Hodgkin lymphoma.



Review

- ▶ Chemotherapy is the most widely used and most effective treatment for Hodgkin lymphoma.
- ▶ Some steroids have anti-cancer effects and may be used with chemotherapy.
- ▶ Radiation therapy is often given after chemotherapy but sometimes is used alone to treat Hodgkin lymphoma.
- ▶ A stem cell transplant destroys bone marrow then replaces it by adding healthy stem cells into your body. It is an option if chemotherapy with or without radiation therapy fails.
- ▶ Immunotherapy is a newer type of cancer treatment that increases the activity of your immune system. By doing so, it improves your body's ability to find and destroy cancer cells.
- ▶ Immunotherapy medicines may be used to treat Hodgkin lymphoma that doesn't respond to treatment (refractory) or that returns after treatment (relapsed).
- ▶ Rituximab (Rituxan®) is a targeted therapy widely used alone or in combination with chemotherapy to treat NLPHL.

4

Classic Hodgkin lymphoma (CHL)

- 35 Risk assessment
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This chapter presents the treatment options for classic Hodgkin lymphoma. CHL may be treated with chemotherapy alone, or with both chemotherapy and radiation therapy. A stem cell transplant may be needed if the cancer doesn't respond to treatment.

Risk assessment

Stage I–II CHL may have certain features that make it harder to treat, or that are known to lead to poorer outcomes. Your doctor may refer to these as “unfavorable” risk factors.

These unfavorable risk factors include large (“bulky”) tumors in your lymph nodes or chest, B symptoms, a fast erythrocyte sedimentation rate (ESR), and having cancer in 3 or more groups of lymph nodes. These risk factors are also listed in [Guide 4](#).

Treatment of stage I–II CHL is based in part on whether the cancer has any of these risk factors.

In order to plan the best treatment, doctors often group people with stage I–II CHL into one of 3 categories, depending on which risk factors (if any) they have. The risk groups are explained below.

- **Low-risk** early disease means that the cancer doesn't have any of the risk factors listed in [Guide 4](#).
- **Medium-risk** early disease means that the cancer has one or more risk factors listed in [Guide 4](#), but not large (bulky) tumors.
- **High-risk** early disease means that the cancer is large (bulky) and there may also be other risk factors that are listed in [Guide 4](#).

Guide 4 Risk factors for stage I–II CHL

Large (“bulky”) cancer. This means that there are either large tumors in one or more lymph nodes, or there is a large tumor in the area between your lungs.

B symptoms (fevers, night sweats, and extreme weight loss without dieting)

Fast erythrocyte sedimentation rate (ESR) (50 or higher)

3 or more areas of cancer

Low-risk early CHL

Low-risk early disease means the cancer doesn't have any of the risk factors listed in [Guide 4](#) on the previous page.

Two treatment approaches

There are 2 main approaches to treating low-risk early CHL:

- Combination therapy (treatment with both chemotherapy and radiation therapy)
- Chemotherapy alone

Option 1: Combination therapy

This approach uses both chemotherapy and radiation therapy. **Treatment begins with 2 cycles of chemotherapy with the ABVD regimen.** After finishing chemotherapy, you should have a PET/CT scan to see if the cancer improved. Further treatment depends on the results of the PET scan (the Deauville score).

Deauville score of 1 or 2

1 more cycle of ABVD chemotherapy and radiation therapy are recommended.

Deauville score of 3

2 more cycles of ABVD chemotherapy and radiation therapy are recommended.

Deauville score of 4

More chemotherapy is needed. You can continue ABVD for 2 more cycles, or switch to escalated BEACOPP for 2 cycles. After finishing chemotherapy, you should have another PET scan. Further treatment depends

Guide 5

Deauville score of 4 after 2 cycles of ABVD chemotherapy

Step 1: Chemotherapy	Continue with the ABVD regimen for 2 more cycles or switch to escalated BEACOPP for 2 cycles.
Step 2: Restage	PET/CT scan to see if the cancer improved. A new (“interim”) Deauville score will be given.
Step 3: Treatment based on interim Deauville score	<p>Interim Deauville score of 1–3:</p> <ul style="list-style-type: none"> • Option 1: Radiation therapy alone. • Option 2: Continue the same chemotherapy regimen for 2 more cycles. Radiation therapy may be given in addition to chemotherapy. <p>Interim Deauville score of 4–5:</p> <ul style="list-style-type: none"> • Biopsy. If the biopsy is negative, see treatment options directly above for Deauville 1–3. If the biopsy is positive, start treatment for refractory CHL (see page 46).

on the results of the new (interim) PET scan (the Deauville score). [See Guide 5.](#)

Deauville score of 5

If the Deauville score is 5 after 2 cycles of ABVD chemotherapy, there are two possibilities.

Your doctor may recommend more chemotherapy with a different regimen (escalated BEACOPP). Depending on the results of chemotherapy, a biopsy may be needed. [See Guide 6.](#)

Your doctor may want to do a biopsy before giving further treatment. If the biopsy is negative, you would then continue chemotherapy, but with a different regimen (escalated BEACOPP). [See Guide 6.](#) If the biopsy is positive, treatment for refractory CHL is recommended (see page 46).

Option 2: Chemotherapy alone

This approach for treating stage I–II low-risk CHL uses chemotherapy alone as the initial treatment. Keep in mind that radiation therapy may be needed later, depending on the results of chemotherapy.

Treatment begins with 2 cycles of chemotherapy with the ABVD regimen, followed by a PET/CT scan. Further treatment depends on the results of the PET scan (the Deauville score).

Deauville score of 1–2

More chemotherapy is recommended. You may have 1 or 2 additional cycles of ABVD chemotherapy.

Other combination therapy options for low-risk early CHL

The Stanford V regimen

Combination therapy for low-risk early CHL usually starts with chemotherapy with the ABVD regimen. However, the "B" in ABVD stands for bleomycin. Bleomycin can damage the lungs and cause a disease called pulmonary fibrosis. Older adults with CHL may not be able to tolerate bleomycin. Another combination therapy option for low-risk early CHL is the Stanford V regimen, followed by radiation therapy if the cancer responds to chemotherapy.

The German Hodgkin Study Group (GHSg) HD10 study

An important research study of low-risk early CHL found that—in some people who meet very specific criteria—fewer cycles of chemotherapy may be just as effective (and less toxic) when followed by radiation therapy. If you meet the same criteria as the participants in the study, your doctor may recommend a slightly different combination therapy approach that could involve less chemotherapy.

Deauville score of 3

Continue ABVD chemotherapy for 2 more cycles.

Deauville score of 4

More chemotherapy is needed. You can continue ABVD for 2 more cycles, or switch to escalated BEACOPP for 2 cycles. After chemotherapy, you should have another PET scan. Further treatment depends on the results of the new PET scan. [See Guide 5](#) on page 37.

Deauville score of 5

There are two possibilities. Your doctor may recommend more chemotherapy with a different regimen (escalated BEACOPP). Depending on the results of chemotherapy, a biopsy may be needed. [See Guide 6](#). Your doctor may want to do a biopsy before giving further treatment. If

the biopsy is negative, you would then continue chemotherapy, but with a different regimen (escalated BEACOPP). [See Guide 6](#). If the biopsy is positive, treatment for refractory CHL is recommended (see page 46).

Guide 6**Deauville score of 5 after 2 cycles of ABVD chemotherapy****Step 1: More chemotherapy**

Switch to escalated BEACOPP chemotherapy for 2 cycles.

Step 2: Restage

PET/CT scan. A new (interim) Deauville score will be given.

Step 3: Treatment based on interim Deauville score**Interim Deauville score of 1–3:**

- Radiation therapy alone, or
- 2 more cycles of escalated BEACOPP chemotherapy. You may have radiation therapy in addition to chemotherapy.

Interim Deauville score of 4–5:

- Biopsy to differentiate refractory CHL from a different type of lymphoma. If the biopsy is positive, treatment for refractory CHL is recommended (see page 46). If the biopsy is negative, you should switch to escalated BEACOPP chemotherapy for 2 cycles. You may also have radiation therapy.

Medium-risk early CHL

Medium-risk stage I–II CHL means that the cancer isn't bulky, but it does have one or more of the other risk factors listed below.

- B symptoms
- A fast erythrocyte sedimentation rate (ESR)
- Cancer in more than 3 areas

There are 2 main approaches for initial treatment of medium-risk early CHL:

- Combination therapy (chemotherapy and radiation therapy)
- Chemotherapy alone

Treatment with combination therapy is described first. Treatment with chemotherapy is explained on page 41.

Combination therapy

This approach uses both chemotherapy and radiation therapy. **Treatment begins with 2 cycles of chemotherapy with the ABVD regimen, followed by a PET/CT scan.** Further treatment depends on the results of the PET scan (the Deauville score).

Deauville score of 1 or 2

Two more cycles of ABVD chemotherapy and radiation therapy are recommended. The treatments are given during the same time period, not one after the other.

This will bring the total number of cycles of ABVD chemotherapy you've had to 4. After

Guide 7

Combination therapy for medium-risk early CHL

Step 1: Chemotherapy	2 cycles of chemotherapy with the ABVD regimen.
Step 2: Restage	PET/CT scan to see if the cancer improved. A Deauville score will be given.
Step 3: Treatment based on Deauville score	<p>Deauville score of 1 or 2:</p> <ul style="list-style-type: none"> • 2 more cycles of ABVD chemotherapy and radiation therapy. <p>Deauville score of 3 or 4:</p> <ul style="list-style-type: none"> • 2 cycles of chemotherapy (either continue ABVD or switch to escalated BEACOPP) followed by radiation therapy. You may have a PET/CT scan in between chemotherapy and radiation therapy. <p>Deauville score of 5:</p> <ul style="list-style-type: none"> • Biopsy. If the biopsy is negative, see the treatment options for a Deauville score of 3 or 4 above. If the biopsy is positive, treatment for refractory (persistent) CHL is recommended. See page 46.

4 cycles of chemotherapy with the ABVD regimen, your doctor may order lung function tests to see how well your lungs are working.

Deauville score of 3 or 4

Chemotherapy and radiation therapy are recommended, but not at the same time. You should have 2 cycles of chemotherapy first. There are two options for chemotherapy:

- Continue ABVD chemotherapy for 2 more cycles. This option is preferred if the Deauville score is 3.
- Switch to escalated BEACOPP chemotherapy for 2 cycles. This option is preferred if the Deauville score is 4.

After finishing chemotherapy, your doctor may order another PET/CT scan to see how well the cancer responded to treatment. After chemotherapy (and a PET/CT scan, if you had one), radiation therapy is recommended.

Deauville score of 5

Biopsy (testing) of the cancer is recommended. The purpose of testing the cancer is to differentiate refractory CHL from a different type of lymphoma.

If the biopsy is negative, see the treatment options for a Deauville score of 3 or 4 on the previous page. If the biopsy is positive, treatment for refractory (persistent) CHL is recommended. See page 46.

Other options for combination therapy

The combination therapy approach described here includes chemotherapy with the ABVD regimen. This is the most common chemotherapy regimen used with radiation therapy to treat medium-risk early CHL.

However, there are other options that may be a better choice for some people, for one or more reasons. The other options include:

- 12 weeks of the Stanford V regimen and radiation therapy
- 2 cycles of escalated BEACOPP followed by 2 cycles of ABVD and radiation therapy

Chemotherapy alone

This approach for treating early, medium-risk CHL uses chemotherapy alone as the initial treatment. Radiation therapy may be needed later, depending on the results of initial treatment with chemotherapy.

Treatment begins with 2 cycles of chemotherapy with the ABVD regimen, followed by a PET/CT scan. Further treatment depends on the results of the PET scan (the Deauville score).

Deauville score of 1, 2, or 3

4 cycles of AVD chemotherapy (does not include bleomycin) are recommended.

Deauville score of 4

See [Guide 5](#) on page 37. More chemotherapy is needed. You can continue ABVD for 2 more cycles, or switch to escalated BEACOPP for 2 cycles. After finishing chemotherapy, you should have another PET scan. Further treatment depends on the results of the new PET scan (the Deauville score).

Deauville score of 5

See [Guide 6](#) on page 38. There are two possibilities. Your doctor may recommend more chemotherapy with a different regimen (escalated BEACOPP). Depending on the results of chemotherapy, a biopsy may be needed.

Or, your doctor may want to do a biopsy before giving further treatment. If the biopsy is negative, you would then continue chemotherapy, but with a different regimen (escalated BEACOPP). See [Guide 6](#) on page 38. If the biopsy is positive, treatment for refractory CHL is recommended (see page 46).

High-risk early CHL

High-risk early CHL means that the cancer is large (bulky). The cancer may also have one or more of the other 3 risk factors listed in [Guide 4](#) on page 35. Everyone with bulky, early-stage CHL should have chemotherapy first. There are two options for chemotherapy:

- The ABVD regimen
- The Stanford V regimen

While both regimens are appropriate treatment options, the ABVD regimen is preferred by NCCN experts for bulky stage I–II CHL.

Preferred option: ABVD chemotherapy

Treatment begins with 2 cycles of chemotherapy with the ABVD regimen. This is the preferred treatment for most people with bulky, early-stage CHL. After finishing chemotherapy, a PET/CT scan should be performed. Further treatment depends on the results of the PET scan (the Deauville score).

Deauville score of 1–3

If the Deauville score is 1, 2, or 3 after 2 cycles of ABVD chemotherapy, there are two options:

- 2 more cycles of ABVD chemotherapy and radiation therapy
- 4 cycles of AVD chemotherapy (does not include bleomycin). You may also have radiation therapy.

Deauville score of 4

If the Deauville score is 4 after 2 cycles of ABVD chemotherapy, there are three options:

- Continue ABVD chemotherapy for 2 more cycles followed by radiation therapy. You may have another PET/CT scan between chemotherapy and radiation.
- Switch to escalated BEACOPP chemotherapy for 2 cycles, followed by radiation therapy. You may have another PET/CT scan between chemotherapy and radiation.
- Switch to escalated BEACOPP chemotherapy for 3 cycles, followed by a PET/CT scan. After the PET/CT scan, continue escalated BEACOPP for 1 more cycle.

Deauville score of 5

If the Deauville score is 5 after 2 cycles of ABVD chemotherapy, there are three options:

- **Option 1:** Test the cancer by doing a biopsy. If the biopsy is negative, see the treatment options directly above for a Deauville score of 4. If the biopsy is positive, treatment for refractory CHL is recommended. See page 46.
- **Option 2:** Switch to escalated BEACOPP chemotherapy for 2 cycles, followed by radiation therapy. You may have another PET/CT scan between chemotherapy and radiation. After radiation therapy, you can begin follow-up care.
- **Option 3:** Start treatment for refractory CHL. See page 46.

Other option: Stanford V chemotherapy

Another option for treating high-risk (bulky) stage I–II CHL is chemotherapy with the Stanford V regimen. Twelve weeks of this regimen is recommended. After finishing chemotherapy, a PET/CT scan should be performed. Further treatment depends on the results of the PET scan (the Deauville score).

Deauville score of 1–4

Radiation therapy is recommended. NCCN experts recommend treating tumors that were bigger than 5 cm wide (about 2 inches) at the time of diagnosis. Ideally, radiation therapy should start within 2–3 weeks. After radiation therapy, you can begin follow-up care. You should have another PET/CT scan within 3 months to make sure the cancer is gone.

Deauville score of 5

If the Deauville score is 5 after chemotherapy with the Stanford V regimen, a biopsy is recommended. If the biopsy is positive, treatment for refractory CHL is recommended. See page 46.

If the biopsy is negative, radiation therapy is recommended. You can then begin follow-up care. You should have another PET/CT scan within 3 months to make sure the cancer is gone.

Advanced CHL (stage III–IV)

This section explains the recommended treatment options for CHL that has spread below the diaphragm, and possibly outside the lymphatic system.

Prognostic scores

Cancer researchers have developed a scoring system used to help guide treatment decisions for people with advanced CHL.

The seven risk factors below have been shown to contribute to poor treatment outcomes in people with stage III-IV CHL.

- Age 45 years or older
- Male gender
- Stage IV disease
- Albumin level below 4 g/dL
- A low hemoglobin level for your age and sex (commonly known as anemia)
- A high number of white blood cells in the blood (called *leukocytosis*)
- An extremely low level of lymphocytes in the blood (called *lymphocytopenia*)

The score is calculated by adding the number of these risk factors that apply to you or your cancer. The total is called the International Prognostic Score (IPS).

Overview of treatment

Chemotherapy is always used to treat stage advanced CHL. Radiation therapy may be given in addition to chemotherapy. The three most common chemotherapy regimens used to treat advanced CHL are listed below. The

ABVD regimen is the best option for most people.

- ABVD chemotherapy. **This is the best option for most people.**
- Escalated-dose BEACOPP chemotherapy. This regimen may be an option for some people younger than age 60 with an IPS score of 4 or higher.
- Brentuximab vedotin plus AVD chemotherapy. This may be a good option for some people without nerve damage and with an IPS score of 4 or higher, or who can't have bleomycin.

ABVD chemotherapy

This treatment pathway is recommended for most people with stage III–IV CHL. Treatment begins with 2 cycles of chemotherapy with the ABVD regimen, followed by a PET/CT scan. Further treatment depends on the results of the PET scan (the Deauville score) and may include chemotherapy, radiation therapy, or both.

Deauville score of 1, 2, or 3

The next step is to have 4 cycles of AVD (not ABVD) chemotherapy. AVD chemotherapy does not include bleomycin. After chemotherapy, there are two options.

- No further treatment (observation)
- Radiation therapy to high-risk areas

Deauville score of 4 or 5

If the Deauville score is 4, you can either continue ABVD chemotherapy for 2 more cycles, or switch to escalated BEACOPP chemotherapy for 2 cycles.

If the Deauville score is 5, switching to escalated BEACOPP for 2 cycles is recommended. Your doctor may want to do a biopsy of any new tumors before starting more treatment.

After chemotherapy with either ABVD or escalated BEACOPP, you should have another PET/CT scan to see if the cancer improved. Further treatment depends on the new (interim) Deauville score.

If the [interim Deauville score is 1, 2, or 3](#), continue chemotherapy with the same regimen (either ABVD or escalated BEACOPP) for 2 more cycles. Radiation therapy may be given during the same time period.

If the [interim Deauville score is 4 or 5](#), a biopsy is recommended. If the biopsy is negative, continue chemotherapy with the same regimen (either ABVD or escalated BEACOPP) for 2 more cycles. Radiation therapy may be given during the same time period. If the biopsy is positive, treatment for refractory (persistent) CHL is recommended. See page 46.

Escalated BEACOPP chemotherapy

This pathway may be an option for some people younger than age 60 who have an IPS score of 4 or higher. Treatment begins with 2 cycles of chemotherapy with the escalated BEACOPP regimen, followed by a PET/CT scan. Further treatment depends on the Deauville score.

Deauville score of 1, 2, or 3

More chemotherapy is needed. There are three options:

- Continue escalated BEACOPP for 2 more cycles

- Switch to ABVD chemotherapy for 4 cycles
- Switch to AVD chemotherapy (does not include bleomycin) for 4 cycles

After chemotherapy, you may have radiation therapy to high-risk areas.

Deauville score of 4

Continue escalated BEACOPP chemotherapy for 2 more cycles (bringing you to 4 cycles total). Next, a PET/CT scan is done to see if the cancer improved. Further treatment depends on the new (interim) Deauville score.

If the interim Deauville score is 1, 2, or 3, continue escalated BEACOPP chemotherapy for 2 more cycles. After chemotherapy, you may have radiation therapy to high-risk areas.

If the interim Deauville score is 4 or 5, a biopsy is recommended.

- If the biopsy is negative, continue escalated BEACOPP chemotherapy for 2 more cycles. After chemotherapy, you may have radiation therapy to high-risk areas.
- If the biopsy is positive, treatment for refractory (persistent) CHL is recommended. See page 46.

Deauville score of 5

A biopsy is recommended. If the biopsy is negative, continue escalated BEACOPP chemotherapy for 4 more cycles. You may also have radiation therapy to high-risk areas.

If the biopsy is positive, treatment for refractory (persistent) CHL is recommended. See page 46.

Brentuximab vedotin and AVD

Chemotherapy with this regimen may be a good option for people who:

- Don't suffer from nerve problems or damage (called "neuropathy")
- Have an IPS score of 4 or higher
- Can't have bleomycin

Treatment begins with 2 cycles of chemotherapy with brentuximab vedotin plus AVD. You should then have a PET/CT scan in order to restage the cancer. Further treatment depends on the Deauville score.

Continuing chemotherapy with brentuximab vedotin and AVD for 4 more cycles is recommended for all Deauville scores (1, 2, 3, 4, and 5). An additional option for a Deauville score of 5 is called "alternative frontline

therapy." This may include chemotherapy with escalated BEACOPP or treatment for refractory (persistent) disease. After chemotherapy, you should then have another PET/CT scan. Further treatment depends on the new (interim) Deauville score.

If the interim Deauville score is 1 or 2, you can begin follow-up care.

If the interim Deauville score is 3 or 4, there are two options. One option is to watch and wait (no treatment). The other is to have radiation therapy to high-risk areas.

If the interim Deauville score is 5, treatment for refractory (persistent) CHL is recommended. See page 46.

Guide 8**Brentuximab vedotin and AVD for advanced CHL**

Step 1: Chemotherapy	2 cycles of brentuximab vedotin plus AVD
Step 2: Restage	PET/CT scan to see if the cancer improved. A Deauville score will be given.
Step 3: More chemotherapy	<p>Continue chemotherapy with brentuximab vedotin and AVD (possibly different regimen if Deauville score is 5) for 4 more cycles, followed by PET/CT scan. Further treatment based on new (interim) Deauville score.</p> <p>Interim Deauville score of 1 or 2: Watch and wait (no treatment)</p> <p>Interim Deauville score of 3 or 4:</p> <ul style="list-style-type: none"> • Option 1: Watch and wait (no treatment) • Option 2: Radiation therapy <p>Interim Deauville score of 5: Treatment for refractory CHL (see page 46)</p>

If CHL doesn't respond to treatment

Cancer that doesn't respond to treatment is called *refractory* or resistant. There is no "best" way of treating refractory CHL. Treatment should be customized to the unique characteristics of your cancer.

If CHL doesn't respond to treatment, the first step is to do a biopsy. If a biopsy confirms that the cancer is refractory CHL, more systemic therapy (chemotherapy) is recommended.

Second-line treatment is given when initial treatment (first-line therapy) doesn't work or stops working. Second-line systemic therapy (chemotherapy) is recommended for everyone with refractory CHL. [See Guide 9](#) for the recommended second-line chemotherapy regimens. After systemic therapy, the cancer should be restaged by doing another PET/CT scan.

Deauville score of 1 to 3

High-dose therapy with autologous stem cell rescue (HDT/ASCR) is recommended for everyone who can have them. Radiation therapy may be given in addition to HDT/ASCR. After HDT/ASCR (and radiation therapy, if you have it), there are two options. If your doctor thinks the cancer is likely to return, 1 year of maintenance therapy with brentuximab vedotin (Adcetris®) is recommended. You can then begin follow-up care.

If you can't have high-dose therapy with autologous stem cell rescue, taking a watch-and-wait approach (observation) is recommended. Radiation therapy may also be an option. You can then begin follow-up care.

Deauville score of 4

If the Deauville score is 4 after second-line systemic therapy, there are three options.

Guide 9

Second-line chemotherapy regimens for refractory CHL

Brentuximab vedotin (Adcetris®)

Brentuximab vedotin (Adcetris®) and bendamustine (Treanda®, Bendeka™)

Brentuximab vedotin (Adcetris®) and nivolumab (Opdivo®)

DHAP: Dexamethasone, cisplatin, and high-dose cytarabine (Cytosar-U®)

ESHAP: Etoposide (Etopophos®), methylprednisolone, high-dose cytarabine (Cytosar-U®), and cisplatin

Gemcitabine (Gemzar®), bendamustine (Treanda®, Bendeka™), and vinorelbine (Navelbine®)

GVD: Gemcitabine (Gemzar®), vinorelbine (Navelbine®), and liposomal doxorubicin (Doxil®)

ICE: Ifosfamide, carboplatin, and etoposide (Etopophos®)

IGEV: Ifosfamide, gemcitabine (Gemzar®), and vinorelbine (Navelbine®)

Option 1: High-dose therapy with autologous stem cell rescue (HDT/ASCR). Radiation therapy may also be used. Whether or not you need more treatment depends on how likely the cancer is to return. If your doctor thinks you are at low or average risk of the cancer returning, you can take a watch-and-wait approach and begin follow-up care. If your doctor thinks the cancer is likely to return, 1 year of maintenance therapy with brentuximab vedotin (Adcetris®) is recommended. You can then begin follow-up care.

Option 2: Radiation therapy alone. You can then begin follow-up care.

Option 3: More systemic therapy (chemotherapy). Radiation therapy may also be given. Options for chemotherapy include other second-line regimens that you didn't already receive (see Guide 9), or third-line and beyond regimens (see Guide 10). You can then begin follow-up care.

Deauville score of 5

If the Deauville score is 5 after second-line systemic therapy, there are two options.

Option 1: More chemotherapy. Radiation therapy may also be given. Options for chemotherapy include other second-line regimens that you didn't already receive (see Guide 9), or third-line and beyond regimens (see Guide 10).

Option 2: Radiation therapy alone. If the cancer improves after chemotherapy, radiation therapy, or both, having a stem cell transplant may be an option. It may be either autologous or allogeneic. You can then begin follow-up care.

Guide 10

Third-line and beyond chemotherapy regimens for refractory CHL

Bendamustine (Treanda®, Bendeka™)

C-MOPP (cyclophosphamide, vincristine, procarbazine, and prednisone)

Everolimus (Afinitor®)

GCD: Gemcitabine (Gemzar®), carboplatin, and dexamethasone

Lenalidomide (Revlimid®)

MINE: Etoposide (Etopophos®), ifosfamide, mesna (Mesnex®), and mitoxantrone (Novantrone®)

Mini-BEAM: Carmustine (BiCNU®), cytarabine, etoposide, and melphalan

Nivolumab (Opdivo®)

Pembrolizumab (Keytruda®)

CHL in older adults

While CHL is often curable in younger adults, treatment outcomes for older adults are not as good. People older than age 60 often have other, sometimes serious, health problems. They may also not be able to do a wide range of day-to-day tasks and activities. In addition, the cancer itself tends to have different features in older adults, which can make it harder to treat.

Chemotherapy

Like in younger adults, the main treatment for CHL in older adults is chemotherapy. However, the standard chemotherapy regimens for CHL are too harsh and potentially dangerous to use in older adults. For example, most of the chemotherapy regimens used to treat CHL in younger adults include the drug bleomycin (Blenoxane®). Bleomycin can damage the lungs and cause a disease called pulmonary fibrosis. Pulmonary fibrosis is a buildup of scar tissue in the lungs that makes it hard to breathe, and causes other side effects. Older adults with CHL may not be able to tolerate chemotherapy that includes bleomycin.

Unfortunately, there isn't a lot of research on alternatives to standard treatments for older patients. The goal of choosing a treatment regimen is to try to find the most effective treatment that will cause the least amount of harm. Your doctor should consider your overall health, the features of the cancer, and the harshness of a chemotherapy regimen when recommending a treatment option.

The treatment regimens in [Guide 11](#) are likely to be less harmful to older adults with CHL than standard treatment regimens. Unfortunately, treatment outcomes for older adults with CHL

are usually poor, even if one of these milder regimens is used. For this reason, joining a clinical trial is recommended if there is one available to you. If your doctor feels that you should not have any chemotherapy at all, treatment with radiation therapy alone is an option.

Older adults with CHL are more likely to have:

- ✓ B symptoms
- ✓ Other health conditions or limitations
- ✓ The Epstein-Barr virus
- ✓ A subtype of classic Hodgkin lymphoma called "mixed cellularity Hodgkin lymphoma (MCHL)"

Guide 11

Treatment options for older adults with CHL

Stage I–II favorable CHL	2 cycles of chemotherapy with the ABVD regimen (bleomycin is optional). May be followed by 2 cycles of AVD chemotherapy and radiation therapy. (Preferred)
	4 cycles of chemotherapy with the CHOP regimen (cyclophosphamide, doxorubicin, vincristine, and prednisone) and radiation therapy
	3 cycles of chemotherapy with the VEPEMB regimen (vinblastine, cyclophosphamide, prednisolone, procarbazine, etoposide, mitoxantrone, and bleomycin) with or without radiation therapy
Stage I–II unfavorable CHL Stage III–IV CHL	2 cycles of chemotherapy with the ABVD regimen (bleomycin is optional), followed by a PET scan. <ul style="list-style-type: none"> • If the PET scan is negative, 4 cycles of chemotherapy with the AVD regimen is recommended. • If the PET scan is positive, discuss your treatment options with your doctor.
	Chemotherapy with brentuximab vedotin (Adcetris®) and dacarbazine
	6 cycles of chemotherapy with one of the below regimens, with or without radiation therapy: <ul style="list-style-type: none"> • CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) • PVAG (prednisone, vinblastine, doxorubicin, and gemcitabine) • VEPEMB (vinblastine, cyclophosphamide, prednisolone, procarbazine, etoposide, mitoxantrone, and bleomycin)
CHL that doesn't respond to treatment or that comes back after treatment Options for helping with symptoms caused by the cancer (palliative therapy)	Chemotherapy with bendamustine (Treanda®, Bendeka™)
	Chemotherapy with brentuximab vedotin (Adcetris®)
	Radiation therapy
	Targeted therapy with nivolumab (Opdivo®)
	Targeted therapy with pembrolizumab (Keytruda®)
	Treatment options listed in Guide 9 and Guide 10

Review

- ▶ Stage I–II CHL may have certain features that make it harder to treat or that are known to lead to poorer outcomes. Treatment is based in part on whether the cancer has any of these risk factors.
- ▶ The risk factors include large or “bulky” tumors in your lymph nodes or chest, B symptoms, a fast erythrocyte sedimentation rate, and having cancer in three or more groups of lymph nodes.
- ▶ There are two main approaches for the initial treatment of CHL: chemotherapy and combination therapy (chemotherapy and radiation therapy).
- ▶ It is important to have another PET/CT scan within 3 months of finishing treatment. If the PET/CT finds no signs of cancer, you can begin follow-up care.
- ▶ While CHL is often curable in younger adults, treatment outcomes for older adults are not as good. The chemotherapy regimens for CHL are too harsh and potentially dangerous to use in older adults.
- ▶ There are milder chemotherapy regimens that are likely to be less harmful to older adults. Joining a clinical trial is also recommended.
- ▶ High-dose therapy with autologous stem cell rescue is the best way to treat CHL that doesn’t respond to treatment (refractory), or that returns after treatment (relapsed).

5

Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL)

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- 56 Review



NLPHL is a very rare type of Hodgkin lymphoma. It is often slow-growing and may return long after treatment (relapse). However, more treatment is not always needed for relapsed NLPHL. Over time, NLPHL can transform into an aggressive type of non-Hodgkin's lymphoma.

About NLPHL

NLPHL is usually found at an early stage in most people, and doesn't tend to have any high-risk features when it is diagnosed. NLPHL can transform into an aggressive type of non-Hodgkin's lymphoma called diffuse large B-cell lymphoma (DLBCL).

NLPHL is more likely to transform into an aggressive B-cell lymphoma if any of the following are found at the time of diagnosis.

- Large tumor(s) (the medical term for this is "bulky disease")
- Cancer below the diaphragm
- Cancer in the spleen

Overview of treatment

The three main treatments for NLPHL are:

- Radiation therapy
- Chemotherapy
- Targeted therapy with rituximab (Rituxan®)

Depending on the cancer stage, they may be used alone or combined. Treatment of NLPHL depends in part on the following:

- Whether the lymph nodes with cancer are large (bulky)
- Whether the cancer is only above the diaphragm (stage I–II) or whether it has spread below the diaphragm (stage III–IV)
- If the cancer is in only in 2 groups of lymph nodes above the diaphragm (stage II), treatment also depends on whether the lymph node groups with cancer are next to each other (contiguous). If the lymph node groups with cancer aren't next to each other, it is called non-contiguous disease.



SNAPSHOT NLPHL

- A very rare form of Hodgkin lymphoma that is usually found at an early stage
- Known for being slow-growing and returning long after treatment (late relapse)
- Can transform into an aggressive (fast-growing) type of non-Hodgkin's lymphoma
- Radiation therapy alone is an option for treating early (stage IA–IIA) NLPHL

Initial treatment

This section describes the initial treatment options for NLPHL, according to stage.

Stage I-II

Stage IA and IIA

Most stage IA and IIA tumors are small (not bulky). Radiation therapy is recommended to treat these small, early-stage tumors.

Some people with stage IA NLPHL may be able to safely skip radiation therapy. This may be the case if cancer was found in only one lymph node that was totally removed. In this situation, while radiation therapy is preferred, having no further treatment is an option.

Large or non-contiguous tumors

While uncommon, stage IA and IIA tumors can be large (bulky). Stage IIA NLPHL may also be non-contiguous. This means that cancer is in 2 groups of lymph nodes above the diaphragm, but the groups are not next to each other.

NCCN experts recommend the combined use of chemotherapy, the targeted therapy rituximab (Rituxan®), and radiation therapy to treat bulky stage IA and bulky or non-contiguous stage IIA NLPHL. [Guide 12](#) lists the most common chemotherapy regimens given with Rituxan® to treat NLPHL. When used in combination with radiation therapy, chemotherapy is generally only given for 3 to 4 months.

Radiation therapy alone may be an option for a small number of people with stage IIA non-contiguous disease.

Stage IB and IIB

NCCN experts recommend the combined use of chemotherapy, the targeted therapy rituximab (Rituxan®), and radiation therapy to treat stage IB and stage IIB NLPHL. [Guide 12](#) lists the most common chemotherapy regimens given with Rituxan to treat NLPHL. When used in combination with radiation therapy, chemotherapy is generally only given for 3 to 4 months.

Radiation therapy alone may be an option for a small number of people with stage IB disease.

Guide 12

The most commonly used chemotherapy regimens for NLPHL

ABVD and Rituxan®	Doxorubicin, bleomycin, vinblastine, dacarbazine, and rituximab
CHOP and Rituxan®	Cyclophosphamide, doxorubicin, vincristine, prednisone, and rituximab
CVP and Rituxan®	Cyclophosphamide, vinblastine, prednisolone, and rituximab
Rituxan® alone	Rituximab

Stage III–IV

This section describes the initial treatment options for stage III–IV (advanced) NLPHL.

Before starting treatment

Over time, NLPHL can turn into a fast-growing type of non-Hodgkin's lymphoma called DLBCL. Before beginning treatment for advanced NLPHL, your doctor may want to confirm that the cancer hasn't transformed. This is important to know because B-cell lymphoma is managed differently than NLPHL. The cancer type is confirmed by removing a sample of one or more tumors below your diaphragm and testing them in a laboratory.

Treatment

Treatment with both chemotherapy and Rituxan® (a targeted therapy given with chemotherapy) is recommended for everyone with advanced (stage III–IV) NLPHL. The most common chemotherapy regimens given with rituximab (Rituxan®) to treat NLPHL are shown in [Guide 12](#). Your doctor may also recommend treatment with radiation therapy in addition to chemotherapy and rituximab (Rituxan®).

Other options include:

- Watch-and-wait. Having no further treatment is an option for people with no cancer symptoms.
- Treatment with rituximab (Rituxan®) alone.
- Radiation therapy alone to relieve symptoms caused by the cancer.

After initial treatment

After finishing initial treatment, you should have a PET/CT scan to learn if the cancer improved.

If the cancer improves but you are still having symptoms, radiation therapy is recommended (only if you haven't already had it). If the cancer improves and you don't have any symptoms, you don't need any more treatment. You can begin follow-up care. See the chapter titled, *When treatment is over*.

If the cancer doesn't improve—or gets worse—your doctor should make sure that it hasn't transformed into a non-Hodgkin's lymphoma. This is done by removing samples of one or more tumors below your diaphragm and testing them in a laboratory (a biopsy).

If the biopsy is negative and you don't have any symptoms, taking a watch-and-wait approach is recommended. No further treatment is needed and you can begin follow-up care. See the chapter called, *When treatment is over*.

If the biopsy is positive, treatment for refractory NLPHL is recommended. "Refractory" is the medical term for cancer that does not respond to treatment.

Refractory or relapsed NLPHL

If NLPHL doesn't respond to treatment or returns after a cancer-free period, second-line chemotherapy that includes rituximab (Rituxan®) is recommended. [See Guide 13](#). Keep in mind that NLPHL can be very slow-growing and some people may not need aggressive treatment. Treatment decisions should be based on your general health and the features of the cancer. There isn't a "best" way to treat refractory or relapsed NLPHL.

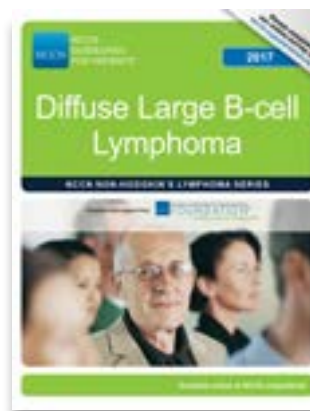
NLPHL can transform into an aggressive type of non-Hodgkin's lymphoma. Before starting second-line chemotherapy, it is a good idea to make sure the cancer hasn't transformed. This is done by testing one or more areas of cancer below the diaphragm.

If the biopsy is negative and you don't have any symptoms, taking a watch-and-wait approach is recommended.

If the biopsy is positive for NLPHL, treatment for relapsed NLPHL is recommended. There are several options:

- Watch-and-wait (no treatment)
- Treatment with rituximab alone. Some people may continue treatment with rituximab alone for 2 years. This is called *maintenance therapy*.
- Second-line systemic therapy alone. [See Guide 13](#).
- Radiation therapy and second-line systemic therapy
- Radiation therapy alone

If the biopsy confirms that the cancer has transformed, see the *NCCN Guidelines for Patients: Diffuse Large B-cell Lymphoma*.



Guide 13 Second-line systemic therapy regimens for NLPHL

DHAP and Rituxan®	Dexamethasone, cisplatin, high-dose cytarabine, and rituximab
ESHAP and Rituxan®	Etoposide, methylprednisolone, high-dose cytarabine, cisplatin, and rituximab
ICE and Rituxan®	Ifosfamide, carboplatin, etoposide, and rituximab
IGEV and Rituxan®	Ifosfamide, gemcitabine, vinorelbine, and rituximab

Review

- NLPHL is a very rare type of Hodgkin lymphoma that can transform into an aggressive type of non-Hodgkin's lymphoma called diffuse large B-cell lymphoma (DLBCL).
- The three main treatments for NLPHL are radiation therapy, chemotherapy, and the targeted therapy rituximab (Rituxan®). Depending on the cancer stage, they may be used individually or together.
- Radiation therapy is the preferred treatment for most people with non-bulky stage IA and IIA NLPHL.
- Combination therapy with chemotherapy, Rituxan® (a targeted therapy given with chemotherapy), and radiation therapy is recommended for initial treatment of:
 - Bulky stage IA NLPHL
 - Bulky or non-contiguous stage IIA NLPHL
 - Stage IB and stage IIB NLPHL
- Radiation therapy alone may be an option for a small number of people with stage IIA non-contiguous NLPHL and stage IB NLPHL.
- Combination therapy with chemotherapy and Rituxan® (a targeted therapy given with chemotherapy) is recommended for everyone with advanced (stage III–IV) NLPHL. Your doctor may also recommend treatment with radiation therapy in addition to chemotherapy.

6

When treatment is over

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- 61 Long-term follow-up care
- 66 Review



While Hodgkin lymphoma can usually be cured, its treatment can cause serious health problems—including other cancers—down the line. When treatment is over, it is important to see an oncologist who understands the unique risks and health issues faced by Hodgkin lymphoma survivors.

The first 5 years

During the first 5 years after treatment, it is very important to monitor for the return of Hodgkin lymphoma. The care you should have is explained below and listed in [Guide 14](#).

Physical exams

Physical exams are an important part of follow-up care. They are given more frequently in the years immediately after treatment, and then spaced farther apart in later years. During the first 1 to 2 years, you should have a physical exam every 3 to 6 months. They are then given every 6 to 12 months for the next 3 years. Annual (yearly) exams are recommended after that.

Blood tests

There is no recommended schedule for bloodwork in the first 5 years after finishing treatment. Your doctor may order one or more blood tests at the time of your physical exams, or may only order them if there is reason to suspect the cancer has returned.

Blood tests your doctor may order include a complete blood count (CBC), erythrocyte sedimentation rate (ESR), and a chemistry



Good to know

There isn't a "one-size-fits-all" care plan that all Hodgkin lymphoma survivors should follow after treatment. The types of follow-up tests you should have—and how often you should have them—should be based on your specific cancer circumstances. This includes:

- Your age
- The cancer stage when you were diagnosed
- Your social habits
- The treatments you had

profile. An ESR is usually only needed if your initial ESR was high. If you had radiation therapy to the neck, you should have a thyroid-stimulating hormone (TSH) test at least once a year.

Imaging tests

You may have a computed tomography (CT) scan of your neck, chest, abdomen, and pelvis as soon as 6 months after finishing treatment, and again at 1 and 2 years. Or, your doctor may only order a CT scan if you have symptoms, or if there are other reasons to suspect the cancer has returned. A contrast agent should be

used during any follow-up CT scans. You may need a PET/CT if the results of your last PET/CT suggested a poor response to treatment.

However, having PET scans on a regular basis to monitor for the return of Hodgkin lymphoma is not recommended.

Guide 14

Follow-up during the first 5 years after treatment

Health history and physical exam	Every 3–6 months for 1–2 years, then every 6–12 months until year 3, then once a year
Vaccines	<ul style="list-style-type: none"> • Get the influenza vaccine (“the flu shot”) every year • Other vaccines as needed
Blood tests	<p>The following tests should be done as needed, or as directed by your doctor:</p> <ul style="list-style-type: none"> • CBC • ESR (if it was high when you were first diagnosed) • Chemistry profile • People who had radiation therapy to the neck should also have TSH testing at least annually
Imaging tests	<ul style="list-style-type: none"> • CT scan of your neck, chest, abdomen, and pelvis (with contrast) at 6, 12, and 24 months after completing treatment, or as directed by your doctor. • You only need a PET/CT scan if your last Deauville score was 4 or 5. There is no need to have PET scans on a regular basis.
Counseling	<p>All people treated for Hodgkin lymphoma should be counseled on:</p> <ul style="list-style-type: none"> • What to expect at the end of treatment • Reproductive issues • Healthy habits after treatment • The psychosocial effects of cancer and its treatment • The cardiovascular risks of cancer and its treatment • Breast self-exams • The risk of skin cancer

Survivorship counseling

There are both short- and long-term health effects of Hodgkin lymphoma and its treatment. It is important for you to be aware of—and to understand—the unique risks and health issues faced by Hodgkin lymphoma survivors.

Ask your doctor about:

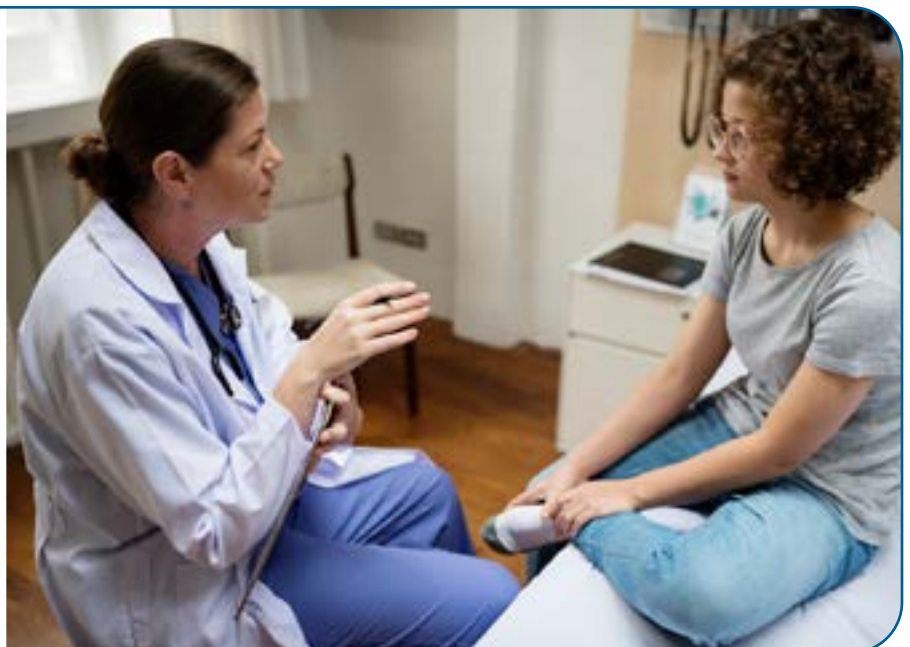
- What to expect now that treatment is over
- Issues related to fertility and family planning
- The importance of leading a healthy lifestyle after cancer treatment
- Your increased risk of other types of cancer (eg, skin cancer and breast cancer) and steps you can take to help prevent getting them (eg, doing breast self-exams)
- The importance of taking care of your mental and emotional health

Did you know?

An individual is considered a cancer survivor from the time of diagnosis, during and immediately after treatment, and for the rest of his or her life.

Survivorship counseling

Hodgkin lymphoma survivors are encouraged to undergo counseling on survivorship, including long-term treatment effects, preventing new cancers, and healthy behaviors. Ask your doctor about survivorship clinics near you.



Long-term follow-up care

Side effects of Hodgkin lymphoma and its treatment can start years after finishing treatment. These are called “late” side effects. The most serious late effects that long-term Hodgkin survivors experience are:

- Other cancers
- Heart disease
- Hypothyroidism
- Fertility issues

The longer you are monitored after finishing treatment, the more likely you are to experience some of these side effects. The long-term care you should receive is described below and summarized in [Guide 15](#).

Physical exams

Physical exams continue to be an important part of follow-up care. Beginning in the sixth year after treatment, you should have a

physical exam once a year. Your doctor should closely monitor changes in your blood pressure. Any signs of heart damage or disease should be noted and promptly managed.

Blood tests

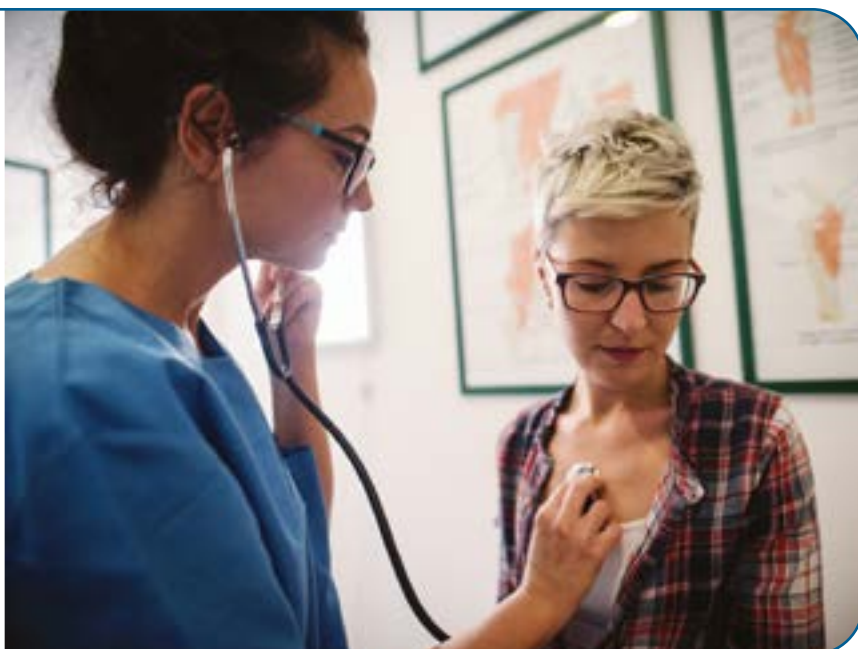
You should have a CBC and a chemistry profile once a year beginning in the sixth year after treatment. If your neck was treated with radiation, continue to have your TSH level measured at least once a year.

Due to the increased risk of heart damage or disease over time, extra bloodwork to test for lipid disorders and diabetes is needed after 5 years. Lipids are fats that your body uses for energy. Cholesterol is a lipid. You should have a test called a lipids panel twice per year. A lipids panel typically measures your:

- Total cholesterol level
- Triglyceride level
- The levels of “good” (HDL) and “bad” (LDL) cholesterol

Physical exams

Physical exams are needed more frequently immediately after treatment, and then spaced farther apart. Starting in the sixth year after treatment, a physical exam is recommended once per year.



Guide 15

Follow-up starting 6 years after treatment

Health history and physical exam	Annual physical exam and updating of health history, including an assessment of cardiovascular risk factors
Vaccines	<ul style="list-style-type: none"> • People treated with radiation therapy to the spleen or who had a splenectomy should be re-vaccinated against pneumonia, meningitis, and <i>haemophilus influenzae</i> type B (“Hib”) 5–7 years after treatment. • Continue to get the influenza vaccine (“the flu shot”) every year. • Other vaccines as needed
Monitoring for cardiovascular side effects	<ul style="list-style-type: none"> • Some people should have an exercise stress test or an echocardiogram every 10 years after treatment. • People who had radiation therapy to the neck may need an ultrasound of the carotid artery every 10 years.
Blood tests	<p>The following tests should be done as needed, or as directed by your doctor:</p> <ul style="list-style-type: none"> • CBC, ESR (if it was high when you were first diagnosed), and chemistry profile • People who had radiation therapy to the neck should also have TSH testing at least annually.
Breast cancer screening	<ul style="list-style-type: none"> • Women who had radiation therapy to the chest or armpit area should have mammograms once a year starting 8–10 years after treatment or at age 40, whichever comes first. • Women who had radiation therapy to the chest between the ages of 10–30 should also have breast MRI in addition to mammography. • Some women will be referred to a breast specialist.
Screening for other cancers	Get screened for other cancers based on your age and gender, including cervical, colorectal, endometrial, lung, and prostate cancer.
Counseling	All people treated for Hodgkin lymphoma should receive counseling on reproductive issues, healthy habits after treatment, the psychosocial effects of cancer and its treatment, the cardiovascular risks of cancer and its treatment, breast self-exams, and the risk of skin cancer.

Glucose—a simple sugar—is your body’s main source of energy. A fasting glucose test measures the amount of glucose in your blood. If your blood glucose levels are high, it could be a sign of diabetes. If your blood glucose levels are low, it could be a sign of hypothyroidism. A fasting glucose test is recommended once a year beginning in the sixth year after finishing treatment.

Thyroid problems

About half of Hodgkin lymphoma survivors who had radiation therapy to the neck or upper chest have thyroid problems later in life. The most common problem is hypothyroidism, in which the thyroid gland doesn’t make enough of the thyroid hormone. Weight gain, constipation, dry skin, and sensitivity to cold temperatures are symptoms of an underactive thyroid.

Your doctor should do a careful thyroid examination during your annual physical exam.

Thyroid function tests should also be done at least once a year to rule out hypothyroidism, especially in people who had radiation therapy to the neck.

Thyroid exam

About half of Hodgkin lymphoma survivors who had radiation therapy to the neck or upper chest have thyroid problems later in life. A careful thyroid examination is an important part of your annual physical exam.



Screening for other cancers

Anyone who has had Hodgkin lymphoma is at risk of getting other types of cancer, especially if radiation therapy was used as part of first-line treatment. These “secondary cancers” often occur more than 10 years after finishing treatment for Hodgkin lymphoma. Lung cancer and breast cancer are the most common

secondary cancers in Hodgkin lymphoma survivors.

Women who had radiation therapy to the chest or armpit area should start screening for breast cancer 8 to 10 years after finishing treatment, or at age 40 (whichever comes first). Women who had radiation therapy to the chest between

Breast cancer screening

Many Hodgkin lymphoma survivors get breast cancer later in life. Women who had radiation therapy to the chest or armpit area should start screening for breast cancer 8 to 10 years after finishing treatment, or at age 40 (whichever comes first).



Breast self exam

In addition to screening with mammography and MRI, NCCN experts also encourage doing monthly breast self-exams, and having a breast exam by a health care professional once a year.



age 10 and age 30 should be screened with both mammography and breast magnetic resonance imaging (MRI). NCCN experts also encourage doing monthly breast self-exams, and having a breast exam by a health care professional once a year.

Screening for cervical, colorectal, endometrial, lung, and prostate cancer is also recommended, and should follow the recommendations of the American Cancer Society.

Heart disease

Hodgkin lymphoma survivors have a higher long-term risk of getting diseases that affect the heart or blood vessels. This is called heart disease or cardiovascular disease. Symptoms of heart disease can start at any age, but damage to the heart or blood vessels is usually found more than 5 to 10 years after finishing treatment.

The biggest risk factors for developing heart disease in Hodgkin lymphoma survivors are:

- Treatment with radiation therapy to the area between the lungs
- Treatment with chemotherapy medicines called anthracyclines. Doxorubicin is an anthracycline used in several chemotherapy regimens widely used to treat Hodgkin lymphoma, including ABVD, escalated BEACOPP, and Stanford V.

Everyone treated for Hodgkin lymphoma should have their blood pressure taken at least once a year and the levels closely monitored, even if there are no symptoms of heart disease.

Your doctor may order an exercise stress test or echocardiogram when you are done treatment. If you had radiation therapy to the neck, your doctor may also order an ultrasound of your carotid artery. The goal is to get a baseline (starting) measurement of your cardiovascular health. The testing may then be repeated every 10 years, and the results will be compared to your baseline (starting) results.

Exercise stress test

In order to monitor for signs of heart disease, you may have an exercise stress test every 10 years after finishing treatment.



Review

- ▶ While Hodgkin lymphoma can usually be cured, its treatment can cause serious health problems—including other cancers—down the line.
- ▶ The most serious late effects that long-term Hodgkin survivors experience are other cancers, heart disease, hypothyroidism, and fertility issues.
- ▶ When treatment is over, it is important to see an oncologist who understands the unique risks and health issues faced by Hodgkin lymphoma survivors.
- ▶ There isn't a “one-size-fits-all” care plan that all Hodgkin lymphoma survivors should follow after treatment. The types of follow-up tests you have—and how often you have them—should be based on your specific cancer circumstances.
- ▶ Your doctor should provide you with a summary of your cancer treatment that includes the details of any radiation therapy you had, a listing of your organs that may be at risk for future health problems, and the total amount of doxorubicin with which you were treated.

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Making treatment decisions

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Having cancer is very stressful. There is a lot to learn in what feels like a short amount of time. This chapter can help you make decisions that reflect your beliefs, wishes, and values.

It's your choice

The role patients want in choosing their treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may feel uneasy because you don't know much about cancer. You've never heard the words used to describe cancer, tests, or treatments. Likewise, you may think that your judgment isn't any better than your doctors'.

Letting others decide which option is best may make you feel more at ease. But, whom do you

want to make the decisions? You may rely on your doctors alone to make the right decisions. However, your doctors may not tell you which to choose if you have more than one good option. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, you still have to agree by signing a consent form.

On the other hand, you may want to take the lead or share in decision-making. Most patients do. In shared decision-making, you and your doctors share information, weigh the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you are likely to get a higher quality of care and be more satisfied. You'll likely get the treatment you want, at the place you want, and by the doctors you want.

Informed consent

Even if others decide which treatment you will receive, you still have to agree by signing a consent form.



Questions to ask your doctors

You may meet with experts from different fields of medicine. Try to talk with each expert. Prepare questions before your visit and ask questions if the person isn't clear. You can also record your talks and get copies of your medical records. It may be helpful to have your spouse, partner, or a friend with you at these visits. They can help to ask questions and remember what was said. Below are some suggested questions to ask.

What's my diagnosis and prognosis?

Cancer can greatly differ even when people have a tumor in the same organ. Your doctor should clearly explain the type of cancer you have. This is your diagnosis. Your doctor should also be able to tell you how he or she expects your cancer to respond to treatment. This is your prognosis.

1. Where did the cancer start?
2. Is this cancer common?
3. What is the cancer stage? Does this stage mean the cancer has spread far?
4. Is this a fast- or slow-growing cancer?
5. What other test results are important to know?
6. How often are these tests wrong?
7. Would you give me a copy of the pathology report and other test results?
8. How likely is it that I'll be cancer-free after treatment?

What are my options?

There is no single treatment practice that is best for all patients. There is often more than one treatment option along with clinical trial options. Your doctor will review your test results and recommend treatment options.

1. What will happen if I do nothing?
2. Can I just carefully monitor the cancer?
3. Do you consult NCCN recommendations when considering options?
4. Are you suggesting options other than what NCCN recommends? If yes, why? What are these other options based on?
5. Do your suggested options include clinical trials? Please explain why.
6. How do my age, health, and other factors affect my options?
7. What if I am pregnant?
8. Which option is proven to work best? Which options lack scientific proof?
9. What are the benefits of each option? Does any option offer a cure? Are my chances any better for one option than another? Less time-consuming? Less expensive?
10. What are the risks of each option? What are possible complications? What are the rare and common side effects? Short-lived and long-lasting side effects? Serious or mild side effects? Other risks?
11. What can be done to prevent or relieve the side effects of treatment?
12. What are my chances that the cancer will return?
13. How soon should I start treatment? If there are delays in starting my treatment, how will this impact my treatment options?

Weighing your options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions on which option is best for you. This can be very confusing. Your spouse or partner may disagree with which option you want. This can be stressful. In some cases, one option hasn't been shown to work better than another, so science isn't helpful. Some ways to decide on treatment are discussed next.

Second opinion

After finding out you have cancer, it is normal to want to start treatment as soon as possible. While cancer can't be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care.

Getting a second opinion doesn't mean you don't trust the first doctor. In fact, most doctors who are diagnosed with cancer will see more than one doctor before beginning treatment. What's more, some health plans require a second opinion. If your health plan doesn't cover the cost of a second opinion, you have the choice of paying for it yourself.

If the two opinions are the same, you may feel better about the treatment you accept to have. If the two opinions differ, think about getting a third opinion. Choosing your cancer treatment is a very important decision. It can affect your length and quality of life.

Support groups

In addition to speaking with health experts, it may help to talk to patients who have walked in your shoes. Support groups often consist of

people at different stages of treatment. Some may be in the process of deciding while others may be finished with treatment. At support groups, you can ask questions and hear about the experiences of other people with Hodgkin lymphoma. Keep in mind that your cancer may have different characteristics (eg, stage, number of unfavorable risk factors) than other people. Therefore, you may have different treatment options than others.

Compare benefits and downsides

Every option has benefits and downsides. Consider these when deciding which option is best for you. Talking to others can help identify benefits and downsides you haven't thought of. For example, you can decide how aggressive you want to be with treatment at the cost of increasing negative long-term side effects. Scoring each factor from 0 to 10 can also help since some factors may be more important to you than others. You should feel comfortable discussing your goals of care with your health care team.

Websites

BMT InfoNet

<https://www.bmtinonet.org/>

nbmtLINK

<https://www.nbmtlink.org/>

The Leukemia & Lymphoma Society (LLS)

<https://www.lls.org/>

National Cancer Institute

<https://www.cancer.gov/types/lymphoma>

NCCN

www.nccn.org/patients

U.S. National Library of Medicine Clinical Trials Database

www.clinicaltrials.gov

Review

- ▶ Shared decision-making is a process in which you and your doctors plan treatment together.
- ▶ Asking your doctors questions is vital to getting the information you need to make informed decisions.
- ▶ Getting a second opinion, attending support groups, and comparing risks and benefits may help you decide which treatment is best for you.



Words to know

abdomen

The area of the body between the chest and pelvis. Contains the pancreas, stomach, intestines, liver, gallbladder, and other organs.

allogeneic stem cell transplant

A cancer treatment that replaces abnormal blood stem cells with healthy donor cells. Also called allogeneic hematopoietic cell transplant (HCT).

autologous stem cell transplant

A treatment that destroys your bone marrow then rebuilds it with your healthy stem cells. Also called high-dose therapy with autologous stem cell rescue (HDT/ASCR).

B symptoms

High fevers, heavy night sweats, and fast weight loss without dieting caused by Hodgkin lymphoma.

biopsy

Removal of small amounts of tissue or fluid to be tested for disease.

blood chemistry profile

A lab test of the amount of 8 chemicals in a sample of blood.

body plethysmograph

A test done in a small room with a small tube to measure how much air is in your lungs after inhaling or exhaling.

bone marrow

Soft, sponge-like tissue in the center of most bones where blood cells are made.

bone marrow aspiration

A procedure that removes a liquid bone marrow sample to test for disease.

bone marrow biopsy

Removal of a small amount of solid bone and bone marrow to test for disease.

cancer stage

A rating of the extent of cancer in the body.

chemotherapy

The use of medicines that stop the growth of cancer cells.

classic Hodgkin lymphoma (CHL)

The most common type of Hodgkin lymphoma.

clinical trial

A type of research that studies how well medical tests and treatments work in people.

complete blood count (CBC)

A test of the number of blood cells in a sample.

comprehensive metabolic panel

Tests of about 14 chemicals in your blood.

computed tomography (CT)

A test that uses x-rays from many angles to make pictures of areas inside the body.

contiguous lymphoma

Lymphoma in which the lymph nodes containing cancer are next to each other.

contrast

A dye put into your body to make clearer pictures during imaging tests.

core needle biopsy

The removal of a tissue sample with a wide needle for examination under a microscope. Also called core biopsy.

Deauville scale

A rating by doctors of treatment response based on comparing the uptake of a radiotracer by cancer sites to two other sites.

diaphragm

The thin muscle below the lungs and heart that helps a person to breathe.

diffuse large B-cell lymphoma (DLBCL)

A common type of B-cell non-Hodgkin's lymphoma that is usually fast-growing.

echocardiogram

A test that uses sound waves to make pictures of the heart.

ejection fraction

The amount of blood pumped out of the left side of your heart.

erythrocyte sedimentation rate (ESR)

A test for inflammation based on how much clear liquid is at the top of a tube of blood after one hour.

excisional biopsy

A procedure that removes entire lymph nodes to test for cancer cells.

external beam radiation therapy (EBRT)

Radiation therapy received from a machine outside the body.

fatigue

Severe tiredness despite getting enough sleep that limits one's ability to function.

fertility specialist

An expert who helps men and women have babies.

fine-needle aspiration (FNA)

Use of a thin needle to remove fluid or tissue from the body to test for disease.

gas diffusion test

A test that uses harmless gas to measure how much a person can breathe out.

general anesthesia

A drug-induced, sleep-like state for pain relief.

Hodgkin lymphoma

A cancer that starts in a type of white blood cell (lymphocyte). Reed-Sternberg cells are present.

immune system

The body's natural defense against infection and disease.

immunohistochemistry (IHC)

A test of cancer cells to find specific cell traits involved in abnormal cell growth.

involved-site radiation therapy (ISRT)

Treatment with high-energy rays (radiation) that is delivered to lymph nodes and nearby sites with cancer.

lactate dehydrogenase

A protein that helps to make energy in cells.

liver

Organ that removes waste from the blood and helps to digest food.

liver function test

Test that measures chemicals in the blood that are made or processed by the liver.

local anesthesia

A drug-induced loss of feeling in a small area of the body.

lung function test

A test used to measure how well the lungs work. Also called pulmonary function test.

lymph

A clear fluid containing white blood cells.

lymphatic system

The tissues and organs that produce, store, and carry white blood cells that fight infections and other diseases.

lymph node

Small groups of special disease-fighting cells located throughout the body.

lymphocyte

A type of immune cell that is made in the bone marrow and is found in the blood and in lymph tissue.

mediastinum

The area of the chest between the lungs.

myelosuppression

A condition in which bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and platelets.

noncontiguous lymphoma

Lymphoma in which the lymph nodes containing cancer are on the same side of the diaphragm, but are not next to each other.

positron emission tomography/computed tomography (PET/CT) scan

A procedure that uses two types of imaging techniques (PET and CT) to create detailed pictures of areas inside the body.

positron emission tomography (PET) scan

A test that uses a small amount of radioactive glucose (sugar) and a scanner to see where glucose is being used in the body.

spleen

An organ that is part of the lymphatic system and helps protect the body from disease. It is located on the left side of the abdomen near the stomach.

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800.789.7366
penmedicine.org/cancer

Fred & Pamela Buffett Cancer Center
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nebraskamed.com/cancer

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University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
Cancer Institute
Cleveland, Ohio
800.641.2422 • UH Seidman Cancer Center
uhhospitals.org/services/cancer-services
866.223.8100 • CC Taussig Cancer Institute
my.clevelandclinic.org/departments/cancer
216.844.8797 • Case CCC
case.edu/cancer

City of Hope National Medical Center
Los Angeles, California
800.826.4673
cityofhope.org

Dana-Farber/Brigham and
Women's Cancer Center
Massachusetts General Hospital
Cancer Center
Boston, Massachusetts
877.332.4294
dfbwc.org
massgeneral.org/cancer

Duke Cancer Institute
Durham, North Carolina
888.275.3853
dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427
foxchase.org

Huntsman Cancer Institute
at the University of Utah
Salt Lake City, Utah
877.585.0303
huntsmancancer.org

Fred Hutchinson Cancer
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Seattle, Washington
206.288.7222 • seattlecca.org
206.667.5000 • fredhutch.org

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410.955.8964
hopkinskimmelfcancercenter.org

Robert H. Lurie Comprehensive
Cancer Center of Northwestern
University
Chicago, Illinois
866.587.4322
cancer.northwestern.edu

Mayo Clinic Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
800.446.2279 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/departments-centers/mayo-clinic-cancer-center

Memorial Sloan Kettering
Cancer Center
New York, New York
800.525.2225
mskcc.org

Moffitt Cancer Center
Tampa, Florida
800.456.3434
moffitt.org

The Ohio State University
Comprehensive Cancer Center -
James Cancer Hospital and
Solove Research Institute
Columbus, Ohio
800.293.5066
cancer.osu.edu

O'Neal Comprehensive
Cancer Center at UAB
Birmingham, Alabama
800.822.0933
uab.edu/onealcancercenter

Roswell Park Comprehensive
Cancer Center
Buffalo, New York
877.275.7724
roswellpark.org

Siteman Cancer Center at Barnes-
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University School of Medicine
St. Louis, Missouri
800.600.3606
siteman.wustl.edu

St. Jude Children's Research Hospital
The University of Tennessee
Health Science Center
Memphis, Tennessee
888.226.4343 • stjude.org
901.683.0055 • westclinic.com

Stanford Cancer Institute
Stanford, California
877.668.7535
cancer.stanford.edu

UC San Diego Moores Cancer Center
La Jolla, California
858.657.7000
cancer.ucsd.edu

UCSF Helen Diller Family
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San Francisco, California
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cancer.ucsf.edu

University of Colorado Cancer Center
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coloradocancercenter.org

University of Michigan
Rogel Cancer Center
Ann Arbor, Michigan
800.865.1125
rogelcancercenter.org

The University of Texas
MD Anderson Cancer Center
Houston, Texas
800.392.1611
mdanderson.org

University of Wisconsin
Carbone Cancer Center
Madison, Wisconsin
608.265.1700
uwhealth.org/cancer

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
800.811.8480
vicc.org

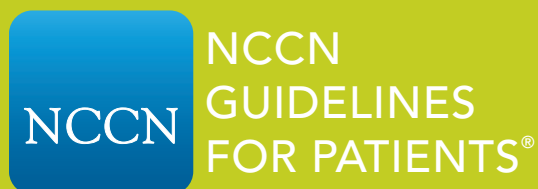
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Smilow Cancer Hospital
New Haven, Connecticut
855.4.SMILOW
yalecancercenter.org

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