



HODGKIN DISEASE

What is cancer?

Cancer develops when cells in a part of the body begin to grow out of control. Although there are many kinds of cancer, they all start because of out-of-control growth of abnormal cells.

Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide more rapidly until the person becomes an adult. After that, cells in most parts of the body divide only to replace worn-out or dying cells and to repair injuries.

Because cancer cells continue to grow and divide, they are different from normal cells. Instead of dying, they outlive normal cells and continue to form new abnormal cells.

Cancer cells develop because of damage to DNA. This substance is in every cell and directs all its activities. Most of the time when DNA becomes damaged the body is able to repair it. In cancer cells, the damaged DNA is not repaired. People can inherit damaged DNA, which accounts for inherited cancers. Many times though, a person's DNA becomes damaged by exposure to something in the environment, like smoking.

Cancer usually forms as a tumor. Some cancers, like leukemia, do not form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Often, cancer cells travel to other parts of the body, where they begin to grow and replace normal tissue. This process is called metastasis. Regardless of where a cancer may spread, however, it is always named for the place it began. For instance, breast cancer that spreads to the liver is still called breast cancer, not liver cancer.

Not all tumors are cancerous. Benign (non-cancerous) tumors do not spread (metastasize) to other parts of the body and, with very rare exceptions, are not life threatening.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Cancer is the second leading cause of death in the United States. Nearly half of all men and a little over one third of all women in the United States will develop cancer during their lifetimes. Today, millions of people are living with cancer or have had cancer. The risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking and eating a better diet. The sooner a cancer is found and treatment begins, the better are the chances for living for many years.

What Is Hodgkin Disease?

Hodgkin disease (Hodgkin lymphoma) is a type of *lymphoma*, a cancer that starts in cells of the lymph system, which is part of the body's immune system. There are 2 kinds of lymphomas:

- Hodgkin disease (named after Dr. Thomas Hodgkin, who recognized it in 1832)
- non-Hodgkin lymphoma

For information on non-Hodgkin lymphoma, see the American Cancer Society document, *Non-Hodgkin Lymphoma*.

The Lymph System and Lymphoid Tissue

To better understand Hodgkin disease, it helps to know about the body's lymph system. The lymph system (also known as the lymphatic system) is composed mainly of lymphoid tissue, lymph vessels, and a clear fluid called lymph.

Lymphoid tissue includes the lymph nodes and related organs that are part of the body's immune and blood-forming systems, such as the spleen and bone marrow.

Lymphocytes

Lymphoid tissue is made up of cells called lymphocytes, which are a type of infection-fighting white blood cell. The 2 major types of lymphocytes are known as B lymphocytes (B cells) and T lymphocytes (T cells).

- **B lymphocytes** or B cells help protect the body from invading germs. They do this by maturing into plasma cells, which make antibodies (immune proteins). These

antibodies attach to germs, such as bacteria, marking them for destruction. *The vast majority of cases of Hodgkin disease start in B lymphocytes.*

- **T lymphocytes** or T cells can directly destroy certain kinds of bacteria or cells infected with viruses or fungi, or they can help other immune system cells do their job better.

Organs That Contain Lymphoid Tissue

Because lymphoid tissue is found in many parts of the body, Hodgkin disease can start almost anywhere. The major sites of lymphoid tissue are listed below.

Lymph nodes: Lymph nodes are small, bean-shaped organs found under the skin in the neck, under the arms, and in the groin. They are also found in many other places in the body such as inside the chest, abdomen, and pelvis.

The lymph nodes are connected by a system of *lymphatic vessels*. These vessels are like veins, except that instead of carrying blood, they carry lymph (a clear fluid containing waste products and excess fluid from tissues) and immune system cells traveling between lymph nodes and other tissues.

Lymph nodes increase in size when they fight an infection. Lymph nodes that grow in reaction to infection are called reactive nodes or hyperplastic nodes and are often tender to the touch. An enlarged lymph node is not usually a sign of a serious problem. Enlarged lymph nodes in the neck are often felt in people with sore throats or colds. But a large lymph node is also the most common sign of Hodgkin disease. See the section, "How Is Hodgkin Disease Diagnosed?" for more information.

Spleen: The spleen is an organ found under the lower part of the rib cage on the left side of the body. The spleen makes lymphocytes and other immune system cells to help fight infection. It also stores healthy blood cells and filters out damaged blood cells, bacteria, and cell waste.

Bone marrow: The bone marrow is the spongy tissue inside the bones, which functions as the "factory" in which new white blood cells (including some lymphocytes), red blood cells, and platelets are made.

Thymus: The thymus is a small organ that lies behind the upper part of the breastbone and in front of the heart. It is important in the development of T lymphocytes.

Start and Spread of Hodgkin Disease

Because lymphoid tissue is found in many parts of the body, Hodgkin disease can start almost anywhere. Most often it starts in lymph nodes in the upper part of the body. The most common sites are in the chest, in the neck, or under the arms.

The major route of spread of Hodgkin disease is through the lymphatic vessels to nearby lymph nodes and only later in the course of disease to more distant nodes. Hodgkin disease spreads through the body in a stepwise fashion from lymph node to lymph node. Rarely, and late in the disease, it may invade the bloodstream and spread to other sites in the body, including the liver, lungs, and/or bone marrow.

The Hodgkin Disease Cell

The cancer cells in Hodgkin disease are unique and are called *Reed-Sternberg cells*, after the 2 doctors who first described them. These cells are an abnormal type of B lymphocyte. Under a microscope, Reed-Sternberg cells are much larger than normal lymphocytes and also look different from the cells of non-Hodgkin lymphomas and other cancers. Enlarged lymph nodes contain a minority of Reed-Sternberg cells and a majority of normal cells of the immune system. It is mainly these other cells that account for the bulk of the enlarged lymph nodes.

Types of Hodgkin Disease

There are different types of Hodgkin disease. These types are classified by their appearance under the microscope. This is important because types of Hodgkin disease may grow and spread differently and may be treated differently. The 2 main types are *classical Hodgkin disease* (which has several subtypes) and *nodular lymphocyte predominance Hodgkin disease*.

Classical Hodgkin Disease

Classical Hodgkin disease (HD) accounts for about 95% of all cases of Hodgkin disease in developed countries. It has 4 subtypes, all of which have classical appearing Reed-Sternberg cells.

Nodular sclerosis Hodgkin disease: This is the most common type of Hodgkin disease in developed countries, accounting for about 70% to 80% of cases. It occurs mainly in younger people, with equal occurrence in men and women. It tends to start in lymph nodes in the neck or chest (mediastinum). Under the microscope, the lymph nodes contain fibrous bands that criss-cross the node and encircle abnormal nodules of lymph tissue.

Mixed cellularity Hodgkin disease: This is the second most common type (15% to 30%) and is seen mostly in older adults. It can occur in any lymph node but most often occurs in

the upper half of the body. Under the microscope, many different kinds of cells can be seen on the biopsy specimen, including Reed-Sternberg cells and normal immune system cells (lymphocytes, eosinophils, and plasma cells).

Lymphocyte-rich Hodgkin disease: This subtype accounts for about 5% of Hodgkin disease cases. It usually occurs in the upper half of the body and is rarely found in more than a few lymph nodes. Under the microscope it looks very much like mixed cellularity, except that most of the cells are small lymphocytes.

Lymphocyte-depleted Hodgkin disease: This is the least common form of Hodgkin disease, making up only about 1% of cases. It is seen mainly in older people. The disease is more likely to involve lymph nodes in the abdomen as well as the spleen, liver, and bone marrow. When looking at the cells under the microscope, there are few normal lymphocytes or other immune system cells, and many Reed-Sternberg cells.

Nodular Lymphocyte Predominant Hodgkin Disease

Nodular lymphocyte predominant Hodgkin disease (NLPHD) accounts for about 5% of Hodgkin disease. This type mostly involves lymph nodes in the neck and under the arm. It can occur at any age. It contains large cells, often called "popcorn" cells (because they look like popcorn), which are variants of Reed-Sternberg cells. Under the microscope, there is a pattern of sheets of lymphocytes arranged in nodules.

All types of Hodgkin disease are malignant because as they grow they may compress, invade, and destroy normal tissue and spread to other tissues. There is no benign (non-cancerous) form of Hodgkin disease.

Hodgkin disease occurs in both children and adults. Because Hodgkin disease is similar in both children and adults, this document discusses treatment in both groups.

What Are the Key Statistics About Hodgkin Disease?

The American Cancer Society estimates that in 2008 about 8,220 new cases of Hodgkin disease will be diagnosed in the United States. Of these new cases, 3,820 will occur in females and 4,400 in males. These numbers have not changed much over the past few years.

Hodgkin disease can occur in both children and adults. It is most common in early adulthood (age 15 to 40, especially in a person's 20s), where it is mostly of the nodular sclerosis subtype, and in late adulthood (after age 55), where the mixed cellularity subtype is more common. Hodgkin disease is rare before 5 years of age. About 10% to 15% of cases are diagnosed in children and teenagers.

An estimated 1,350 people (650 females, 700 males) will die of Hodgkin disease in the United States during 2008. Because of advances in treatment, survival rates have improved considerably since the early 1970s. By 2004, over 138,000 people had been diagnosed with this disease at some time and were still alive.

The 1-year relative survival rate for all patients after treatment is about 94%; the 5-year and 10-year rates are about 85% and 82%, respectively. At 15 years, the relative survival rate is about 74%, while at 20 years it is about 63%.

The survival rate (for example) refers to the percentage of patients who live *at least* that long after their cancer is diagnosed. (For example, the 5-year survival rate includes all people who live at least 5 years after being diagnosed.) Survival rates are used to produce a standard way of discussing prognosis. Of course, many people live much longer than these cutoffs. *Relative* survival rates are calculated in ways that exclude the impact of diseases other than cancer on survival; that is, people with Hodgkin disease who die of other causes are not counted.

Certain factors such as the stage of the disease and a patient's age affect these rates. For about the first 15 years after treatment, the main cause of death in these patients is recurrent Hodgkin disease (Hodgkin disease that comes back). By 15 to 20 years after treatment, death due to other causes is more common.

Of course, current 5-year survival rates are based on people with Hodgkin disease who were diagnosed and initially treated more than 5 years ago. Advances in treatment have produced a more favorable outlook for recently diagnosed patients. For a discussion on 5-year survival by stage of disease, see the section, "How Is Hodgkin Disease Staged?"

What Are the Risk Factors for Hodgkin Disease?

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for cancers of the lung, mouth, larynx, bladder, kidney, pancreas, and several other organs.

But risk factors don't tell us everything. Having a risk factor, or even several, does not mean that you will get the disease. Likewise, not having any known risk factors doesn't mean you won't get the disease.

Scientists have found a few risk factors that may make a person more likely to develop Hodgkin disease, although it's not always clear why these factors increase risk.

Epstein-Barr Virus (EBV) Infection/Mononucleosis

There is an increased risk of Hodgkin disease in people who have had infectious mononucleosis (sometimes called "mono" for short), an infection caused by the *Epstein-Barr virus*. The risk of developing Hodgkin disease in people who have had infectious mononucleosis appears to be a few times higher than in people who have not had the disease, although the overall risk is still very small.

The Epstein-Barr virus is found within the DNA of Reed-Sternberg cells in about half of all patients with Hodgkin disease. But the other half of patients with Hodgkin disease have no evidence of Epstein-Barr virus in their cancer cells.

Age

Hodgkin disease is most common in early adulthood (age 15 to 40, especially in a person's 20s) and in late adulthood (after age 55).

Gender

Hodgkin disease occurs slightly more often in males than in females.

Geography

Hodgkin disease is most common in the United States, Canada, and northern Europe, and is least common in Asian countries.

Family History

There is a higher risk for Hodgkin disease in brothers and sisters of young people with this disease. The risk is very high for an identical twin of a person with Hodgkin disease. But a family association is still uncommon, and accounts for only around 5% of all cases.

It's not clear why family history might increase risk. Some families may have a higher rate of Hodgkin disease because of similar early childhood exposures to infections (such as Epstein-Barr virus), inherited genes that make them more susceptible, or some combination of these factors. Some researchers have found certain changes in the genes responsible for immunity in patients with Hodgkin disease.

Socioeconomic Status

The risk of Hodgkin disease is greater in people with a higher socioeconomic background.

Do We Know What Causes Hodgkin Disease?

The exact cause of Hodgkin disease is not known. However, scientists have found that the disease is associated with a few conditions, particularly infection with the Epstein-Barr virus. Some researchers think that this leads to DNA changes in B lymphocytes, leading to the development of the Reed-Sternberg cell and Hodgkin disease.

Recently, scientists have been able to isolate the Reed-Sternberg cell to learn more about Hodgkin disease. They have found many gene abnormalities that stimulate the cell to grow and divide and that also prevent the cell from dying. Reed-Sternberg cells also make substances called *cytokines*, which attract many other cells into the lymph node, enlarging these nodes abnormally. Despite these advances, scientists have yet to discover what sets off these processes. An abnormal reaction to the Epstein-Barr virus or to other as yet unidentified infections may be that initiating event in some cases. But further work will be required to understand the ultimate "cause" of Hodgkin disease.

Can Hodgkin Disease Be Prevented?

Since scientists and doctors have not yet found preventable risk factors for Hodgkin disease (infectious mononucleosis cannot be prevented), it is not possible to prevent the disease at this time.

Can Hodgkin Disease Be Found Early?

At this time, there are no specific screening tests that are recommended for early detection of Hodgkin disease. The best strategy for early diagnosis is prompt attention to possible symptoms.

Some patients have early symptoms that cause them to seek medical attention. The most common symptom is enlargement of one or more lymph nodes forming a lump or bump, most often on the side of the neck, the arm pit, or the groin (although this is more often a sign of something other than Hodgkin disease). Other symptoms can include unexplained fever that doesn't go away, drenching night sweats that often require changing of bed sheets or night clothes, and unexplained weight loss in excess of 10% of normal body weight. Severe and persistent itching can be another symptom of Hodgkin disease. However, very early in the course of disease, many people with Hodgkin disease may not have any symptoms.

How Is Hodgkin Disease Diagnosed?

Most people with Hodgkin disease see their doctor because they have felt a lump that hasn't gone away, they develop some of the symptoms listed below, or they just don't feel well and go in for a checkup.

Signs and Symptoms of Hodgkin Disease

You or your child can have Hodgkin disease and feel perfectly well. However, there are some symptoms that this disease may cause.

Lump(s) Under the Skin

You may notice a lump in the neck, under the arm, or in the groin, which is an enlarged lymph node. Sometimes this may go away, only to come back. Eventually, it may not go away, and although it doesn't hurt, it may become more noticeable and lead you to go to the doctor. There may even be several areas of enlarged lymph nodes.

But Hodgkin disease is not the most common cause of lymph node swelling. Most lymph node enlargement, especially in children, is caused by an infection. The node should return to its normal size within a couple of weeks or months after the infection goes away.

Other cancers can also cause lymph node swelling. If your lymph nodes have enlarged to more than an inch, especially if you haven't had a recent infection, it is best to have your doctor examine the lymph nodes so that any disease found can be treated without delay.

Generalized (non-specific) Symptoms

Some patients with Hodgkin disease have fever, drenching night sweats, or weight loss. The fever can come and go over several days or weeks. Itching, tiredness, and decreased appetite are other symptoms that may occur. Sometimes the only symptom may be being tired all the time. However, infections, other types of cancer, or other conditions can also produce these symptoms.

Cough or Trouble Breathing

When Hodgkin disease affects lymph nodes inside the chest, the swelling of these nodes may compress the windpipe (trachea) and make you cough or even have trouble breathing, especially when lying down.

If you or your child has any of these symptoms, discuss them with your doctor without delay. The sooner a correct diagnosis is made, the sooner treatment can be started and the more effective the treatment will be.

Medical History and Physical Exam

If symptoms suggest the possibility of Hodgkin disease, the doctor will want to get a thorough medical history, including how long the symptoms have been present.

Next, the doctor will perform a complete physical exam. This provides information about whether there are any enlarged lymph nodes and whether there is any sign of an infection that might be causing the symptoms. The doctor will pay special attention to the lymph nodes and will inspect other areas of the body that may be involved. Because infections are the most common cause of enlarged lymph nodes, especially in children, the doctor will look for an infection in the part of the body near the swollen lymph nodes. If the doctor suspects that Hodgkin disease may be causing the symptoms, he or she will recommend a biopsy of the area.

Biopsy Procedures to Diagnose Hodgkin Disease

The only way to know for sure whether Hodgkin disease is present is by removing a sample of the lymph node and looking at it under the microscope. This procedure is called a *biopsy*. The goal of a biopsy is to get enough of a sample to be sure of the diagnosis, as well as to identify the type of Hodgkin disease if it's present. There are different types of biopsy methods, and doctors choose one based on the unique aspects of your situation.

Excisional or Incisional Biopsy

This is the preferred and most commonly used procedure. After giving anesthesia, the doctor cuts through the skin to remove the entire lymph node (*excisional biopsy*) or a small part of a larger tumor or node (*incisional biopsy*). If the node is near the skin surface, this is a fairly simple operation that can sometimes be done with numbing medicine (local anesthesia). But if the node is inside the chest or abdomen, the patient is given general anesthesia (where he or she is in a deep sleep). This type of biopsy almost always provides enough of a tissue sample to make a diagnosis of the exact type of Hodgkin disease.

Fine Needle Aspiration (FNA) Biopsy

FNA involves using a thin needle attached to a syringe to withdraw (aspirate) a small amount of fluid and tiny bits of tissue from a lymph node or organ in the body. This procedure avoids the need for minor surgery. It is useful for some cancers, but the FNA often does not remove

enough tissue for a reliable diagnosis of Hodgkin disease (or to determine the type of HD). If the doctor suspects that your lymph node swelling is caused by an infection or by the spread of cancer from another organ (such as the breast, lungs, or thyroid), FNA may be the first type of biopsy done. But an excisional biopsy may still be needed to diagnose Hodgkin disease properly, even after an FNA has been done.

Once Hodgkin disease has been diagnosed and treated, the FNA is sometimes used to check areas in other parts of the body that might represent Hodgkin disease spreading or coming back.

Lab Tests Used to Diagnose and Classify Hodgkin Disease

All biopsy specimens are looked at under a microscope by a doctor called a *pathologist*, who is specially trained to recognize changes in cells and tissues caused by cancer and other diseases. The doctor looks at the appearance, as well as the size and shape of the cells and determines whether any of them are Reed-Sternberg cells. Sometimes the first biopsy does not provide a definite answer and more biopsies are needed.

Looking at the tissue under the microscope can often reveal whether Hodgkin disease is the diagnosis (and what type it is), but sometimes testing called *immunohistochemistry* is needed. This consists of special stains of the specimen to look for the presence of certain proteins on the surface of the Reed-Sternberg cells, such as CD15 and CD30. These are typically found in the classical type of Hodgkin disease. Tests for other proteins may point to non-Hodgkin lymphoma rather than Hodgkin disease or to other diseases entirely.

How Is Hodgkin Disease Staged?

Staging is the process of finding out how far a cancer has spread. It is important because it helps determine which treatments are best for each patient. Staging also helps doctors predict the outlook for recovery.

Hodgkin disease generally starts in one set of lymph nodes and spreads directly to a nearby set without skipping areas, at least until late in the disease. Growth (invasion) into nearby organs can sometimes occur as well. Rarely, Hodgkin disease will involve only one organ or one site other than lymph nodes, such as the lung. The current staging system is based on these facts.

Once a biopsy has been done to confirm the presence and determine the type of Hodgkin disease, the next step is to stage the disease. Information from the medical history and physical exam that were discussed in the section, "How Is Hodgkin Disease Diagnosed?" is taken into account, as well as the results of biopsies and imaging tests.

Imaging Tests Used to Stage Hodgkin Disease

One or more of the following tests may be used to help determine the extent of the Hodgkin disease in the body.

Chest X-ray

Hodgkin disease often causes enlargement of lymph nodes in the chest (mediastinal and hilar lymph nodes), which can usually be seen on a plain chest x-ray.

Computed Tomography (CT)

This test gives your doctor a better look at lymph nodes in the chest, abdomen, and pelvis, as well as other organs.

The CT scan is an x-ray procedure that produces detailed cross-sectional images of the body. Instead of taking one picture like an x-ray, a CT scanner takes many pictures as it rotates around the patient. A computer combines these pictures into an image of a "slice" of the body. The machine creates many images or pictures of the parts of the body that are being studied.

Often after the first set of pictures is taken, you or your child will receive an intravenous (IV) injection of a contrast dye, or you may also be asked to drink a solution of contrast material. This helps better outline structures in the body. A second set of CT scan pictures is then taken.

You or your child may need an IV line through which the contrast dye is injected. Right after the dye is injected into the vein, you may feel very warm. This feeling is normal, and will usually go away in a few seconds. Some people are allergic to the dye and get hives or a flushed feeling or, rarely, have more serious reactions like trouble breathing and low blood pressure. *Be sure to tell the doctor if you or your child has ever had a reaction to any contrast material used for x-rays.*

CT scans take longer than regular x-rays. You need to lie still on a table while they are being done. During the test, the table moves in and out of the scanner, a ring-shaped machine that completely surrounds the table. You might feel a bit confined by the ring you have to lie in when the pictures are being taken.

In some cases, a CT can be used to guide a biopsy needle precisely into a suspicious area. For this procedure, called a *CT-guided needle biopsy*, you remain on the CT scanning table while a radiologist (a doctor specially trained to perform these kinds of tests) moves a biopsy needle through the skin and toward the location of the mass. CT scans are repeated until the

needle is within the mass. A biopsy sample is then removed to be looked at under a microscope.

Magnetic Resonance Imaging (MRI)

This test is rarely used in Hodgkin disease, but if your doctor is concerned about spread to the spinal cord or brain, MRI is very useful for looking at these areas.

MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body. A contrast material might be injected, just as with CT scans, but is used less often.

MRI scans take longer than CT scans -- often up to an hour. You may have to lie inside a narrow tube, which is confining and can upset people with a fear of enclosed spaces. Newer, "open" MRI machines can help with this if needed. The MRI machine makes loud buzzing or clicking noises that you may find disturbing. Some places provide headphones to block this out.

Positron Emission Tomography (PET)

PET scans involve injecting glucose (a form of sugar) that contains a small amount of radioactivity into the blood. Because cancer cells in the body are growing rapidly, they absorb large amounts of the radioactive sugar. A special camera can then create a picture of areas of radioactivity in the body.

PET scans can help tell if an enlarged lymph node contains Hodgkin disease or is benign. The picture is not finely detailed like a CT or MRI scan, but it can provide helpful information about your whole body.

PET scans are sometimes used to tell if a lymphoma is responding to treatment. Some doctors will repeat the PET scan after 2 or 3 courses of chemotherapy. If it is working, the lymph nodes will no longer take up the radioactive glucose. PET scans can also be used after treatment in helping decide whether an enlarged lymph node still contains cancer or is merely scar tissue.

Recently, newer devices have been developed that combine the PET scan with a CT scan. PET/CT scans can help pinpoint the exact location of the lymphoma.

Gallium Scan

During this test, the radiologist injects a small dose of radioactive gallium into a vein. It is attracted to lymph tissue in the body. A few days later a special camera is used to detect the radioactivity, showing the location of the gallium. These tests can find tumors that might be Hodgkin disease in lymph nodes and other organs.

The gallium scan was used before PET scans were available and can still be useful in finding lymphoma deposits that the PET scan may miss. It is also useful in distinguishing infections from lymphomas when the diagnosis is not clear.

Lymphangiogram

This test uses x-ray to look at lymph nodes in the pelvis and abdomen. The first step in this procedure is to inject some blue dye under the skin between the toes. The lymphatic vessels pick up this dye, become blue, and can be recognized by the doctor, who then injects a small amount of contrast material into the vessels. This material is carried through the lymphatic vessels and reaches lymph nodes in the pelvis and abdomen. The contrast material appears white on x-ray images, which helps doctors detect enlarged lymph nodes that may be affected by Hodgkin disease. With CT, gallium, and PET scans now available, the lymphangiogram is rarely used.

Other Tests

Blood Tests

Blood tests aren't used to stage Hodgkin disease, but they may be useful in getting a sense of how advanced the disease is and how well a person might tolerate certain treatments.

Hodgkin disease cells do not appear in the blood, but a complete blood count can sometimes reveal signs of Hodgkin disease. Anemia (not having enough red blood cells) can be a sign of a more advanced Hodgkin disease. A high white blood cell count is another possible sign, although it can also be caused by infections. Blood tests to check liver and kidney function may also be done.

Bone Marrow Biopsy and Aspiration

In some cases, tests may be done to tell if the Hodgkin disease is in the bone marrow. These include bone marrow aspiration and biopsy -- two tests that are usually done at the same time. The samples are usually taken from the back of the pelvic (hip) bone, although in some cases they may be taken from the sternum (breastbone) or other bones.

In bone marrow *aspiration*, you lie on a table (either on your side or on your belly). After cleaning the area, the skin over the hip and the surface of the bone are numbed with local anesthetic, which may cause a brief stinging or burning sensation. A thin, hollow needle is then inserted into the bone and a syringe is used to suck out a small amount of liquid bone marrow (about 1 teaspoon). Even with the anesthetic, most patients still have some brief pain when the marrow is removed.

A bone marrow *biopsy* is usually done just after the aspiration. A small piece of bone and marrow (about 1/16 inch in diameter and 1/2 inch long) is removed with a slightly larger needle that is twisted as it is pushed down into the bone. The biopsy may also cause some brief pain. Once the biopsy is done, pressure will be applied to the site to help stop any bleeding.

The samples are then viewed under a microscope to look for signs of Hodgkin disease.

Ann Arbor Staging System

The staging system for Hodgkin disease is known as the Ann Arbor system. It has 4 stages, labeled with the Roman numerals I, II, III, and IV. If Hodgkin disease affects an organ outside of the lymph system, but is next to a known area of lymph node involvement, the letter "E" is added to the stage (for example, stage IE or IIE). If it involves the spleen, the letter "S" is added.

Stage I: Either of the following means that the disease is a stage I:

- HD is found in only 1 lymph node area (I).
- The cancer is found only in one area of a single organ outside of the lymph system (IE).

Stage II: Either of the following means that the disease is a stage II:

- HD is found in 2 or more lymph node areas on the same side of (above or below) the diaphragm -- the muscle beneath the lungs that moves up and down to help you breathe (II).
- The cancer extends locally from the lymph node(s) into a nearby organ (IIE).

Stage III: Either of the following means that the disease is a stage III:

- HD is found in lymph node areas on both sides of (above and below) the diaphragm (III).
- The HD is present in lymph nodes above and below the diaphragm, and has also spread to nearby organs (IIIE), to the spleen (IIIS), or to both (IIIE,S).

Stage IV: The following means that the disease is a stage IV:

- HD has spread widely through 1 or more organs outside of the lymph system, such as liver, bone marrow, or lung. Cancer cells may or may not be found in nearby lymph nodes.

Other modifiers may also be used to describe the Hodgkin disease stage.

"Bulky" Disease

This term is used to describe tumors in the chest that are at least 1/3 as wide as the chest or tumors in other areas that are at least 10 centimeters (about 4 inches) across. It is usually designated by adding the letter "X". Bulky disease may require more intensive treatment.

A vs. B

Each stage may also be assigned an "A" or "B". The letter "A" is added if the person doesn't have certain symptoms that can be caused by Hodgkin disease. The letter "B" is added (stage IIIB, for example) if any B symptoms are present:

- loss of more than 10% of body weight over the previous 6 months
- fever of 100° or greater without any known cause (except the Hodgkin disease)
- drenching night sweats

If any of these is present, then more intensive treatment is usually recommended.

Resistant or Recurrent Hodgkin Disease

The terms *resistant* or *progressive* disease are used when the disease does not go away or progresses while you are still being treated with initial therapy. *Recurrent* or *relapsed* disease means that Hodgkin disease initially responded well to treatment and went away, but it has now come back. If Hodgkin disease returns, it may do so in the area of the body where it first started or in another part of the body. This may occur shortly after treatment or years later.

Survival Rates by Stage

The 5-year survival rate refers to the percentage of patients who live *at least* 5 years after their cancer is diagnosed. Five-year survival rates are used to produce a standard way of discussing prognosis. Of course, many people live much longer than 5 years. Five-year *relative* survival rates are calculated in ways that exclude the impact of diseases other than cancer on survival.

Current 5-year survival rates are based on people with Hodgkin disease who were diagnosed and initially treated more than 5 years ago. Advances in treatment since then mean that people diagnosed today likely have a more favorable outlook than the numbers below.

Stage	5-year Survival Rate
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I	90% to 95%
II	90% to 95%
III	80% to 85%
IV	About 60 to 70%

These numbers are taken from a large international database described in the American Cancer Society Atlas of Clinical Oncology (see "References" section). The patients were all adults treated well before 1990. The stage I and II patients had no B symptoms.

More recent studies have found overall 5-year survival rates to be higher than those listed above. For example, studies from Germany and Italy that used intensive therapy reported a 90% 5-year survival in patients with more advanced disease. It is too early to tell if these people are cured or if their disease will eventually come back.

It's important to keep in mind that these numbers are general statistics, and they may not apply to an individual person's situation. Factors other than stage, including the person's age and the prognostic factors listed below, also affect a person's outlook.

Other Prognostic Factors

Certain factors, if present, regardless of stage, tend to make the prognosis (outlook) more serious and often influence the doctor to make the treatment more intense. These are:

- having B symptoms or bulky disease
- being male
- age over 45
- a high white blood cell count (above 15,000)
- a low red blood cell count (hemoglobin level below 10.5)
- a low blood lymphocyte count (below 600)
- a low blood albumin level

How Is Hodgkin Disease Treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

This section starts by describing the types of treatments used for Hodgkin disease. This is followed by a discussion of the typical treatment options based on the stage of the disease, as well as other prognostic factors when these are important.

In recent years, many advances have been made in treating Hodgkin disease. Most newly-diagnosed patients can be cured with chemotherapy and radiation therapy. Treatment for Hodgkin disease is based largely on the stage of the disease. However, factors that are unique to an individual may alter standard therapy. Some of these factors include the person's age and general health, and the type and site(s) of the disease.

Making Treatment Decisions

After Hodgkin disease is staged, the cancer care team will discuss treatment options with you. Take the time to think about all of your choices. In choosing a treatment plan, consider your health and the type and stage of the Hodgkin disease. Be sure that you understand all the risks and side effects of the various treatments before making a decision.

Seeking a second opinion can give you more information and help you feel confident about the treatment plan that you choose. Your doctor should be willing to help you find another cancer doctor who can give you a second opinion. Some insurance companies actually require a second opinion before they will agree to pay for certain treatments.

For almost all patients with Hodgkin disease, complete cure is the main goal. But treatment can have side effects that often don't show up for many years. Because of this, doctors always try and choose a curative treatment with the lowest risk of these potential side effects. The 2 main methods of treating Hodgkin disease are *chemotherapy* (the use of cancer-killing drugs) and *radiation therapy* (the use of high-energy rays or particles to kill cancer cells and shrink tumors).

In certain circumstances, the best approach may involve using 1 or both of these treatments. High-dose chemotherapy with blood-forming stem cell transplants, discussed later, is being used for certain patients when the other treatments haven't been successful. In most cases, except for biopsy and staging, surgery rarely has a role in the treatment of Hodgkin disease.

Chemotherapy

Chemotherapy is the use of drugs to kill cancer cells. The drugs can be taken as pills or injected into a vein under the skin. Chemotherapy is systemic therapy, which means the drugs enter the bloodstream and circulate throughout the body to reach and destroy cancer cells wherever they may be.

Multiple drugs are always used in the chemotherapy regimens for Hodgkin disease because different drugs kill cancer cells in different ways. The combinations of drugs used to treat

Hodgkin disease are often referred to by abbreviations that are easier to remember than the full drug names. Although other combinations may be used, the standard in the United States is a 4 drug combination called **ABVD**, which consists of:

- **A**driamycin (doxorubicin)
- **B**leomycin
- **V**inblastine
- **D**acarbazine

Other commonly used regimens include:

BEACOPP

- **B**leomycin
- **E**toposide
- **A**driamycin (doxorubicin)
- **C**yclophosphamide
- **O**ncovin (vincristine)
- **P**rocarbazine
- **P**rednisone

Stanford V

- Doxorubicin (Adriamycin)
- Mechlorethamine (Nitrogen mustard)
- Vincristine
- Vinblastine
- Bleomycin
- Etoposide
- Prednisone

Radiation is also used together with chemotherapy in the Stanford V regimen.

Other chemotherapy combinations may also be used for Hodgkin disease. Most contain the same drugs as listed above, but they are given in different doses and schedules. Perhaps the most important issue is that your doctor is familiar with using the regimen prescribed and understands its side effects.

Possible Side Effects

Chemotherapy drugs work by attacking cells that are dividing quickly, which is why they work against most types of lymphoma cells. But other cells in the body, such as those in the bone marrow, the lining of the mouth and intestines, and the hair follicles, also divide

quickly. These cells are also likely to be affected by chemotherapy, which can lead to side effects.

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are taken. These side effects can include:

- hair loss
- mouth sores
- loss of appetite
- nausea and vomiting
- increased chance of infections (due to low white blood cell counts)
- easy bruising or bleeding (due to low blood platelet counts)
- fatigue (due to low red blood cell counts)

These side effects are usually short-term and go away after treatment is finished.

There are often ways to lessen these side effects. For example, drugs are usually given to help prevent or reduce nausea and vomiting.

Drugs known as growth factors (G-CSF or GM-CSF, for example) are sometimes given to help the white blood cells recover from the effects of chemotherapy and thus reduce the chance of infection. Antibiotics may also be given before signs of infection appear, but they are usually given at the earliest sign of an infection, such as a fever.

If your white blood cell counts are very low during treatment, you can help reduce the risk of infection by carefully avoiding exposure to germs. During this time, your doctor may advise that you:

- Wash your hands often.
- Avoid fresh, uncooked fruits and vegetables and other foods that might carry germs.
- Avoid fresh flowers and plants because they may carry mold.
- Make sure other people wash their hands before they come in contact with you.
- Avoid large crowds and people who are sick (wearing a surgical mask offers some protection in these situations).

If your platelet counts are very low, you may be given drugs or platelet transfusions to help protect against bleeding. Fatigue caused by anemia (very low red blood cell counts) can be treated with drugs or with red blood cell transfusions.

Some chemotherapy drugs may have long-term side effects that occur many years after therapy has ended. These can affect a patient's heart, lungs, growth, and ability to have children. If the patient is old enough and is scheduled to receive drugs that cause sterility, sperm banking should be considered before chemotherapy is started.

Chemotherapy can increase the risk of developing a second type of cancer later in life (such as leukemia), especially in those patients who have received radiation therapy along with chemotherapy.

The severity of long-term side effects can vary, depending on the patient's age at the time of treatment and other factors. Long-term effects are discussed in more detail in the section, "What Happens After Treatment for Hodgkin Disease?"

Ask your doctor to explain all of the possible side effects of chemotherapy and your particular chances of having them.

Radiation Therapy

Radiation therapy uses high-energy rays (or particles) to destroy cancer cells or slow their rate of growth.

When radiation is used to treat Hodgkin disease, it is done with a carefully focused beam of radiation, delivered from a machine outside the body. This is known as *external beam radiation*. It is most useful when the disease is localized to one part of the body. Radiation is also used together with chemotherapy when the Hodgkin disease involves a large or bulky tumor mass, usually in the chest. In this circumstance, the chemotherapy alone or radiation alone will not cure the patient, but both treatments together are usually effective in getting rid of the disease.

Extended Field Radiation

At one time, the major site of disease and surrounding "normal" lymph node areas were usually treated with radiation, just in case the Hodgkin disease had spread, even though the doctors could not actually detect it in these areas. This is called extended field radiation.

- If the Hodgkin disease was in the upper body, radiation was given to the *mantle field*, which included lymph node areas in the neck, chest, and under the arms. Sometimes this was extended to also include lymph nodes in the upper abdomen.
- *Inverted Y field* radiation therapy included the lymph nodes in the upper abdomen, the spleen, and the lymph nodes in the pelvis).
- When inverted Y field radiation was given together with mantle field radiation, the combination was called *total nodal radiation*.

Mantle field, inverted Y field, or total nodal radiation is seldom given in combination with chemotherapy at this time.

Involved Field Radiation

Doctors have found that in some cases, treating only the known areas of disease with radiation may also produce a cure. This is called involved field radiation and is now the preferred form of radiation therapy when used along with chemotherapy, although they are not given at the same time. Chemotherapy is given first, followed by involved field radiation given to areas that were initially involved.

The main drawback of external beam radiation is that it only kills Hodgkin cells in the precise area where the radiation has been given. Thus, if there are Hodgkin cells hidden in other areas of the body, radiation alone is not likely to be successful.

Possible Side Effects

Radiation can damage nearby healthy tissue. Some people have skin changes similar to sunburn, which slowly fades away. Other possible short-term side effects include fatigue, nausea, or diarrhea.

Radiation therapy can also have long-term side effects. The most serious of these is the development of another cancer in the part of the body that was irradiated (exposed to radiation). This is described in the section, "What Happens After Treatment for Hodgkin Disease?"

In children, another possible side effect is the failure of bones, such as the spine, to grow normally if they are irradiated.

Radiation to the chest can damage the thyroid gland so that patients become hypothyroid (their thyroid gland doesn't make enough thyroid hormone). This leads to fatigue and weight gain. Treatment with pills containing thyroid hormone can take care of this problem.

In the past, radiation was thought to have fewer side effects than chemotherapy and was preferred when possible. But as more patients have been able to live out their normal life spans after successful treatment for Hodgkin disease, we have seen more long-term complications from radiation. Cancers develop in the treated area at the rate of about 1% per year. Radiation to the chest also carries with it an increased risk of heart disease (such as heart attacks). Radiation to the neck may increase the risk of stroke many years later. Because of these problems, doctors are slowly moving away from using radiation or at least, limiting the dose and areas of the body that are treated.

To reduce the risk of side effects, doctors carefully calculate the exact dose of radiation needed and aim the beam as accurately as they can to hit the cancer and minimize exposure of the normal surrounding tissues. This requires a great deal of planning. Ask your doctor about the possible side effects of radiation therapy.

High-Dose Chemotherapy and Bone Marrow or Peripheral Blood Stem Cell Transplant

For some patients the only curative therapy is very high doses of chemotherapy followed by the infusion of previously collected blood-forming stem cells. High-dose chemotherapy and stem cell transplant is now used in the following circumstances for patients with Hodgkin disease:

- when Hodgkin disease doesn't go away completely after standard treatment with chemotherapy and/or radiation therapy
- when Hodgkin disease seems to completely go away after chemotherapy and/or radiation, but then comes back at some later time

The usual doses of chemotherapy drugs can cause serious side effects to quickly dividing tissues such as the bone marrow. Even though higher doses of these drugs might be more effective in treating Hodgkin disease, they are not given because the severe damage to bone marrow cells would cause lethal shortages of blood cells, and other vital organs would likely be damaged as well.

A stem cell transplant (SCT) allows doctors to use higher doses of chemotherapy. After treatment is finished, the patient receives a transplant of blood-forming stem cells to restore the bone marrow.

Blood-forming stem cells used for a transplant are obtained either from the blood (for a peripheral blood stem cell transplant, or PBSCT) or from the bone marrow (for a bone marrow transplant, or BMT). Peripheral blood stem cells are obtained from a procedure similar to a blood donation, while bone marrow donation is usually done in an operating room under general anesthesia (where the donor is asleep). Bone marrow transplants were more common in the past, but they have largely been replaced by PBSCTs.

Types of Transplants

There are 2 main types of stem cell transplants: autologous and allogeneic. They differ with regard to the source of the blood-forming stem cells.

Autologous stem cell transplant: In this type of transplant, a patient's own stem cells are removed from his or her bone marrow or peripheral blood. They are collected on several occasions in the weeks before treatment. The cells are frozen and stored while the person gets treatment (high-dose chemotherapy and/or radiation) and then are reinfused into the patient's blood. This is the more commonly used type of transplant for Hodgkin disease.

Allogeneic stem cell transplant: In this type of transplant, the stem cells come from someone else -- usually a donor whose tissue type is almost identical to the patient's. Tissue type is based on certain substances present on the surface of cells in the body. These substances can cause the immune system to react against the cells. Therefore, the closer a tissue "match" is between the donor and the recipient, the better the chance the transplanted cells will "take" and begin making new blood cells.

The donor may be a brother or sister or a matched unrelated donor (MUD). The stem cells from an unrelated donor come from volunteers whose tissue type has been stored in a central registry and matched with that of the patient. Sometimes umbilical cord stem cells are used. These "cord blood" stem cells come from blood drained from the umbilical cord and placenta after a baby is born and the umbilical cord is cut.

In treating Hodgkin disease, an allogeneic transplant is generally used only if an autologous transplant has failed, largely because it is more toxic than the autologous transplant.

With either type of transplant, the blood-forming stem cells are carefully frozen and stored before treatment. The patient then receives high-dose chemotherapy and sometimes whole body radiation treatment as well. (Radiation shields are used to protect the lungs, heart, and kidneys from damage during radiation therapy.)

This destroys remaining cancer cells, but it also kills all or most normal cells in the bone marrow. After therapy, the frozen stem cells are thawed and returned to the body like a blood transfusion. The stem cells settle into the patient's bone marrow over the next several days and start to grow and make new blood cells.

The Transplant Procedure

The patient getting the stem cell transplant may be admitted to the bone marrow transplant (BMT) unit of the hospital or receive treatment as an outpatient depending on a number of factors.

If done as an inpatient, the patient is usually admitted to the hospital on the day before chemotherapy begins. He or she will usually stay in the hospital (BMT unit) until after the high-dose chemotherapy and the stem cells have been given, and until the stem cells have started to work, making new blood cells again.

If done as an outpatient, patients and families must be able to spot complications requiring their doctor's attention. Unless they live close to the transplant center, they will be asked to stay in a nearby hotel.

After the proper education, the patient starts high-dose chemotherapy and may be given high-dose whole body radiation. The chemotherapy and radiation treatments are meant to destroy any remaining cancer cells. They also kill the normal cells of the bone marrow and the

immune system. This prevents the stem cell transplant (graft) from being rejected. Once treatment is complete, the stem cells (autologous or allogeneic) are given through a vein or venous access line, just like a blood transfusion. The stem cells migrate to the bone marrow.

In an allogeneic SCT, the person getting the transplant is given drugs such as cyclosporine, methotrexate, tacrolimus, or prednisone to prevent acute graft-versus-host-disease (GVHD). In this condition, the immune cells in the donor's marrow or cord blood (the graft) attack the patient's body (the host).

For the next 3 to 4 weeks the patient is given as much supportive therapy as needed. This can include IV nutrition; antibiotics to treat bacteria, viral, and fungal infections; red blood cell and/or platelet transfusions; or other medicines as needed.

Usually around 2 to 3 weeks after the stem cells have been infused, they begin making new white blood cells. This is followed by the new platelet production and, several weeks later, by new red blood cell production. Because of the high risk of serious infections right after treatment, patients remain in protective isolation (where exposure to germs is kept to a minimum) until a measure of their white blood cells, the absolute neutrophil count (ANC), rises above 500. They can usually leave the hospital when their ANC nears 1,000.

Patients then typically make regular visits to the outpatient transplant clinic for about 6 months, after which time their care is continued by their regular oncologist or internist. At this point, they only come back to the clinic for their regular exams or if they have symptoms that should be checked by their doctor.

Practical Points

Bone marrow or peripheral blood SCT is a complex treatment. If the doctors think a patient may benefit from a transplant, it should be done at a hospital where the staff has experience with the procedure and with managing the recovery phase. Some stem cell transplant programs may not have experience in certain types of transplants, especially transplants from unrelated donors.

SCT is very expensive (more than \$100,000) and often requires a lengthy hospital stay. Because some insurance companies may view it as an experimental treatment, they may not pay for the procedure. It is important to find out what your insurer will cover before deciding on a transplant and to have an idea of what you might have to pay.

Possible Side Effects

Side effects from a stem cell transplant are generally divided into early and long-term effects. The early complications and side effects are basically the same as those caused by any other type of high-dose chemotherapy (see the "Chemotherapy" section of this document), and are

caused by damage to the bone marrow and other quickly growing tissues of the body. They can include low blood cell counts (with increased risks of infection and bleeding), nausea, vomiting, loss of appetite, mouth sores, and hair loss.

Complications and side effects that can persist for a long time or that may occur many years after the transplant include:

- graft-versus-host disease (GVHD), which occurs only in allogeneic (donor) transplants (see below)
- infertility and premature menopausal symptoms in female patients (caused by damage to the ovaries)
- infertility in male patients
- damage to the thyroid gland that can cause problems with metabolism
- cataracts (damage to the lens of the eye that can affect vision)
- damage to the lungs, causing shortness of breath
- bone damage called aseptic necrosis (if damage is severe, the patient may need to have part of the affected bone and the joint replaced)
- possible development of leukemia several years later

Graft-versus-host disease (GVHD): This is one of the most serious complications of allogeneic (donor) stem cell transplants. It occurs because the immune system of the patient is taken over by that of the donor. The donor immune system then may "see" the patient's own body tissues as foreign and may react against them. Symptoms can include severe skin rashes with itching, mouth sores (which can affect eating), nausea, and severe diarrhea. Liver damage may cause yellowing of the skin and eyes (jaundice). The lungs may also be damaged. The patient may also become easily fatigued and develop muscle aches.

GVHD is often described as either acute or chronic, based on how soon after the transplant it begins. Sometimes GVHD can become disabling, and if it is severe enough, it can be fatal. Usually, immune suppressing drugs can be used to control GVHD.

On the positive side, the graft-versus-host disease also leads to "graft-versus-lymphoma" activity. Any lymphoma cells remaining after the chemotherapy and radiation therapy are often killed by immune reactions of the donor cells since the lymphoma cells are seen as foreign by the donor's immune system as well. Mild graft-versus-host disease can be a good thing.

Non-myeloablative Transplant (Mini-Transplant)

Most patients over the age of 55 can't tolerate a standard allogeneic transplant that uses high doses of chemotherapy. Some may be able to have a non-myeloablative transplant (also known as a mini-transplant or reduced-intensity transplant), where they receive lower doses of chemotherapy and radiation that do not completely destroy the cells in their bone marrow. They then receive the allogeneic (donor) stem cells. These cells enter the body and establish

a new immune system, which sees the lymphoma cells as foreign and attacks them (a "graft-versus-lymphoma" effect).

Doctors have learned that if they use small doses of certain chemotherapy drugs and low doses of total body radiation, an allogeneic transplant can still work with much less toxicity. In fact, a patient can receive a non-myeloablative transplant as an outpatient.

The major complication is graft-versus-host disease, which may damage the patient's body tissue. Researchers are looking for ways to eliminate the graft-versus-host response while keeping the graft-versus-lymphoma effect.

For more information on these procedures, see the American Cancer Society document, *Bone Marrow & Peripheral Blood Stem Cell Transplants*.

Hodgkin Disease in Children

The types of Hodgkin disease that develop in children are different from those that develop in adults. Although there are exceptions, childhood cancers tend to respond better to chemotherapy. Children's bodies also tend to tolerate chemotherapy better than adults'. But because chemotherapy can have some long-term side effects, children who survive their cancer need careful attention for the rest of their lives.

Treatment Differences

Although the treatment for Hodgkin disease is generally the same for adults and children, there are some differences.

If the child is sexually mature and has reached, or almost reached, full development of muscles and bone mass, the treatment is usually the same as that given to adults. But if the child has not reached his or her potential body size, then chemotherapy will likely be favored over radiation therapy. Radiation could affect bone and muscle growth and prevent children from reaching their normal size. The major goal is to cure the child without causing long-term problems.

In order to cure children, doctors often combine chemotherapy with low doses of radiation. The chemotherapy drugs tend to be combinations of multiple drugs rather than just the usual adult 4-drug regimen ABVD. The success of this approach has been excellent, with cure rates of 85% to 100% of children with more advanced disease.

Childhood Cancers Are Treated at Special Centers

Childhood cancer patients and their families have special needs that can be best met by specialized cancer centers for children and adolescents. Being treated in specialized centers offers them the advantage of a team of experts who know the differences between adult and childhood cancers, as well as the unique needs of children with cancers. This team usually includes the following:

- pediatric oncologist -- a doctor who specializes in cancers of children
- pathologist -- a doctor who specializes in diagnosing disease in tissue samples
- surgeon -- a doctor who performs operations
- radiation oncologist-- a doctor who specializes in using radiation to treat cancer
- pediatric oncology nurse -- a nurse who specializes in caring for children with cancer and their families
- nurse practitioners -- a registered nurse with a master's or doctoral degree

Since the 1960s, most children with cancer have been treated at specialized centers designed for them. These centers have psychologists, social workers, child life specialists, nutritionists, rehabilitation and physical therapists, and educators who can support and educate the entire family.

Nearly 90% of children with cancer in the United States are treated at a center that is a member of the Children's Oncology Group (COG). These centers are associated with either a university or a children's hospital.

Clinical Trials

You have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is deciding which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you. Clinical trials are one way to get state-of-the-art cancer care. Still, they are not right for everyone.

Here we will give you a brief review of clinical trials. Talking to your health care team, your family, and your friends can help you make the best treatment choice for you.

What Are Clinical Trials?

Clinical trials are carefully controlled research studies that are done with patients. These studies test whether a new treatment is safe and how well it works in patients, or they may test new ways to diagnose or prevent a disease. Clinical trials have led to many advances in cancer prevention, diagnosis, and treatment.

The Purpose of Clinical Trials

Clinical trials are done to get a closer look at promising new treatments or procedures in patients. A clinical trial is only done when there is good reason to believe that the treatment, test, or procedure being studied may be better than the one used now. Treatments used in clinical trials are often found to have real benefits and may go on to become tomorrow's standard treatment.

Clinical trials can focus on many things, such as:

- new uses of drugs that are already approved by the US Food and Drug Administration (FDA)
- new drugs that have not yet been approved by the FDA
- non-drug treatments (such as radiation therapy)
- medical procedures (such as types of surgery)
- herbs and vitamins
- tools to improve the ways medicines or diagnostic tests are used
- medicines or procedures to relieve symptoms or improve comfort
- combinations of treatments and procedures

Researchers conduct studies of new treatments to try to answer the following questions:

- Is the treatment helpful?
- What's the best way to give it?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Are there more or fewer side effects than the standard treatment used now?
- Do the benefits outweigh the side effects?
- In which patients is the treatment most likely to be helpful?

Phases of Clinical Trials

There are 4 phases of clinical trials, which are numbered I, II, III, and IV. We will use the example of testing a new cancer treatment drug to look at what each phase is like.

Phase I clinical trials: The purpose of a phase I study is to find the best way to give a new treatment safely to patients. The cancer care team closely watches patients for any harmful side effects.

For phase I studies, the drug has already been tested in lab and animal studies, but the side effects in patients are not fully known. Doctors start by giving very low doses of the drug to the first patients and increase the doses for later groups of patients until side effects appear or

the desired effect is seen. Doctors are hoping to help patients, but the main purpose of a phase I trial is to test the safety of the drug.

Phase I clinical trials are often done in small groups of people with different cancers that have not responded to standard treatment, or that keep coming back (recurring) after treatment. If a drug is found to be reasonably safe in phase I studies, it can be tested in a phase II clinical trial.

Phase II clinical trials: These studies are designed to see if the drug works. Patients are given the best dose as determined from phase I studies. They are closely watched for an effect on the cancer. The cancer care team also looks for side effects.

Phase II trials are often done in larger groups of patients with a specific cancer type that has not responded to standard treatment. If a drug is found to be effective in phase II studies, it can be tested in a phase III clinical trial.

Phase III clinical trials: Phase III studies involve large numbers of patients -- most often those who have just been diagnosed with a specific type of cancer. Phase III clinical trials may enroll thousands of patients.

Often, these studies are randomized. This means that patients are randomly put in one of two (or more) groups. One group (called the control group) gets the standard, most accepted treatment. Another group (or more than one group) will get the new treatment being studied. All patients in phase III studies are closely watched. The study will be stopped early if the side effects of the new treatment are too severe or if one group has much better results than the others.

Phase III clinical trials are usually needed before the FDA will approve a treatment for use by the general public.

Phase IV clinical trials: Once a drug has been approved by the FDA and is available for all patients, it is still studied in other clinical trials (sometimes referred to as phase IV studies). This way more can be learned about short-term and long-term side effects and safety as the drug is used in larger numbers of patients with many types of diseases. Doctors can also learn more about how well the drug works, and if it might be helpful when used in other ways (such as in combination with other treatments).

What It Will Be Like to Be in a Clinical Trial

If you are in a clinical trial, you will have a team of experts taking care of you and watching your progress very carefully. Depending on the phase of the clinical trial, you may receive more attention (such as having more doctor visits and lab tests) than you would if you were treated outside of a clinical trial. Clinical trials are specially designed to pay close attention to you.

However, there are some risks. No one involved in the study knows in advance whether the treatment will work or exactly what side effects will occur. That is what the study is designed to find out. While most side effects go away in time, some may be long-lasting or even life threatening. Keep in mind, though, that even standard treatments have side effects. Depending on many factors, you may decide to enter (enroll in) a clinical trial.

Deciding to Enter a Clinical Trial

If you would like to take part in a clinical trial, you should begin by asking your doctor if your clinic or hospital conducts clinical trials. There are requirements you must meet to take part in any clinical trial. But whether or not you enter (enroll in) a clinical trial is completely up to you.

Your doctors and nurses will explain the study to you in detail. They will go over the possible risks and benefits and give you a form to read and sign. The form says that you understand the clinical trial and want to take part in it. This process is known as giving your informed consent. Even after reading and signing the form and after the clinical trial begins, you are free to leave the study at any time, for any reason.

Taking part in a clinical trial does not keep you from getting any other medical care you may need.

To find out more about clinical trials, talk to your cancer care team. Here are some questions you might ask:

- Is there a clinical trial that I could take part in?
- What is the purpose of the study?
- What kinds of tests and treatments does the study involve?
- What does this treatment do? Has it been used before?
- Will I know which treatment I receive?
- What is likely to happen in my case with, or without, this new treatment?
- What are my other choices and their pros and cons?
- How could the study affect my daily life?
- What side effects can I expect from the study? Can the side effects be controlled?
- Will I have to stay in the hospital? If so, how often and for how long?
- Will the study cost me anything? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment would I be entitled to?
- What type of long-term follow-up care is part of the study?
- Has the treatment been used to treat other types of cancers?

How Can I Find Out More About Clinical Trials That Might Be Right for Me?

The American Cancer Society offers a clinical trials matching service for patients, their family, and friends. You can reach this service at 1-800-303-5691 or on our Web site at <http://clinicaltrials.cancer.org>.

Based on the information you give about your cancer type, stage, and previous treatments, this service can put together a list of clinical trials that match your medical needs. The service will also ask where you live and whether you are willing to travel so that it can look for a treatment center that you can get to.

You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials.

For even more information on clinical trials, the American Cancer Society has a document called *Clinical Trials: What You Need to Know*. You can read this on the Web site, www.cancer.org, or have it sent to you by calling 1-800-ACS-2345.

Complementary and Alternative Treatments

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that are different from mainstream (standard) medical treatment. These treatments can include vitamins, herbs, and special diets, or acupuncture and massage—among many others. You may have a lot of questions about these treatments. Here are some you may have thought of already:

- How do I know if the treatment is safe?
- How do I know if it works?
- Should I try one or more of these treatments?
- What does my doctor know/think about these treatments? Should I tell the doctor that I'm thinking about trying them?
- Will these treatments cause a problem with my standard medical treatment?
- What is the difference between "complementary" and "alternative" treatments?
- Where can I find out more about these treatments?

The Terms Can Be Confusing

Not everyone uses these terms the same way, so it can be confusing. The American Cancer Society uses *complementary* to refer to medicines or treatments that are used *along with* your regular medical care. *Alternative* medicine is a treatment used *instead of* standard medical treatment.

Complementary Treatments

Complementary treatment methods, for the most part, are not presented as cures for cancer. Most often they are used to help you feel better. Some methods that can be used in a complementary way are meditation to reduce stress, acupuncture to relieve pain, or peppermint tea to relieve nausea. There are many others. Some of these methods are known to help and could add to your comfort and well being, while others have not been tested. Some have been proven not to be helpful. A few have even been found harmful.

There are many complementary methods that you can safely use right along with your medical treatment to help relieve symptoms or side effects, to ease pain, and to help you enjoy life more. For example, some people find methods such as aromatherapy, massage therapy, meditation, or yoga to be useful.

Alternative Treatments

Alternative treatments are those that are used instead of standard medical care. These treatments have not been proven to be safe and effective in clinical trials. Some of these treatments may even be dangerous or have life-threatening side effects. The biggest danger in most cases is that you may lose the chance to benefit from standard treatment. Delays or interruptions in your standard medical treatment may give the cancer more time to grow.

Deciding What to Do

It is easy to see why people with cancer may consider alternative treatments. You want to do all you can to fight the cancer. Sometimes mainstream treatments such as chemotherapy can be hard to take, or they may no longer be working.

Sometimes people suggest that their treatment can cure your cancer without having serious side effects, and it's normal to want to believe them. But the truth is that most non-standard treatments have not been tested and proven to be effective for treating cancer.

As you consider your options, here are 3 important steps you can take:

- Talk to your doctor or nurse about any treatment you are thinking about using.
- Check the list of "red flags" below.
- Contact the American Cancer Society at 1-800-ACS-2345 to learn more about complementary and alternative treatments in general and to learn more about the specific treatments you are thinking about.

Red Flags

You can use the questions below to spot treatments or methods to avoid. A "yes" answer to any one of these questions should raise a "red flag."

- Does the treatment promise a cure for all or most cancers?
- Are you told not to use standard medical treatment?
- Is the treatment or drug a "secret" that only certain people can give?
- Does the treatment require you to travel to another country?
- Do the promoters attack the medical or scientific community?

The Decision Is Yours

Decisions about how to treat or manage your cancer are always yours to make. If you are thinking about using a complementary or alternative method, be sure to learn about it and talk to your doctor about it. With reliable information and the support of your health care team, you may be able to safely use methods that can help you while avoiding those that could be harmful.

Treatment Options by Stage (Classical Hodgkin Disease)

The exact type of treatment the doctor recommends depends in large part on the patient's age at diagnosis, the stage of the disease, whether or not the disease is "bulky," and other prognostic factors. For an adolescent who has achieved full growth, the treatment is usually the same as that for an adult. This section summarizes the choices available according to the stage of cancer and points out some differences in therapy for adults and children.

Remember that your treatment decision is based on many factors, including:

- the kind of Hodgkin disease you have
- the extent of the Hodgkin disease in your body
- results of blood and other lab tests
- your general health
- your age
- your medical history

Because of this combination of factors, your treatment may be a little different from the general outline given below. Regardless of which factors you may have, it is important that your doctor have experience in treating Hodgkin disease.

Stage IA and IIA, Non-bulky Disease

This group includes Hodgkin disease that is confined to one side of the diaphragm (above or below), is not bulky, and that doesn't cause any of the "B" symptoms.

The preferred treatment option for most patients is chemotherapy (usually 2 or 4 cycles of ABVD), followed by involved field radiation to the initial site of the disease. Less commonly used options may include either radiation therapy alone (often given over more extensive area) or chemotherapy alone (usually for 4 or 6 cycles) in selected patients.

A newer strategy being studied by some doctors to decide if radiation should be given (regardless of the location of the Hodgkin disease) is to perform a PET scan after 2 courses of chemotherapy. If the scan doesn't show any active disease, then chemotherapy is given for another 2 courses without adding radiation. If the PET scan shows active disease, some doctors are adding radiation and others giving more intensive chemotherapy. Clinical trials are in progress to learn more about using PET scans to help choose the best treatment plan for each patient.

In children and adolescents with Hodgkin disease, treatment generally starts with chemotherapy alone, used at the lowest dose that is likely to result in a cure. If the disease doesn't completely go away with initial treatment, radiation therapy or more chemotherapy might be added. If radiation is used, the dose and field would be kept as small as possible. If radiation therapy is used below the diaphragm in girls and young women, the ovaries should be protected. Radiation damage of the ovaries might prevent them from ever being able to become pregnant.

Stage IA and IIA, Bulky Disease

This group includes Hodgkin disease that is confined to one side of the diaphragm (above or below) and that doesn't cause any of the "B" symptoms, but is bulky in terms of tumor mass.

Treatment is generally more intense than with non-bulky disease. The most common option is chemotherapy (usually ABVD for 4 to 6 cycles or other regimens such as Stanford V or BEACOPP), followed by involved-field radiation therapy to the sites of the tumor. For those who don't respond to treatment, high-dose chemotherapy (and possibly radiation) followed by a stem cell transplant may be recommended.

In children and adolescents, treatment is likely to consist of chemotherapy combined with radiation therapy, although the dose and field of radiation would be kept as small as possible.

Stage IB or IIB (Non-bulky), or Stage III or IV (Bulky or Non-bulky)

Doctors generally treat these stages with chemotherapy at full doses. Although ABVD (for at least 6 cycles) can be used, some doctors favor more intense treatment with the Stanford V or BEACOPP regimen. As long as the cancer is still shrinking, chemotherapy will be continued.

Any remaining areas of enlarged lymph nodes are then treated with radiation, if needed. Once again, PET scans might be used during treatment to assess how much treatment you need. For those who don't respond to treatment, high-dose chemotherapy (and possibly radiation) followed by a stem cell transplant may be recommended.

In children, treatment includes chemotherapy, either alone or in combination with low-dose radiation therapy to areas with bulky disease (areas that contain a lot of Hodgkin disease). Clinical trials are now under way to determine which option is better.

Resistant Hodgkin Disease

Treatment for Hodgkin disease should remove all traces of the cancer. Once initial treatment is complete, the doctor will likely do further tests to look for any signs of Hodgkin disease, such as CT and/or PET scans. If the Hodgkin disease is still there, most experts think that more of the same treatment will not cure the patient.

Sometimes, radiation therapy to a single area of disease that remains after chemotherapy might be curative. If radiation alone was the initial treatment, using chemotherapy (with or without more radiation) might also be curative. But if your cancer has not completely responded to the combination of these treatments, most doctors would recommend high-dose chemotherapy and an autologous stem cell transplant, if possible.

Recurrent or Relapsed Hodgkin Disease

Treatment in this situation depends both on where the disease comes back and on the treatment that you received before the relapse. If initial treatment was radiation therapy without chemotherapy, chemotherapy is usually given for recurrent disease.

If chemotherapy without radiation therapy was used first, and the cancer comes back only in the lymph nodes, you could receive radiation therapy to the lymph nodes with or without more chemotherapy.

Although chemotherapy with different drugs can be used for people with recurrent Hodgkin disease, radiation usually can not be repeated in the same area. If, for example, Hodgkin disease in the chest was treated with radiation and it came back in the chest, this patient could not be treated with more radiation to the chest. This holds true no matter how long ago the Hodgkin disease was first treated.

If the Hodgkin disease has returned within a few months of the original treatment, high-dose chemotherapy with an autologous stem cell transplant may be recommended. On the other hand, if the disease has returned after a long period, then repeating different chemotherapy drugs might also be curative. These are decisions that need to be made by you and your cancer care team.

Treating Nodular Lymphocyte Predominant Hodgkin Disease (NLPHD)

Because of the way it grows and responds to treatment, this rare type of Hodgkin disease (HD) is sometimes treated slightly differently than classic HD.

As with classic HD, chemotherapy plus radiation therapy is an appropriate option for most stages. But in people with early stage NLPHD and without any "B" symptoms, radiation therapy alone is often appropriate. Another option for people who can't tolerate radiation therapy is to observe the disease closely without any active treatment.

If the disease is more advanced or if B symptoms are present, chemotherapy plus radiation is more likely to be recommended. Another option in some cases may be the monoclonal antibody drug rituximab (Rituxan), although this is still under study.

Hodgkin Disease in Pregnancy

If a woman is pregnant and diagnosed with Hodgkin disease, there are several approaches that can be successful. In about half of cases, a woman can wait until the baby is born and then begin treatment. This is the approach that is safest for the baby.

If the Hodgkin disease requires treatment, single agent chemotherapy or full multi-agent chemotherapy may be given, based upon the circumstances. Radiation is not often given because of concerns about the long-term effects to the unborn baby. However, a few studies suggest that as long as very careful precautions are taken to aim the radiation precisely and limit the doses, pregnant women with Hodgkin disease in lymph nodes in the neck, underarm area, or inside the chest ("mediastinum") may be able to receive this treatment with little or no apparent risk of birth defects or childhood cancer.

More Treatment Information

For more details on treatment options -- including some that may not be addressed in this document -- the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. Those are available on the NCCN Web site (www.nccn.org).

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

What Should You Ask Your Doctor About Hodgkin Disease?

As you deal with your cancer or your child's cancer and the process of treatment, you need to have honest, open discussions with the cancer care team. You should feel free to ask any question that's on your mind, no matter how minor it might seem. Among the questions you might want to ask are:

- What type of Hodgkin disease is it?
- What is the stage? What does the staging mean?
- What are the treatment choices? Which do you recommend? Why?
- Does one type of treatment reduce the risk of recurrence more than another?
- What short-term side effects can be expected from treatment? What can be done about these side effects?
- What are the possible long-term side effects?
- Will the treatment affect my (my child's) ability to have children? Can we do anything about this?
- What are the other risks of treatment?
- How long will it take to recover from treatment?
- When will it be okay to go back to work or school?
- What are the chances that the cancer will recur? How will I know if the cancer has recurred? What should I look out for?
- What should I do to be ready or get my child ready for treatment?
- How will this cancer affect other illnesses or medical problems and their treatment?
- Should I get a second opinion?

You will no doubt have other questions. Be sure to write your questions down so that you remember to ask them during visits with your cancer care team. Also keep in mind that doctors are not the only ones who can provide you with information. Other health care professionals, such as nurses and social workers, may have the answers you seek.

What Happens After Treatment for Hodgkin Disease?

Completing treatment can be both stressful and exciting. You will be relieved to finish treatment, yet it is hard not to worry about cancer coming back. (When cancer returns, it is called recurrence.) This is a very common concern among those who have had cancer.

It may take a while before your confidence in your own recovery begins to feel real and your fears are somewhat relieved. You can learn more about what to look for and how to learn to live with the possibility of cancer coming back in the American Cancer Society document, *Living with Uncertainty: The Fear of Cancer Recurrence*, available at 1-800-ACS-2345.

Follow-up Care

After treatment is over, it is very important to keep all follow-up appointments. You or your child will need follow-up care for many years after treatment for Hodgkin disease.

Make a special effort to keep all appointments with your cancer care team and follow their instructions carefully. During these visits, the doctor will ask about symptoms, do physical exams, and may order blood tests or imaging studies such as CT scans or x-rays. Doctor visits are usually recommended every few months for the first several years after treatment. Gradually, the length of time between visits can be increased, but even after 5 years they should be done at least yearly. Follow-up is needed to check for cancer recurrence or spread, as well as possible side effects of certain treatments. This is the time for you to ask your health care team any questions you need answered and to discuss any concerns you might have.

Watching for Long-term Side Effects

Each type of treatment for Hodgkin disease has side effects that may last for a few months. Some, like loss of fertility, may be permanent. Because so many people are living for a long time after their treatment, we are now learning about serious side effects that happen years after treatment is over.

Second cancers: One of the most serious side effects of Hodgkin disease treatment is developing a second cancer. Acute myelogenous leukemia (AML), also called acute non-lymphocytic leukemia (ANLL), is a serious type of cancer that can develop in about 5% of patients receiving certain types of treatment for Hodgkin disease. This usually occurs in the first few years after treatment and is seen more often in older people.

Many doctors think that using the ABVD combination instead of the older MOPP combination (particularly when extensive radiation treatment is also used) lowers this risk. This is why there is a trend toward using ABVD instead of MOPP and, if radiation is needed, using as little as possible.

While radiation alone does not increase the risk for leukemia much, it can have other long-term side effects. The most serious of these is the development of other forms of cancer in the part of the body that received the radiation.

Women who receive chest radiation before they are 30 years old have a much higher risk of breast cancer. They should be especially careful about following American Cancer Society recommendations for early detection of breast cancer and should talk to their doctor about starting mammogram screening at an early age.

Both men and women receiving chest radiation have a higher chance of developing lung cancer, mesothelioma (a cancer of the lining of the lungs), and thyroid cancer. It should be no surprise that the chance of getting lung cancer is much higher in smokers, so not smoking is especially important among survivors of Hodgkin disease. Although there are no accepted screening tests for these cancers, follow-up physical exams, blood tests for thyroid problems, and chest x-rays as suggested by your doctor may be helpful.

Cancer of muscle or bone, called sarcomas, can also develop in the radiated area. Likewise, digestive tract cancers such as colon cancer are also more likely.

Another type of cancer, non-Hodgkin lymphoma, develops in about 2% of patients with Hodgkin disease. It is thought that this risk is due mostly to the disease itself and not the treatment.

Fertility issues: A less serious but still important long-term effect of chemotherapy and radiation therapy is a loss of fertility. Men lose their ability to produce sperm if they are treated with nitrogen mustard (the "M" in the MOPP chemotherapy regimen). Sperm production may return but usually does not.

Likewise, women may stop ovulating and menstruating with chemotherapy. This may or may not return to normal. Radiation given to the ovaries will permanently sterilize a woman unless the ovaries are surgically placed outside the radiation field. Moving the ovaries does not affect cure rates because Hodgkin disease almost never spreads to the ovaries.

Infections: For unknown reasons, the immune system of people with Hodgkin disease does not work properly. Treatments such as radiation, chemotherapy, and surgical removal of the spleen (splenectomy) can add to this problem. Splenectomy was once done commonly but now is a rare procedure for people with Hodgkin disease. Before they have their spleen removed, all patients should be immunized against the pneumonia bacteria, pneumococcus. *Haemophilus influenzae* and meningococcus immunizations are also important in children. All adults should keep up with their influenza vaccinations (flu shots). Keeping up with vaccinations and careful, prompt treatment of infections are very important.

Thyroid problems: The thyroid gland may also be affected by treatment. Many people who have had radiation of their thyroid, which happens with mantle field radiation, will become hypothyroid (their thyroid gland does not make enough thyroid hormone) and may need thyroid medication. Thyroid function should be tested at least yearly.

Heart disease and strokes: Another complication of radiation can occur because of damage done to blood vessels. In particular, patients who have had radiation to the chest have a

higher than normal risk of developing coronary artery disease and heart attacks. This has become less of a problem with more modern techniques of radiation treatment. It is important to avoid smoking and maintain a healthy diet to help avoid this problem. The chemotherapy drug doxorubicin (Adriamycin) can also cause heart damage and increase radiation therapy damage.

Radiation to the neck increases the chance of stroke because of damage done to the blood vessels in the neck that supply the brain. Smoking and high blood pressure increase the risk of stroke. Once again it is important to avoid smoking. It is also important to have regular check-ups with your doctor and have any high blood pressure treated.

Seeing a New Doctor

At some point after your cancer diagnosis and treatment, you may find yourself in the office of a new doctor. Your original doctor may have moved or retired, or you may have moved or changed doctors for some reason. It is important that you be able to give your new doctor the exact details of your diagnosis and treatment. Make sure you have the following information handy:

- a copy of your pathology report from any biopsy or surgery
- if you had surgery, a copy of your operative report
- if you were hospitalized, a copy of the discharge summary that every doctor must prepare when patients are sent home from the hospital
- if there was radiation, a final summary of the dose and field
- finally, since some drugs can have long-term side effects, a list of your drugs, drug doses, and when you took them

It is also important to keep medical insurance. Even though no one wants to think of their cancer coming back, it is always a possibility. If it happens, the last thing you want is to have to worry about paying for treatment. Should your cancer come back the American Cancer Society document, *When Your Cancer Comes Back: Cancer Recurrence* gives you information on how to manage and cope with this phase of your treatment. You can get this document by calling 1-800-ACS-2345.

Lifestyle Changes to Consider During and After Treatment

Having cancer and dealing with treatment can be time-consuming and emotionally draining, but it can also be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even begin this process during cancer treatment.

Make Healthier Choices

Think about your life before you learned you had cancer. Were there things you did that might have made you less healthy? Maybe you drank too much alcohol, or ate more than you needed, or smoked, or didn't exercise very often. Emotionally, maybe you kept your feelings bottled up, or maybe you let stressful situations go on too long.

Now is not the time to feel guilty or to blame yourself. However, you can start making changes today that can have positive effects for the rest of your life. Not only will you feel better but you will also be healthier. What better time than now to take advantage of the motivation you have as a result of going through a life-changing experience like having cancer?

You can start by working on those things that you feel most concerned about. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society's Quitline™ tobacco cessation program at 1-800-ACS-2345.

Diet and Nutrition

Eating right can be a challenge for anyone, but it can get even tougher during and after cancer treatment. For instance, treatment often may change your sense of taste. Nausea can be a problem. You may lose your appetite for a while and lose weight when you don't want to. On the other hand, some people gain weight even without eating more. This can be frustrating, too.

If you are losing weight or have taste problems during treatment, do the best you can with eating and remember that these problems usually improve over time. You may want to ask your cancer team for a referral to a dietitian, an expert in nutrition who can give you ideas on how to fight some of the side effects of your treatment. You may also find it helps to eat small portions every 2 to 3 hours until you feel better and can go back to a more normal schedule.

One of the best things you can do after treatment is to put healthy eating habits into place. You will be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Try to eat 5 or more servings of vegetables and fruits each day. Choose whole grain foods instead of white flour and sugars. Try to limit meats that are high in fat. Cut back on processed meats like hot dogs, bologna, and bacon. Get rid of them altogether if you can. If you drink alcohol, limit yourself to 1 or 2 drinks a day at the most. And don't forget to get some type of regular exercise. The combination of a good diet and regular exercise will help you maintain a healthy weight and keep you feeling more energetic.

Rest, Fatigue, Work, and Exercise

Fatigue is a very common symptom in people being treated for cancer. This is often not an ordinary type of tiredness but a "bone-weary" exhaustion that doesn't get better with rest. For some, this fatigue lasts a long time after treatment, and can discourage them from physical activity.

However, exercise can actually help you reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel physically and emotionally improved and can cope better.

If you are ill and need to be on bed rest during treatment, it is normal to expect your fitness, endurance, and muscle strength to decline some. Physical therapy can help you maintain strength and range of motion in your muscles, which can help fight fatigue and the sense of depression that sometimes comes with feeling so tired.

Any program of physical activity should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis 3 times a week. If you haven't exercised in a few years but can still get around, you may want to think about taking short walks.

Talk with your health care team before starting, and get their opinion about your exercise plans. Then, try to get an exercise buddy so that you're not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, though, you will need to balance activity with rest. It is okay to rest when you need to. It is really hard for some people to allow themselves to do that when they are used to working all day or taking care of a household. (For more information about fatigue, please see the American Cancer Society publication, *Cancer-Related Fatigue and Anemia Treatment Guidelines for Patients*.)

Exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- It strengthens your muscles.
- It reduces fatigue.
- It lowers anxiety and depression.
- It makes you feel generally happier.
- It helps you feel better about yourself.

And long term, we know that exercise plays a role in preventing some cancers. The American Cancer Society, in its guidelines on physical activity for cancer prevention, recommends that adults take part in at least 1 physical activity for 30 minutes or more on 5

days or more of the week. Children and teens are encouraged to try for at least 60 minutes a day of energetic physical activity on at least 5 days a week.

How About Your Emotional Health?

Once your treatment ends, you may find yourself overwhelmed by emotions. This happens to a lot of people. You may have been going through so much during treatment that you could only focus on getting through your treatment.

Now you may find that you think about the potential of your own death, or the effect of your cancer on your family, friends, and career. You may also begin to re-evaluate your relationship with your spouse or partner. Unexpected issues may also cause concern -- for instance, as you become healthier and have fewer doctor visits, you will see your health care team less often. That can be a source of anxiety for some.

This is an ideal time to seek out emotional and social support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or individual counselors.

Almost everyone who has been through cancer can benefit from getting some type of support. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or realistic to go it all by yourself. And your friends and family may feel shut out if you decide not to include them. Let them in -- and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-ACS-2345 and we can put you in touch with an appropriate group or resource.

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life -- making healthy choices and feeling as well as possible, physically and emotionally.

What Happens if Treatment Is No Longer Working?

If cancer continues to grow after one kind of treatment, or if it returns, it is often possible to try another treatment plan that might still cure the cancer, or at least shrink the tumors enough to help you live longer and feel better. On the other hand, when a person has received several different medical treatments and the cancer has not been cured, over time the cancer tends to become resistant to all treatment. At this time it's important to weigh the possible

limited benefit of a new treatment against the possible downsides, including continued doctor visits and treatment side effects.

Everyone has his or her own way of looking at this. Some people may want to focus on remaining comfortable during their limited time left.

This is likely to be the most difficult time in your battle with cancer -- when you have tried everything medically within reason and it's just not working anymore. Although your doctor may offer you new treatment, you need to consider that at some point, continuing treatment is not likely to improve your health or change your prognosis or survival.

If you want to continue treatment to fight your cancer as long as you can, you still need to consider the odds of more treatment having any benefit. In many cases, your doctor can estimate the response rate for the treatment you are considering. Some people are tempted to try more chemotherapy or radiation, for example, even when their doctors say that the odds of benefit are less than 1%. In this situation, you need to think about and understand your reasons for choosing this plan.

No matter what you decide to do, it is important that you be as comfortable as possible. Make sure you are asking for and getting treatment for any symptoms you might have, such as pain. This type of treatment is called "palliative" treatment.

Palliative treatment helps relieve these symptoms, but is not expected to cure the disease; its main purpose is to improve your quality of life. Sometimes, the treatments you get to control your symptoms are similar to the treatments used to treat cancer. For example, radiation therapy might be given to help relieve bone pain from bone metastasis. Or chemotherapy might be given to help shrink a tumor and keep it from causing a bowel obstruction. But this is not the same as receiving treatment to try to cure the cancer.

At some point, you may benefit from hospice care. Most of the time, this can be given at home. Your cancer may be causing symptoms or problems that need attention, and hospice focuses on your comfort. You should know that receiving hospice care doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. It just means that the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult stage of your cancer.

Remember also that maintaining hope is important. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that are filled with happiness and meaning. In a way, pausing at this time in your cancer treatment is an opportunity to refocus on the most important things in your life. This is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do.

What's New in Hodgkin Disease Research and Treatment?

Important research into Hodgkin disease is under way right now in many university hospitals, medical centers, and other institutions around the country.

Each year, scientists get closer to finding out what causes the disease and how to improve treatment. In the past few years, for example, scientists have made advances in sub-typing and classifying the various types of Hodgkin disease.

Tailoring Treatment

In general, cure rates for Hodgkin disease are high, but long-term side effects of treatment are an important issue. A very active area of research is directed at learning which patients can be treated with gentler therapy and which patients need stronger treatment. A related area of research is developing less toxic and easier therapies that do not have serious long-term side effects, yet still cure as many patients as possible. New drug combinations containing as many as 8 different drugs are being developed. The reasoning behind this approach is that even though more drugs are needed, by using less of each drug, fewer side effects may occur.

Chemotherapy

New chemotherapy drugs and drug combinations are being studied in patients with Hodgkin disease. Some drugs, such as vinorelbine, idarubicin, and gemcitabine, are already used to treat other cancers, and are now showing promise against Hodgkin disease. They have helped patients who have relapsed after other chemotherapy treatments. Studies are in progress to see if these drugs could be more effective than the ones we use now.

Newer drugs that work differently than typical chemotherapy drugs are now being studied as well. For example, a class of drugs known as histone deacetylase (HDAC) inhibitors has shown promise in early clinical studies against relapsed Hodgkin disease.

Stem Cell Transplants

Evidence is growing that autologous stem cell transplants can benefit certain patients with recurrent or advanced-stage Hodgkin disease.

A newer approach is the non-myeloablative allogeneic (from a donor) stem cell transplant, or "mini-transplant." In this procedure, the patient is given a stem cell transplant from a compatible donor, such as a sibling, but does not receive the high doses of chemotherapy and radiation therapy usually given in transplantation. Instead, the patient receives just enough chemotherapy to allow the transplant to "take." Once the transplant takes, it begins developing immunity to the cancer and may actually cause the cancer to shrink or go away.

This procedure is still being developed, but it has already helped some patients with Hodgkin disease.

Monoclonal Antibodies

Antibodies are proteins normally made by the immune system to help fight infections. Each antibody is designed to attack only a specific target (usually a protein on the surface of an unwanted cell). Monoclonal antibodies are manmade versions of these immune system proteins. Some can kill cancer cells by themselves. Others have radioactive molecules or cell poisons attached to them, which help kill the cancer cells. An advantage of these drugs is that in general they seem to have few side effects. This makes the idea of combining them with chemotherapy very attractive because they do not add much to the toxicity of the chemotherapy.

At this time, there are no monoclonal antibodies specifically licensed for use in patients with Hodgkin disease, although several are being studied. One such monoclonal antibody, which attaches to a molecule called CD30 in Hodgkin cells, contains radioactive iodine. In early tests, it has had some success in treating relapsed Hodgkin disease.

Rituximab (Rituxan) is a monoclonal antibody against the CD20 molecule that is mainly used to treat non-Hodgkin lymphoma. It seems to be helpful in treating some cases of relapsed Hodgkin disease, particularly the nodular lymphocyte predominant type, since this most closely resembles non-Hodgkin lymphoma. Studies are under way to better clarify its role in treating Hodgkin disease.

Additional Resources

More Information From Your American Cancer Society

The following related information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-ACS-2345.

After Diagnosis: A Guide for Patients and Families (also available in Spanish)

Caring for the Patient With Cancer at Home (also available in Spanish)

Understanding Chemotherapy: A Guide for Patients and Families (also available in Spanish)

Understanding Radiation Therapy: A Guide for Patients and Families (also available in Spanish)

The following book is available from the American Cancer Society. Call us at 1-800-ACS-2345 to ask about cost or to place your order.

Caregiving: A Step-By-Step Resource for Caring for the Person With Cancer at Home

National Organizations and Web Sites*

In addition to the American Cancer Society, other sources of patient information and support include:

Lymphoma Research Foundation
Telephone: 1-800-500-9976
Internet Address: www.lymphoma.org

National Cancer Institute
Telephone: 1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615
Internet Addresses: www.cancer.gov

The Leukemia & Lymphoma Society
Telephone: 1-800-955-4572 or 1-914-949-5213
Internet Address: www.lls.org

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

The American Cancer Society is happy to address almost any cancer-related topic. If you have any more questions, please call us at 1-800-ACS-2345 at any time, 24 hours a day.

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