Non-Hodgkin Lymphoma in Children

What are the differences between cancers in adults and children?

The types of cancers that develop in children are often different from the types that develop in adults. Childhood cancers are often the result of DNA changes in cells that take place very early in life, sometimes even before birth. Unlike many cancers in adults, childhood cancers are not strongly linked to lifestyle or environmental risk factors.

There are exceptions, but childhood cancers tend to respond better to treatments such as chemotherapy. Children's bodies also tend to tolerate chemotherapy better than adults' bodies do. But cancer treatments such as chemotherapy and radiation therapy can have long-term side effects, so children who survive cancer need careful attention for the rest of their lives.

Since the 1960s, most children and teens with cancer have been treated at specialized centers designed for them. Being treated in these centers offers the advantage of a team of specialists who know the differences between adult and childhood cancers, as well as the unique needs of children with cancer and their families. This team usually includes pediatric oncologists, surgeons, radiation oncologists, pathologists, pediatric oncology nurses, and nurse practitioners.

These centers also have psychologists, social workers, child life specialists, nutritionists, rehabilitation and physical therapists, and educators who can support and educate the entire family.

Most children with cancer in the United States are treated at a center that is a member of the Children's Oncology Group (COG). All of these centers are associated with a university or children's hospital. As we have learned more about treating childhood cancer, it has become even more important that treatment be given by experts in this area.

Any time a child or teen is diagnosed with cancer, it affects every family member and nearly every aspect of the family's life. You can read more about coping with these changes in our documents on children with cancer.

What is non-Hodgkin lymphoma in children?

Cancer starts when cells in the body begin to grow out of control. Cells in nearly any part of the body can become cancer, and can spread to other areas of the body. To learn more about how cancers start and spread, see *What Is Cancer?*

Lymphoma is a type of cancer that starts in cells called *lymphocytes*, which are part of the body's immune system. There are 2 kinds of lymphomas:

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

These types of lymphomas behave, spread, and respond to treatment differently, so it is important to tell them apart.

Both types of lymphoma are more common in adults, but they can also occur in children and teens. Among this younger age group, NHL tends to occur in younger children, while Hodgkin disease is more likely to affect older children and teens.

Hodgkin disease is very similar in adults and children, and treatment is the same for both. For more information on this disease, see our document *Hodgkin Disease*.

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

The lymph system and lymphoid tissue

To understand NHL, it helps to know about the body's lymph system.

The lymph system (also known as the *lymphatic system*) is part of the body's immune system, which helps fight infections and some other diseases. It also helps fluids move around within the body. The lymph system is made up mainly of:

- **Lymphoid tissue:** includes the lymph nodes and related organs (see below) that are part of the body's immune and blood-forming systems
- **Lymph:** a clear fluid that travels through the lymph system, carrying waste products and excess fluid from tissues, as well as lymphocytes and other immune system cells
- **Lymphatic vessels:** small tubes, similar to blood vessels, through which lymph travels to different parts of the lymph system

Lymphocytes

Lymphoid tissue is made up mainly of cells called *lymphocytes*, a type of white blood cell. The 2 main types of lymphocytes are *B lymphocytes* (B cells) and *T lymphocytes* (T cells). Normal B cells and T cells do different jobs.

B lymphocytes: B cells normally help protect the body against germs (bacteria or viruses) by making proteins called antibodies. The antibodies attach to the germs, marking them for destruction by other parts of the immune system.

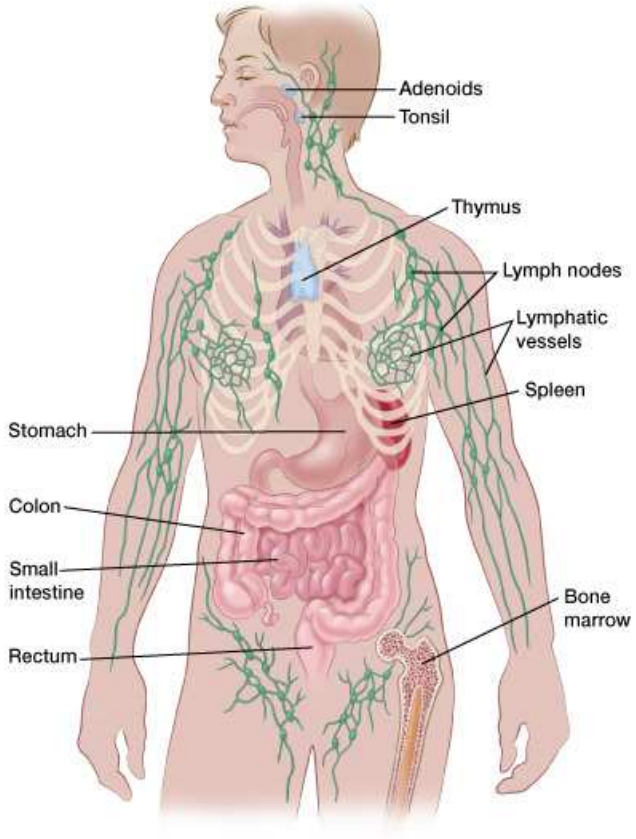
T lymphocytes: There are several types of T cells, each with a special job. Some T cells directly destroy cells infected with viruses, fungi, or certain kinds of bacteria. Other types of T cells play a role in either boosting or slowing the activity of other immune system cells.

Both types of lymphocytes can develop into lymphoma cells, but B-cell lymphomas are much more common in the United States than T-cell lymphomas. Different types of lymphoma can develop from both B and T lymphocytes, based on how mature the cells are when they become cancerous and other factors.

Treatment for lymphoma depends on which type it is, so determining the exact type of lymphoma is important.

Organs that have lymphoid tissue

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



The major sites of lymphoid tissue are:

Lymph nodes: Lymph nodes are bean-sized collections of lymphocytes and other immune cells throughout the body. They can sometimes be felt under the skin in the neck, under the arms, and in the groin. Lymph nodes are connected to each other by a system of lymphatic vessels.

Lymph nodes get bigger when they fight infection. Lymph nodes that grow because of infection are called *reactive nodes* or *hyperplastic nodes* and are often painful when they are touched. An enlarged lymph node in a child is not usually a sign of a serious problem. Lymph nodes in the neck are often enlarged in children with sore throats or colds. But a large lymph node is also the most common sign of lymphoma. Lymph node enlargement is discussed more in "Signs and symptoms of non-Hodgkin lymphoma in children."

Spleen: The spleen is an organ 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.

Thymus: The thymus is a small organ behind the upper part of the breast bone and in front of the heart. Before birth, the thymus plays a vital role in development of T lymphocytes. The thymus shrinks and becomes less important as people get older, but it continues to play a role in immune system function.

Adenoids and tonsils: These are collections of lymphoid tissue in the back of the throat. They help make antibodies against germs that are breathed in or swallowed. They are easy to see when they become enlarged during an infection, which occurs often in children, or if a lymphoma develops.

Digestive tract: Lymphoid tissue is also in the stomach and intestines, as well as many other organs.

Bone marrow: The bone marrow (the soft inner part of certain bones) makes red blood cells, blood platelets, and white blood cells. Red blood cells carry oxygen from the lungs to the rest of the body. Platelets help control bleeding by plugging up small holes in blood vessels. White blood cells fight infections. The main types of white blood cells are granulocytes and lymphocytes. Bone marrow lymphocytes are mainly B cells. Lymphomas sometimes start from bone marrow lymphocytes.

Types of non-Hodgkin lymphoma in children

Lymphomas are most often classified by how the cancer cells look under the microscope. Key features include the size and shape of the cells and how they are arranged (their pattern of growth).

- Size is described as large or small.
- Shape is described as cleaved (showing folds or indentations) or non-cleaved.
- The growth pattern may be either diffuse (cancer cells are scattered) or follicular (cells are arranged in clusters).

Not every lymphoma is described using all 3 features (size, shape, and growth pattern). Special lab tests are often needed to accurately classify lymphomas. These are discussed in the section, “How is non-Hodgkin lymphoma diagnosed in children?”

The most common types of non-Hodgkin lymphoma (NHL) in children are different from those in adults. Nearly all NHLs in children belong to 1 of 3 main types:

- Lymphoblastic lymphoma
- Burkitt lymphoma (small non-cleaved cell lymphoma)
- Large cell lymphoma

All 3 types are high grade (meaning they grow quickly) and diffuse, but it is important to distinguish among them because they are treated differently.

There are many other types of NHL. These are much more common in adults and are rare in children, so they are not discussed further in this document.

Lymphoblastic lymphoma

Lymphoblastic lymphoma accounts for about 25% to 30% of NHL in children. It is most common in teens, and boys are affected about twice as often as girls.

The cancer cells of this lymphoma are very young lymphocytes called *lymphoblasts*. They are the same cells as those seen in acute lymphoblastic leukemia (ALL) in children. In fact, if more than 25% of the bone marrow is made up of lymphoblasts, the disease is classified and treated as ALL instead of lymphoma.

Most cases of lymphoblastic lymphoma develop from T cells and are called *precursor T-lymphoblastic lymphomas*. These lymphomas often start in the thymus, forming a mass in the area behind the breast bone and in front of the trachea (windpipe). This can cause problems breathing, which may be the first symptom of lymphoblastic lymphoma.

Less often, this cancer develops in the tonsils, lymph nodes of the neck, or other lymph nodes. It can spread very quickly to the bone marrow, other lymph nodes, the surface of the brain, and/or the membranes that surround the lungs and heart.

A small fraction of lymphoblastic lymphomas develop from B cells (called *precursor B-lymphoblastic lymphomas*). These lymphomas more often begin in lymph nodes outside the chest, particularly in the neck. They can also involve the skin and bones.

Lymphoblastic lymphoma can grow very quickly and can often interfere with breathing, so it needs to be diagnosed and treated quickly.

Burkitt lymphoma

Burkitt lymphoma, also known as *small non-cleaved cell lymphoma*, accounts for about 40% of childhood NHL in the United States. It is most often seen in boys, usually when they are around 5 to 10 years old.

A subtype of Burkitt lymphoma, sometimes called *Burkitt-like lymphoma* or *non-Burkitt lymphoma*, shares some features with diffuse large B-cell lymphoma (described below) when seen under the microscope, but it is still treated like Burkitt lymphoma.

Burkitt lymphoma is named after the doctor who first described it in African children. In certain parts of Africa, Burkitt lymphoma accounts for nearly all childhood NHL and over half of all childhood cancers. In African children this lymphoma usually develops in the jaw or other facial bones.

Burkitt lymphomas in other parts of the world, including the United States, almost always start in the abdomen (belly). Typically, a child will develop a large tumor in his or her abdomen that can sometimes block the bowels (intestines). This can cause belly pain, nausea, and vomiting. Burkitt lymphoma can also sometimes start in the neck or tonsils, or rarely in other parts of the body.

This lymphoma develops from B lymphocytes, and it is one of the fastest growing cancers known. It can spread to other organs, including the surface of the brain or inside the brain. Because of this, it must be diagnosed and treated quickly.

Large cell lymphomas

These lymphomas start in more mature forms of T cells or B cells and can grow almost anywhere in the body. They are not as likely to spread to the bone marrow or brain, nor do they grow as quickly as other childhood lymphomas. These lymphomas tend to occur more often in older children and teens. There are 2 main subtypes of large cell lymphoma.

Anaplastic large cell lymphoma (ALCL): This lymphoma represents about 10% of all NHL in children. It usually develops from mature T cells. It may start in lymph nodes in the neck or other areas, and may be found in the skin, lungs, bone, digestive tract, or other organs.

Diffuse large B-cell lymphoma: This lymphoma accounts for about 15% of childhood lymphomas. It starts in B cells, as the name implies. These lymphomas often grow as large masses in the mediastinum (the space between the lungs), in which case they are referred to as *primary mediastinal B-cell lymphomas*. But they are also sometimes found in other areas such as lymphoid tissue in the neck or abdomen, or in the bones.

Treatment is basically the same for both types of large cell lymphoma, although the cure rate tends to be slightly higher for the diffuse large B-cell type.

What are the key statistics for non-Hodgkin lymphoma in children?

Non-Hodgkin lymphoma (NHL) accounts for about 5% of all childhood cancers. (Hodgkin disease accounts for about another 3%.)

In children up to age 14, most lymphomas are non-Hodgkin lymphomas, with about 500 of these cancers being diagnosed in the United States each year. If all children and teens up to age 19 are included, the numbers of Hodgkin and non-Hodgkin lymphomas are about equal, and there are about 900 cases of NHL diagnosed each year.

Non-Hodgkin lymphoma is about 2 to 3 times more common in boys than in girls, and it is more common in white children than black children.

About 2% of all non-Hodgkin lymphomas occur in children and teens. Overall, the risk of non-Hodgkin lymphoma in children increases with age. It can occur at any age but is uncommon in children younger than 3.

Visit the American Cancer Society's Cancer Statistics Center for more key statistics.Statistics on survival can be found in the section "Survival rates for childhood non-Hodgkin lymphoma."

What are the risk factors for non-Hodgkin lymphoma in children?

A risk factor is anything that might affect a person's chance of getting cancer. Different cancers have different risk factors.

Lifestyle-related risk factors such as body weight, physical activity, diet, and tobacco use play a major role in many adult cancers. But these factors usually take many years to influence cancer risk, and they are not thought to have much of an effect on the risk of childhood cancers, including non-Hodgkin lymphoma (NHL).

Researchers have found some factors that can increase children's risk of NHL. But most children with NHL do not have any known risk factors for this disease that can be changed.

Age, gender, and race

Non-Hodgkin lymphoma is rare in children in general, but it is more common in older children than in younger ones. It is also more common in boys than in girls and in white children than in black children. The reasons for these gender and racial differences are not known.

Having a weakened immune system

Some types of immune system problems have been linked with a higher risk of NHL in children.

Congenital (present at birth) immune deficiency syndromes

Some genetic (inherited) syndromes can cause children to be born with an abnormal immune system. Along with an increased risk of serious infections, these children also have a higher risk of developing NHL (and sometimes other cancers as well). These syndromes include:

- Wiskott-Aldrich syndrome
- Severe combined immunodeficiency syndrome (SCID)
- Ataxia-telangiectasia
- Common variable immunodeficiency
- Bloom syndrome
- X-linked lymphoproliferative syndrome

Organ transplants

Children who have received organ transplants are treated with drugs that weaken their immune system to prevent it from attacking the new organs. These children have an increased risk of developing NHL that is almost always caused by Epstein-Barr virus infection (see below). The risk depends on which drugs and what doses are used.

HIV/AIDS

Infection with human immunodeficiency virus (HIV), also known as the AIDS virus, can weaken the immune system in children and adults. Children with HIV generally get the infection from contact with their mother's blood, usually before or during birth.

HIV infection is a risk factor for developing NHL, so doctors may recommend that children with NHL be tested for HIV infection.

Radiation exposure

Radiation exposure may be a minor risk factor in childhood NHL.

Survivors of atomic bombs and nuclear reactor accidents have an increased risk of developing some types of cancer. Leukemia and thyroid cancers are the most common, but there is a slightly increased risk of NHL as well.

Patients treated with radiation therapy for other cancers have a slightly increased risk of developing NHL later in life. However, it usually takes many years for this to happen, so these secondary cases of NHL are more common in adults than children.

The possible risks from fetal or childhood exposure to lower levels of radiation, such as from x-ray tests or CT scans, are not known for sure. Any increase in risk for NHL or

other cancers is likely to be small, but to be safe, most doctors recommend that pregnant women and children not get these tests unless they are absolutely needed.

Epstein-Barr virus infection

In areas of Africa where Burkitt lymphoma is common, chronic infection with both malaria and the Epstein-Barr virus (EBV) is an important risk factor. EBV has been linked with as many as 90% of Burkitt lymphomas in Africa. In the United States, EBV has been linked with about 15% of Burkitt lymphomas.

EBV infection is life-long, although in most people it doesn't cause serious problems. In Americans who are first infected with EBV as teens or young adults, it can cause infectious mononucleosis, sometimes known simply as *mono*. Most Americans have been infected with EBV by the time they are adults, but the infection seems to occur later in life in the United States than in Africa, which may help explain why it is less likely to cause childhood lymphoma here. Another factor may be that in certain parts of Africa, children's immune systems also have to deal with other infections, such as malaria, which, together with EBV, may cause the body to make more lymphocytes.

Exactly how EBV is linked to Burkitt lymphoma is not completely understood, but it seems to have to do with the ability of the virus to infect and alter B lymphocytes. (For more information, see the section, "Do we know what causes non-Hodgkin lymphoma in children?")

Other possible risk factors

Some research has suggested that a family history of NHL (in a brother, sister, or parent) might raise the risk of lymphoma. Lymphoma risk may also be higher in children of older mothers. More research is needed to confirm these findings, but the increased risk, if any, is likely to be small overall.

Do we know what causes non-Hodgkin lymphoma in children?

The exact cause of most cases of childhood non-Hodgkin lymphoma (NHL) is not known. However, scientists have found that the risk of this cancer is higher if the child has any of the conditions described in the section, "What are the risk factors for non-Hodgkin lymphoma in children?" Many of these conditions are related to problems with the immune system.

Scientists have found that certain changes in the DNA inside normal lymphocytes can make them become lymphoma cells. Normal human cells grow and function based mainly on the information contained in each cell's chromosomes. Human DNA is packaged in 23 pairs of chromosomes, which are long molecules of DNA in each cell. DNA is the chemical that makes up our genes – the instructions for how our cells

function. We look like our parents because they are the source of our DNA. But our genes affect more than the way we look.

Some genes control when our cells grow, divide into new cells, and die. Certain genes that help cells grow and divide or help them live longer are called *oncogenes*. Others that slow down cell division or make cells die at the right time are called *tumor suppressor genes*.

Each time a cell prepares to divide into 2 new cells, it must make a new copy of the DNA in its chromosomes. This process is not perfect, and errors can occur in the DNA. Cancers can be caused by DNA mutations (changes) that turn on oncogenes or turn off tumor suppressor genes.

For example, *translocations* are a type of DNA change that can cause NHL to develop. A translocation means that DNA from one chromosome breaks off and attaches to a different chromosome. When this happens, oncogenes can be turned on or tumor suppressor genes can be turned off.

Some people inherit DNA changes from a parent that increase their risk for some types of cancer. But NHL is not one of the cancer types often caused by these inherited mutations.

Usually, DNA changes related to NHL occur during life rather than having been inherited before birth. In rare cases, these acquired changes result from exposure to radiation or other factors. But often they occur for no apparent reason.

The combination of immune deficiencies (from inherited conditions, drug treatment, or HIV infection) and Epstein-Barr virus (EBV) infection can cause some types of NHL. EBV infects B lymphocytes. It can make the cells grow, divide, and live longer than they should. In young adults infected with EBV, it often causes infectious mononucleosis, also known as *mono*. Mono is usually not a serious disease because the person's immune system destroys the B cells that are infected with EBV. But when children have an immune deficiency, EBV-infected B cells may grow and accumulate. These cells have an increased risk for DNA changes. If these changes affect certain oncogenes or tumor suppressor genes, lymphoma may develop.

Scientists have learned a lot about the gene changes commonly seen in lymphoma cells. This is being used to develop better tests to detect and classify certain types of NHL. Some of these discoveries are being used to create new treatments as well.

Most children who develop NHL in the United States do not have an immune deficiency or evidence of EBV infection. Even though researchers have found many of the key DNA changes in lymphoma cells, they still do not know what causes them in children without these risk factors.

Can non-Hodgkin lymphoma in children be prevented?

The risk of many adult cancers can be reduced by doing certain things such as staying at a healthy weight or quitting smoking, but there is no known way to prevent most childhood cancers.

Most children (and adults) with non-Hodgkin lymphoma (NHL) have no risk factors that can be changed, so at this time there is no way to prevent these lymphomas. For now, the best way to reduce the risk for NHL is to try to prevent known risk factors such as a weakened immune system.

The most common cause of acquired immune problems is HIV infection. HIV is spread among adults mostly through unprotected sex and sharing needles contaminated by injection drug users. Blood transfusions are now an extremely rare source of HIV infection.

Children generally get HIV infection from contact with their mother's blood, usually before or during birth. Treating the pregnant woman with anti-HIV drugs can greatly reduce the risk of infecting her infant. HIV can also be passed on in breast milk, so HIV-positive mothers are advised not to breastfeed.

Some cases of NHL are caused by the treatment of other cancers with radiation and chemotherapy or by the use of immune-suppressing drugs to avoid rejection of transplanted organs. Doctors are trying to find better ways to treat these conditions without raising the risk of lymphoma. But for now, the small risk of developing NHL several years later due to treatment must be balanced against the risks of these life-threatening diseases themselves.

Because most children with NHL do not have known risk factors that can be changed, it's important to note that there is nothing these children or their parents could have done to prevent this cancer.

Can non-Hodgkin lymphoma in children be found early?

Non-Hodgkin lymphoma (NHL) in children is uncommon, and there are no widely recommended screening tests for this cancer. (Screening is testing for cancer in people without any symptoms.) Still, in some cases NHL can be found early.

The best way to find this cancer early is to be aware of the possible signs and symptoms of this disease and to take your child to the doctor if something concerns you.

Careful, regular medical checkups are important for children, especially those with known risk factors for NHL, such as those who have certain inherited immune deficiencies, who have had cancer treatment or an organ transplant, or who have an HIV

infection. These children do not usually develop NHL, but it is important for parents and doctors to know the possible symptoms and signs of lymphoma.

Signs and symptoms of non-Hodgkin lymphoma in children

Childhood non-Hodgkin lymphoma (NHL) can cause many different signs and symptoms, depending on where it is in the body. In some cases it might not cause any symptoms until it grows quite large. Common symptoms include:

- Enlarged lymph nodes (seen or felt as lumps under the skin)
- Swollen abdomen (belly)
- Feeling full after only a small amount of food
- Shortness of breath or cough
- Fever
- Weight loss
- Night sweats
- Fatigue (extreme tiredness)

Enlarged lymph nodes

Non-Hodgkin lymphoma may grow in lymph nodes under the skin (on the sides of the neck, in the underarm area, above the collar bone, or in the groin area). The enlarged nodes are often seen or felt as lumps under the skin. They are often noticed by the child, parent, or a health care professional. Enlarged lymph nodes in children are more often caused by infections than by NHL.

Lymphoma in the abdomen (belly)

If the lymphoma grows inside the abdomen, it can make it swollen and painful. There may also be a buildup of fluid that causes even more swelling.

Lymphoma can sometimes enlarge the spleen and make it press on the stomach. This can make a child feel full after eating only a small amount of food.

When lymphoma causes swelling near the intestines, bowel movements may be blocked, which may lead to abdominal pain, nausea, or vomiting.

The lymphoma may also block urine from leaving the kidneys. This can lead to kidney problems, which can cause low urine output, tiredness, loss of appetite, nausea, or swelling in the hands or feet.

Lymphoma in the chest

When lymphoma starts in the thymus or lymph nodes in the chest, it can press on the nearby trachea (windpipe). This can lead to coughing, shortness of breath, and trouble breathing.

The superior vena cava (SVC) is a large vein that carries blood from the head and arms back to the heart. It passes next to the thymus and lymph nodes inside the chest. Lymphomas in this area may push on the SVC, which can make the blood back up in the veins. This is can lead to swelling in the face, neck, arms, and upper chest (sometimes with a bluish-red skin color). It can also cause trouble breathing, as well as headaches, dizziness, and a change in consciousness if it affects the brain. This condition, known as *SVC syndrome*, can be life-threatening, and needs to be treated right away.

Lymphoma in the brain and spinal cord

Some types of lymphoma can spread to the area around the brain and spinal cord. This can cause problems such as headache, vision changes, facial numbness, and trouble speaking.

Lymphoma in the skin

Some lymphomas can affect the skin itself. They can cause itchy, red or purple lumps or nodules under the skin.

General symptoms

Along with causing symptoms and signs in the part of the body where it starts, NHL can also cause general symptoms such as:

- Fever and chills
- Sweating (particularly at night)
- Unexplained weight loss

When talking about lymphoma, doctors sometimes call these *B symptoms*. B symptoms are often found in more rapidly growing lymphomas.

Other symptoms can be caused by low blood cell counts. Blood counts can become low if lymphoma spreads to the bone marrow and crowds out the normal, healthy cells that make new blood cells. This can lead to problems like:

- Severe or frequent infections (from low white blood cell counts)
- Easy bruising or bleeding (from low blood platelet counts)
- Fatigue and pale skin (from low red blood cell counts [anemia])

Many of the signs and symptoms above are more likely to be caused by something other than a lymphoma, such as an infection. Still, if your child has any of these symptoms, check with the doctor so that the cause can be found and treated, if needed.

How is non-Hodgkin lymphoma diagnosed in children?

Non-Hodgkin lymphoma (NHL) is usually found when a child is brought to a doctor because of signs or symptoms he or she is having. The doctor might suspect a child could have a lymphoma based on the signs and symptoms, but tests are needed to confirm the diagnosis. The exams and tests below are used to diagnose the disease, to find out what type of lymphoma it is, and to learn how advanced it is.

Medical history and physical exam

If any signs and symptoms suggest a child might have lymphoma, the doctor will want to get a thorough medical history to learn more about the symptoms and how long they have been present. The doctor might also ask if there is any history of possible risk factors, such as immune system problems.

During the physical exam, the doctor will probably focus on any enlarged lymph nodes or other areas of concern. For example, the abdomen may be felt for signs of an enlarged spleen or liver. Enlarged lymph nodes in children are usually caused by infections, so the doctor will look for an infection in the part of the body near any swollen lymph nodes.

Because infections are the most common cause of enlarged lymph nodes, this is often what doctors think of first, so the diagnosis of NHL in a child can sometimes be delayed. There is usually little cause for concern in children with swollen lymph nodes unless they are very large (more than 1 inch across). Even in these instances, the child is usually watched closely for a time or given a course of antibiotics first to see if the nodes will shrink. If not, more tests are done, usually a biopsy removing a swollen node (or a large portion of it) (see next section). But if the lymph nodes seem to be growing quickly or the child’s health seems to be getting worse, a biopsy may be needed right away.

Biopsy

A doctor can’t make a diagnosis of NHL in a child based only on symptoms or a physical exam. Most of the symptoms NHL can cause are more often caused by non-cancerous problems, like infections. They may also be caused by other kinds of cancers. If a child does have NHL, it’s important to tell which type it is, because each type is treated slightly differently.

For these reasons, an accurate diagnosis is needed, and the only way to do this is to remove some or all of an abnormal lymph node (or tumor) for viewing under a microscope and other lab tests. This is called a *biopsy*.

Types of biopsies used to diagnose non-Hodgkin lymphoma

There are several types of biopsies. Doctors choose which one to use based on the situation. The goal is to get a sample large enough to make an accurate diagnosis as quickly as possible, with as few side effects as possible.

Excisional or incisional biopsy: These are the most common types of biopsy done if lymphoma is suspected. An exception might be for large tumors in chest, for which a needle biopsy (described below) might be used instead.

In these procedures, a surgeon cuts through the skin to remove either an entire lymph node (excisional biopsy) or a small part of a large tumor (incisional biopsy).

If the node is near the skin surface, this is an operation that might be done with either local anesthesia (numbing medicine used only at the biopsy site) and sedation or with general anesthesia (where the child is in a deep sleep). If the node is inside the chest or abdomen, then general anesthesia is usually needed.

This method almost always provides enough of a sample to diagnose the exact type of NHL.

Fine needle aspiration (FNA) or core needle biopsy: In an FNA biopsy, the doctor uses a very thin, hollow needle attached to a syringe to withdraw (aspirate) a small amount of tissue from an enlarged lymph node or a tumor mass. For a core needle biopsy, the doctor uses a larger needle to remove a slightly larger piece of tissue.

If an enlarged lymph node is near the surface, the doctor can aim the needle while feeling the node. If the enlarged node or tumor is deep in the body (such as in the chest or abdomen), the doctor can guide the needle while watching it on a CT scan or ultrasound (see discussion of imaging tests later in this section).

The main advantage of a needle biopsy is that it does not require surgery. This can be especially important for tumors in the chest, because general anesthesia (where the child is in a deep sleep) can sometimes be dangerous for these children. It is also useful when the lymphoma is in other sites outside of the lymph nodes, such as the bones.

In children, needle biopsies can often be done using local anesthesia to numb the area, along with sedation to make the child sleepy. General anesthesia is needed less often.

The main drawback of needle biopsies (especially FNA) is that in some cases the needle might not remove enough of a sample to make a definite diagnosis. Most doctors don’t use needle biopsies if they strongly suspect lymphoma (unless other types of biopsies can’t be done for some reason). But if the doctor suspects that lymph node swelling is caused by an infection (even after antibiotics), a needle biopsy may be the first type of biopsy done. If a biopsy is needed, doctors typically prefer to do a core biopsy instead of FNA. An excisional biopsy might still be needed to diagnose and classify lymphoma, even after a needle biopsy has been done.

Once lymphoma has been diagnosed, needle biopsies are sometimes used to check areas in other parts of the body that might be lymphoma spreading or coming back after treatment.

Other types of biopsies

These other types of biopsies are not normally used to diagnose lymphoma, but they might be done to help determine the extent of spread if a lymphoma has already been diagnosed.

Bone marrow aspiration and biopsy: These tests help determine if a lymphoma has reached the bone marrow. The 2 tests are usually done at the same time. The biopsy samples are usually taken from the back of the pelvic (hip) bones, although in some cases they may be taken from the front of the hip bones or from other bones.

For a bone marrow *aspiration*, the skin over the hip and the surface of the bone is numbed with local anesthetic. In most cases, children will be given other medicines to make them drowsy or brief general anesthesia so they are asleep during the biopsy. 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.

A bone marrow *biopsy* is usually done just after the aspiration. A small piece of bone and marrow is removed with a slightly larger needle that is put into the bone. Once the biopsy is done, pressure will be applied to the site to help stop any bleeding.

Lumbar puncture (spinal tap): This test is used to look for lymphoma cells in the cerebrospinal fluid (CSF), which is the liquid that bathes the brain and spinal cord.

For this test, the doctor first numbs an area in the lower part of the back near the spine. The doctor usually also gives the child medicine to make him or her sleep during the procedure. A small, hollow needle is then placed between the bones of the spine to withdraw some of the fluid.

In children already diagnosed with lymphoma, a lumbar puncture can also be used to put chemotherapy drugs into the CSF to try to prevent or treat the spread of lymphoma to the spinal cord and brain.

Pleural or peritoneal fluid sampling: If lymphoma spreads to the thin membranes that line the inside of the chest and abdomen it can cause fluid to build up. Pleural fluid (inside the chest) or peritoneal fluid (inside the abdomen) can be removed using a hollow needle put through the skin into the chest or abdomen.

Before the procedure, the doctor uses a local anesthetic to numb the skin and may give the child other medicines so they are drowsy or asleep during the procedure. The fluid is then drawn out and looked at under the microscope to check for lymphoma cells.

When this procedure is used to remove fluid from the chest, it’s called a *thoracentesis*. When it is used to collect fluid from inside the abdomen, it’s known as a *paracentesis*.

Lab tests on biopsy samples to diagnose and classify lymphoma

All biopsy samples and fluids are looked at under a microscope by a pathologist (a doctor with special training in using lab tests to identify cancer cells). The doctor looks at the size and shape of the cells and how they are arranged. This may reveal not only if a child has lymphoma, but also what type of lymphoma it is. Because diagnosing lymphoma can be tricky, it helps if the pathologist specializes in diseases of the blood.

Pathologists can sometimes tell which kind of lymphoma a child has by looking at the cells, but usually other types of lab tests are needed to confirm the diagnosis.

Immunohistochemistry

In this test, a part of the biopsy sample is treated with special antibodies (man-made versions of immune system proteins) that attach only to specific molecules on the cell surface. These antibodies cause color changes, which can be seen under a microscope. This test can help distinguish different types of NHL from one another and from other diseases.

Flow cytometry

Like immunohistochemistry, this test looks for certain substances on the outer surface of cells that help identify what types of cells they are. But this test can look at many more cells than immunohistochemistry can.

For this test, a sample of cells is treated with special antibodies that stick to the cells only if these substances are on their surfaces. The cells are then passed in front of a laser beam. If the cells now have antibodies attached to them, the laser will cause them to give off light, which can be measured and analyzed by a computer. Groups of cells can be separated and counted by these methods.

This is the most commonly used test for *immunophenotyping* – classifying lymphoma cells according to the substances (antigens) on their surfaces. Different types of lymphocytes have different antigens on their surface. These antigens may also change as each cell matures.

Flow cytometry can help determine whether lymph node swelling is due to lymphoma, some other cancer, or a non-cancerous disease. It has also become very useful in helping doctors determine the exact type of lymphoma so that they can select the best treatment.

Cytogenetics

Doctors use this technique to evaluate the chromosomes (long strands of DNA) in the lymphoma cells. They look at the cells under a microscope to see if the chromosomes have any translocations (where part of one chromosome has broken off and is now attached to another chromosome), as happens in certain types of lymphoma. Some

lymphoma cells may also have too many chromosomes, too few chromosomes, or other chromosome changes. These changes can be used to help identify the type of lymphoma.

Cytogenetic testing usually takes about 2 to 3 weeks because the lymphoma cells must grow in lab dishes for a couple of weeks before their chromosomes are ready to be viewed under the microscope.

Molecular genetic tests

These tests look more closely at lymphoma cell DNA. They can detect most changes that can be seen under a microscope on cytogenetic tests, as well as others that can't be seen.

Fluorescent in situ hybridization (FISH): FISH is similar to cytogenetic testing. It uses pieces of DNA that only attach to specific parts of chromosomes. The DNA is linked to fluorescent dyes that can be seen with a special microscope. FISH can find most chromosome changes (such as translocations) that can be seen under a microscope on standard cytogenetic tests, as well as some changes too small to be seen with usual cytogenetic testing.

FISH can be used to look for specific changes in chromosomes. It can be used on regular blood or bone marrow samples. It is very accurate and can usually provide results within a couple of days, which is why this test is now used in many medical centers.

Polymerase chain reaction (PCR): This is a very sensitive DNA test that can also find some chromosome changes too small to be seen under a microscope, even if there are very few lymphoma cells in a sample.

Blood tests

Blood tests measure the amounts of certain types of cells and chemicals in the blood. They are not used to diagnose lymphoma, but they might be one of the first types of tests done in children with symptoms to help the doctor determine what is going on.

If a child has been diagnosed with lymphoma, these tests can also sometimes help determine how advanced the lymphoma is.

The complete blood count (CBC) is a test that measures the levels of different cells in the blood, such as the red blood cells, the white blood cells, and the platelets. In children already known to have lymphoma, low blood cell counts might mean that the lymphoma is growing in the bone marrow and damaging new blood cell production.

Blood levels of a chemical called *LDH* will often be abnormally high in patients with fast-growing lymphomas.

Blood chemistry tests can help detect liver or kidney problems caused by the spread of lymphoma cells or certain chemotherapy drugs. Blood tests can also help determine if treatment is needed to correct low or high blood levels of certain minerals. Tests may also be done to make sure the blood is clotting properly.

For some types of lymphoma, the doctor might also want to order other blood tests to see if the child has been infected with certain viruses, such as the Epstein-Barr virus (EBV), hepatitis B virus (HBV), or human immunodeficiency virus (HIV). Infections with some of these viruses can affect your child's treatment.

Imaging tests to diagnose and stage non-Hodgkin lymphoma

Imaging tests use x-rays, sound waves, magnetic fields, or radioactive substances to create pictures of the inside of the body. In a child with known or suspected lymphoma, these tests might be done to look more closely at an abnormal area that might be lymphoma, to learn how far the lymphoma may have spread, or to find out if treatment has been effective. Children with NHL usually get some (but not all) of the following imaging tests.

Chest x-ray

A chest x-ray may be done to look for enlarged lymph nodes inside the chest.

Computed tomography (CT or CAT) scan

The CT scan is an x-ray test that produces detailed, cross-sectional images of the body. Unlike a regular x-ray, CT scans can show the detail in soft tissues (such as internal organs). They can help tell if any lymph nodes or organs in the body are enlarged. CT scans can be used to look for enlarged lymph nodes or other masses in the chest, abdomen, pelvis, head, and neck.

Instead of taking one picture, like a standard x-ray does, a CT scanner takes many pictures as it rotates around the child. A computer then combines these pictures into images of slices of the part of the body being studied.

Before the scan, your child may be asked to drink a contrast solution and/or get an intravenous (IV) injection of a contrast dye that helps better outline abnormal areas in the body. Your child may need an IV line through which the contrast dye will be injected. The injection can cause some flushing (redness and warm feeling). Some people are allergic and get hives or, rarely, more serious reactions like trouble breathing and low blood pressure. Be sure to tell the doctor if your child has any allergies or has ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays. A CT scanner has been described as a large donut, with a narrow table in the middle opening. Your child will need to lie still on the table while the scan is being done. During the test, the table slides in and out of the scanner. Some younger children may be given medicine to help keep them calm or even asleep during the test to help make sure the pictures come out well.

CT-guided needle biopsy: CT scans can also be used to guide a biopsy needle precisely into a suspected tumor or enlarged lymph node. For this procedure, the child remains asleep on the CT scanning table, while a radiologist advances a biopsy needle through the

skin and toward the mass. CT scans are repeated until the needle is within the mass. A biopsy sample is then removed and looked at under a microscope.

Ultrasound (sonogram)

Ultrasound uses sound waves and their echoes to produce a picture of internal organs or masses.

Ultrasound can be used to look at lymph nodes near the surface of the body or to look inside the abdomen (belly) for enlarged lymph nodes or organs such as the liver, spleen, and kidneys. (It can't be used to look inside the chest because the ribs block the sound waves.) It is also sometimes used to help guide a biopsy needle into an enlarged lymph node.

For this test, a small wand called a *transducer* is moved around on the skin (which is first lubricated with gel). The transducer gives off sound waves and picks up the echoes as they bounce off the organs. The echoes are converted by a computer into a black and white image on a computer screen.

This is usually an easy test to have, and it uses no radiation. Your child simply lies on a table, and a technician moves the transducer over the part of the body being looked at. The test is not usually painful, but it might be uncomfortable if the transducer is pressed down hard on the abdomen.

Magnetic resonance imaging (MRI) scan

An MRI scan, like a CT scan, gives detailed images of soft tissues in the body. This test is not used as often as CT scans for lymphoma, but MRI is very useful for looking at the brain and spinal cord if a child has symptoms that might be caused by problems in the nervous system.

MRI scans use radio waves and strong magnets instead of x-rays, so there is no radiation. The energy from the radio waves is absorbed and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into very detailed images of parts of the body.

A contrast material called *gadolinium* is often injected into a vein before the scan to better see details. The contrast material usually does not cause allergic reactions.

MRI scans take longer than CT scans, often up to an hour. Your child may have to lie inside a narrow tube, which can be distressing, so sedation is sometimes needed. Newer, more open MRI machines may be another option, although your child will still have to lie still. The MRI machine makes loud buzzing and clicking noises that your child may find disturbing. Some places provide headphones or earplugs to help block this noise out.

Positron emission tomography (PET) scan

For a PET scan, a form of radioactive sugar (known as *fluorodeoxyglucose* or *FDG*) is injected into the blood. (The amount of radioactivity used is very low and will pass out of the body within a day or so.) Because lymphoma cells grow quickly, they absorb large amounts of the sugar. After about an hour, your child will be moved onto a table in the PET scanner. He or she will lie on the table for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body. The picture is not finely detailed like a CT or MRI scan, but it provides helpful information about the whole body.

PET scans can be used for many reasons in a child with lymphoma:

- They can help tell if an enlarged lymph node contains lymphoma or is benign.
- They can help spot small areas in the body that might be lymphoma, even if the area looks normal on a CT scan.
- They can help tell if a lymphoma is responding to treatment. Some doctors will repeat the PET scan after 1 or 2 courses of chemotherapy. If the chemotherapy is working, the lymph nodes will no longer take up as much of the radioactive sugar.
- They can be used after treatment in helping decide whether an enlarged lymph node still contains lymphoma or is merely scar tissue.

Some newer machines can do both a PET and CT scan at the same time (PET/CT scan). This lets the doctor compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT scan.

Bone scan

This test is not usually needed unless a child is having bone pain or has lab test results that suggest the lymphoma might have reached the bones.

For a bone scan, a radioactive substance called *technetium* is injected into the blood. (The amount of radioactivity used is very low and will pass out of the body within a day or so.)

The substance travels to damaged areas of the bone over a couple of hours. Your child then lies on a table for about 30 minutes while a special camera detects the radioactivity and creates a picture of the skeleton. Younger children may be given medicine to help keep them calm or even asleep during the test.

A bone scan can detect bone damage from lymphoma. But a bone scan may also pick up non-cancerous problems, so other tests might be needed to be sure.

How is non-Hodgkin lymphoma staged in children?

Once non-Hodgkin lymphoma (NHL) is diagnosed, tests are done to determine the stage (extent of spread) of the disease. A child's treatment and prognosis (outlook) depend, to a large extent, on the lymphoma's stage.

Staging is based on the results of the physical exam, biopsies, and imaging tests (CT scan, PET scan, etc.), which are described in the section, "How are non-Hodgkin lymphomas diagnosed in children?"

A staging system is a standard way for the cancer care team to sum up how far a cancer has spread. The staging system most often used to describe the spread of NHL in children is called the St. Jude staging system. This is different from the staging system used for lymphomas in adults (the Ann Arbor staging system).

St. Jude staging system

The St. Jude system divides NHL in children into 4 stages. In general, stage I and II lymphomas are considered limited-stage disease and are treated the same way. Stage III and IV lymphomas are usually thought of as advanced-stage disease and are also treated alike.

Stage I

The lymphoma is in only one place, either as a single tumor *not* in lymph nodes *or* in lymph nodes in one part of the body (the neck, groin, underarm, etc.). The lymphoma is not in the chest or abdomen (belly).

Stage II

Stage II lymphomas are not in the chest, and one of the following applies:

- The lymphoma is a single tumor and is also in nearby lymph nodes in only one part of the body (the neck, groin, underarm, etc.).
- The lymphoma is more than one tumor and/or in more than one set of lymph nodes, all of which are either above or below the diaphragm (the thin breathing muscle that separates the chest and abdomen). For example, this might mean nodes in the underarm and neck area are affected but not the combination of underarm and groin nodes.
- The lymphoma started in the digestive tract (usually at the end of the small intestine) and can be removed by surgery. It might or might not have reached nearby lymph nodes.

Stage III

For stage III lymphomas, one of the following applies:

- The lymphoma started in the chest (usually in the thymus or lymph nodes in the center of the chest or the lining of the lung).
- The lymphoma started in the abdomen and has spread too widely within the abdomen to be completely removed by surgery.
- The lymphoma is located next to the spine (and may be elsewhere as well).
- The lymphoma is more than one tumor or in more than one set of lymph nodes that are both above and below the diaphragm. For example, the lymphoma is in both underarm and groin lymph nodes.

Stage IV

The lymphoma is in the central nervous system (brain or spinal cord) or the bone marrow when it is first found. (If more than 25% of the bone marrow is cancer cells, called *blasts*, the cancer is classified as acute lymphoblastic leukemia [ALL] instead of lymphoma.)

Survival rates for childhood non-Hodgkin lymphoma

Advances in treatment have increased the overall survival rates for children with non-Hodgkin lymphoma (NHL) dramatically in recent decades. The 5-year survival rate is used for many types of cancer to refer to the percentage of patients who live *at least* 5 years after being diagnosed with cancer. With regard to children with NHL, those who are still alive and free of disease after 5 years are likely to have been cured, as it is rare for these cancers to return after this much time.

Survival rates give doctors a standard way to discuss and compare the prognosis (outlook) for people with cancer. Some parents want to know the survival statistics for children in similar situations, while others might not find the numbers helpful, or might not want to know them. If you would rather not read about survival rates, please skip to the next section, “How is non-Hodgkin lymphoma treated in children?”

Current survival rates are based on children diagnosed and treated many years ago. Improvements in treatment since then may mean that the outlook is better for children diagnosed recently.

Survival statistics can sometimes be useful as a general guide, but they can’t predict what will happen in any child’s case. A number of factors, including the type of lymphoma, the location and size of the tumor(s), and how well the lymphoma responds to treatment, also affect the outlook. Your child’s doctor can tell you if the numbers below apply to your child’s situation.

The ranges of numbers given below are based on the results of several studies that have used different treatment regimens or included slightly different groups of patients.

Lymphoblastic lymphoma

With intensive treatment, around 90% of children with limited stage (stage I or II) lymphoblastic lymphoma can be cured.

The cure rate for more advanced (stage III or IV) lymphoblastic lymphomas is generally higher than 80%.

Burkitt and Burkitt-like lymphoma

Treatment of limited stage (stage I and II) Burkitt lymphomas is usually very successful, with a cure rate of over 90%.

The cure rate for children with more advanced (stage III or IV) Burkitt lymphoma ranges from about 80% to 90%.

Large cell lymphomas

The cure rate is over 90% for limited stage (stage I and II) diffuse large B-cell lymphomas and is slightly lower for anaplastic large cell lymphomas.

The cure rate for children with advanced (stage III or IV) diffuse large B-cell lymphoma ranges from about 80% to 90%. For advanced anaplastic large cell lymphoma, the cure rate is about 60% to 75%.

How is non-Hodgkin lymphoma treated in children?

General treatment information

Children and teens with non-Hodgkin lymphoma (NHL) and their families have special needs. These needs can be met best by cancer centers for children and teens, working closely with the child's primary care doctor. Treatment in these centers gives you the advantage of having teams of specialists who know the differences between cancers in adults and those in children and teens, as well as the unique needs of younger people with cancer.

For childhood lymphomas, this team is typically led by a pediatric oncologist, a doctor who uses chemotherapy and other medicines to treat children's cancers. Many other specialists may be involved in your child's care as well, including other doctors, physician assistants, nurse practitioners, nurses, psychologists, social workers, rehabilitation specialists, and other health professionals. For more information, see our document *Children Diagnosed With Cancer: Understanding the Health Care System*.

After lymphoma is diagnosed and tests have been done to determine its stage, your child's cancer care team will discuss the treatment options with you. The most important

factors in choosing a treatment include the type and stage of the cancer, although other factors can also play a role. The intensive treatment for childhood lymphoma can possibly cause serious side effects. It's important to discuss all of the options as well as their possible side effects with your child's doctors so you can make an informed decision. (For a list of some questions to ask, see the section "What should you ask your child's doctor about non-Hodgkin lymphoma?")

Chemotherapy (sometimes along with other drugs) is the main treatment for all children with NHL, because it can reach all parts of the body and kill lymphoma cells wherever they may be. Even if the lymphoma appears to be limited to a single swollen lymph node, NHL in a child has often spread by the time it is diagnosed. Lymphoma cells are probably in other organs, but these are too small to be felt by the doctor or seen on imaging tests. Sometimes high-dose chemotherapy followed by a stem cell transplant might be needed if the lymphoma comes back after treatment.

Other types of treatment, such as surgery and radiation, play a much smaller role in treating childhood lymphoma.

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-of-the art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service at 1-800-303-5691 for a list of studies that meet your medical needs, or see "Clinical Trials" to learn more.

Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your cancer or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used along with your regular medical care. Alternative treatments are used instead of a doctor's medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be dangerous.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision. See *Complementary and Alternative Medicine* to learn more.

Help getting through cancer treatment

Your cancer care team will be your first source of information and support, but there are other resources for help when you need it. Hospital- or clinic-based support services are an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, support groups, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained specialists on call 24 hours a day, every day.

The next few sections describe the types of treatments used for NHL in children. This is followed by a description of the most common approaches used based on the type and stage (extent) of the lymphoma.

The treatment information given here is not official policy of the American Cancer 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.

Chemotherapy for non-Hodgkin lymphoma in children

Chemotherapy (chemo) is the main treatment for non-Hodgkin lymphoma (NHL) in children. Chemo uses anti-cancer drugs that are usually given into a vein or taken by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment very useful for cancers that tend to spread widely, such as NHL. In some cases where the lymphoma may have reached the brain or spinal cord, chemo may also be given into the cerebrospinal fluid (known as *intrathecal* chemo).

Children with NHL get a combination of several chemo drugs over a period of time. The number of drugs, their doses, and the length of treatment depend on the type and stage of the lymphoma. Some of the drugs commonly used to treat childhood lymphoma include:

- Cyclophosphamide (Cytoxan)
- Vincristine (Oncovin)
- Doxorubicin (Adriamycin)
- Prednisone
- Dexamethasone
- Cytarabine, also known as ara-C (Cytosar)
- Methotrexate

- L-asparaginase (Elspar), PEG-L-asparaginase (pegaspargase, Oncaspar)
- Etoposide (VePesid, others)
- 6-mercaptopurine (Purinethol)
- Ifosfamide (Ifex)

Doctors give chemo in cycles. Each chemo cycle generally lasts for several weeks. A period of treatment is followed by a rest period to allow the body time to recover. Most chemo treatments are given on an outpatient basis (in the doctor's office or clinic or hospital outpatient department), but some – especially at the start of treatment – may need to be given while the child stays in the hospital.

For more information on chemotherapy, see the Chemotherapy section of our website.

Possible risks and side effects of chemotherapy

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow (where new blood cells are made), 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 chemo depend on the type and dose of drugs given and how long they are taken. These side effects can include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea
- 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-lived and go away after treatment is finished. If serious side effects occur, chemotherapy may have to be reduced or delayed.

There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. Infections can be very serious in people getting chemo. Drugs known as growth factors can be given to keep the blood cell counts higher.

Tumor lysis syndrome is a possible side effect of chemotherapy in children who have large numbers of lymphoma cells in the body before treatment. It occurs most often with

the first cycle of chemo. When chemo kills these cells, they break open and release their contents into the bloodstream. This can overwhelm the kidneys, which aren't able to get rid of all of these substances at once. Excess amounts of certain minerals may also cause problems for the heart and nervous system. This can be prevented by making sure the child gets lots of fluids during treatment and by giving drugs such as bicarbonate, allopurinol, and rasburicase, which help the body get rid of these substances.

Some possible side effects occur only with certain drugs. For example, drugs such as doxorubicin can damage the heart. Your child's doctor may order heart function tests (like a MUGA scan or echocardiogram) if your child is getting one of these drugs.

Be sure to ask your child's doctor or nurse about any specific side effects you should watch for and about what you can do to help reduce them.

Along with the side effects listed above, there are possible long-term effects of chemotherapy in children, such as possible effects on fertility later in life. These are described in the section, "Late and long-term effects of treatment for non-Hodgkin lymphoma in children."

Other drugs for non-Hodgkin lymphoma in children

In recent years, new drugs that target specific parts of cancer cells have been developed. These drugs work differently from standard chemotherapy drugs. They sometimes work when chemo drugs don't, and they often have different (and less severe) side effects. Some of these drugs might be useful in certain cases of childhood non-Hodgkin lymphoma (NHL).

Monoclonal antibodies

Antibodies are proteins normally made by the body's immune system to help fight infections. Man-made versions, called *monoclonal antibodies*, can be designed to attack a specific target, such as a substance on the surface of lymphoma cells.

Several monoclonal antibodies are now being used to treat lymphoma in adults. Some of these are now being studied for use in children as well.

Rituximab (Rituxan): This antibody attaches to a substance called CD20 on the surface of some types of lymphoma cells. This attachment seems to cause the lymphoma cell to die. Rituximab is being studied for use along with chemotherapy. The treatments are given as intravenous (IV) infusions in the doctor's office or clinic.

Common side effects are usually mild but can include chills, fever, nausea, rashes, fatigue, and headaches during or after the infusion. Even if these symptoms occur with the first rituximab infusion, it is unusual for them to recur with later doses. Rituximab can also increase a person's risk of some types of infections.

Brentuximab vedotin (Adcetris): This is an anti-CD30 antibody attached to a chemotherapy drug. Some lymphoma cells have the CD30 molecule on their surface. The

antibody acts like a homing signal, bringing the chemo drug to the lymphoma cells, where it enters the cells and causes them to die when they try to divide into new cells.

Brentuximab can be used to treat anaplastic large cell lymphoma (ALCL) that has come back after other treatments. So far it has been used mainly in adults, but it is now being studied in children as well. It is given as an infusion into a vein (IV) every 3 weeks.

Common side effects include nerve damage (neuropathy), low blood counts, fatigue, fever, nausea and vomiting, infections, diarrhea, and cough.

Other new drugs

Other drugs that target parts of lymphoma cells are now being studied for use in children as well.

For example, the *anaplastic lymphoma kinase (ALK)* gene is often abnormal in ALCL. Crizotinib (Xalkori) is a newer drug that targets cells with an abnormal *ALK* gene. In early studies, this drug has shown very promising results in children with ALCL that is no longer responding to other treatments. Doctors are now studying the use of this drug along with chemotherapy in treating ALCL.

High-dose chemotherapy and stem cell transplant for non-Hodgkin lymphoma in children

High-dose chemotherapy and stem cell transplant is not used as the first treatment for non-Hodgkin lymphoma (NHL) in children, but a transplant may be an option if the first treatment does not work or if the lymphoma comes back after treatment.

A stem cell transplant lets doctors give higher doses of chemotherapy than the body would normally tolerate. Giving higher doses of chemo might be more likely to kill all of the lymphoma cells, but doctors can’t do it routinely because it destroys the bone marrow, which is where new blood cells are made. This could lead to life-threatening infections, bleeding, and other serious problems because of low blood cell counts.

For a stem cell transplant doctors first give high doses of chemotherapy and, sometimes, radiation therapy. After the chemotherapy, the child gets a transplant of blood-forming stem cells to restore the bone marrow. These stem cells can be taken either from the child before treatment (*autologous stem cell transplant*) or donated from another person (*allogeneic stem cell transplant*).

Autologous stem cell transplant

In an autologous stem cell transplant, blood-forming stem cells are removed from your child’s bone marrow or blood on several occasions in the weeks before treatment. The stem cells are carefully frozen and stored.

Your child then receives high doses of chemotherapy and sometimes radiation treatment to destroy the lymphoma cells, which also destroys the cells in the bone marrow. The

frozen stem cells are then thawed and returned to the child as a blood transfusion after the treatment.

For childhood NHL, this type of transplant is done more often than an allogeneic transplant (unless the lymphoma has already reached the bone marrow).

Allogeneic stem cell transplant

In an allogeneic stem cell transplant, the stem cells come from someone else. This type of transplant may be used if lymphoma cells are found in a child's own bone marrow in order to avoid returning lymphoma cells to the child after treatment.

The stem cell donor's tissue type (also known as the *HLA type*) needs to match the patient's tissue type as closely as possible to help prevent the risk of major problems with the transplant. Usually this donor is a brother or sister if they have the same tissue type as the patient. If a parent is a close match to the child, the parent's cells can sometimes be used. If there are no relatives with a good match, the cells may come from an HLA-matched, unrelated donor – a stranger who has volunteered to donate their cells – if one can be found.

The stem cells for an allogeneic stem cell transplant are usually collected from a donor's bone marrow or blood on several occasions. In some cases, the source of the stem cells may be blood collected from an umbilical cord attached to the placenta (which is rich in stem cells) after a baby is born. Regardless of the source, the stem cells are then frozen and stored until they are needed for the transplant.

How stem cells are transplanted

The child will typically be admitted to the stem cell transplant unit of the hospital on the day before the high-dose chemo begins. He or she will usually stay in the hospital until after the chemo and the stem cells have been given, and until the stem cells have started making new blood cells again (see below).

The child gets high-dose chemotherapy and sometimes radiation treatment to the entire body. (Radiation shields are used to protect the lungs, heart, and kidneys from damage during radiation therapy.) This should destroy any remaining cancer cells, as well as the normal cells in the bone marrow.

After treatment, the frozen stem cells are thawed and given as a blood transfusion. The stem cells then travel to the child's bone marrow. Usually within a couple of weeks after the stem cells have been infused, they begin making new white blood cells. This is later followed by new platelet and red blood cell production.

In the meantime, the child is at high risk for serious infections because of a low white blood cell count, as well as bleeding because of a low platelet count. During this time, blood and platelet transfusions and treatment with IV antibiotics are often used to help prevent or treat infections or bleeding problems.

Because of the high risk of serious infections right after treatment, patients usually stay in a special hospital room in protective isolation (guarding against exposure to germs) until the part of their white blood cell count known as the *absolute neutrophil count*, or ANC, rises above 500. They may be able to leave the hospital when their ANC is near 1,000.

The child is then seen in an outpatient clinic almost every day for several weeks. Because platelet counts often take longer to return to a safe level, the child may get platelet transfusions as an outpatient. Patients may make regular visits to the outpatient clinic for about 6 months, after which time their care may be continued by their regular doctors.

Practical points

A stem cell transplant procedure is a complex treatment that can cause life-threatening side effects. If the doctors think your child may benefit from a transplant, the best place to have this done is at a nationally recognized cancer center where the staff has experience with the procedure and with managing the recovery period.

Stem cell transplants often require a long hospital stay and can be very expensive (costing well over $100,000). Be sure to get written approval from your insurer if it is recommended for your child. Even if the transplant is covered by your insurance, co-pays or other costs could easily amount to many thousands of dollars. Find out what your insurer will cover before the transplant so you will have an idea of what you might have to pay.

Possible side effects

The possible side effects from a stem cell transplant are generally divided into early (short-term) and late (long-term) effects.

Early or short-term side effects

The early complications and side effects are basically the same as those caused by high-dose chemotherapy (see the “Chemotherapy” section of this document), and can be severe. They can include:

- Low blood cell counts (with fatigue and increased risks of infection and bleeding)
- Nausea and vomiting
- Loss of appetite
- Mouth sores
- Diarrhea
- Hair loss

One of the most common and serious short-term effects is the increased risk of serious infections. Antibiotics are often given to try to prevent this. Other side effects, like low

red blood cell and platelet counts, may require blood product transfusions or other treatments.

Late and long-term side effects

Some complications and side effects can persist for a long time or may not occur until years after the transplant. These can include:

- Graft-versus-host disease (GVHD), which can occur in allogeneic (donor) transplants (see below).
- Radiation damage to the heart or lungs
- Problems with the thyroid or other hormone-making glands
- Problems with fertility
- Damage to bones or problems with bone growth
- Development of another cancer (including leukemia) years later

GVHD happens when the donor's immune system cells attack tissues of the patient's skin, liver, and digestive tract. Symptoms can include severe skin rashes, diarrhea, weakness, fatigue, mouth sores, nausea, yellowing of the skin and eyes (jaundice), and muscle aches. GVHD can also cause lung damage, leading to problems breathing. In severe cases, GVHD can be life-threatening. GVHD is often described as either acute or chronic, based on how soon after the transplant it begins. Drugs that weaken the immune system are often given to try to keep GVHD under control, although they can have their own side effects.

Be sure to talk to your child's doctor before the transplant to learn about possible long-term effects your child may have. More information on possible long-term effects can be found in the section, "Late and long-term effects of treatment for non-Hodgkin lymphoma in children."

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

Radiation therapy for non-Hodgkin lymphoma in children

Radiation therapy uses high-energy rays to kill cancer cells. This was once a very common treatment for children with non-Hodgkin lymphoma (NHL). But as doctors have developed more effective chemotherapy treatments, radiation therapy has been used less.

Radiation focused on a cancer from a source outside the body is called *external beam radiation*. This is the type of radiation therapy most often used to treat NHL. Before treatment starts, the radiation team takes careful measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation.

The treatment itself is much like getting an x-ray, but the radiation is stronger. It is painless, but some younger children might still need to be sedated to help make sure they don't move during the treatment. Each treatment lasts only a few minutes, although the setup time – getting your child into place for treatment – usually takes longer. Most often, radiation treatments are given 5 days a week for several weeks.

There are a few instances in which radiation therapy may be used.

- Sometimes radiation is used along with chemotherapy, such as in patients where the lymphoma has reached the brain or spinal cord.
- It may be used as a form of urgent treatment in children with symptoms caused by large tumors in the chest.
- It may be used as part of treatment for children receiving high-dose chemotherapy and stem cell transplant.
- It can be used to relieve symptoms caused by lymphoma in internal organs, such when it is causing pain because it is pressing on nerves.

Possible risks and side effects of radiation therapy

Short-term side effects of radiation therapy depend on where the beams are aimed. It may cause sunburn-like skin problems or hair loss in the area being treated. Radiation therapy that includes large parts of the body can cause fatigue. Radiation of the abdomen can sometimes cause nausea, vomiting, or diarrhea. Often these effects go away after a short while.

Possible long-term side effects of radiation therapy in children can be more serious, and may occur after many years.

- Radiation therapy to the chest may damage the lungs or heart, which could raise the risk of lung or heart problems later in life. In the long term, radiation to the chest may also increase the risk of lung cancer (especially in smokers) and of breast cancer.
- Radiation therapy to the brain might cause headaches and problems such as memory loss, personality changes, and trouble learning at school.
- Radiation to other parts of the body may slow a child's growth or increase the risks for certain other cancers, such as those of muscle or bone (called sarcomas) or of the digestive tract.

Because of these possible long-term effects, doctors try to avoid using radiation therapy in children or limit the doses used whenever possible. For more on possible long-term effects, see the section, "Late and long-term effects of treatment for non-Hodgkin lymphoma in children."

More information on radiation therapy can be found in the radiation therapy section of our website, or in our document *Understanding Radiation Therapy: A Guide for Patients and Families.*

Surgery for non-Hodgkin lymphoma in children

Surgery often has a limited role in treating non-Hodgkin lymphoma (NHL) since it's unlikely to cure it by itself, and normal organs might be damaged in the process.

Surgery is sometimes used as the first treatment for early-stage Burkitt lymphoma that is in only one area (such as part of the intestine) to try to remove as much of the tumor as possible before chemotherapy. If the lymphoma can be removed completely, doctors might be able to give a less intensive chemotherapy regimen.

Other uses of surgery include:

- To get biopsy samples for lab tests to determine the exact type of NHL if non-surgical procedures (needle biopsy, bone marrow biopsy, etc.) could not get enough tissue.
- To insert a small plastic tube, called a *central venous catheter* or *venous access device* (VAD), into a large blood vessel near the heart. The end of the tube stays just under the skin or sticks out in the chest area or upper arm. The VAD is left in place during treatment to give intravenous (IV) drugs such as for chemotherapy and to take blood samples. This lowers the number of needle sticks needed during treatment.
- To relieve some emergency situations, such as if a lymphoma has blocked a child's intestines.

Possible risks and side effects of surgery

Possible complications of surgery depend on the location and extent of the operation and the child's health beforehand. Serious complications, although rare, can include problems with anesthesia, bleeding, blood clots, wound infections, and pneumonia. Most children will have some pain for a while after the operation, although this can usually be helped with medicines if needed.

For more information on surgery as a treatment for cancer, see our document *Understanding Cancer Surgery: A Guide for Patients and Families*.

Treatment of non-Hodgkin lymphoma in children, by type and stage

In general, all children with non-Hodgkin lymphoma are treated with chemotherapy, but the treatments differ depending on the type and stage of the lymphoma. This treatment is intense and might cause serious side effects, so it is very important that it is given in a children's cancer center, especially when it is first started.

Lymphomas in children (especially Burkitt lymphomas) tend to grow very quickly and may already be quite large by the time they're diagnosed, so it is important to start treatment as soon as possible. These lymphomas usually respond well to chemotherapy, which can kill large numbers of lymphoma cells in a short period of time. A concern is that this can cause *tumor lysis syndrome*, a side effect in which the inner contents of the dead cells enter the blood and can cause problems with the kidneys and other organs.

Doctors try to prevent this by making sure the child gets lots of fluids before and during treatment, and by giving certain drugs to help the body get rid of these substances.

It is assumed even children with early stage (stage I or II) lymphomas have more widespread disease than can be detected with exams or imaging tests. Because of this, local treatments such as surgery or radiation therapy alone are very unlikely to cure them. Therefore, chemotherapy is an important part of treatment for all children.

Treatment of lymphoblastic lymphoma

Stages I and II: In general, treatment for these early stage lymphomas is similar to the treatment of acute lymphoblastic leukemia (ALL). Chemotherapy is given in 3 phases (induction, consolidation, and maintenance) using many drugs. For example, the BFM regimen uses combinations of many different drugs for the first several months, followed by less intense treatment with methotrexate and 6-mercaptopurine in pill form for a total of about 2 years. Shorter and less intensive treatments, such as the chemotherapy combinations called CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) and COMP (cyclophosphamide, vincristine, methotrexate, and prednisone) have also been used.

Chemotherapy, usually with methotrexate, is also given into the spinal fluid (known as *intrathecal* chemo) for at least 4 doses, each separated by a week. This helps kill any lymphoma cells in the brain or spinal cord.

The total length of treatment may be as long as 2 years.

Stages III and IV: The treatment for children with advanced lymphoblastic lymphoma lasts for about 2 years. Treatment is typically more intensive than for earlier stage lymphomas. It is given as 3 phases of chemotherapy (induction, consolidation, and maintenance) using many drugs. This is very similar to the treatment of high-risk acute lymphoblastic leukemia (ALL). For more information, see the treatment section of the document, *Childhood Leukemia*.

Intrathecal chemotherapy is also given into the spinal fluid to kill any lymphoma cells that may have reached the brain or spinal cord. In some cases, radiation therapy may be given to the brain and spinal cord as well.

Treatment of Burkitt and Burkitt-like lymphoma

Chemotherapy is the main form of treatment for these lymphomas. Studies are now being done to determine whether adding a monoclonal antibody such as rituximab to chemotherapy will make treatment more effective.

Stages I and II: Treatment of these lymphomas may include surgery prior to chemotherapy if the tumor is in only one area. If there is a large abdominal tumor, it is important that as much of it as possible be removed. After that, chemotherapy is given.

Several different chemo drugs are used. The length of treatment ranges from about 9 weeks to 6 months. Most pediatric oncologists feel that the 9-week treatment is adequate if all of the tumor is removed with surgery first.

Chemotherapy into the spinal fluid is needed only if the lymphoma is growing around the head or neck.

Stages III and IV: Children with more advanced Burkitt lymphoma need more intensive chemotherapy. Because these lymphomas tend to grow quickly, the chemotherapy cycles are short, with little rest between courses of treatment.

For example, a treatment plan known as the French LMB protocol regimen alternates between different combinations of drugs every 3 to 4 weeks for a total of about 6 to 8 months. Other similar treatment regimens are the German BFM protocol and the St. Jude Total B regimen.

Chemotherapy must also be given into the spinal fluid.

Treatment of large cell (including anaplastic) lymphoma

Chemotherapy is the main form of treatment for these lymphomas. Studies are being done to determine whether adding other drugs to chemotherapy might make treatment more effective.

Stages I and II: Treatment for these lymphomas usually consists of chemotherapy with 4 or more drugs given for around 3 to 6 months. For diffuse large B-cell lymphoma, treatment may include surgery in addition to chemotherapy. The usual chemotherapy regimen contains a 4-drug combination of cyclophosphamide, vincristine, prednisone, and either doxorubicin or methotrexate. (These are known as the CHOP or COMP regimens.)

Chemotherapy is given into the spinal fluid only if the lymphoma is near the head or neck.

Stages III and IV: Large cell lymphomas don’t often reach the bone marrow or spinal fluid, but if they do they require more intensive treatment.

Chemotherapy includes several drugs given over 9 to 12 months. Many doctors treat advanced large B-cell lymphomas as they would Burkitt lymphoma (see above).

Intrathecal chemotherapy is given into the spinal fluid as well.

Current clinical trials are focusing on the length of chemotherapy, which drugs are important in treating large cell lymphoma, and whether the different types of large cell lymphoma can be treated similarly. Newer drugs that might help treat anaplastic large cell lymphoma, such as brentuximab vedotin (Adcetris) and crizotinib (Xalkori), are also being studied.

Treatment of recurrent lymphoma

Generally, if the lymphoma comes back after the first therapy, it is much harder to treat. When possible, more intensive chemotherapy, usually including a stem cell transplant, is recommended. This is often done in a clinical trial. Clinical trials of newer forms of treatment may also be an option.

More treatment information about non-Hodgkin lymphoma in children

For more details on treatment options – including some that may not be addressed in this document – the National Cancer Institute (NCI) and the Children's Oncology Group (COG) are good sources of information.

The NCI provides information by phone (1-800-4-CANCER) and on its website (www.cancer.gov). Detailed information intended for use by cancer care professionals is also available at www.cancer.gov.

The COG is the world's largest organization devoted to childhood cancer research. The COG website, www.childrensoncologygroup.org, provides information to help support children and their families from diagnosis, through treatment, and beyond.

What should you ask your child's doctor about non-Hodgkin lymphoma?

It is important to have open, honest discussions with your child's 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 non-Hodgkin lymphoma does my child have?
- What is the stage (extent) of the lymphoma, and what does that mean in our case?
- What tests need to be done before we can decide on treatment?
- Do we need to see other doctors?
- How much experience do you have treating this type of lymphoma?
- Should we get a second opinion before starting treatment?
- What are our treatment choices?
- What do you recommend and why?
- How soon do we need to start treatment?
- What should we do to be ready for treatment?

- How long will treatment last? What will it be like? Where will it be done?
- How much of the treatment will need to be done in the hospital?
- How will treatment affect our daily activities?
- What are the risks and side effects of the treatments you suggest?
- Which side effects start shortly after treatment and which ones might develop later on?
- Will treatment affect my child's ability to learn, grow, and develop?
- What are the chances of curing the lymphoma?
- What would our options be if the treatment doesn't work or if the lymphoma comes back?
- What type of follow-up will my child need after treatment?

You should also talk with your child's doctor before treatment to find out about the possible long-term side effects. For example, you may want to ask about how it may affect your child's fertility later on. Here are some questions you might want to ask about the risk of infertility with treatment:

- Will this treatment have an effect on my child's ability to have children someday?
- Is there anything that can be done to prevent or lower the risk of infertility? Would this interfere with my child's cancer treatment?
- If my child becomes infertile, what are their options for having a family?
- Should we talk to a fertility specialist?
- Once my child finishes treatment, how will we know if they might have fertility problems?

Along with these sample questions, be sure to write down your own. For instance, you might want more information about recovery times so that you can plan your work and school schedules. Or you may want to ask about clinical trials for which your child may qualify.

What happens during and after treatment for non-Hodgkin lymphoma in children?

During and after treatment for lymphoma, the main concerns for most families are the short- and long-term effects of the lymphoma and its treatment, and concerns about the lymphoma coming back.

It is certainly normal to want to put the lymphoma and its treatment behind you and to get back to a life that doesn't revolve around cancer. But it's important to realize that follow-up care is a central part of this process that offers your child the best chance for recovery and long-term survival.

Follow-up exams

It is very important for your child to have regular follow-up exams with the cancer care team for several years after treatment. The doctors will continue to watch for possible signs of lymphoma, as well as for short-term and long-term side effects of treatment. Doctor visits will be more frequent at first, but the time between visits may be extended as time goes on.

Checkups after treatment of non-Hodgkin lymphoma typically include careful physical exams, lab tests, and sometimes imaging tests such as CT scans. If the lymphoma recurs (comes back), it is usually while the child is still getting treatment or just after. It is unusual for childhood lymphoma to return if there are no signs of the disease within a year or so after treatment.

A benefit of follow-up care is that it gives you a chance to discuss questions and concerns that come up during and after your child's recovery. For example, almost any cancer treatment can have side effects. Some might last for only a short time, but others can last longer or might not show up until months or even years later. It is important to report any new symptoms to the doctor right away so that the cause can be found and treated, if needed.

It is also important to keep health insurance coverage. Tests and doctor visits cost a lot, and even though no one wants to think of the lymphoma coming back, this could happen.

Social, emotional, and other issues in treating non-Hodgkin lymphoma

Social and emotional issues may come up during and after treatment. Factors such as the child's age when diagnosed and the extent of treatment may play a role here.

Some children may have emotional or psychological issues that need to be addressed during and after treatment. Depending on their age, they may also have some problems with normal functioning and school work. These can often be overcome with support and encouragement. Doctors and other members of the health care team can also often recommend special support programs and services to help children after treatment.

Many experts recommend that school-aged patients attend school as much as possible. This can help them maintain a sense of daily routine and keep their friends informed about what is happening.

Friends can be a great source of support, but patients and parents should know that some people have misunderstandings and fears about cancer. Some cancer centers have a school re-entry program that can help in these situations. In this program, health

educators visit the school and tell students about the diagnosis, treatment, and changes that the cancer patient may go through. They also answer any questions from teachers and classmates. (For more information, see our document *Children Diagnosed With Cancer: Returning to School*.)

Centers that treat many children with lymphoma may have programs to introduce new patients to children or teens who have finished their treatment. This can give patients and their families an idea of what to expect during and after treatment, which is very important. Seeing another patient with lymphoma doing well after treatment is often helpful. Support groups also might be helpful.

Parents and other family members can also be affected, both emotionally and in other ways. Some common family concerns during treatment include financial stresses, traveling to and staying near the cancer center, the possible loss of a job, and the need for home schooling. Social workers and other professionals at cancer centers can help families sort through these issues.

During treatment, children and their families tend to focus on the daily aspects of getting through it and beating the lymphoma. But once treatment is finished, a number of emotional concerns can arise. Some of these might last a long time. They can include things like:

- Dealing with physical changes that can result from the treatment
- Worries about the lymphoma returning or new health problems developing
- Feelings of resentment for having had lymphoma or having to go through treatment when others do not
- Concerns about being treated differently or discriminated against (by friends, classmates, coworkers, employers, etc.)
- Concerns about dating, marrying, and having a family later in life

No one chooses to have lymphoma, but for many childhood lymphoma survivors, the experience can eventually be positive, helping to establish strong self-values. Other survivors may have a harder time recovering, adjusting to life after cancer, and moving on. It is normal to have some anxiety or other emotional reactions after treatment, but feeling overly worried, depressed, or angry can affect many aspects of a young person’s growth. It can get in the way of relationships, school, work, and other aspects of life.

With support from family, friends, other survivors, mental health professionals, and others, many people who have survived cancer can thrive in spite of the challenges they’ve had to face. If needed, doctors and other members of the health care team can often recommend special support programs and services to help children after cancer treatment.

Late and long-term effects of treatment for non-Hodgkin lymphoma in children

Because of major advances in treatment, most children treated for lymphoma are living into adulthood, so their health as they get older has come more into focus in recent years.

Just as the treatment of childhood lymphoma requires a very specialized approach, so does follow-up and monitoring for late effects of treatment. Careful follow-up after treatment is very important. The earlier problems are recognized, the more likely it is they can be treated effectively.

Childhood lymphoma survivors are at risk, to some degree, for several possible late effects of their cancer treatment. This risk depends on a number of factors, such as the type of lymphoma, the type of treatments they received, dosages of cancer treatment, and age at the time treatment. It's important to discuss what these possible effects might be with your child's medical team so you know what to watch for and report to the doctor.

Late effects of treatment can include:

- Heart or lung problems after getting certain chemotherapy drugs or getting radiation therapy to the chest
- Slowed or decreased growth and development (especially after a stem cell transplant)
- Bone damage or thinning of bones (osteoporosis)
- Changes in sexual development and ability to have children (see below)
- Changes in intellectual function with learning difficulties
- Development of second cancers, such as leukemia, later in life. These are not common, but they can occur. (For more information, see our document *Second Cancers Caused by Cancer Treatment*.)

Cancer treatment might affect sexual development and ability to have children later in life. Talk with your child's cancer care team about the risk of treatment affecting fertility, and ask if there are options for preserving fertility. For more information, see our documents *Fertility and Women With Cancer* and *Fertility and Men With Cancer*.

There may be other possible complications from treatment as well. Your child's doctor should carefully review any possible problems with you before your child starts treatment.

Along with physical side effects, survivors of childhood cancer may have emotional or psychological issues. They also may have some problems with normal functioning and school work. These can often be addressed with support and encouragement. Doctors and other members of the health care team can also often recommend special support programs and services to help children after cancer treatment.

Long-term follow-up guidelines

To help increase awareness of late effects and improve follow-up care for childhood cancer survivors throughout their lives, the Children's Oncology Group (COG) has developed long-term follow-up guidelines for survivors of childhood cancers. These guidelines can help you know what to watch for, what types of screening tests should be done, and how late effects may be treated.

It is very important to discuss possible long-term complications with your child's health care team, and to make sure there is a plan in place to watch for these problems and treat them, if needed. To learn more, ask your child's doctors about the COG survivor guidelines. You can also download them for free at the COG website: www.survivorshipguidelines.org. The guidelines are written for health care professionals. Patient versions of some of the guidelines are available (as "Health Links") on the site as well, but we urge you to discuss them with a doctor.

For more about some of the possible long-term effects of treatment, see our document *Children Diagnosed With Cancer: Late Effects of Cancer Treatment.*

Keeping good medical records of your child's treatment for non-Hodgkin lymphoma

As much as you might want to put the experience behind you once treatment is done, it is also very important to keep good records of your child's medical care during this time. Eventually, your child will grow up, be on his or her own, and have new doctors. It is important that your child be able to give the new doctors the details of the cancer diagnosis and treatment. Gathering the details soon after treatment may be easier than trying to get them at some point in the future. There are certain pieces of information that your child's doctors should have, even into adulthood. These include:

- A copy of the pathology reports from any biopsies or surgeries.
- If your child had surgery, a copy of the operative report(s).
- If your child stayed in the hospital, copies of the discharge summaries that doctors prepare when patients are sent home.
- A list of the final doses of each chemotherapy drug or other drug your child received. (Certain drugs have specific long-term side effects.)
- If radiation therapy was given, a summary of the type and dose of radiation and when and where it was given.

What’s new in research and treatment of non-Hodgkin lymphoma in children?

Research on the causes, diagnosis, and treatment of childhood non-Hodgkin lymphoma (NHL) is being done at many medical centers, university hospitals, and other institutions around the world.

Genetics

As noted in the section, “Do we know what causes non-Hodgkin lymphoma in children?” scientists are making great progress in understanding how changes in the DNA inside normal lymphocytes can cause them to develop into lymphoma cells.

Understanding the gene changes that often occur in lymphoma cells can help explain why these cells grow too quickly, live too long, and do not develop into normal, mature cells. This information is being used to develop new treatments for lymphoma.

This progress has also led to vastly improved and very sensitive tests for detecting and monitoring this disease. Tests such as the polymerase chain reaction (PCR) can identify lymphoma cells based on some of these gene changes. This test is useful in determining how completely the lymphoma has been destroyed by treatment and whether a relapse is likely if further treatment is not given.

Clinical trials of new treatments

Most children with NHL are treated at major medical centers, where treatment often involves taking part in clinical trials to get the most up-to-date care. Several important questions are now being studied in clinical trials, such as:

- Can early stage (stages I and II) lymphomas be treated with less intense chemotherapy regimens?
- What is the best length of treatment of each type of NHL?
- Can less intense treatment provide as good an outcome as the highly intense treatments and thus help children possibly avoid some long-term side effects?
- Can new chemotherapy drugs and new combinations of drugs improve cure rates?
- Can the safety and effectiveness of stem cell transplants be improved on?
- Can newer, targeted drugs such as monoclonal antibodies be added to current treatments to make them better? (See “Other drugs for non-Hodgkin lymphoma in children.”)

Additional resources for non-Hodgkin lymphoma in children

More information from your American Cancer Society

We have a lot more information that you might find helpful. Explore www.cancer.org or call our National Cancer Information Center toll-free number, 1-800-227-2345. We're here to help you any time, day or night.

National organizations and websites*

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

American Childhood Cancer Organization (formerly Candlelighters)
Toll-free number: 1-855-858-2226
Website: www.acco.org

> Offers information for children and teens with cancer, their siblings, and adults dealing with children with cancer. Also offers books and a special kit for children newly diagnosed with cancer, as well as some local support groups.

Children's Oncology Group (COG)
Website: www.childrensoncologygroup.org

> Provides key information from the world's largest organization devoted to childhood cancer research to help support children and their families from the time of diagnosis, through treatment, and beyond. Also has a searchable database to find the COG center closest to you.

CureSearch for Children's Cancer
Toll-free number: 1-800-458-6223
Website: www.curesearch.org

> Provides up-to-date information about childhood cancer from pediatric cancer experts. Has sections on the website for patients, families, and friends to help guide them on how to support the child with cancer.

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

> Has an Information Resource Center, staffed by health care professionals, available via the toll free number; free publications on lymphoma, as well as other related topics (some materials are also available in Spanish); family support groups for patients, family, and friends are available in most geographical areas; free education teleconferences and webcasts (schedule is available on the website;

also has a program to assist patients with significant financial need to cover some of the costs associated with transportation, drug co-pays, and insurance premiums.

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

Provides accurate, up-to-date information about cancer for patients and their families, including clinical trials information. Offers a special booklet for teen siblings of a child with cancer at: www.cancer.gov/cancertopics/when-your-sibling-has-cancer.

National Children's Cancer Society, Inc.
Toll-free number: 1-800-5-FAMILY (1-800-532-6459).
Website: www.children-cancer.org

Services include an online support network for parents of children with cancer, educational materials, and financial assistance for treatment-related expenses.

National Dissemination Center for Children with Disabilities (NICHCY)
Toll-free number: 1-800-695-0285 (also for TTY)
Website: www.nichcy.org

Provides information about disabilities and disability-related issues for families, educators, and other professionals.

Websites for teens and children

Starlight Children's Foundation
Toll-free number: 1-310-479-1212
Website: www.starlight.org

Website has animated stories and interactive programs to teach kids about chemo and procedures that are done in the hospital; also has videos specifically for teens and provides a safe, monitored online support group for teens with cancer.

Group Loop (a subsite of the **Cancer Support Community** just for teens)
Toll-free number: 1-888-793-9355
Website: www.grouploop.org

An online place for teens with cancer or teens who know someone with cancer to connect with other teens away from the pressures of classes, responsibilities, and treatment schedules. Has online support groups, chat rooms, information, and more.

Teens Living with Cancer
Website: www.teenslivingwithcancer.org/

An online-only resource dedicated to teens coping with a cancer diagnosis and treatment. It focuses on teen issues and provides resources to support teens, their families, and friends.

SuperSibs! powered by Alex's Lemonade Stand
Toll-free number: 1-866-333-1213
Website: www.supersibs.org

Supports, honors, and recognizes brothers and sisters of children diagnosed with cancer so they may face the future with strength, courage, and hope. Alex's Lemonade Stand is restarting SuperSibs in 2014 so there may be some delays with resuming support services.

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

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