Non-Hodgkin Lymphoma Overview

This overview is based on the more detailed information in our document *Non-Hodgkin Lymphoma*.

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide to make new cells, and die in an orderly way. During the early years of a person's life when they are growing, normal cells divide faster. Once the person becomes an adult, most cells divide only to replace worn-out, damaged, or dying cells.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of this out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells keep on growing and form new cancer cells. In most types of cancer, the cancer cells form a tumor (this does not always happen with lymphoma). Cancer cells can also grow into (invade) other tissues, something that normal cells can’t do. Being able to grow out of control and invade other tissues is what makes a cell a cancer cell.

Sometimes cancer cells spread to other parts of the body. There they begin to grow and form new tumors. This process is called *metastasis*.

No matter where a cancer may spread, it is always named (and treated) based on the place where it started. For instance, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is still prostate cancer, not bone cancer.

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. This is why people with cancer need treatment that is aimed at their own kind of cancer.

Not all tumors are cancer. Tumors that aren't cancer are called *benign*. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into other tissues. Because of this, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

What is non-Hodgkin lymphoma?

Non-Hodgkin lymphoma (also called non-Hodgkin's lymphoma, NHL, or just lymphoma) is cancer that starts in cells called *lymphocytes*, which are part of the body's immune system. Lymphocytes are in the lymph nodes and other lymphoid tissues (such as the spleen and bone marrow). Other types of cancer (lung or colon cancers, for example), can start in other organs and then spread to lymph nodes or other lymphoid tissue. But these cancers are **not** lymphomas. Lymphomas start in the lymphoid tissue and can then spread to other organs.

The main types of lymphomas are:

- Hodgkin lymphoma (also known as Hodgkin's lymphoma, Hodgkin disease, or Hodgkin's disease) is named after Dr. Thomas Hodgkin, who first described it.
- Non-Hodgkin lymphoma (NHL)

Different types of lymphomas behave, spread, and respond to treatment differently.

The information here is about NHL in adults. Our other documents focus on *Non-Hodgkin Lymphoma in Children*, *Lymphoma of the Skin*, and *Hodgkin Disease*.

The rest of this document is only about non-Hodgkin lymphoma in adults.

The lymph system and lymphoid tissue

To better understand what lymphoma is, it helps to know something about the body's lymph system. The lymph system is made up of lymphoid tissue (found in many places in the body), lymph vessels, and a clear fluid called *lymph*.

Lymphoid tissue includes the lymph nodes and collections of lymphocytes in other organs (like the intestines), the spleen, and bone marrow.

Lymphocytes

The main kind of cell found in lymphoid tissue is a type of white blood cell called the *lymphocyte*. The main types of lymphocytes are: *B cells* and *T cells*. Normal B cells and T cells do different jobs within the immune system.

B lymphocytes: B cells help protect the body against germs by making proteins called *antibodies*. The antibodies attach to the germs and attract other immune system cells that

surround and digest the germs. Antibodies also attract certain blood proteins that can kill bacteria. Most lymphomas start in the B cells.

T lymphocytes: There are several types of T cells and each has a special job. Some T cells help destroy cells infected with germs. Other types of T cells help boost or slow the work of other immune system cells.

Different types of lymphoma can develop from these different types of lymphocytes. The different types of lymphoma are treated differently, so finding out the exact type of lymphoma is important.

Start and spread of NHL

Because lymphoid tissue is found in many parts of the body, lymphomas can start almost anywhere.

Types of NHL

About half of all cases of NHL are one of the 2 types listed below, but there are also many other types. Ask your doctor for information about your type of NHL and what that means for your treatment choices and chances for survival. You can also find more detailed information about many of the other types in our separate detailed guide, *Non-Hodgkin Lymphoma*.

Diffuse large B-cell lymphoma: This kind makes up about 1 of every 3 cases of lymphoma. It can affect any age group but is mostly found in older people. This kind of lymphoma grows quickly, but often responds well to treatment.

Follicular lymphoma: About 1 out of 5 cases of lymphoma in the United States are of this type. The cells tend to grow in a circular pattern in the lymph nodes. Follicular lymphoma is found most often in older people and is rare in very young people. It tends to grow slowly. These lymphomas often don’t need treatment when they are first found. Instead, treatment might be delayed until the lymphoma is causing problems. Although standard treatment will not often cure this cancer, people may live many years with it. Over time, some follicular lymphomas change into a fast-growing diffuse B-cell type.

How many people get non-Hodgkin lymphoma?

The American Cancer Society’s estimates for non-Hodgkin lymphoma (NHL) for 2015 are:

- About 71,850 new cases of NHL

- About 19,790 deaths from NHL

These numbers include both adults and children. This cancer is slightly more common in men than in women. A person's risk of getting NHL during his or her lifetime is about 1 in 50.

Although some types of NHL are among the most common childhood cancers, more than 9 out of 10 cases occur in adults. The types of NHL found in children are often very different from those seen in adults. For more information, see our document *Non-Hodgkin Lymphoma in Children*.

What are the risk factors for non-Hodgkin lymphoma?

A risk factor is something that affects a person's chance of getting a disease like cancer. Some risk factors, such as smoking, can be controlled. Others, like a person's age or race can't be changed. But risk factors don't tell us everything. Having a risk factor, or even several risk factors, does not mean that you will get the disease. And many people who get the disease may have had few or no known risk factors. Even if a person with non-Hodgkin lymphoma (NHL) has a risk factor, it is often very hard to know what part that risk factor may have played in the lymphoma.

Scientists have found a few risk factors that could make a person more likely to get lymphoma. There are many types of lymphoma, and some of these factors have been linked only to certain types.

- Age – the risk of NHL goes up with age
- Gender – overall, NHL is more common inmen than in women
- Race – in the United States, whites are more likely than African Americans or Asian Americans to get NHL.
- Exposure to certain chemicals or chemotherapy drugs
- Radiation exposure – such as from the atomic bomb, nuclear reactor accidents, or treatment for another cancer
- Having a weakened immune system – like from HIV infection or having had an organ transplant
- Autoimmune diseases ─ such as rheumatoid arthritis, systemic lupus erythematosus (SLE, or lupus), celiac sprue
- Certain infections

- Being very overweight (obese) may also increase risk
- Eating a diet high in fat and meats may also increase your risk, but this needs to be studied more
- Breast implants are linked to NHL in the breast

Can non-Hodgkin lymphoma be prevented?

Most people who have non-Hodgkin Lymphoma (NHL) do not have any known risk factors that can be changed, and the cause of their cancer is unknown. For now, the best way to prevent some cases of this cancer is to prevent known risk factors, such as a weak immune system.

HIV infection is mostly spread among adults through sex or sharing dirty needles by IV drug users. Stopping the spread of HIV would prevent many deaths from NHL. For people who have HIV, treatment with anti-HIV drugs can lower the risk of NHL.

Infection with the bacterium *H. pylori* has been linked to lymphoma in the stomach, so treating *H. pylori* infections might lower this risk, but this has not been proven yet.

Doctors are trying to find ways to treat cancer and do organ transplants without increasing the risk of lymphoma. But for now, the benefits of these treatments still usually outweigh the small risk of developing lymphoma many years later.

Being very overweight or eating a diet high in fat and meats may increase your risk of non-Hodgkin lymphoma, so staying at a healthy weight and eating a healthy diet might help lower your risk of getting lymphoma. More research is needed to confirm this.

Can non-Hodgkin lymphoma be found early?

At this time, no special tests can find non-Hodgkin lymphoma (NHL) early.

The best course of action is to pay attention to any possible symptoms of this disease. People with medical problems that increase the risk of NHL, such as a weakened immune system, HIV infection, autoimmune disease, or earlier treatment for cancer, should see their doctors regularly and let them know if any new problems occur.

Signs and symptoms of non-Hodgkin lymphoma

NHL may cause many different signs and symptoms, depending on where it is in the body. Sometimes it doesn't cause any symptoms until it has grown quite large. Common signs and symptoms include:

- Enlarged lymph nodes (sometimes felt as lumps under the skin)
- Swollen abdomen (belly)
- Feeling full after only a small amount of food
- Chest pain or pressure
- Shortness of breath or cough
- Fever
- Weight loss
- Night sweats
- Fatigue (extreme tiredness)
- Low red blood cell counts (anemia)

How is non-Hodgkin lymphoma diagnosed?

If there is a reason to think that you may have non-Hodgkin lymphoma, your doctor will want to get a complete medical history, with information about your symptoms, risk factors, family history, and other medical conditions. Next, the doctor will do an exam, paying special attention to the lymph nodes and other places of the body that might be involved, including the spleen and liver. If you have swollen lymph nodes, the doctor will look for an infection in that area. Enlarged lymph nodes are more likely to be caused by an infection than by lymphoma.

If the doctor suspects that NHL might be causing the symptoms, he or she will recommend you have some other tests.

Imaging tests to find and stage NHL

Imaging tests are ways to take pictures of the inside of the body. These tests are used to help find a place that might be cancer, to learn how far a cancer may have spread, and to find out whether treatment is working.

Chest x-ray

An x-ray of the chest may be done to look for swollen lymph nodes in this area.

CT scan (computed tomography)

The CT scan is a special type of x-ray test that takes many pictures as it moves around the body. A computer then combines these to make a detailed picture. A CT scan is useful in looking for lymphoma in the belly (abdomen), pelvis, chest, head, and neck. CT scans can also be used to help guide a biopsy needle into a swollen lymph node.

CT scans take longer than regular x-rays. You need to lie still on a table while they are being done. Before any pictures are taken, you may be asked to drink a liquid that helps outline the intestine for the scan. After the first set of pictures is taken, you may also get an intravenous (IV) injection of a "dye" to help outline the structures in your body. A second set of CT scan pictures is then taken. Sometimes the dye causes flushing (a feeling of warmth, especially in the face), hives, or, rarely, a serious allergic reaction like trouble breathing or low blood pressure. Be sure to tell the doctor if you have any allergies or have ever had a reaction to any contrast material used for x-rays.

MRI scan (magnetic resonance imaging)

MRI scans use radio waves and strong magnets instead of x-rays to take pictures. This test is not used as often as CT scans for lymphoma, but if your doctor is concerned about spread to the spinal cord or brain, MRI is very useful for looking at these areas. A contrast substance (called *gadolinium*) may be put into a vein before the scan to better show details. It is different from the dye used for CT scans, so being allergic to one doesn’t mean you are allergic to the other. Still, be sure to let the doctor know if you have had a problem with it in the past.

MRIs take longer than CT scans and you may have to lie in a narrow tube, which upsets some people. Special, open MRI machines may sometimes be an option. The drawback of the more open machines is that the pictures aren’t as clear.

The machine makes loud buzzing and clicking noises, but some places will give you earplugs or headphones to help block this out.

Ultrasound

This test uses sound waves to make a picture of the inside of the body. It is a very easy test to have. For most scans, a kind of wand is moved along your skin over the part of your body being looked at. No radiation is used. An ultrasound can find tumors under the skin or in the belly and can show if the kidneys have become swollen because the flow of urine has been blocked by swollen lymph nodes.

PET scan (positron emission tomography)

PET scans use a form of sugar that has a radioactive atom attached to it. The sugar mixture is put into a vein and travels throughout the body. Cancer cells take up the

radioactive sugar more than other cells, and then a special camera is used spot the areas of radioactivity.

PET is useful when looking for lymphoma all over the body. It can help tell whether a swollen lymph node has cancer in it. It is also used during and after treatment to find out whether an enlarged lymph node still contains cancer or just has scar tissue. For patients with lymphoma, a machine that combines the PET scan with a CT scan (PET/CT scan) is often used.

Gallium scan

In this test a radioactive substance is put into a vein. It goes to lymph tissues in the body. A special camera is used to show these areas. This test can find tumors that might be NHL in bones and other organs. This test is not used as much now as in the past because most doctors do a PET scan instead. But it can still sometimes be useful in finding areas of lymphoma that the PET scan may miss.

Bone scan

For bone scans, a different radioactive substance is used. After it is put into the blood, it travels to areas of the bone that are damaged. This test is not usually done unless a person is having bone pain or has lab test results that suggest the lymphoma may have reached the bones. The scan will show bone damage caused by lymphoma, but will also pick up other problems, such as arthritis and fractures. Lymphoma in the bone can also be seen on a PET scan, so this test isn’t used if a PETscan has been done.

Tests to diagnose NHL

Lymph node biopsy

Because swollen lymph nodes are more often caused by infection, not cancer, doctors often give antibiotics and wait a few weeks to see if the nodes stay large. If the nodes stay the same or keep on getting bigger, either a small piece of the node or the whole node is often removed for testing. This is called a *biopsy*.

A doctor with special training (a pathologist) looks at the biopsy samples with a microscope to look for lymphoma and see what type it is. Sometimes the first biopsy does not give a final answer and another biopsy or other tests are needed.

The doctor might use other lab tests to diagnose and classify NHL such as immunohistochemistry, cytogenetics, flow cytometry, FISH, and PCR. These tests are explained in our detailed guide, *Non-Hodgkin Lymphoma*.

There are a few kinds of biopsies:.

- Excisional biopsy: a surgeon cuts through the skin to remove an entire lymph node (or tumor)
- Incisional biopsy: a surgeon cuts through the skin to remove only a small part of a lymph node (or tumor) (.
- Needle biopsy: a needle is used to remove part of the lymph node or tumor

Bone marrow aspiration and biopsy

NHL sometimes involves the bone marrow – the soft inner part of some bones where blood cells are made. A bone marrow aspiration and biopsy are done to check the bone marrow, often at the same time. A sample of bone marrow and a sliver of bone are removed with a large needle, usually from the back of the hip bone.

Other tests done for NHL

Lumbar puncture (spinal tap)

This test looks to see if lymphoma has spread to the tissue around the brain and spinal cord. It is not needed for most patients with lymphoma. In this test, the doctor removes a sample of the fluid around the brain and spinal cord (called cerebrospinal fluid or CSF). This is done with a needle placed between the bones of the spine into the area around the spinal cord.

Blood tests

Blood tests may be used to measure the amounts of certain types of cells and chemicals in the blood. They are not used to find out if a person has lymphoma, but they can be helpful in deciding how advanced the lymphoma is and how fast it is growing. Blood tests can also help find liver or kidney problems caused by either the spread of lymphoma side effects of certain chemotherapy drugs. Tests may also be done to make sure blood is clotting like it should.

Depending on what treatment you will get, your doctor may also order other blood tests to check for viral infections that may affect your treatment.

Tests of heart and lung function

These tests are not used to help find non-Hodgkin lymphoma, but they might be done if you are going to get certain chemotherapy drugs that could affect the heart or the lungs.

- Your heart function may be checked with an echocardiogram (an ultrasound of the heart) or a MUGA scan.

- Your lung function may be checked with pulmonary function tests, in which you breathe into a tube hooked up to a machine.

Staging of non-Hodgkin lymphoma

Staging is the process of finding out how far the cancer has spread. This is very important because the treatment and the patient's outlook for survival depend on the exact type, location, and stage of the cancer.

Tests used to gather information for staging

- Physical exam
- Biopsies
- Blood tests
- Imaging tests such as CT scans
- Bone marrow aspiration and biopsy (often, but not always done)
- Lumbar puncture (spinal tap – this may not need to be done)

Ann Arbor staging system

A staging system is a way for members of the cancer care team to sum up the extent of a cancer's spread. The Ann Arbor staging system is the one most often used for non-Hodgkin lymphoma (NHL). The stages are described by Roman numerals I through IV (1 through 4). As a rule, the higher the number, the more advanced the cancer. Letters can be added after the number based on certain factors:

- If the lymphoma affects a single organ or tissue outside of the lymph system (for example, a bone) the letter E is added (for example, stage IIE)
- The letter S is added if the lymphoma affects the spleen
- The letter B is added if a person has any B symptoms (fever, night, sweats, or weight loss). If no B symptoms are present, the letter A is added instead.

The letter X is added if there is "bulky disease" meaning either the lymphoma in the chest is at least one-third as wide as the chest, or tumors in other places that are at least 4 inches across. For more details about this staging system, see "How is non-Hodgkin lymphoma staged" in our document *Non-Hodgkin Lymphoma*.

The type and stage of the lymphoma give useful information about a person's outlook. But for some types of lymphomas (such as fast-growing ones) knowing the stage is not too helpful on its own. In these patients, other factors can give doctors a better idea about their outlook (prognosis).

Other factors that affect prognosis (outlook) for non-Hodgkin lymphoma

The prognosis (outlook) for people with lymphoma can vary widely, depending on both the type and stage of the lymphoma. For some types of lymphomas, knowing the stage is not very helpful on its own. In these cases, other factors can give doctors a better idea about a person's outlook. Some of these other factors include:

- The person's age
- Whether or not the lymphoma is in organs outside the lymph system
- How well a person can complete normal daily activities
- The results of certain lab tests

For some types of lymphoma, these factors are combined into a *prognostic index*, which gives the doctor an overall idea of a person's likely prognosis and whether more intense treatment might be needed. To learn more about survival rates for different types of NHL, please see our document *Non-Hodgkin Lymphoma*.

Keep in mind that every person's situation is unique and these factors can't predict exactly what will happen in your case. Talk with your cancer care team if you have questions about your own chances of a cure, or how long you might survive your cancer. They know your situation best.

How is non-Hodgkin lymphoma 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.

About treatment

In recent years, much progress has been made in treating non-Hodgkin lymphoma (NHL). The treatment options depend on the kind of lymphoma, its stage, and the prognostic factors mentioned in the section "Staging of non-Hodgkin lymphoma." Of course, no 2 people are exactly alike, and treatments are often tailored to each person. It

is often a good idea to get a second opinion. This can give you more information and help you feel more confident about the treatment plan you choose.

The main types of treatment for non-Hodgkin lymphoma are:

- Chemotherapy
- Radiation
- Immunotherapy
- Targeted therapy
- Stem cell transplant

In rare cases, surgery is also used.

Based on your treatment options, you may have different types of doctors on your treatment team, such as:

- A hematologist: a doctor who treats disorders of the blood, including lymphomas.
- A medical oncologist: a doctor who treats cancer with medicines.
- A radiation oncologist: a doctor who treats cancer with radiation therapy.

It is important to discuss all of your treatment options as well as their possible side effects with your doctors to help make the decision that best fits your needs. (See the section "What are some questions I can ask my doctor about non-Hodgkin lymphoma?") If time permits, it is often a good idea to seek a second opinion. Your doctor should be willing to help you find another cancer doctor who can give you a second opinion.

Chemotherapy for non-Hodgkin lymphoma

Chemotherapy (often called *chemo*) is the use of drugs to kill cancer cells. Usually the drugs are given into a vein (IV) or by mouth (as pills). Once the drugs enter the bloodstream, they spread through the body, making this treatment very useful for lymphoma. Chemo drugs are also sometimes put right into the spinal fluid to treat lymphoma cells in the brain or spinal cord.

Doctors give chemo in cycles, in which a round of treatment is followed by a rest period to allow the body time to recover. Each chemo cycle usually lasts for a few weeks. Most treatments are given in the doctor's office (or clinic) on an outpatient basis, but some must be given in the hospital.

A patient might start on one combination of drugs and later be switched to a different combination if the first one doesn't seem to be working.

For NHL, the antibody drug rituximab (Rituxan®) is often given along with chemo.

Possible side effects

Chemo drugs kill cancer cells, but they also damage normal cells, causing side effects. The exact side effects depend on the type and dose of drugs used and the length of time they are taken. Side effects can include the following:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea
- Greater chance of infection (from low white blood cell counts)
- Easy bruising or bleeding (from low platelet counts)
- Fatigue (from low red blood cell counts)

Most of these side effects are short term and go away after treatment ends. There are often ways to lessen these side effects. For example, there are drugs to help prevent or reduce nausea and vomiting.

Certain chemo drugs have specific possible side effects. For instance, some drugs can damage the heart, lungs, kidneys, liver, testicles, ovaries or brain. If serious side effects occur, chemo may have to be reduced or stopped, at least for a short time.

Chemotherapy can also cause side effects that might not occur until years after treatment. For example, in rare cases, people may develop leukemia several years later.

Tumor lysis syndrome can be a side effect of chemo. It occurs when many cancer cells die in a short period, often during treatment with chemo. When the cells die, they break open and release their contents into the bloodstream. This "cell waste" can affect the kidneys, heart, and nervous system. Because this only happens if many cells die at once, it is most common in the first cycle of chemo. To prevent this problem, the patient may be given extra fluids and certain drugs.

For more information about chemotherapy, see our document *A Guide to Chemotherapy*. If you want to know more about the chemo drugs used to treat NHL, see our document *Non-Hodgkin Lymphoma*.

Radiation therapy for non-Hodgkin lymphoma

Radiation therapy is treatment with high energy rays (such as x-rays) or particles to kill cancer cells or shrink tumors. Radiation given from a source outside the body (external beam radiation) is the kind most often used to treat non-Hodgkin lymphoma (NHL). The treatment is much like getting an x-ray, but the radiation is more intense. Getting radiation treatment is painless and each treatment only takes a few minutes, although

getting you ready takes longer. Most often, radiation treatments are given 5 days a week for several weeks.

Radiation might be used as the main treatment for lymphomas that are found early (stage I or II), because these tumors respond very well to radiation. For more advanced lymphomas and for some lymphomas that spread quickly, radiation is sometimes given after chemotherapy. Radiation can also be used to ease symptoms in organs such as the brain and spinal cord or to decrease pain when tumors are pressing on nerves.

People who are getting a stem cell transplant may get radiation to the whole body along with high-dose chemotherapy to try to kill lymphoma cells throughout the body. Radiation can also be given in the form of a drug in some cases (see the section about immunotherapy for more details).

Possible side effects

Radiation can cause side effects, which can vary based on the area being treated. Common side effects include:

- Skin changes ranging from mild redness to blistering and peeling
- Extreme tiredness (fatigue)
- Low blood counts
- Upset stomach (more common if the radiation is to the belly)
- Vomiting (more common if the radiation is to the belly)
- Diarrhea (more common if the radiation is to the belly)

Often these problems go away after radiation is stopped.

If radiation is given with chemotherapy, the side effects tend to be worse.

Radiation can also cause long-term side effects. Ask your doctor what you can expect.

For more information about radiation therapy, see our document *Understanding Radiation Therapy: A Guide for Patients and Families*.

Immunotherapy for non-Hodgkin lymphoma

Immunotherapy is treatment that uses the patient’s immune system to fight cancer. There are 2 main ways this is done. The patient's own immune system may be made to work better, or the patient can be given man-made versions of the normal parts of the immune system to fight the cancer.

Monoclonal antibodies

These are man-made versions of the antibodies made by the immune system to help fight infections. Instead of attacking germs, they can be designed to attack lymphoma cells. Many monoclonal antibodies are now approved as treatments for lymphoma. Most of them, like rituximab (Rituxan), ofatumumab (Arzerra®), obinutuzumab (Gazyva™), and alemtuzumab (Campath®) are plain antibodies. Others are antibodies along with something else attached to them to attack the cancer cells. Ibritumomab (Zevalin®) for example, has a radioactive molecule attached to it. Brentuximab vedotin (Adcetris®) is a monoclonal antibody with a chemotherapy drug attached.

Rituximab is the most commonly used immunotherapy drug in treating non-Hodgkin lymphoma. It is often used along with chemotherapy, but can also be used by itself.

Patients get these treatments as IV infusions in the doctor's office or clinic.

Common side effects are usually mild and might include chills, fever, nausea, rashes, tiredness, and headaches. The antibodies that have radioactive substances attached also tend to lower blood counts. Another important concern is that some of these can cause dormant hepatitis infections to become active again.

More information about how these antibodies are used to treat NHL can be found in our document *Non-Hodgkin Lymphoma*.

Interferon

Interferon is a protein made by white blood cells to help fight infections. Some studies suggest that giving man-made interferon can make some types of lymphoma shrink or stop growing. Side effects from this treatment can include tiredness, fever, chills, headaches, muscle and joint aches, and mood changes. Because of these side effects, interferon is not used very often.

Immunomodulating agents

These drugs are thought to work against certain cancers by affecting parts of the immune system, but exactly how they work isn’t clear. They are sometimes used to help treat certain types of lymphoma, often after other treatments have been tried. Both of the immunomodulating agents used for lymphoma, thalidomide (Thalomid®) and lenalidomide (Revlimid®), are more often used to treat a cancer called multiple myeloma.

Common side effects include low blood counts, painful nerve damage, and serious blood clots. Thalidomide can also cause drowsiness, fatigue, and severe constipation.

Because thalidomide causes severe birth defects if taken during pregnancy, it should not be used by women who are or may become pregnant. Access to thalidomide and

lenalidomide is tightly controlled to prevent women from taking it when they are pregnant.

Targeted therapy to treat non-Hodgkin lymphoma

As doctors have learned more about the changes in cells that cause cancer, they have been able to create newer drugs that are aimed right at these changes. These drugs are often referred to as *targeted therapy*. They work differently from standard chemo drugs and often have different side effects. These drugs include bortezomib (Velcade®), ibrutinib (Imbruvica®), and idelalisib (Zydelig®).

More information about the use of these drugs for NHL can be found in our document *Non-Hodgkin Lymphoma*.

Bone marrow or peripheral blood stem cell transplant for non-Hodgkin lymphoma

Stem cell transplants are sometimes used to treat lymphoma patients who are in remission (that is, they seem to be disease-free after treatment) or who have had the cancer come back (relapse) during or after treatment.

In a stem cell transplant, patients are given higher doses of chemotherapy (chemo) than would normally be safe. Sometimes radiation is given, too. This treatment destroys the bone marrow, which keeps new blood cells from being made. Normally, this could lead to life-threatening infections, bleeding, and other problems due to low blood cell counts. To get around this problem, after chemo (and sometimes radiation treatment) is finished, the patient gets an infusion of blood-forming stem cells to restore the bone marrow. Blood-forming stem cells are very early cells that can make new blood cells. They are different from embryonic stem cells.

Here are the main types of stem cell transplants.

Autologous stem cell transplant: For this type of transplant, blood-forming stem cells come from the patient's own blood or, less often, from the bone marrow (before the transplant). This is the most common type of transplant used to treat lymphoma, but it generally isn't an option if the lymphoma has spread to the bone marrow or blood. If that happens, it may be hard to get a stem cell sample with no lymphoma cells in it.

Donor (allogeneic) stem cell transplant: In this approach, the stem cells come from someone else. The best results occur when the donor has a tissue type that is very close to the patient’s. Often this means a close relative like a brother or sister.

Some things to keep in mind

Stem cell transplant is a complex treatment that can have severe and even deadly side effects, so it is important to have it done at a hospital where the staff has experience with the procedure.

To learn more about stem cell transplants, see our document *Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants).*

Surgery for non-Hodgkin lymphoma

Surgery may be done to get a tissue sample (biopsy) to figure out the type of lymphoma, but it is not often used to treat non-Hodgkin lymphoma (NHL). In rare cases, surgery may be used to treat lymphomas that start in organs such as the spleen, the stomach, or the thyroid and that have not spread beyond these organs. For lymphoma that is only in one place, radiation treatment is more common than surgery.

Palliative and supportive care in the treatment of non-Hodgkin lymphoma

Palliative (or supportive) care is treatment aimed at symptoms to improve your quality of life. It is often given when cancer treatment is no longer working, but it can also be given along with standard cancer treatment. Sometimes, the treatments you get to control your symptoms are the same as treatments used to treat cancer, like chemotherapy or radiation. The difference is the goal of treatment – to help symptoms, not to make the cancer go away. For instance, when lymph nodes become enlarged, they may press on nerves and cause pain. Radiation therapy to these areas may help relieve the pain. Pain medicines can also be given.

Symptoms such as fatigue can be caused by low red blood blood counts. Sometimes, a patient will need blood transfusions or treatment with drugs that help make new blood cells.

Some patients with non-Hodgkin lymphoma are more prone to infection because they have low levels of antibodies to fight germs. They may be helped by giving them infusions of antibodies.

Nausea and loss of appetite can be treated with drugs and high-calorie food supplements. If the lymphoma has spread to the lungs, patients may get short of breath. Oxygen may be used to help treat this symptom.

Be sure to tell your health care team about any symptoms you are having, including any side effects from treatment. There are often ways to help control or lessen these symptoms. This is an important part of your overall treatment plan.

For more information on palliative care and getting help with side effects, see the Palliative or Supportive Care section of our website.

Clinical trials for non-Hodgkin lymphoma

You may 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 carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our website at www.cancer.org/clinicaltrials. 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 website at www.cancer.gov/clinicaltrials.

You must meet requirements to take part in any clinical trial. But if you do qualify for a clinical trial, you still get to decide whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the art cancer treatment. Sometimes they may be the only way to get access to some newer treatments. They are also the only way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

You can get a lot more information on clinical trials, in our document called *Clinical Trials: What You Need to Know*. You can read it on our website or call our toll-free number and have it sent to you.

Complementary and alternative therapies for non-Hodgkin lymphoma

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to social media groups and websites may offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What are complementary and alternative therapies?

It can be confusing because not everyone uses these terms the same way, and they are used to refer to many different methods. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help you feel better. Some examples of methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not to be helpful, and a few are even harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may be harmful, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with few or no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

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

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking of using.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at. You can also check them out in the Complementary and Alternative Medicine section of our website.

The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your

doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

What are some questions I can ask my doctor about non-Hodgkin lymphoma?

It’s important to have frank, open discussions with your cancer care team. They want to answer all of your questions, no matter how minor they might seem. For instance, consider asking these questions:

- What kind of NHL do I have?
- Has my biopsy been reviewed at by a pathologist who is an expert on lymphoma?
- Are there other tests that need to be done before we can decide on treatment?
- Will I need to see other doctors?
- What is the extent (stage) of my disease and what does that mean for me?
- What are my prognostic factors and do they affect my options?
- How much experience do you have treating this type of lymphoma?
- Should I get a second opinion before starting treatment? Can you suggest someone?
- What are my treatment options? Do we need to start treatment right away?
- What treatment do you recommend, and why?
- What risks or side effects might there be from this treatment?
- What should I do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?
- How will treatment affect my daily activities?
- What is my outlook for survival?
- What are the chances that the cancer will come back with this treatment plan? What would we do if the treatment doesn't work or if the lymphoma comes back?
- What type of follow-up will I need after treatment?

Along with these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so that you can plan

your work or activity schedule. Or you might want to ask about clinical trials. You can find more information about communicating with your health care team in our document *Talking With Your Doctor*.

Moving on after treatment for non-Hodgkin lymphoma

For many people with non-Hodgkin lymphoma, treatment may remove or destroy the cancer. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about the lymphoma growing or coming back. (When cancer comes back after treatment, it is called *recurrence*.) This is a very common concern in people who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to live with this uncertainty and are leading full lives. Our document *Living With Uncertainty: The Fear of Cancer Recurrence* can give you more information on this.

For some, the lymphoma may never go away completely. These people still might get treatments to help keep the lymphoma in check for as long as possible. Learning to live with lymphoma as more of a chronic disease can be hard and very stressful. It has its own type of uncertainty. Our document *When Cancer Doesn't Go Away* has more on this

Follow-up care

Lymphomas are a varied group of diseases that call for different treatments and can have very different outlooks. Your care after treatment will depend to a large extent on what type of lymphoma you have, what type of treatment you received, and how well it worked.

If you have finished treatment, your doctors will still want to watch you closely. It is very important to go to all of your follow-up appointments. During these visits, your doctors will ask about any problems you may have, examine you, and might order lab tests or imaging tests to look for signs of recurrence or treatment side effects.

Almost any cancer treatment can have side effects. Some may last for a few weeks or months, but others can last the rest of your life. This is the time for you to talk to your cancer care team about any changes or problems you notice, and any questions or concerns you have.

You might need to have frequent blood tests to check that you have recovered from treatment and to look for signs of problems such as the return of the cancer. Blood counts can also sometimes become abnormal because of a disease called *myelodysplasia*, which is a defect of the bone marrow that can lead to leukemia. Some chemotherapy drugs can

cause this disease. For more on this, see our document *Myelodysplastic Syndromes*. A person can also develop leukemia a few years after being treated for lymphoma.

If the lymphoma does recur at some point, further treatment will depend on what treatments you've had before, how long it's been since treatment, and your health.

It is important to keep health insurance. While you hope your cancer won't come back, it could happen. If it does, you don't want to have to worry about paying for treatment. Should your cancer come back, our document *When Your Cancer Comes Back: Cancer Recurrence* can help you manage and cope with this phase of your treatment.

Seeing a new doctor

At some point after your cancer is found and treated, you may find yourself seeing a new doctor who doesn’t know anything about your medical history. It is important to give your new doctor the exact details of your diagnosis and treatment. Make sure you have this information handy and always keep copies for yourself:

- A copy of your pathology report from any biopsy or surgery
- Copies of imaging tests (CT or MRI scans, etc.), which can usually be stored on a CD, DVD, etc.
- If you had surgery, a copy of your operative report
- If you were in the hospital, a copy of the discharge summary that the doctor wrote when you were sent home
- If you had radiation treatment, a copy of the treatment summary (you need to get this from the doctor)
- If you had drug treatment (such as chemotherapy, immunotherapy, or targeted therapy), a list of your drugs, drug doses, and when you took them

Lifestyle changes after non-Hodgkin lymphoma

Having cancer and dealing with treatment can take a lot of time and energy, but it can also be a time to look at your life in new ways.

Make healthier choices

For many people, finding out they have cancer helps them focus on their health in ways they may not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on alcohol, or give up tobacco. Even things like keeping your stress level under control may help. Now is a good time to think about making changes that can

have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. 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 at 1-800-227-2345 for information and support.

Eating better

Eating right is hard for many people, but it can be even harder during and after cancer treatment. If treatment caused weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do after treatment is to start healthy eating habits. You may be surprised at the long-term benefits of some simple changes. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of cancer, as well as having many other health benefits.

Get more information in our document *Nutrition and Physical Activity During and After Cancer Treatment: Answers to Common Questions*.

Rest, fatigue, and exercise

Feeling tired (fatigue) is very common during and after cancer treatment. This is not a normal type of tiredness but a "bone-weary" exhaustion that doesn't get better with rest. For some people, fatigue lasts a long time after treatment and can keep them from staying active. But exercise can actually help reduce fatigue and the sense of depression that sometimes comes with feeling so tired.

If you are very tired, though, you will need to balance activity with rest. It is OK to rest when you need to. To learn more about fatigue and other side effects, please see the Physical Side Effects section of our website or “More information about non-Hodgkin lymphoma” to get a list of available information.

If you were very ill or weren't able to do much during treatment, it is normal that your fitness, staying power, and muscle strength declined. You need to find a physical activity plan that fits your own needs. Talk with your health care team before starting. Get their input on your activity plans. Then try to get a buddy so that you're not doing it alone.

Physical activity can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.

- It makes your muscles stronger.
- It reduces fatigue.
- It lowers anxiety and depression.
- It can make you feel generally happier.
- It helps you feel better about yourself.

Long term, we know that getting regular physical activity plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

Can I lower my risk of the lymphoma growing or coming back?

Most people want to know if there are certain lifestyle changes they can make to reduce their risk of cancer progressing or coming back. Unfortunately, for most cancers there is little solid evidence to guide people. This doesn't mean that nothing will help – it's just that for the most part this is an area that hasn't been well studied. Most studies have looked at lifestyle changes as ways of preventing cancer in the first place, not slowing it down or keeping it from coming back.

At this time, not enough is known about non-Hodgkin lymphoma to say for sure if there are things you can do that will be helpful. Healthy behaviors such as not smoking, eating well, and keeping a healthy weight may help, but no one knows for sure. But we do know that these types of changes can have positive effects on your health that can extend beyond your risk of lymphoma or other cancers.

How about your emotional health after non-Hodgkin lymphoma?

During and after treatment, you may be surprised by the flood of emotions you go through. This happens to a lot of people.

You may find yourself thinking about death and dying. You may find that you think about the effect of your cancer on things like your family, friends, and career. Money may be a concern as the medical bills pile up. Unexpected issues may also cause concern – for instance, as you get better and need fewer doctor visits, you will see your health care team less often. This can be hard for some people.

This is a good time to look for emotional and social support. You need people you can turn to. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or private counselors.

The cancer journey can feel very lonely. You don't need to go it alone. Your friends and family may feel shut out if you decide not 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 1-800-227-2345 and we can put you in touch with a group or resource that may work for you. You can also read our document *Distress in People with Cancer* or see the Emotional Side Effects section of our website for more information.

If treatment for non-Hodgkin lymphoma stops working

Because lymphoma is a group of diseases, the chance of it growing or coming back after treatment varies among types. When lymphomas come back, they tend to do so in the same part of the body they started in. For instance, if the lymphoma began in lymph nodes in the belly, this is the most likely place it will recur. If the bone marrow was affected, it will most likely return there. In many cases, the lymphoma will respond to new kinds of chemotherapy (chemo) or other drugs.

For general information on dealing with a recurrence, see our document *When Your Cancer Comes Back: Cancer Recurrence*.

But when a person has had many different treatments and the cancer has not been cured, over time the cancer tends to resist all treatment. At this time you may have to weigh the possible benefits of a new treatment against the downsides, like treatment side effects and clinic visits. Everyone has their own way of looking at this.

This is likely to be the hardest time in your battle with cancer – when you have tried everything within reason and it's just not working anymore. Your doctor may offer you new treatment, but you will need to talk about how likely the treatment is to improve your health or change your outlook for survival.

No matter what you decide to do, it is important for you to feel as good as possible. Make sure you are asking for and getting treatment for pain, nausea, or any other problems you may have. This type of treatment is called *palliative care*. Palliative care helps relieve symptoms, but it is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose. The main purpose of palliative care is to improve the quality of your life, or to help you feel as good as you can for as long as you can. Sometimes this means using drugs to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat cancer. For instance, radiation might be used to help relieve bone pain caused by cancer that has spread to the bones. Or chemo might be used to help shrink a tumor and keep it from blocking the bowels. But this is not the same as treatment to try to cure the cancer. You can learn more about physical and emotional changes, as well as plans and preparations for yourself and your family, in our document *Nearing the End of Life*.

At some point you may want to think about hospice care. Most of the time it is given at home. Your cancer may be causing symptoms or problems that need to be treated. Hospice focuses on your comfort. You should know that having hospice care doesn't mean you can't have treatment for the problems caused by your cancer or other health issues. It just means that the purpose of your care is to help you live life as fully as possible and to feel as well as you can. You can learn more about this in our document, *Hospice Care*.

What's new in non-Hodgkin lymphoma research?

Research into the causes, prevention, and treatment of non-Hodgkin lymphoma (NHL) is being done in many medical centers throughout the world.

Genetics

Scientists are making great progress in learning about the genetics of lymphoma. They are learning more about how genes change to make cells grow too fast, live too long, and not grow into mature cells. This research may help them to find drugs to block the process.

New tests to find and classify lymphoma are also being studied. Some of these tests might be able to predict how the cancer will respond to chemo, to show how completely the cancer has been destroyed by treatment, or to find out whether the cancer is likely to come back (relapse).

Treatment

Much of the research being done on NHL is focused on looking at new and better ways to treat this disease.

Chemotherapy

New chemotherapy (chemo) drugs are being studied in clinical trials. In recent years, these studies have led to the approval of newer drugs for use against certain types of lymphoma. Others studies are looking at new ways to combine drugs using different doses or drugs in a different order.

Targeted therapies

As researchers have learned more about cancer cells, they have developed newer drugs that target certain parts of these cells. These are different from standard chemo drugs,

which work by attacking all cells that are growing quickly. The newer drugs focus on the cancer cells. They often have different side effects, and they work in some cases where chemo doesn't. These drugs are now being studied in clinical trials.

Lymphoma vaccines

Scientists are also looking at whether it's possible to use a vaccine to help a person's immune system reject the lymphoma. Doctors have known for some time that people's immune systems may help fight their cancer. In rare cases, these people's immune systems have killed the cancers, and they have been cured. Scientists are now searching for ways to boost this immune reaction by the use of vaccines.

Unlike vaccines in children, the goal of these vaccines is to create an immune reaction in people who already have an early cancer or to keep the cancer from coming back after treatment. So far, there have been a few successes with this approach. It is a major area of research in lymphoma treatment. At this time lymphoma vaccines are only available in clinical trials.

More information about non-Hodgkin lymphoma

From the American Cancer Society

The following information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

More details about lymphoma

Lymphoma of the Skin

Non-Hodgkin Lymphoma Detailed Guide (also in Spanish)

Living with cancer

Health Professionals Associated With Cancer Care

Talking With Your Doctor (also in Spanish)

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

Nutrition for the Person With Cancer During Treatment: A Guide for Patients and Families (also in Spanish)

Coping With Cancer in Everyday Life (also in Spanish)

Cancer treatments

A Guide to Cancer Surgery (also in Spanish)

A Guide to Chemotherapy (also in Spanish)

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

Targeted Therapy

Immunotherapy

Clinical Trials: What You Need to Know

Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants)

Cancer treatment side effects

Caring for the Patient With Cancer at Home: A Guide for Patients and Families (also in Spanish)

Distress in People With Cancer

Anxiety, Fear, and Depression

Nausea and Vomiting

Guide to Controlling Cancer Pain (also in Spanish)

Get Relief From Cancer Pain

Pain Diary

Anemia in People With Cancer

Fatigue in People With Cancer

Family and caregiver concerns

Talking With Friends and Relatives About Your Cancer (also in Spanish)

Helping Children When A Family Member Has Cancer: Dealing With Diagnosis (also in Spanish)

What It Takes to Be a Caregiver

Insurance and financial issues

In Treatment: Financial Guidance for Cancer Survivors and Their Families (also in Spanish)

Health Insurance and Financial Assistance for the Cancer Patient (also in Spanish)

Your American Cancer Society also has books that you might find helpful. Call us at 1-800-227-2345 or visit our bookstore online at cancer.org/bookstore to find out about costs or to place an order.

National organizations and websites*

Along with the American Cancer Society, other sources of information and support include:

Lymphoma

Leukemia & Lymphoma Society
Toll-free number: 1-800-955-4572
Website: www.lls.org

Lymphoma Research Foundation
Toll-free number: 1-800-500-9976
Website: www.lymphoma.org

National Cancer Institute
Toll-free number: 1-800-4-CANCER (1-800-422-6237)
Website: www.cancer.gov

National Coalition for Cancer Survivorship
Toll-free number: 1-888-650-9127
1-877-NCCS-YES (622-7937) for some publications and Cancer Survivor Toolbox® orders
Website: www.canceradvocacy.org

Bone marrow and peripheral blood stem cell transplants

National Bone Marrow Transplant Link (nbmtLINK)
Toll-free number: 1-800-LINK-BMT (1-800-546-5268)
Website: www.nbmtlink.org

Be the Match (formerly National Marrow Donor Program)
Toll-free number: 1-800-MARROW-2 (1-800-627-7692)
Website: www.bethematch.org

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

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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For additional assistance please contact your American Cancer Society
1-800-227-2345 or www.cancer.org