Childhood Leukemia

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide into new cells, and die in an orderly way. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

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

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but often the DNA damage is caused by mistakes that happen while a normal cell is reproducing or by something in our environment. In adults the cause of the DNA damage may be something obvious, like cigarette smoking. But often no clear cause is found, especially for many childhood cancers.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells are in the blood and blood-forming organs and circulate through other tissues where they grow.

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

What are the differences between cancers in adults and children?

The types of cancers that develop in children are often different from those that develop in adults. Childhood cancers are often the result of gene changes inside 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 some long-term side effects, so children who have had cancer will 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 has 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. To find a listing of COG institutions by state, go to their website.

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 document, *Children Diagnosed With Cancer: Dealing With Diagnosis.*

What is childhood leukemia?

Leukemia is a cancer that starts in early blood-forming cells. Most often, leukemia is a cancer of the white blood cells, but some leukemias start in other blood cell types.

Any of the cells from the bone marrow can turn into a leukemia cell. Once this change takes place, the leukemia cells don't go through the normal process of maturing. Leukemia cells might reproduce quickly, and not die when they should. They survive and build up in the bone marrow, crowding out normal cells. In most cases, the leukemia cells spill into the bloodstream fairly quickly. From there it can go to other parts of the body such as the lymph nodes, spleen, liver, central nervous system (the brain and spinal cord),

testicles, or other organs, where they can keep other cells in the body from functioning normally.

Some other childhood cancers, such as neuroblastoma or Wilms tumor, start in other organs and can spread to bone marrow, but these cancers are not leukemia.

Normal bone marrow, blood, and lymphoid tissue

To understand the different types of leukemia, it helps to know about the blood and lymph systems.

Bone marrow

Bone marrow is the soft inner part of bones. New blood cells (red blood cells, white blood cells, and platelets) are made there. In infants, active bone marrow is found in almost all bones of the body, but by the teenage years it is found mainly in the flat bones (skull, shoulder blades, ribs, and pelvis) and vertebrae (the bones that make up the spine).

Bone marrow is made up of a small number of blood stem cells, more mature blood-forming cells, fat cells, and supporting tissues that help cells grow. Blood stem cells go through a series of changes to make new blood cells. During this process, the cells develop into 1 of the 3 main types of blood cell components:

Red blood cells

Red blood cells carry oxygen from the lungs to all other tissues of the body, and take carbon dioxide back to the lungs to be removed.

Platelets

Platelets are actually cell fragments that are made by a type of bone marrow cell called a *megakaryocyte*. They are released into the blood, where they are important in stopping bleeding by plugging holes in blood vessels caused by cuts or bruises.

White blood cells

White blood cells, also known as *leukocytes*, help the body fight infections. The 3 main types of white blood cells are lymphocytes, granulocytes, and monocytes.

Lymphocytes: These are the main cells that make up lymphoid tissue, a major part of the body's immune system. Lymphoid tissue is found in many places in the body, including the lymph nodes, thymus, spleen, tonsils and adenoids, and bone marrow. It is also scattered through the digestive system and respiratory system.

Lymphocytes develop from cells called *lymphoblasts* to become mature, infection-fighting cells. There are 2 main types of lymphocytes:

- **B lymphocytes** (B cells) help protect the body against germs such as bacteria and viruses. They make proteins called *antibodies* that attach to the germ, marking it for destruction by other parts of the immune system.

- **T lymphocytes** (T cells) also help protect the body against germs. Some types of T cells destroy germs directly, while others play a role in either boosting or slowing the activity of other immune system cells.

Acute lymphocytic (lymphoblastic) leukemia (ALL), the most common type of childhood leukemia, develops from early forms of lymphocytes. It can start in either early B cells or T cells at different stages of maturity. Although both B cells and T cells can develop into leukemia, B-cell leukemias are much more common than T-cell leukemias. For more information, see the section, “How is childhood leukemia classified?”

Granulocytes: These white blood cells have granules in them, which are spots that can be seen under the microscope. The granules contain enzymes and other substances that can destroy germs, such as bacteria. The 3 types of granulocytes – *neutrophils*, *basophils*, and *eosinophils* – are distinguished by the size and color of their granules. Granulocytes develop from blood-forming cells called *myeloblasts* to become mature, infection-fighting cells.

Monocytes: These white blood cells, which are related to granulocytes, also help protect the body against bacteria. They start in the bone marrow as blood-forming *monoblasts* and develop into mature monocytes. After circulating in the bloodstream for about a day, monocytes enter body tissues to become *macrophages*, which can destroy some germs by surrounding and digesting them.

Types of leukemia in children

Leukemia is often described as being either acute (fast growing) or chronic (slow growing). Almost all childhood leukemia is acute.

Acute leukemias

The main types of acute leukemia are:

- Acute lymphocytic (lymphoblastic) leukemia (ALL): About 3 out of 4 cases of childhood leukemia are ALL. This leukemia starts from the lymphoid cells in the bone marrow.

- Acute myelogenous leukemia (AML): This type of leukemia, also called *acute myeloid leukemia*, *acute myelocytic leukemia*, or *acute non-lymphocytic leukemia*), accounts for most of the remaining cases. AML starts from the myeloid cells that form white blood cells (other than lymphocytes), red blood cells, or platelets.

- **Hybrid or mixed lineage leukemias:** In these rare leukemias, the cells have features of both ALL and AML. In children, they are generally treated like ALL and respond to treatment like ALL.

Both ALL and AML can be further divided into different subtypes. For more information on these subtypes, see the section, “How is childhood leukemia classified?”

Chronic leukemias

Chronic leukemias are much more common in adults than in children. They tend to grow more slowly than acute leukemias, but they are also harder to cure. Chronic leukemias can also be divided into 2 types.

- Chronic myelogenous leukemia **(CML):** This leukemia rarely occurs in children. Treatment is similar to that used for adults (see “Treatment of children with chronic myelogenous leukemia.”) For more detailed information on CML, see our document, *Leukemia--Chronic Myeloid*.
- Chronic lymphocytic leukemia **(CLL):** This leukemia is extremely rare in children, so it is not discussed further in this document. For more information on CLL, see our document, *Leukemia--Chronic Lymphocytic*.

Juvenile myelomonocytic leukemia (JMML)

This rare type of leukemia is neither chronic nor acute. It begins from myeloid cells, but it usually doesn’t grow as fast as AML or as slow as CML. It occurs most often in young children (under age 4). Symptoms can include pale skin, fever, cough, easy bruising or bleeding, trouble breathing (from too many white blood cells in the lungs), and an enlarged spleen and lymph nodes.

What are the key statistics for childhood leukemia?

Leukemia is the most common cancer in children and teens, accounting for almost 1 out of 3 cancers. Overall, however, childhood leukemia is a rare disease.

About 3 out of 4 leukemias among children and teens are acute lymphocytic leukemia (ALL). Most of the remaining cases are acute myelogenous leukemia (AML).

ALL is most common in early childhood, peaking between 2 and 4 years of age. Cases of AML are more spread out across the childhood years, but it is slightly more common during the first 2 years of life and during the teenage years.

ALL is slightly more common among white children than among African-American and Asian-American children, and it is more common in boys than in girls. AML occurs about equally among boys and girls of all races.

Chronic leukemias are rare in children. Most of these are chronic myelogenous leukemia (CML), which tends to occur more in teens than in younger children.

Survival statistics for childhood leukemia are in another section of this document.

What are the risk factors for childhood leukemia?

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, smoking is a risk factor for several types of cancer in adults.

Lifestyle-related risk factors such as diet, body weight, physical activity, 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 play much of a role in childhood cancers, including leukemias.

There are a few known risk factors for childhood leukemia.

Genetic risk factors

Genetic risk factors are those that are part of our DNA (the substance that makes up our genes). They are most often inherited from our parents. While some genetic factors increase the risk of childhood leukemia, most cases of leukemia are not linked to any known genetic causes.

Inherited syndromes

Several inherited disorders increase a child's risk of developing leukemia:

- **Down syndrome (trisomy 21):** Children with Down syndrome have an extra (third) copy of chromosome 21. In ways that are not completely understood, this extra chromosome 21 causes mental retardation and a characteristic facial appearance. Children with Down syndrome are many times more likely to develop either acute lymphocytic leukemia (ALL) or acute myeloid leukemia (AML) than are other children, with an overall risk of about 2% to 3%. Down syndrome has also been linked with transient leukemia (also known as *transient myeloproliferative disorder*) – a leukemia-like condition within the first month of life, which often resolves on its own without the use of chemotherapy.

- **Klinefelter syndrome:** This is a genetic condition in which males have an extra "X" chromosome. This causes infertility, prevents normal development of some male features (such as body hair, deep voice, etc.), and is linked to a slightly increased risk of developing leukemia.

- **Li-Fraumeni syndrome:** This is a rare condition caused by a change in the *TP53* tumor suppressor gene. People with this change have a higher risk of developing several kinds of cancer, including leukemia, bone or soft tissue sarcomas, breast cancer, adrenal gland cancer, and brain tumors.

Several other genetic disorders (such as neurofibromatosis and Fanconi anemia) also carry an increased risk of leukemia, as well as some other types of cancers.

Inherited immune system problems

Certain inherited diseases cause children to be born with immune system problems. These include:

- Ataxia telangiectasia
- Wiskott-Aldrich syndrome
- Bloom syndrome

Along with an increased risk of getting serious infections from reduced immune defenses, these children might also have an increased risk of leukemia.

Having a brother or sister with leukemia

Siblings (brothers and sisters) of children with leukemia have a slightly increased chance (2 to 4 times normal) of developing leukemia, but the overall risk is still low. The risk is much higher among identical twins. If an identical twin develops childhood leukemia, the other twin has about a 1 in 5 chance of getting leukemia as well. This risk is even higher if the leukemia develops in the first year of life.

Having a parent who develops leukemia as an adult does not seem to raise a child's risk of leukemia.

Lifestyle-related risk factors

Lifestyle-related risk factors for some adult cancers include being overweight, smoking, drinking excessive amounts of alcohol, and getting too much sun exposure. Lifestyle-related factors are important in many adult cancers, but they are unlikely to play a role in most childhood cancers.

Some studies have suggested that if a mother drinks a lot of alcohol during pregnancy it might increase the risk of leukemia in her child, but not all studies have found such a link.

Environmental risk factors

Environmental risk factors are influences in our surroundings, such as radiation and certain chemicals, that increase the risk of getting diseases such as leukemias.

Radiation exposure

Exposure to high levels of radiation is a risk factor for childhood leukemia. Japanese atomic bomb survivors had a greatly increased risk of developing AML, usually within 6 to 8 years after exposure. If a fetus is exposed to radiation within the first months of development, there may also be an increased risk of childhood leukemia, but the extent of the risk is not clear.

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. Some studies have found a slight increase in risk, while others have found no increased risk. Any risk increase 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.

Exposure to chemotherapy and certain other chemicals

Children and adults treated for other cancers with certain chemotherapy drugs have a higher risk of getting a second cancer, usually AML, later in life. Drugs such as cyclophosphamide, chlorambucil, etoposide, and teniposide have been linked to a higher risk of leukemia. These leukemias usually develop within 5 to 10 years of treatment, and they tend to be hard to treat.

Exposure to chemicals such as benzene (a solvent used in the cleaning industry and to manufacture some drugs, plastics, and dyes) may cause AML in adults and, rarely, in children. Chemical exposure is more strongly linked to an increased risk of AML than to ALL.

Several studies have found a possible link between childhood leukemia and household exposure to pesticides, either during pregnancy or early childhood. Some studies have also found a possible increased risk among mothers with workplace exposure to pesticides before birth. However, most of these studies had serious limitations in the way they were done. More research is needed to try to confirm these findings and to provide more specific information about the possible risks.

Immune system suppression

Children who are getting intensive treatment to suppress their immune function (mainly organ transplant patients) have an increased risk of certain cancers, such as lymphoma and ALL.

Uncertain, unproven, or controversial risk factors

Other factors that have been studied for a possible link to childhood leukemia include:

- Exposure to electromagnetic fields (such as living near power lines)
- Living near a nuclear power plant
- Infections early in life
- Mother’s age when child is born
- Parent’s smoking history
- Fetal exposure to hormones such as diethylstilbestrol (DES) or birth control pills
- Father’s workplace exposure to chemicals and solvents

- Chemical contamination of ground water

So far, most studies have not found strong links between any of these factors and childhood leukemia. Researchers continue to study these exposures.

Do we know what causes childhood leukemia?

The exact cause of most cases of childhood leukemia is not known. Most children with leukemia do not have any known risk factors.

Still, scientists have made great progress in understanding how certain changes in the DNA inside normal bone marrow cells can cause them to become leukemia cells. Normal human cells grow and function based mainly on the information contained in each cell's DNA. DNA is the chemical that makes up our genes – the instructions for how our cells function. We usually look like our parents because they are the source of our DNA. But our genes affect more than the way we look.

Some genes have instructions for controlling when our cells grow, divide into new cells, and die. Certain genes that help cells grow and divide are called *oncogenes*. Others that slow down cell division or cause cells to die at the right time are called *tumor suppressor genes*.

Cancers can be caused by DNA mutations (or other types of changes) that turn on oncogenes or turn off tumor suppressor genes. These gene changes can be inherited from a parent (as is sometimes the case with childhood leukemias), or they may happen randomly during a person's lifetime if cells in the body make mistakes as they divide to form 2 new cells.

A common type of DNA abnormality that can lead to leukemia is known as a chromosome *translocation*. Human DNA is packaged in 23 pairs of chromosomes. In a translocation, DNA from one chromosome breaks off and becomes attached to a different chromosome. The point on the chromosome where the break occurs can affect oncogenes or tumor suppressor genes. For example, a translocation seen in nearly all cases of childhood chronic myeloid leukemia (CML) and in some cases of childhood acute lymphocytic leukemia (ALL) is a swapping of DNA between chromosomes 9 and 22, which leads to what is known as the *Philadelphia chromosome*. This creates an oncogene known as *BCR-ABL*. Many other changes in chromosomes or in specific genes have been found in childhood leukemias as well.

Some children inherit DNA mutations from a parent that might increase their risk for cancer (see the section "What are the risk factors for childhood leukemia?"). For instance, a condition called *Li-Fraumeni syndrome*, which results from an inherited mutation of the *TP53* tumor suppressor gene, increases a person's risk of developing leukemia, as well as some other cancers.

Certain inherited diseases can increase the risk of developing leukemia, but most cases of childhood leukemia do not seem to be caused by inherited mutations. Usually, DNA

mutations related to leukemia develop after conception rather than having been inherited. Some of these acquired mutations may occur early, even before birth. In rare cases, acquired mutations may result from exposure to radiation or cancer-causing chemicals, but most often they occur for no apparent reason.

A few studies have suggested that some childhood leukemias may be caused by a combination of genetic and environmental factors. For example, certain genes normally control how our bodies break down and get rid of harmful chemicals. Some people have different versions of these genes that make them less effective. Children who inherit these genes may not be as able to break down harmful chemicals if they are exposed to them. The combination of genetics and exposure might increase their risk for leukemia.

Can childhood leukemia be prevented?

Although the risk of many adult cancers can be reduced by lifestyle changes (such as quitting smoking), there is no known way to prevent most childhood cancers at this time. Most adults and children with leukemia have no known risk factors, so there is no sure way to prevent their leukemias from developing.

Some leukemias result from treating cancers with radiation and chemotherapy, or the use of immune-suppressing drugs to avoid rejection of transplanted organs. Doctors are looking for ways to treat patients with cancer and organ transplants without raising the risk of leukemia. But for now, the obvious benefits of treating life-threatening diseases with chemotherapy, radiation therapy, or organ transplants must be balanced against the small chance of developing leukemia several years later.

X-rays or CT scans done before birth or during childhood use much lower levels of radiation than those used for treatment. If there is any increase in risk from these tests, it is likely to be very small, but to be safe, most doctors recommend that pregnant women and children not get these tests unless they are absolutely needed.

There are very few known lifestyle-related or environmental causes of childhood leukemias, so it is important to know that in most cases there is nothing these children or their parents could have done to prevent these cancers.

Can childhood leukemia be found early?

At this time there are no widely recommended blood tests or other screening exams for most children to look for leukemia before it starts to cause symptoms. Childhood leukemia is often found because a child has symptoms that prompt a visit to the doctor. Blood test results are abnormal, which then points to the diagnosis. The best way to find these cancers early is to pay attention to the possible signs and symptoms of this disease (see “Signs and symptoms of childhood leukemia”).

For children known to be at increased risk of leukemia (because of Li-Fraumeni syndrome or Down syndrome, for example), most doctors recommend careful, regular medical checkups and possibly other tests. The same is true for children who have had

other cancers treated with chemotherapy and/or radiation therapy, and for children who have received organ transplants and are taking immune system-suppressing drugs. The risk of leukemia in these children, although higher than in the general population, is still small.

Signs and symptoms of childhood leukemia

As leukemia cells build up in the bone marrow, they can crowd out the normal blood cell-making cells. As a result, a child may not have enough normal red blood cells, white blood cells, and blood platelets. These shortages show up on blood tests, but they can also cause symptoms. The leukemia cells may also invade other areas of the body, which can also cause symptoms.

Many of these symptoms have other causes as well, and most often they are not from leukemia. Still, it's important to let your child's doctor know about them right away so that the cause can be found and treated, if needed.

Fatigue (tiredness), pale skin: Anemia (a shortage of red blood cells) might make a child feel tired, weak, lightheaded, or short of breath. It may also cause pale skin.

Infections and fever: A child with leukemia may develop fever. This is often caused by an infection, which may not improve even with antibiotics. This is because of a lack of normal white blood cells, which would normally help fight the infection. Although children with leukemia may have very high white blood cell counts, the leukemia cells do not protect against infection the way normal white blood cells do. Fever is also sometimes caused by the leukemia cells themselves releasing certain chemicals into the body.

Easy bleeding or bruising: A child with leukemia may bruise easily, have frequent nosebleeds and bleeding gums, or bleed too much from small cuts. There may be pinhead-sized red spots on the skin caused by bleeding from tiny blood vessels. This comes from a lack of blood platelets, which normally stop bleeding by plugging holes in damaged blood vessels.

Bone or joint pain: Some children with leukemia will have bone pain or joint pain. This is from the buildup of leukemia cells near the surface of the bone or inside the joint.

Swelling of the abdomen (belly): Leukemia cells may collect in the liver and spleen, causing them to enlarge. This may be noticed as a fullness or swelling of the belly. The lower ribs usually cover these organs, but when they are enlarged the doctor can often feel them.

Loss of appetite, weight loss: If the spleen and/or liver become large enough, they may press against other organs like the stomach. This can limit the amount of food that can be eaten, leading to a loss of appetite and weight loss over time.

Swollen lymph nodes: Some leukemias spread to lymph nodes. The child, a parent, or a health professional may notice swollen nodes as lumps under the skin in certain areas of the body (such as on the sides of the neck, in underarm areas, above the collarbone, or in

the groin). Lymph nodes inside the chest or abdomen may also swell, but these can only be detected by imaging tests, such as CT or MRI scans.

Lymph nodes often enlarge when they are fighting an infection, especially in infants and children. An enlarged lymph node in a child is more often a sign of infection than leukemia, but it should be checked by a doctor and followed closely.

Coughing or trouble breathing: The T-cell type of acute lymphocytic leukemia (ALL) often affects the thymus, which is a small organ in the chest behind the breastbone (sternum) and in front of the windpipe (trachea). An enlarged thymus or lymph nodes inside the chest can press on the trachea. This can lead to coughing or trouble breathing.

Swelling of the face and arms: The superior vena cava (SVC), a large vein that carries blood from the head and arms back to the heart, passes next to the thymus. Growth of the thymus from the buildup of leukemia cells may press on the SVC, causing the blood to "back up" in the veins. This is known as *SVC syndrome*. It can cause swelling in the face, neck, arms, and upper chest (sometimes with a bluish-red skin color). It can also cause headaches, dizziness, and a change in consciousness if it affects the brain. The SVC syndrome can be life-threatening, and needs to be treated right away.

Headache, seizures, vomiting: A small number of children have leukemia that has already spread to the central nervous system (brain and spinal cord) when they are first diagnosed. Headache, trouble concentrating, weakness, seizures, vomiting, problems with balance, and blurred vision can be symptoms of spread to the central nervous system.

Rashes, gum problems: In children with acute myelogenous leukemia (AML), leukemia cells may spread to the gums, causing swelling, pain, and bleeding. If it has spread to the skin, it can cause small, darkly colored spots that look like common rashes. A collection of AML cells under the skin or in other parts of the body is called a *chloroma* or *granulocytic sarcoma*.

Extreme fatigue, weakness: One rare but very serious consequence of AML is extreme tiredness, weakness, and slurring of speech. This can occur when very high numbers of leukemia cells cause the blood to become too thick and slow the circulation through small blood vessels of the brain.

How is childhood leukemia diagnosed?

Most of the signs and symptoms of childhood leukemia are more likely to have other causes, such as infections. Still, it's important to let your child's doctor know about such symptoms right away so that the cause can be found and treated, if needed.

Exams and tests will be done to determine the cause of the symptoms. If leukemia is found, further tests will be needed to help tell what type it is and how it should be treated.

It's important to diagnose childhood leukemia as early as possible and to determine what type of leukemia it is so that treatment can be tailored to provide the best chance of success.

Medical history and physical exam

If your child has signs and symptoms that suggest they may have leukemia, the doctor will want to get a thorough medical history to learn about the symptoms your child is having and how long they have had them. The doctor may also ask about any history of exposure to possible risk factors. A family history of cancer, especially leukemia, may also be important.

During the physical exam, the doctor will focus on any enlarged lymph nodes, areas of bleeding or bruising, or possible signs of infection. The eyes, mouth, and skin will be looked at carefully, and a nervous system exam may be done. The abdomen will be felt for signs of an enlarged spleen or liver.

Types of tests used to look for leukemia in children

If the doctor thinks your child might have leukemia, samples of cells from your child's blood and bone marrow will need to be checked to be sure of the diagnosis. Your child's doctor may refer you to a *pediatric oncologist*, a doctor who specializes in cancers (like leukemia) in children, to have some of these tests done. If leukemia is found, other tissue and cell samples may also be taken to help guide treatment.

Blood tests

The first tests done to look for leukemia are blood tests. The blood samples are usually taken from a vein in the arm, but in infants and younger children, they may be taken from other veins (such as in the feet or scalp) or from a "finger stick."

Blood counts and blood smears are the usual tests done on these samples. A complete blood count (CBC) is done to determine how many blood cells of each type are in the blood. For a blood smear, a small sample of blood is spread on a glass slide and looked at under a microscope. Abnormal numbers of blood cells and changes in the way these cells look may make the doctor suspect leukemia.

Most children with acute leukemia – lymphocytic or myeloid – will have too many white blood cells and not enough red blood cells and/or platelets. Many of the white blood cells in the blood will be *blasts*, an early type of blood cell normally found only in the bone marrow. Even though these findings may make a doctor suspect that a child has leukemia, usually the disease cannot be diagnosed for sure without looking at a sample of bone marrow cells.

Bone marrow aspiration and biopsy

Bone marrow samples are obtained from a bone marrow aspiration and biopsy – 2 tests that are usually done at the same time. The samples are usually taken from the back of the pelvic (hip) bones, but in some cases they may be taken from the front of the pelvic bones, the breastbone (sternum [very rarely in children]), or other bones.

For a bone marrow *aspiration*, the skin over the hip bone is cleaned and numbed with local anesthetic. In most cases, the child is also given other medicines to reduce pain or even be asleep during the procedure. A thin, hollow needle is then inserted into the bone and a syringe is used to suck out (aspirate) 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 twisted as it is pushed down into the bone. Once the biopsy is done, pressure will be applied to the site to help prevent any bleeding.

These bone marrow tests are used to diagnose leukemia and may be repeated later to tell if the leukemia is responding to treatment.

Lumbar puncture (spinal tap)

This test is used to look for leukemia 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 over 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.

This test is always done in children with leukemia, but it is important for it to be done by an expert. Doctors have found that if the spinal tap isn’t performed expertly and some blood leaks into the CSF, in some cases leukemia cells may get into the fluid and grow there.

In children already diagnosed with leukemia, the first lumbar puncture is also used to give chemotherapy drugs into the CSF to try to prevent or treat the spread of leukemia to the spinal cord and brain.

Lymph node biopsy

This type of biopsy is important in diagnosing lymphomas, but it is rarely needed for children with leukemias.

During this procedure, a surgeon cuts through the skin to remove an entire lymph node (excisional biopsy). If the node is near the skin surface, this is a simple operation. But it is more involved if the node is inside the chest or abdomen. Most often the child will need general anesthesia (the child is asleep).

Lab tests used to diagnose and classify leukemia

Routine microscopic exams

As mentioned above, blood counts and smears are usually the first tests done when leukemia is a possible diagnosis. Any other samples taken (bone marrow, lymph node

tissue, or CSF) are also looked at under a microscope by a pathologist (a doctor who specializes in interpreting lab tests) and may be reviewed by the patient's hematologist/oncologist (a doctor specializing in blood diseases and cancer).

The doctors will look at the size, shape, and staining patterns of the blood cells in the samples to classify them into specific types. (See the section, "How is childhood leukemia classified?" for more information on the types of leukemia.)

A key element is whether the cells look mature (like normal blood cells) or immature (lacking features of normal blood cells). The most immature cells are called *blasts*. Having too many blasts in the sample, especially in the blood, is a typical sign of leukemia.

An important feature of a bone marrow sample is its *cellularity*. Normal bone marrow contains a certain number of blood-forming cells and fat cells. Marrow with too many blood-forming cells is said to be *hypercellular*. If too few blood-forming cells are found, the marrow is called *hypocellular*.

Cytochemistry

In cytochemistry tests, cells from the sample are put on a microscope slide and exposed to chemical stains (dyes) that react only with some types of leukemia cells. These stains cause color changes that can be seen under a microscope. This can help the doctor determine what types of cells are present. For example, one stain causes the granules of most AML cells to appear as black spots under the microscope, but it does not cause ALL cells to change colors.

Flow cytometry and immunohistochemistry

Flow cytometry is used to test the cells from bone marrow, lymph nodes, and blood samples to determine more accurately the exact type of leukemia. It is a very important tool because it may help define the unique traits of the leukemia. It can also be used to measure the response to treatment and the existence of minimal residual disease (MRD, see "Prognostic factors in childhood leukemia") in some types of leukemias.

The test checks for certain substances on the surface of cells that help identify what types of cells they are. The cells in the sample are treated with special antibodies (man-made versions of immune system proteins) that stick only to these substances. 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 is measured and analyzed by a computer.

Flow cytometry can also be used to estimate the amount of DNA in the leukemia cells. This is important to know, especially in ALL, because cells with a high *DNA index* (1.16 or higher, which is more than 16% above normal) are often more sensitive to chemotherapy, and these leukemias have a better prognosis (outlook).

For *immunohistochemistry* tests, cells from the bone marrow or other samples are treated with special man-made antibodies. But instead of using a laser and computer for analysis,

the sample is treated so that certain types of cells change color when seen under a microscope. Like flow cytometry, this test is helpful in distinguishing different types of leukemia from one another and from other diseases.

These tests are used for *immunophenotyping* – classifying leukemia cells according to the substances (antigens) on their surfaces. Different types of cells have different antigens on their surface. These antigens also change as the cells mature. Each patient's leukemia cells should all have the same antigens because they all come from the same original leukemia cell. Lab testing for antigens is a very sensitive way to diagnose and classify leukemias.

Cytogenetics

For this test, chromosomes (pieces of DNA) from leukemia cells are looked at under a microscope to detect any changes. Normal human cells contain 23 pairs of chromosomes, each of which is a certain size and stains a certain way. In some types of leukemia, chromosome changes may be seen.

For instance, sometimes 2 chromosomes swap some of their DNA, so that part of one chromosome becomes attached to part of a different chromosome. This change, called a *translocation*, can usually be seen under a microscope. Recognizing these changes can help identify certain types of acute leukemias and can help determine prognosis (outlook).

Some types of leukemia have cells with an abnormal number of chromosomes (instead of the usual 46) – they may be missing some chromosomes or have extra copies of some. This can also affect a patient's outlook. For example, chemotherapy is more likely to work in cases of ALL where the cells have more than 50 chromosomes and is less likely to be effective if the cells have fewer than 46 chromosomes. (Counting the number of chromosomes by cytogenetics provides similar information to measuring the DNA index by flow cytometry, as described above.)

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

Not all chromosome changes can be seen under a microscope. Other lab tests can often help detect these changes.

Fluorescent in situ hybridization (FISH)

This is similar to cytogenetic testing. It uses pieces of DNA that only attach to specific parts of particular 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 are visible under a microscope in 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 blood or bone marrow samples. It is very accurate and can usually provide results within a couple of days.

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 very few leukemia cells are present in a sample. This test can be very useful in looking for small numbers of leukemia cells (minimal residual disease, or MRD) during and after treatment that might not be detected with other tests.

Other blood tests

Children with leukemia will have tests to measure certain chemicals in the blood to check how well their body systems are working.

These tests are not used to diagnose leukemia, but in children already known to have it, they can help find damage to the liver, kidneys, or other organs caused by the spread of leukemia cells or by certain chemotherapy drugs. Tests are also often done to measure blood levels of important minerals, as well as to ensure the blood is clotting properly.

Children might also be tested for blood infections. It is important to quickly diagnose and treat infections in children with leukemia because their weakened immune systems can allow infections to spread quickly.

Imaging tests

Imaging tests use x-rays, sound waves, magnetic fields, or radioactive particles to produce pictures of the inside of the body. Leukemia does not usually form tumors, so imaging tests aren’t as useful as they are for other types of cancer. But if leukemia is suspected or has been diagnosed, your child’s doctor may order some of these tests to get a better idea of the extent of the disease or to look for other problems, such as infections. (For more details on imaging tests, see our document, *Imaging (Radiology) Tests*.)

Chest x-rays

A chest x-ray can help detect an enlarged thymus or lymph nodes in the chest. If the test result is abnormal, a computed tomography (CT) scan of the chest may be done to get a more detailed view.

Chest x-rays can also help look for pneumonia if your child might have a lung infection.

Computed tomography (CT) scan

The CT scan is a type of 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.

This test can help tell if any lymph nodes or organs in the body are enlarged. It isn't usually needed to diagnose leukemia, but it might be done if the doctor suspects the leukemia is growing in lymph nodes in the chest or in organs like the spleen or liver. It is also sometimes used to look at the brain and spinal cord, but an MRI scan may also be used for this.

Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around your child. A computer then combines these pictures into detailed images of the part of the body that is 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. He or she may need an IV line through which the contrast dye is injected.

The IV injection of contrast dye can cause a feeling of flushing or warmth in the face or elsewhere. Some people are allergic and get hives or, rarely, have 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 people feel a bit confined while the scan is being done. Some children might need to be sedated before the test to help make sure they stay still so the pictures come out well.

PET/CT scan: In recent years, newer devices have been developed that combine the CT scan with a 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 cancer cells in the body grow rapidly, they absorb large amounts of the radioactive sugar. A special camera can then create a picture of areas of radioactivity in the body. The picture from the PET scan is not finely detailed like those from a CT scan, but it provides helpful information about the whole body. The PET/CT scan lets the doctor compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT scan.

Magnetic resonance imaging (MRI) scan

An MRI scan, like a CT scan, gives detailed images of soft tissues in the body. It is most helpful in looking at the brain and spinal cord, so it is most likely to be done if the doctor

has reason to think the leukemia might have spread there (such as if the child has symptoms like headaches, seizures, or vomiting).

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

A contrast material called *gadolinium* is often injected into a vein before the scan to better show 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 is confining and can be distressing, so sedation is sometimes needed. Newer, more open MRI machines may be another option, although they still require that your child be able to lie still. All MRI machines make loud buzzing and clicking noises that your child may find disturbing. Some places provide headphones or earplugs to help block this out.

Ultrasound

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

This test can be used to look at lymph nodes near the surface of the body or to look for enlarged organs inside the abdomen such as the kidneys, liver, and spleen. (It can't be used to look at organs or lymph nodes in the chest because the ribs block the sound waves.)

For this test, a small, microphone-like instrument called a *transducer* is placed on the skin (which is first lubricated with gel). It gives off sound waves and picks up the echoes as they bounce off the organs. The echoes are converted by a computer into an image that is displayed on a computer screen.

This is a fairly 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.

Bone scan

This test is not done often for childhood leukemias, but it may be useful if your child has bone pain that might be from either an infection or cancer in the bones. If your child has already been diagnosed with leukemia or if a PET scan (described above) has already been done, there is usually no need for a bone scan.

For this test, the doctor or nurse injects a small amount of a slightly radioactive chemical into the bloodstream. (The amount of radioactivity used is very low and will pass out of the body within a day or so.) The substance settles in areas of damaged bone throughout the skeleton over the course of 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.

Areas of bone changes appear as hot spots on the skeleton because they attract the radioactivity, but the image isn't very detailed. If an area lights up on the scan, other imaging tests such as x-rays or CT or MRI scans may be done to get a more detailed look at the area. If leukemia is a possibility, a biopsy of the area may be needed to confirm this.

How is childhood leukemia classified?

Classification of the leukemia plays a major role in determining both treatment options and a child's outlook (prognosis). Determining its type (acute lymphocytic, acute myeloid, etc.) and subtype is done by testing samples of the blood, bone marrow, and sometimes lymph nodes or cerebrospinal fluid (CSF), as described in "How is childhood leukemia diagnosed?".

Most types of cancers are assigned numbered stages to describe their extent in the body, based on the size of the tumor and how far the cancer has spread. But leukemia is not staged like most other cancers. It starts in the bone marrow and quickly spreads to the blood, so leukemia cells are already scattered throughout the body. Still, it is important to know whether the leukemia cells have started to collect in other organs such as the liver, spleen, lymph nodes, testicles, or central nervous system (brain and spinal cord).

For instance, if the leukemia cells have spread to the central nervous system in large numbers, they will be seen in samples of CSF. Treatment must be more intense to kill the leukemia cells in the central nervous system. This is why a spinal tap (lumbar puncture) is done as part of the early diagnostic testing.

Acute lymphocytic (lymphoblastic) leukemia (ALL)

Acute lymphocytic leukemia (ALL) is a fast-growing cancer of lymphocyte-forming cells called *lymphoblasts*.

Classification based on how the leukemia cells look (morphology)

In the past, doctors used the French-American-British (FAB) classification to divide ALL into 3 major groups (L1, L2, or L3) based on how the cells looked under the microscope. Some doctors may still refer to these categories. But newer lab tests now let doctors classify ALL based on more than just how the cells look under the microscope.

Classification based on immunophenotype

Doctors have found that cytogenetic tests, flow cytometry, and other lab tests provide more detailed information about the subtype of ALL and the patient's prognosis. These

tests help divide ALL into groups based on the *immunophenotype* of the leukemia, which takes into account:

- The type of lymphocyte (B cell or T cell) the leukemia cells come from
- How mature these leukemia cells are

There are 4 main subtypes of ALL, as shown in the table below:

Subtype	**Frequency**
Early Pre-B cell	60%-65%
Pre-B cell	20%-25%
Mature B cell	2%-3%
T cell	15%-18%

B-cell ALL: About 85% of children with ALL have B-cell ALL.

- The most common subtype of B-cell ALL is “early precursor B” (early pre-B) ALL.
- The “pre-B” form of ALL accounts for 20% to 25% of patients with B-cell ALL.
- Mature B-cell leukemia accounts for about 2% to 3% of childhood ALL. It is also called *Burkitt leukemia*. This disease is essentially the same as Burkitt lymphoma and is treated differently from most leukemias. It’s discussed in detail in our document, *Non-Hodgkin Lymphoma in Children*.

T-cell ALL: About 15% to 18% of children with ALL have T-cell ALL. This type of leukemia affects boys more than girls and generally affects older children more than does B-cell ALL. It often causes an enlarged thymus (a small organ in front of the windpipe), which can sometimes cause breathing problems. It may also spread to the cerebrospinal fluid (the fluid that surrounds the brain and spinal cord) early in the course of the disease.

Aside from the subtype of ALL, other factors are important in determining outlook (prognosis). These are described in the section “Prognostic factors in childhood leukemia.”

Acute myelogenous leukemia (AML)

Acute myelogenous leukemia (AML) is typically a fast-growing cancer of one of the following types of early (immature) bone marrow cells:

- **Myeloblasts:** These cells normally form white blood cells called *granulocytes* (neutrophils, eosinophils, and basophils).
- **Monoblasts:** These cells normally become white blood cells called monocytes and macrophages.

- **Erythroblasts:** These cells mature into red blood cells.
- **Megakaryoblasts:** These cells normally become megakaryocytes, the cells that make platelets.

Two systems have been used to classify AML into subtypes – the French-American-British (FAB) classification and the newer World Health Organization (WHO) classification.

French-American-British (FAB) classification of AML

The older FAB system divides AML into subtypes based on the type of cell involved and how mature it is. In this system, the subtypes of AML are classified mainly based on their morphology (how they look under the microscope) using routine and cytochemical stains. There are 8 subtypes of AML: M0 to M7 (the M refers to myeloid).

- **M0:** This subtype of AML is made up of very immature cells – so immature that they can't be labeled according to the types of cells listed above. This subtype can only be distinguished from ALL by flow cytometry, because the cells lack any distinct features that can be seen by microscope. (Flow cytometry is explained in the section, "How is childhood leukemia diagnosed?") This type of leukemia is very rare in children.
- **M1:** This subtype is made up of immature myeloblasts. It can be recognized by the way the cells look under the microscope after using cytochemical stains.
- **M2:** This subtype is composed of slightly more mature forms of myeloblasts. It is the most common subtype of AML in children, making up a little more than 1 out of every 4 cases.
- **M3:** The M3 subtype is also known as *acute promyelocytic leukemia (APL)*. It is made up of promyelocytes, which are a more mature form of myeloblast. Treatment of APL is different than for other subtypes of AML, as it involves some newer drugs.
- **M4:** This subtype is known as *acute myelomonocytic leukemia*. The cells are an early form of monoblast. The M4 subtype is more common in children less than 2 years of age.
- **M5:** This is known as *acute monocytic leukemia*. It is made up of monoblasts. Like the M4 subtype, it is more common in children less than 2 years of age.
- **M6:** This subtype of AML is known as *acute erythroblastic leukemia* (or *acute erythroleukemia*). It starts in erythroblasts, the cells that normally mature into red blood cells. It is very rare in children.
- **M7:** This subtype is also known as *acute megakaryoblastic leukemia*. The cells are megakaryoblasts, which normally mature into megakaryocytes (the cells that make platelets).

World Health Organization (WHO) classification of AML

The FAB classification system is useful and is still commonly used to group AML into subtypes. But it doesn't take into account many other prognostic factors that doctors have learned about in recent years, such as chromosome changes in the leukemia cells. The newer WHO system includes some of these factors to try to help better classify cases of AML based on a person's outlook. Not all doctors use this new system.

The WHO system divides AML into several broad groups:

AML with certain genetic abnormalities

- AML with a translocation between chromosomes 8 and 21
- AML with a translocation or inversion in chromosome 16
- AML with changes in chromosome 11
- APL (M3), which usually has translocation between chromosomes 15 and 17

AML with multilineage dysplasia (more than one abnormal myeloid cell type is involved)

AML related to previous chemotherapy or radiation

AML not otherwise specified (includes cases of AML that don't fall into one of the above groups; similar to the FAB classification)

- Undifferentiated AML (M0)
- AML with minimal maturation (M1)
- AML with maturation (M2)
- Acute myelomonocytic leukemia (M4)
- Acute monocytic leukemia (M5)
- Acute erythroid leukemia (M6)
- Acute megakaryoblastic leukemia (M7)
- Acute basophilic leukemia
- Acute panmyelosis with fibrosis
- Myeloid sarcoma (also known as granulocytic sarcoma or chloroma)

Hybrid or mixed lineage leukemias

These leukemias have cells with features of both ALL and AML when they are subjected to lab tests. In children, these leukemias are generally treated like ALL and respond to treatment like ALL.

Chronic myelogenous leukemia (CML)

Chronic myelogenous leukemia (CML) is typically a slower-growing cancer of early (immature) myeloid bone marrow cells. CML is not common in children, but it can occur.

The course of CML is divided into 3 phases, based mainly on the number of immature white blood cells – myeloblasts ("blasts") – that are seen in the blood or bone marrow. Different groups of experts have suggested slightly different cutoffs to define the phases, but a common system (proposed by the World Health Organization) is described below.

If the leukemia is not cured with treatment, it can progress to more advanced phases over time.

Chronic phase

This is the earliest phase, in which patients typically have less than 10% blasts in their blood or bone marrow samples. These children usually have fairly mild symptoms (if any), and the leukemia usually responds well to standard treatments. Most patients are in the chronic phase when they are diagnosed.

Accelerated phase

Patients are considered to be in accelerated phase if bone marrow or blood samples have more than 10% but fewer than 20% blasts, or if levels of certain other blood cells are too high or too low.

Children whose CML is in accelerated phase may have symptoms such as fever, poor appetite, and weight loss. CML in the accelerated phase might not respond as well to treatment as CML in the chronic phase.

Blast phase (also called acute phase or blast crisis)

Bone marrow and/or blood samples from a patient in this phase have more than 20% blasts. The blast cells often spread to tissues and organs beyond the bone marrow. These children often have fever, poor appetite, and weight loss. At this point the CML acts much like an aggressive acute leukemia (AML or, less often, ALL).

Not all doctors may agree with or follow these cutoff points for the different phases. If you have questions about what phase your child's CML is in, be sure to have the doctor explain it to you.

Prognostic factors in childhood leukemia (ALL or AML)

Certain differences among patients that affect the leukemia's response to treatment are called *prognostic factors*. They help doctors decide whether a child with leukemia should receive standard treatment or more intensive treatment. Prognostic factors seem to be more important in acute lymphocytic leukemia (ALL) than in acute myelogenous leukemia (AML).

Prognostic factors for children with ALL

Different systems are used to classify childhood ALL risk. In one of the more common systems, children with ALL are divided into standard-risk, high-risk, or very high-risk groups, with more intensive treatment given for higher risk patients. Generally, children at low risk have a better outlook than those at very high risk.

While all of the following are prognostic factors, only certain ones are used to determine which risk group a child falls into. (The first 2 factors – age at diagnosis and initial white blood cell count – are generally considered the most important.) It's important to know that even children with some poor prognostic factors can often still be cured.

Age at diagnosis: Children between the ages of 1 and 9 with B-cell ALL tend to have better cure rates. Children younger than 1 year and children 10 years or older are considered high-risk patients. The outlook in T-cell ALL isn't affected much by age.

White blood cell (WBC) count: Children with ALL who have especially high WBC counts (greater than 50,000 cells per cubic millimeter) when they are diagnosed are classified as high risk and need more intensive treatment.

Subtype of ALL: Children with pre-B or early pre-B-cell ALL generally do better than those with mature B-cell (Burkitt) leukemia. The outlook for T-cell ALL seems to be about the same as that for B-cell ALL as long as treatment is intense enough.

Gender: Girls with ALL may have a slightly higher chance of being cured than boys. As treatments have improved in recent years, this difference has shrunk.

Race/ethnicity: African-American and Hispanic children with ALL tend to have a lower cure rate than children of other races.

Spread to certain organs: Spread of the leukemia into the cerebrospinal fluid, or the testicles in boys, increases the chance of a poor outcome. Enlargement of the spleen and liver is usually linked to a high WBC count, but some doctors view this as a separate sign that the outlook is not as favorable.

Number of chromosomes: Patients are more likely to be cured if their leukemia cells have more than 50 chromosomes (called *hyperdiploidy*), especially if there is an extra chromosome 4, 10, or 17. Hyperdiploidy can also be expressed as a "DNA index" of more than 1.16. Children whose leukemia cells have fewer chromosomes than the normal 46 (known as *hypodiploidy*) have a less favorable outlook.

Chromosome translocations: Translocations result when genetic material (DNA) is swapped between chromosomes. Children whose leukemia cells have a translocation between chromosomes 12 and 21 are more likely to be cured. Those with a translocation between chromosomes 9 and 22 (the Philadelphia chromosome), 1 and 19, or 4 and 11 tend to have a less favorable prognosis. Some of these "poor" prognostic factors have become less important in recent years as treatment has improved.

Response to treatment: Children whose leukemia responds completely (major reduction of cancer cells in the bone marrow) within 1 to 2 weeks of chemotherapy have a better outlook than those whose leukemia does not. Children whose cancer does not respond as well may be given more intensive chemotherapy.

Prognostic factors for children with AML

Prognostic factors are not quite as important in predicting outcome or in altering treatment for AML patients as they are for ALL.

Age at diagnosis: Children younger than age 2 with AML seem to do better than older children (especially teens), although age is not thought to have a strong effect on outlook.

White blood cell (WBC) count: Children with AML whose WBC count is less than 100,000 cells per cubic millimeter at diagnosis are cured more often than those with higher counts.

Down syndrome: Children with Down syndrome who develop AML tend to have a good outlook, especially if the child is 4 years old or younger at the time of diagnosis.

Body weight: Children within the normal weight range tend to do better than children who are underweight or overweight.

Subtype of AML: Some subtypes of AML tend to have a better outlook than others. For example, the acute promyelocytic leukemia (APL) M3 subtype tends to have a good outlook, while undifferentiated AML (M0) and acute megakaryoblastic leukemia (M7) are harder to treat effectively.

Cytogenetics: Children with leukemia cell translocations between chromosomes 15 and 17 (seen in most cases of APL) or between 8 and 21, or with an inversion (rearrangement) of chromosome 16 have a better chance of being cured. Children whose leukemia cells have a chromosomal defect known as *monosomy* 7 have a poorer prognosis. Monosomy 7 means that the leukemia cells have lost one of the copies of chromosome 7.

Myelodysplastic syndrome or secondary AML: Children who first have myelodysplastic syndrome ("smoldering leukemia") or whose leukemia is the result of treatment for another cancer tend to have a less favorable prognosis.

Response to treatment: Children whose leukemia responds quickly to treatment (only one chemotherapy cycle needed to achieve remission) are more likely to be cured than those whose leukemia takes longer to respond or does not respond at all.

Status of acute leukemia after treatment

How well ALL or AML responds to the initial (induction) treatment has an effect on long-term prognosis.

A *remission (complete remission)* is usually defined as having no evidence of leukemia after the 4 to 6 weeks of induction treatment. This means the bone marrow contains fewer than 5% blast cells, the blood cell counts are within normal limits, and there are no signs or symptoms of the disease. A *molecular complete remission* means there is no evidence of leukemia cells in the bone marrow, even when using very sensitive lab tests, such as polymerase chain reaction (PCR). Even when leukemia is in remission, this does not always mean that it has been cured.

Minimal residual disease (MRD) is a term used after treatment when leukemia cells can't be found in the bone marrow using standard lab tests (such as looking at cells under a microscope), but they can still be detected with more sensitive tests (such as flow cytometry or PCR). Details of testing for MRD may vary based on the type of leukemia and other factors. In general, children with detectable MRD during or after induction chemotherapy are more likely to have their leukemia relapse (come back) and may require more intense treatment. Children with more MRD have a greater risk of relapse than those with less MRD.

Active disease means that either there is evidence that the leukemia is still present during treatment or that the disease has relapsed (come back) after treatment. For a patient to be relapsed, more than 5% of the marrow must be made up of blast cells.

Survival rates for childhood leukemias

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some parents may want to know the survival statistics for children in similar situations, while others may not find the numbers helpful, or may even not want to know them. If you would rather not read about the survival rates, skip to the next section, "How is childhood leukemia treated?"

The 5-year survival rate refers to the percentage of patients who live *at least* 5 years after their cancer is diagnosed. With acute leukemias, children who are free of the disease after 5 years are very likely to have been cured, because it very rare for these cancers to return after such a period of time. Current 5-year survival rates are based on children first diagnosed and treated more than 5 years ago. Improvements in treatment since then may result in a more favorable outlook for children diagnosed recently.

The 5-year survival rate for children with ALL has greatly increased over time and is now more than 85% overall.

The overall 5-year survival rate for children with AML has also increased over time, and is now in the range of 60% to 70%. However, survival rates can vary depending on the subtype of AML. For example, most studies suggest that the cure rate for acute

promyelocytic leukemia (APL), a subtype of AML, is now higher than 80%, but rates are lower for some other subtypes of AML.

Accurate survival rates for less common forms of childhood leukemia are harder to find. For juvenile myelomonocytic leukemia (JMML), 5-year survival rates of about 50% have been reported.

For chronic leukemias, which are rare in children, 5-year survival rates are less helpful, because some children may live for a long time with the leukemia without actually being cured. In the past, 5-year survival rates for chronic myelogenous leukemia (CML) were reported to be in the range of 60% to 80%. With newer, more effective medicines developed for CML in recent years, survival rates are likely to be higher now, although these new drugs have not been in use long enough to be sure.

Survival rates are often based on previous outcomes of large numbers of children who had the disease, but they cannot predict what will happen in any particular child's case. Knowing the type of leukemia is important in estimating a child's outlook. But a number of other factors, including the child's age and leukemia characteristics, can also affect outlook. Many of these factors are discussed in the section, "Prognostic factors in childhood leukemia (ALL or AML)." Even when taking these other factors into account, survival rates are at best rough estimates. Your child's doctor is likely to be a good source as to whether these numbers may apply to your child, as he or she knows your situation best.

How is childhood leukemia treated?

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

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

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

Making treatment decisions

Children and teens with leukemia 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 leukemias, 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 nurse practitioners,

nurses, psychologists, social workers, rehabilitation specialists, and other health professionals.

After leukemia is diagnosed and tests have been done to determine its type, your child's cancer care team will discuss the treatment options with you. The most important factor in choosing a treatment is the type of leukemia, but other factors also play a role.

The main treatment for childhood leukemia is chemotherapy. For some children with higher risk leukemias, high-dose chemotherapy may be given along with a stem cell transplant. Other treatments such as targeted drugs, surgery, and radiation therapy may be used in special circumstances.

Treatment of acute forms of childhood leukemia (lymphocytic and myeloid) is usually very intensive, so it is important that it takes place in a center that specializes in treating childhood cancers. Your child's doctor should make sure that treatment reflects your child's risk group (based on certain prognostic factors) and that he or she will be treated according to a protocol or guidelines of the National Cancer Institute or a cooperative study group. This will ensure the most up-to-date treatment.

It's important to ask the cancer care team about any side effects your child might develop as a result of the treatment. They can tell you about common side effects, how long they might last, and how serious they might be.

It's also important that you tell your child's doctors about any drugs, herbal remedies, or other alternative medicines you might be giving your child so that the doctors can determine if they might affect standard treatments.

The next few sections have general comments about types of treatments used for childhood leukemia. This is followed by a discussion of the typical treatment approaches based on the type of leukemia.

Immediate treatment for childhood leukemia

Some children with leukemia are critically ill when they are first diagnosed with leukemia. For example:

- A shortage of normal white blood cells might lead to very serious infections.
- Low levels of platelets or clotting factors in the blood can cause severe bleeding.
- Not having enough red blood cells can lower the amount of oxygen getting to body tissues and put a tremendous strain on the heart.

These problems must often be addressed before treatment of the leukemia can begin. Antibiotics, blood growth factors, and transfusions of platelets and red blood cells may be given to treat or help prevent some of these conditions.

Surgery for childhood leukemia

Surgery has a very limited role in treating childhood leukemia. Because leukemia cells spread throughout the bone marrow and to many other organs through the blood, it's not possible to cure this type of cancer by surgery. Aside from a possible lymph node biopsy, surgery rarely has any role even in the diagnosis, since a bone marrow aspirate and biopsy can usually diagnose leukemia.

Often before chemotherapy is about to start, surgery is needed to insert a small plastic tube, called a *central venous catheter* or *venous access device* (VAD), into a large blood vessel. 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 chemotherapy and to take blood samples. This lowers the number of needle sticks needed during treatment. It's very important for parents to learn how to care for the catheter to keep it from getting infected.

In cases where a boy with leukemia has a relapse of the disease in a testicle, surgery may sometimes be done to remove the testicle (along with giving chemotherapy to treat the rest of the body).

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

Radiation therapy for childhood leukemia

Radiation therapy uses high-energy radiation to kill cancer cells. Radiation is sometimes used to try to prevent or treat the spread of leukemia to the brain or the testicles.

Radiation is also used (rarely) to treat a tumor that is compressing the trachea (windpipe). But chemotherapy is often used instead, as it may work more quickly.

Radiation to the whole body is often an important part of treatment before a bone marrow or peripheral blood stem cell transplant (see the section, "High-dose chemotherapy and stem cell transplant").

External beam radiation therapy, in which a machine delivers a beam of radiation to a specific part of the body, is the type of radiation used most often for childhood leukemia. Before treatment starts, the radiation team will take careful body 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 more intense. It is painless, but some younger children may need to be sedated to 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.

Possible side effects of radiation

The possible short-term side effects depend on where the radiation is aimed. Sunburn-like skin changes and hair loss in the treated area are possible. Radiation to the abdomen can sometimes cause nausea, vomiting, or diarrhea. For radiation that includes large parts of the body, the effects may include fatigue and an increased risk of infection.

Longer-term side effects are also possible and are described in the section “What happens after treatment for childhood leukemia?”

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

Chemotherapy for childhood leukemia

Chemotherapy (chemo) is treatment with anti-cancer drugs that are given into a vein, into a muscle, into the cerebrospinal fluid (CSF), or taken as pills. Except when given into the CSF, these drugs enter the bloodstream and reach all areas of the body, making this treatment useful for cancers such as leukemia.

The treatment of leukemia uses combinations of several chemo drugs. Doctors give chemo in cycles, with each period of treatment followed by a rest period to give the body time to recover. In general, treatment for acute myeloid leukemia (AML) uses higher doses of chemo over a shorter period of time, and acute lymphocytic leukemia (ALL) treatment uses lower doses of chemo over a longer period of time (usually 2 to 3 years).

Some of the drugs commonly used to treat childhood leukemia include:

- Vincristine (Oncovin)
- Daunorubicin, also known as daunomycin (Cerubidine)
- Doxorubicin (Adriamycin)
- Cytarabine, also known as cytosine arabinoside or ara-C (Cytosar)
- L-asparaginase (Elspar), PEG-L-asparaginase (pegaspargase, Oncaspar)
- Etoposide (VePesid, others)
- Teniposide (Vumon)
- 6-mercaptopurine (Purinethol)
- 6-thioguanine
- Methotrexate
- Mitoxantrone

- Cyclophosphamide (Cytoxan)
- Prednisone
- Dexamethasone (Decadron, others)

Children will probably get several of these drugs at different times during the course of treatment, but they do not get all of them.

If you'd like more information on a drug used in your child's treatment or a specific drug mentioned in this section, see our Guide to Cancer Drugs, or call us with the names of the medicines your child is taking.

Possible 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 the length of time they are taken. These side effects may include:

- Hair loss
- Mouth sores
- Loss of appetite
- Diarrhea
- Nausea and vomiting
- Increased risk of infections (because of low white blood cell counts)
- Bruising and bleeding easily (from low platelet counts)
- Fatigue (caused by low red blood cell counts)

The problems with blood cell counts are often caused by the leukemia itself at first. They might get worse during the first part of treatment because of the chemotherapy, but they will probably improve as the leukemia cells are killed off and the normal cells in the bone marrow recover.

The side effects above are usually short-term and go away when treatment is finished. There are often ways to reduce these side effects. For instance, drugs can be given to help prevent or reduce nausea and vomiting. Other drugs known as growth factors can be given to help keep the blood cell counts higher.

Tumor lysis syndrome is another possible side effect of chemotherapy. It can happen in patients who had large numbers of leukemia cells in the body before treatment. 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 affect the heart and nervous system. This problem can be prevented by making sure the child gets lots of fluids during treatment and by giving certain drugs, such as bicarbonate, allopurinol, and rasburicase, which help the body get rid of these substances.

Some chemo drugs can also have specific side effects that are not listed above. 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 these side effects.

Chemotherapy given directly into the cerebrospinal fluid (CSF) around the brain and spinal cord (known as *intrathecal chemotherapy*) can have its own side effects, although these are not common. Intrathecal chemo may cause trouble thinking or even seizures in some children.

Long-term side effects of chemotherapy are also possible. These are discussed in the section, "What happens after treatment for childhood leukemia?"

.For more information on chemotherapy, see our document *Understanding Chemotherapy: A Guide for Patients and Families*.

Targeted therapy for childhood leukemia

In recent years, new drugs that target specific parts of cancer cells have been developed. These targeted 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 may be useful in certain cases of childhood leukemia.

For instance, drugs such as imatinib (Gleevec) and dasatinib (Sprycel) specifically attack cells that have the Philadelphia chromosome (a shortened chromosome 22 that results from a translocation with chromosome 9).

Nearly all children with chronic myeloid leukemia (CML) have this abnormal chromosome in their leukemia cells. These drugs are very effective at controlling the leukemia for long periods of time in most of these children, although it's not yet clear if the drugs can help cure CML.

A small number of children with acute lymphocytic leukemia (ALL) also have the Philadelphia chromosome in their leukemia cells. Studies have shown that the outcome is improved when these drugs are combined with chemotherapy drugs.

These drugs are taken daily as pills. Possible side effects include diarrhea, nausea, muscle pain, fatigue, and skin rashes. These are generally mild. A common side effect is swelling around the eyes or in the hands or feet. Some studies suggest this fluid buildup may be caused by the drugs' effects on the heart. Other possible side effects include lower red

blood cell and platelet counts at the start of treatment. These drugs might also slow a child's growth, especially if used before puberty.

Other targeted drugs are now being tested in clinical trials as well.

For more general information on targeted drugs, see our document *Targeted Therapy*. If you'd like more information on a drug used in your child's treatment or a specific drug mentioned in this section, see our Guide to Cancer Drugs, or call us with the names of the medicines your child is taking.

High-dose chemotherapy and stem cell transplant for childhood leukemia

A stem cell transplant (SCT) can sometimes be used for children whose chances of being cured are poor with standard or even intensive chemotherapy. SCT lets doctors use even higher doses of chemotherapy than would normally be tolerated.

High-dose chemotherapy destroys the bone marrow, which is where new blood cells are formed. This could lead to life-threatening infections, bleeding, and other problems caused by low blood cell counts. A stem cell transplant is given after the chemo to restore the blood-forming stem cells in the bone marrow.

The stem cells used for a transplant come either from the blood (for a peripheral blood stem cell transplant [PBSCT] or an umbilical cord blood transplant) or from the bone marrow (for a bone marrow transplant, or BMT). Bone marrow transplants were more common in the past, but they have largely been replaced by PBSCT and cord blood transplants.

Types of transplants

The 2 main types of stem cell transplants are allogeneic and autologous.

Allogeneic stem cell transplant: For childhood leukemia, the blood-forming stem cells are donated from another person. This is called an *allogeneic transplant*.

The donor's tissue type (also known as the HLA type) should match the patient's tissue type as closely as possible to help prevent the risk of major problems with the transplant. Tissue type is based on certain substances on the surface of cells in the body. These substances can cause the immune system to react against the cells. Therefore, the closer the tissue match between the donor and the recipient, the better the chance the transplanted cells will "take" and begin making new blood cells.

The donor is usually a brother or sister with the same tissue type as the patient. Rarely, it can be an HLA-matched, unrelated donor – a stranger who has volunteered to donate blood-forming stem cells. Sometimes umbilical cord stem cells are used. These stem cells come from blood drained from the umbilical cord and placenta after a baby is born and the umbilical cord is cut. (This blood is rich in stem cells.) Whatever their source, the stem cells are then frozen and stored until they are needed for the transplant.

Autologous stem cell transplant: In an autologous transplant, the patient's own stem cells are removed from his or her bone marrow (bone marrow stem cells) or bloodstream (peripheral blood stem cells, PBSCs). This type of transplant is not used for childhood leukemia, because the risk that the leukemia will come back (relapse) after treatment is greater than with an allogeneic transplant.

When stem cell transplant (SCT) might be used

SCT might be used for a child with ALL whose leukemia doesn't respond well to initial treatment or relapses early after going into remission. It is less clear if SCT should be used for children whose ALL relapses more than 6 months after finishing the initial chemotherapy. These children will often do well with another round of standard dose chemotherapy. SCT may also be recommended for children with some less common forms of ALL, such as those whose leukemias have the Philadelphia chromosome or those with T-cell ALL that doesn't respond well to initial treatment.

Because AML relapses more often than ALL, many doctors recommend SCT for children with AML right after they have gone into remission, if the child has a brother or sister with the same tissue type who can donate stem cells for the transplant. This is especially true if there is a very high risk of relapse (as seen with some subtypes of AML or when there are certain chromosome changes in the cells). There is still some debate about which children with AML need this type of intensive treatment. If a child with AML relapses after his or her first round of standard chemotherapy, most doctors will recommend SCT as soon as the child goes into remission again. In either case, it is important that the leukemia is in remission before getting a stem cell transplant. Otherwise, the leukemia is more likely to return.

SCT might also offer the best chance to cure some less common types of childhood leukemia, such as juvenile myelomonocytic leukemia (JMML) and CML. For CML, newer targeted therapies are likely to be used first for most children, but a transplant might still be needed at some point.

How a stem cell transplant (SCT) is done

A stem cell transplant is a complex treatment that can cause life-threatening side effects. If the doctors think your child can 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.

Typically, the child is admitted to the stem cell transplant unit of the hospital on the day before the treatment 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.) These treatments are meant to destroy any remaining leukemia cells. But they also kill the normal cells in the bone marrow.

After treatment, the frozen stem cells are thawed and given as a blood transfusion. The stem cells settle into the child's bone marrow over the next several days. Usually within a couple of weeks, 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 the hospital in protective isolation (guarding against exposure to germs) until 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 take longer to return to a safe level, they 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.

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

Possible side effects of stem cell transplant (SCT)

The possible side effects from SCT are generally divided into short and long-term effects.

Short-term side effects

The early complications and side effects are basically 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 an increased risk 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 from happening. Other side

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

Long-term and late side effects

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

- Graft-versus-host disease (see below)
- Radiation damage to the 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

Graft-versus-host disease (GVHD) is one of the most serious complications of allogeneic (donor) stem cell transplants. This happens when the donor immune system cells attack tissues of the patient's own cells.

The areas most often affected include the skin, liver, and digestive tract, but other areas may be affected as well. GVHD can be acute or chronic, based on how soon after the transplant it begins. In severe cases, GVHD can be life-threatening. Drugs that weaken the immune system are often given as a part of the transplant to try to prevent GVHD, although they can have their own side effects.

The most common symptoms of GVHD are severe skin rashes and severe diarrhea. If the liver is affected, the damage can lead to jaundice (yellowing of the skin and eyes) or even liver failure. GVHD can also cause lung damage, leading to problems breathing. The patient may feel weak, become tired easily, and have nausea, dry mouth, and muscle aches.

On the good side, graft-versus-host disease can lead to graft-versus-leukemia activity, in which any remaining leukemia cells may be killed by the donor immune cells.

Be sure to talk to your child's doctor before the transplant to learn about possible long-term effects your child might have. More information on long-term effects can be found in the section, "What happens after treatment for childhood leukemia?"

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

Clinical trials for childhood leukemia

You may have had to make a lot of decisions since you've been told your child has leukemia. One of the most important decisions you will make is choosing which treatment is best for your child. You may have heard about clinical trials being done for

this type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

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

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

If you would like your child to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. Children's cancer centers often conduct many clinical trials at any one time, and most children treated at these centers take part in a clinical trial as part of their treatment.

You can also call our clinical trials matching service for a list of clinical trials that meet your child's medical needs. You can reach this service at 1-800-303-5691 or on our website at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials website at www.cancer.gov/clinicaltrials.

Your child will have to meet certain requirements to take part in any clinical trial. If your infant or young child does qualify for a clinical trial, you will have to decide whether or not to enter (enroll) the child into it. Older children, who can understand more, usually must also agree to take part in the clinical trial before the parents' consent is accepted.

You can get a lot more information on clinical trials in our document *Clinical Trials: What You Need to Know*. You can read it on our website or call our toll-free number (1-800-227-2345) to have it sent to you.

Complementary and alternative therapies for childhood leukemia

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

What exactly are complementary and alternative therapies?

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

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

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

Finding out more

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

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

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

The choice is yours

You always have a say in how your child is treated. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help your child while avoiding those that could be harmful.

Treatment of children with acute lymphocytic leukemia

The main treatment for children with acute lymphocytic leukemia (ALL) is chemotherapy, which is usually divided into 3 phases:

- Induction

- Consolidation (also called intensification)
- Maintenance

When leukemia is diagnosed, there are usually about 100 billion leukemia cells in the body. Killing 99.9% of these leukemia cells during the 1-month induction treatment is enough to achieve a remission, but it still leaves about 100 million leukemia cells in the body. These also must be destroyed. An intensive 1- to 2-month program of consolidation treatment and about 2 years of maintenance chemotherapy helps destroy the remaining cancer cells.

As mentioned earlier, children with ALL are typically divided into standard-risk, high-risk, or very high-risk groups to make sure that the correct types and doses of drugs are given. Treatment may be more or less intense, depending on the risk group.

Induction

The goal of induction chemotherapy is to achieve a *remission*. This means that leukemia cells are no longer found in bone marrow samples, the normal marrow cells return, and the blood counts become normal. (A remission is not necessarily a cure.)

More than 95% of children with ALL enter remission after 1 month of induction treatment. This first month is intense and requires frequent visits to the doctor. Your child may spend some or much of this time in the hospital, because serious infections or other complications can occur. It is very important to take all medicines as prescribed. Sometimes complications can be serious enough to be life-threatening, but in recent years, advances in supportive care (nursing care, nutrition, antibiotics, red blood cell and platelet transfusions as needed, etc.) have made these much less common than in the past.

Children with standard-risk ALL often receive 3 drugs for the first month of treatment. These include the chemotherapy drugs L-asparaginase and vincristine, and a steroid drug (usually dexamethasone). A fourth drug in the anthracycline class (daunorubicin is the one most often used) is typically added for high-risk children. Other drugs that may be given early are methotrexate and/or 6-mercaptopurine.

Intrathecal chemotherapy: All children also need chemotherapy into the cerebrospinal fluid (CSF) to kill any leukemia cells that might have spread to the brain and spinal cord. This treatment, known as *intrathecal* chemotherapy, is given through a lumbar puncture (spinal tap). It is usually given twice (more often if the leukemia is high risk) during the first month and 4 to 6 times during the next 1 or 2 months. It is then repeated less often during the rest of consolidation and maintenance. Usually, methotrexate is the drug used for intrathecal chemotherapy. Hydrocortisone (a steroid) and cytarabine (ara-C) may be added, particularly in high-risk children.

Along with intrathecal therapy, some high-risk patients (for example, those with T-cell ALL) and those with high numbers of leukemia cells detected in their CSF when the leukemia is diagnosed may be given radiation therapy to the brain. This was more common in the past, but recent studies have found that many children even with high-risk ALL may not need radiation therapy if they are given more intensive chemotherapy.

Doctors try to avoid giving radiation to the brain if possible, especially in younger children, because no matter how low the dose is kept, it can cause problems with thinking and growth and development.

A possible side effect of intrathecal chemotherapy is seizures during treatment, which happen in a small percentage of children. Children who develop seizures are treated with drugs to prevent them.

Consolidation (intensification)

The next, and usually more intense, consolidation phase of chemotherapy typically lasts about 1 to 2 months. This phase reduces the number of leukemia cells still in the body. Several chemo drugs are combined to help prevent the remaining leukemia cells from developing resistance. Intrathecal therapy (as described above) is continued at this time.

Children with standard-risk ALL are usually treated with drugs such as methotrexate and 6-mercaptopurine or 6-thioguanine, but regimens differ among cancer centers. Vincristine, L-asparaginase, and/or prednisone may also be added.

Children with high-risk leukemia generally receive more intense chemotherapy. Extra drugs such as L-asparaginase, doxorubicin (Adriamycin), etoposide, cyclophosphamide, and cytarabine (ara-C) are often used, and dexamethasone is substituted for prednisone. There may be a second round of intense chemotherapy with the same drugs.

Children with Philadelphia chromosome-positive ALL may benefit from the addition of a targeted drug such as imatinib (Gleevec) or from a stem cell transplant at this time.

Maintenance

If the leukemia remains in remission after induction and consolidation, maintenance therapy can begin. Most treatment plans use daily 6-mercaptopurine and weekly methotrexate, given as pills, often along with vincristine, which is given intravenously, and a steroid (prednisone or dexamethasone). These latter 2 drugs are given for brief periods every 4 to 8 weeks. Other drugs may be added depending on the type of ALL and the risk of recurrence.

During the first few months of maintenance, most treatments include 1 or 2 repeat intensified treatments similar to the initial induction. These 4-week intensifications are called *re-induction* or *delayed intensification*.

Some leukemia patients at higher risk may receive more intense maintenance chemotherapy and intrathecal therapy.

The total duration of therapy (induction, consolidation, and maintenance) for most ALL treatment plans is 2 to 3 years. Because boys are at higher risk for relapse than girls, many doctors favor giving them several more months of treatment.

Treatment of residual disease

These treatment plans may change if the leukemia doesn't go into remission during induction or consolidation. The doctor will probably check the child's bone marrow soon after treatment starts to see if the leukemia is going away. If not, treatment may be intensified or prolonged.

If the leukemia seems to have gone away by standard lab tests, the doctor may do more sensitive tests to look for small numbers of leukemia cells that may remain. If any are found, then chemotherapy again may be intensified or prolonged.

Treatment of recurrent ALL

If the ALL recurs (comes back) at some point during or after treatment, the child will most likely be treated again with chemotherapy. Much of the treatment strategy depends on how soon the leukemia returns after the first treatment. If the relapse occurs after a long time-interval, the same drugs may still be effective, so the same or similar treatment may be used to try to get the leukemia into a second remission.

If the time interval is shorter, more aggressive chemotherapy with other drugs may be needed. The most commonly used chemo drugs are vincristine, L-asparaginase, anthracyclines (doxorubicin, daunorubicin, mitoxantrone), cyclophosphamide, cytarabine (ara-C), and epipodophyllotoxins (etoposide, teniposide). The child will also receive a steroid (prednisone or dexamethasone). Intrathecal chemotherapy will also be given.

For children whose leukemia comes back within 6 months of starting treatment or for children with T-cell ALL who relapse, a stem cell transplant may be considered, especially if there is a brother or sister who is a good tissue type match. Stem cell transplants may also be used for other children who relapse after a second course of chemotherapy.

Some children have an *extramedullary relapse*, meaning that leukemia cells are found in one part of the body (such as the cerebrospinal fluid [CSF] or the testicles) but are not detectable in the bone marrow. In addition to intensive chemotherapy as described above, children with spread to the CSF may get more intense intrathecal chemotherapy, sometimes with radiation to the brain and spinal cord (if that area had not been already treated with radiation). Boys with relapse in a testicle may get radiation to the area, and in some cases may have the affected testicle removed by surgery.

Philadelphia chromosome-type ALL

For children with certain types of ALL, such as those with the Philadelphia chromosome or other high-risk genetic changes, standard chemotherapy for ALL (as outlined above) may not be as effective. A stem cell transplant may be advised if induction treatment yields a remission and a suitable stem cell donor is available.

Newer, targeted drugs such as imatinib (Gleevec) and dasatinib (Sprycel) are designed to kill leukemia cells that contain the Philadelphia chromosome. These drugs are taken as

pills and seem to have limited side effects. Adding these drugs to chemotherapy seems to help improve outcomes, according to studies done so far.

Treatment of children with acute myelogenous leukemia

Treatment of most children with acute myelogenous leukemia (AML) is divided into 2 phases of chemotherapy:

- Induction
- Consolidation (intensification)

Compared to treatment for ALL, the treatment for AML generally uses higher doses of chemotherapy but for a shorter time. Because of the intensity of treatment and the risk of serious complications, children with AML need to be treated in cancer centers or hospitals that have experience with this disease.

Treatment of the M3 subtype (acute promyelocytic leukemia, or APL) is slightly different, and is described in the next section.

Induction

Treatment for AML uses different combinations of drugs than those used for ALL. The drugs most often used are daunorubicin (daunomycin) and cytarabine (ara-C), which are each given for several days in a row. The schedule of treatment may be repeated in 10 days or 2 weeks, depending on how intense doctors want the treatment to be. A shorter time between treatments causes more severe side effects but may be more effective in killing leukemia cells.

If the doctors think that the leukemia might not respond to just 2 drugs alone, they may add etoposide and/or 6-thioguanine. Children with very high numbers of white blood cells or whose leukemia has certain chromosome abnormalities may fall into this group.

Treatment with these drugs is repeated until the bone marrow shows no more leukemia. This usually occurs after 2 or 3 cycles of treatment.

Preventing relapse in the central nervous system: In most cases, intrathecal chemotherapy (given directly into the cerebrospinal fluid, or CSF) is also given to help prevent leukemia from relapsing in the brain or spinal cord. Radiation therapy to the brain is used less often.

Consolidation (intensification)

About 85% to 90% of children with AML go into remission after induction therapy. This means no signs of leukemia are detected using standard lab tests, but it does not necessarily mean that the leukemia has been cured.

Consolidation (intensification) begins after the induction phase. The purpose is to kill any remaining leukemia cells by using more intensive treatment.

Some children have a brother or sister who would be a good stem cell donor. For these children, a stem cell transplant is often recommended once the leukemia is in remission, especially if the AML has some poorer prognostic factors. Most studies have found this improves the chance for long-term survival over chemotherapy alone, but it is also more likely to cause serious complications. For children with good prognostic factors, some doctors may recommend just giving intensive chemotherapy, and reserving the stem cell transplant in case the AML relapses.

For most children without a good stem cell donor, consolidation consists of the chemotherapy drug cytarabine (ara-C) in high doses. Daunorubicin may also be added. It is usually given for at least several months.

Intrathecal chemotherapy (into the cerebrospinal fluid) is usually given every 1 to 2 months for as long as intensification continues.

Maintenance chemotherapy is not needed for children with AML (other than those with APL, as described in the next section).

An important part of treatment for AML is supportive care (proper nursing care, nutritional support, antibiotics, and blood transfusions). The intensity of treatment needed for AML usually destroys much of the bone marrow (causing severe shortages of blood cells) and can cause other serious complications. Without antibiotic treatment of infections or transfusion support, the current high remission rates would not be possible.

Refractory or recurrent AML

Less than 15% of children have *refractory AML* (leukemia that does not respond to initial treatment). These leukemias are often very hard to cure, and doctors may recommend a stem cell transplant if it can be done.

Generally, the outlook for a child whose AML relapses (comes back) after treatment is slightly better than if a remission were never achieved, but this depends on how long the initial remission was. In more than half of cases of relapse, a second remission can be achieved with more chemotherapy. The chance of getting a second remission is better if the first remission lasted for at least a year, but long-term second remissions are rare without a stem cell transplant. Many different combinations of standard chemo drugs have been used in these situations, but the results have been mixed.

Most children whose leukemia has relapsed are good candidates for clinical trials testing new treatment regimens. The hope is that some sort of a remission can be attained so that a stem cell transplant can be considered. Some doctors may advise a stem cell transplant even if there is no remission. This can sometimes be successful.

Treatment of children with acute promyelocytic leukemia (APL)

Treatment of acute promyelocytic leukemia, or APL, the M3 subtype of acute myeloid leukemia (AML), differs from the usual AML treatment. This leukemia usually responds well to treatment.

Induction

Many children with APL have blood-clotting problems at the time APL is diagnosed, which can cause serious problems during early treatment. Because of this, children with APL must be treated carefully and are often given an anticoagulant ("blood thinner") to help prevent or treat this.

Children with APL get a non-chemotherapy drug similar to vitamin A called *all*-trans retinoic acid (ATRA). A remission can often be induced with ATRA alone, but combining it with chemotherapy (usually daunorubicin and cytarabine) gives better long-term results. APL rarely spreads to the brain or spinal cord, so intrathecal chemotherapy is usually not needed.

Along with the possible side effects from the chemotherapy drugs, ATRA can cause a problem called *retinoic acid syndrome*. This can include breathing problems from fluid buildup in the lungs, low blood pressure, kidney damage, and severe fluid buildup elsewhere in the body. It can often be treated by stopping the ATRA for a while and giving a steroid such as dexamethasone.

Consolidation (intensification)

This is usually similar to induction, using both ATRA and chemotherapy (daunorubicin, sometimes along with cytarabine). Because of the success of this treatment, a stem cell transplant is not usually advised as long as the leukemia stays in remission.

Maintenance

Children with APL may receive maintenance therapy with ATRA (often with the chemo drugs methotrexate and 6-mercaptopurine) for about a year.

Relapsed APL

If the leukemia comes back after treatment, most cases can be put into a second remission. Arsenic trioxide is a drug that is very effective in this setting, although it can sometimes cause problems with heart rhythms. Children getting this drug need to have their blood mineral levels watched closely. ATRA plus chemotherapy may be another option. A stem cell transplant may be considered once a second remission is achieved.

Treatment of children with juvenile myelomonocytic leukemia (JMML)

JMML is fairly rare, so it has been hard to study, and there is no single best chemotherapy treatment for this leukemia. An allogeneic stem cell transplant is the treatment of choice when possible, as it offers the best chance to cure JMML. About half of the children with JMML who get a stem cell transplant are still free of leukemia after several years. Sometimes, even if the leukemia recurs, a second stem cell transplant can be helpful.

Because JMML is hard to treat with current chemo drugs, taking part in a clinical trial looking at newer drugs may be a good option for children who cannot get a stem cell transplant.

Treatment of children with chronic myelogenous leukemia (CML)

This leukemia is rare in children, but it does occur. Treatment in children is similar to what is used for adults.

Targeted drugs, such as imatinib (Gleevec) and dasatinib (Sprycel), attack cells with the Philadelphia chromosome, which is the key gene abnormality in CML. These drugs are usually very effective at controlling CML, often for long periods of time and with less severe side effects than chemotherapy drugs. However, these drugs do not seem to cure CML when used alone, and they must be taken every day.

Imatinib is usually the drug tried first. If it does not work or if it becomes less effective over time, another drug may be tried. If targeted drugs are no longer helpful, high-dose chemotherapy with a stem cell transplant offers the best chance for a cure. Doctors are now studying whether adding targeted drugs to stem cell transplant regimens can help increase cure rates.

For more information on CML and its treatment, see our document, *Leukemia--Chronic Myeloid*.

More treatment information

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 treatment information by phone (1-800-4-CANCER) and on its website (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on 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 childhood leukemia?

It's important to have open, honest discussions with your child's cancer care team. They want to answer all of your questions, no matter how small they might seem. For instance, consider these questions:

- What kind of leukemia does my child have?
- Are there any specific factors that might affect my child's prognosis?
- Are there other tests that need to be done before we can decide on treatment?
- Are there other doctors we need to see?
- How much experience do you have treating this type of leukemia?
- Should we get a second opinion?
- What are our treatment choices?
- Should we consider a stem cell transplant? When?
- What do you recommend and why?
- What should we do to be ready for treatment?
- How long will treatment last? What will it be like?
- 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 recommend?
- 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?
- Will treatment affect my child's future ability to have children?
- What are the chances of curing the leukemia?
- What will our options be if the treatment doesn't work or if the leukemia comes back?

- What type of follow-up will we need after treatment?
- Can we talk to support groups or other families who have been through this?

In addition to these sample questions, be sure to write down your own. For instance, you might want more information about how treatment could affect your child's school schedule. Or you might want to ask if your child qualifies for any clinical trials. You may also want to ask about the typical costs of treatment, and what is likely to be covered by insurance.

What happens after treatment for childhood leukemia?

Following treatment for childhood leukemia, the main concerns for most families are the short- and long-term effects of the leukemia and its treatment, and concerns about the leukemia coming back.

It is certainly normal to want to put leukemia 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

For several years after treatment, regular follow-up exams will be very important. The doctors will watch for possible signs of leukemia, as well as for short-term and long-term side effects of treatment.

Checkups typically include careful physical exams, lab tests, and sometimes, imaging tests. These checkups will usually occur monthly during the first year, and then less often for at least 5 years after therapy. After that time, most children see their doctor at least yearly for a checkup.

If leukemia does recur, it is most often while the child is still being treated or within a year or so after finishing treatment. It is unusual for ALL or AML to return if there are no signs of the disease within the next 2 years.

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 may last for a few weeks to several months, but others can last a long time. It is important to report any new symptoms to the doctor right away, so that the cause can be found and treated, if needed.

Social and emotional issues during and after treatment of childhood leukemia

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 can 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 patients with leukemia may have programs to introduce new patients to children or teens who have finished their treatment. This can give patients an idea of what to expect during and after treatment, which can be very important.

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 leukemia. 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 leukemia returning or new health problems developing
- Feelings of resentment for having had leukemia 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 leukemia, but for many childhood leukemia 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.

Late and long-term effects of treatment of childhood leukemia

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

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

Childhood leukemia survivors are at risk, to some degree, for several possible late effects of their treatment. This risk depends on a number of factors, such as the type of leukemia, the type of treatments they received, dosages of cancer treatment, and age at the time of 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.

Children who have been treated for leukemia are at higher risk of developing other cancers later in life. One of the most serious possible side effects of acute lymphocytic leukemia (ALL) therapy is a small risk of getting acute myelogenous leukemia (AML) later on. This occurs in about 5% of patients after they have received chemotherapy drugs called *epipodophyllotoxins* (etoposide, teniposide) or *alkylating agents* (cyclophosphamide, chlorambucil). Of course, the risk of getting these second cancers must be balanced against the obvious benefit of treating a life-threatening disease such as leukemia with chemotherapy. For more information on second cancers, see our document, *Second Cancers Caused by Cancer Treatment*.

Late effects can also include heart or lung problems after receiving certain chemotherapy drugs or radiation therapy to these parts of the body. The risks of heart disease and stroke later in life are much higher among those treated for ALL as children, so careful follow-up is very important. ALL survivors are also more likely to be overweight and to have high blood pressure, which can contribute to these problems.

Treatment that includes radiation therapy to the brain may affect learning ability in some children, as might some types of chemotherapy. Because of this, doctors try to limit treatments that could affect the brain (including radiation) as much as possible.

Some survivors of childhood leukemia might have emotional or psychological problems. They also may have some problems with normal functioning and schoolwork. These can often be helped with support and encouragement.

Some cancer treatments may affect a child's growth, and they may end up a bit shorter as adults. This is especially true after stem cell transplants. This can be helped by treating survivors with growth hormone, if needed.

Cancer treatment may also affect sexual development and ability to have children in some cases. Talk to your child's cancer care team about the risks of infertility with treatment, and ask if there are options for preserving fertility, such as sperm banking. For more information, see our document, *Fertility and Women With Cancer* or *Fertility and Men With Cancer*.

Bone damage or osteoporosis (thinning of the bones) may result from the use of prednisone, dexamethasone, or other steroid drugs.

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

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.
- 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.

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

What's new in childhood leukemia research and treatment?

Researchers are now studying the causes, diagnosis, and treatment of leukemia at many medical centers, university hospitals, and other institutions.

Genetics

As noted in the section "Do we know what causes childhood leukemia?" scientists are making progress in understanding how changes in the DNA inside bone marrow stem cells can cause them to develop into leukemia cells. Understanding the gene changes (such as translocations or extra chromosomes) that occur in leukemia cells can help explain why these cells may grow out of control, and why they do not develop into normal, mature cells. Doctors are now looking to use these changes to help them determine a child's outlook and whether they should receive more or less intensive treatment.

This progress has already led to vastly improved and very sensitive tests for detecting leukemia cells in blood or bone marrow samples. The *polymerase chain reaction* (PCR) test, for example, can identify very small numbers of leukemia cells based on their gene translocations or rearrangements. This test is useful in determining how completely the leukemia has been destroyed by treatment, and whether a relapse will occur if further treatment is not given.

Clinical trials

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

- Why do some children with acute lymphocytic leukemia (ALL) relapse after treatment, and how can this be prevented?
- Are there other prognostic factors that will help identify which children need more or less intensive treatment?
- Can chemotherapy drug resistance in acute myelogenous leukemia (AML) be reversed?
- Are there better drugs or combinations of drugs for treating the different types of childhood leukemia?
- Can drugs, toxins, or radiation be specifically targeted to the leukemia cells by using man-made antibodies? Such antibodies can now be designed to specifically seek out leukemia cells, which are then destroyed by the drug, toxin, or radiation.
- Can natural immune proteins called *biologic response modifiers* help the body's immune system fight the leukemia cells?
- When exactly should a stem cell transplant be used to treat leukemia?
- How effective are stem cell transplants in children who don't have a brother or sister who is a good tissue type match?
- Can a second stem cell transplant help children who relapse after a first stem cell transplant?
- Can the outlook for children with ALL with the Philadelphia chromosome be improved by adding targeted drugs such as imatinib (Gleevec) or dasatinib (Sprycel) to chemotherapy? Early study results of this approach have been promising so far.
- What are the best treatment approaches for children with less common forms of leukemia, such as juvenile myelomonocytic leukemia (JMML) and chronic myeloid leukemia (CML)?

Recently, researchers have had some very early success in using a child's own immune system to fight leukemia. In a small number of children whose ALL was no longer responding to treatment, immune cells were removed from their blood and altered in the lab. They were then given back into the blood, whey they multiplied and attacked the leukemia cells. While the early results from this study are promising, more research is needed before this becomes a standard treatment.

Additional resources for childhood leukemia

More information from your American Cancer Society

Here is more information you might find helpful. You also can order free copies of our documents from our toll-free number, 1-800-227-2345, or read them on our website, www.cancer.org.

Children with cancer

Children Diagnosed With Cancer: Dealing with Diagnosis (also in Spanish)

Pediatric Cancer Centers (also in Spanish)

Children Diagnosed With Cancer: Understanding the Health Care System (also in Spanish)

Children Diagnosed With Cancer: Financial and Insurance Issues

Children Diagnosed With Cancer: Returning to School

Children Diagnosed With Cancer: Late Effects of Cancer Treatment

Health Professionals Associated With Cancer Care

Talking With Your Doctor (also in Spanish)

Coping with cancer

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

Family and Medical Leave Act (FMLA) (also in Spanish)

Nutrition for Children With Cancer (also in Spanish)

What Happened to You, Happened to Me (children's booklet)

When Your Brother or Sister Has Cancer (children's booklet)

When Your Child's Treatment Ends: A Guide for Families (booklet)

Cancer treatment information

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

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

Clinical Trials: What You Need to Know (also in Spanish)

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

Cancer treatment side effects

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

Nausea and Vomiting

Guide to Controlling Cancer Pain (also in Spanish)

Get Relief From Cancer Pain

Anemia in People With Cancer

Fatigue in People With Cancer

Fertility and Women With Cancer

Fertility and Men With Cancer

Second Cancers Caused by Cancer Treatment

Books

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

For family and friends of the child

American Cancer Society Complete Guide to Family Caregiving, Second Edition

Because... Someone I Love Has Cancer (kids' activity book)

For the child with cancer

Imagine What's Possible: Use the Power of Your Mind to Take Control of Your Life During Cancer (grades 4 through 6)

Let My Colors Out (picture book for children ages 5 to 10)

The Long and the Short of It: A Tale About Hair (ages 7 and up)

What's Up with Richard? Medikidz Explain Leukemia (graphic novel for pre-teens and teens)

National organizations and websites*

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

Websites for parents and adults

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.

Childhood Brain Tumor Foundation
Toll-free number: 1-877-217-4166
Website: www.childhoodbraintumor.org

> Though offered by the Childhood Brain Tumor Foundation, services are provided for children with ANY type cancer. Provides information and research options to families so that they may better exercise their rights in making decisions in the areas of medical treatment, schooling, rehabilitation, employment, and insurance reimbursement/coverage.

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 all forms of leukemia, 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)
TTY: 1-800-332-8615
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: 1-800-315-2580
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 4- to 18-year-old 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.*

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

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Last Medical Review: 10/24/2013
Last Revised: 2/3/2014

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