Childhood Leukemia

What is childhood leukemia?

Cancer starts when cells start to grow out of control. Cells in nearly any part of the body can become cancer. To learn more about how cancers start and spread, see *What Is Cancer?* For information about the differences between childhood cancers and adult cancers, see *Cancer in Children*.

Leukemia is a cancer that starts in early blood-forming cells found in the bone marrow, the soft inner part of certain bones. Most often, leukemia is a cancer of the white blood cells, but some leukemias start in other blood cell types.

Any of the blood-forming cells from the bone marrow can turn into a leukemia cell. Once this change takes place, the leukemia cells no longer mature in a normal way. Leukemia cells might reproduce quickly, and not die when they should. These cells build up in the bone marrow, crowding out normal cells. In most cases, the leukemia cells spill into the bloodstream fairly quickly. From there they 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 doing their jobs.

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 hip bones) 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.

Types of blood cells

Red blood cells carry oxygen from the lungs to all other tissues in the body, and take carbon dioxide back to the lungs to be removed. Having too few red blood cells in the body (*anemia*) can make you feel tired, weak, and short of breath because your body tissues are not getting enough oxygen.

Platelets are actually cell fragments made by a type of bone marrow cell called the *megakaryocyte*. Platelets are important in stopping bleeding by plugging up holes in blood vessels. Having too few platelets (*thrombocytopenia*) may cause you to bleed or bruise easily.

White blood cells help the body fight infections. Having too few white blood cells weakens your immune system and can make you more likely to get an infection.

Types of white blood cells

Lymphocytes are mature, infection-fighting cells that develop from *lymphoblasts*, a type of blood stem cell in the bone marrow. Lymphocytes are the main cells that make up lymphoid tissue, a major part of the immune system. Lymphoid tissue is found in the lymph nodes, thymus (a small organ behind the breast bone), spleen, tonsils and adenoids, and bone marrow. It is also scattered through the digestive system and respiratory system. 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 are mature, infection-fighting cells that develop from *myeloblasts*, a type of blood-forming cell in the bone marrow. Granulocytes have granules that show up as spots under the microscope. These granules contain enzymes and other substances that can destroy germs, such as bacteria. The 3 types of granulocytes – *neutrophils*, *basophils*,

and *eosinophils* – are distinguished under the microscope by the size and color of their granules.

Monocytes develop from blood-forming monoblasts in the bone marrow and are related to granulocytes. 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. Macrophages also help lymphocytes recognize germs and start making antibodies to fight 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 childhood leukemias are ALL. This leukemia starts from early forms of lymphocytes 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 leukemia:** In these rare leukemias, the cells have features of both ALL and AML. In children, they are generally treated like ALL and usually respond to treatment like ALL.

Both ALL and AML can be further divided into different subtypes. For more 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 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 *Leukemia--Chronic Myeloid*.
- **Chronic lymphocytic leukemia (CLL):** This leukemia is extremely rare in children. For more information on CLL, see *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 this type of leukemia is slightly more common during the first 2 years of life and during the teenage years.

ALL is slightly more common among Hispanic and 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.

Juvenile myelomonocytic leukemia (JMML) usually occurs in young children, with an average age of about 2.

Visit the American Cancer Society's Cancer Statistics Center for more key statistics.

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 a person's chance of getting a disease such as cancer. Different cancers have different risk factors.

Lifestyle-related risk factors such as tobacco use, diet, body weight, and physical activity 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 leukemias are not linked to any known genetic causes.

Inherited syndromes

Some 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. They 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 treatment.
- **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.

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 conditions cause children to be born with immune system problems. These include:

- Ataxia-telangiectasia
- Wiskott-Aldrich syndrome
- Bloom syndrome
- Schwachman-Diamond 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 one twin develops childhood leukemia, the other

twin has about a 1 in 5 chance of getting leukemia as well. This risk is much 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 smoking, being overweight, drinking too much alcohol, and getting too much sun exposure. These types of factors are important in many adult cancers, but they are unlikely to play a role in most childhood cancers.

Some studies have suggested that a woman drinking a lot of alcohol during pregnancy 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 acute leukemia 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 system (mainly children who have had organ transplants) 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 childhood leukemias is not known. Most children with leukemia do not have any known risk factors.

Still, scientists have learned 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 in each cell’s DNA. The DNA inside our cells makes up

our genes, which are 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 how we look.

Some genes control when our cells grow, divide into new cells, and die at the right time. Certain genes that help cells grow, divide, or stay alive 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 make new cells.

A common type of DNA change 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 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 childhood leukemias 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 might occur early, even before birth. In rare cases, acquired mutations can 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 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 tests 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. The doctor then orders blood tests, which come back as abnormal and point to the diagnosis. The best way to find these leukemias 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 been treated with chemotherapy and/or radiation therapy for other cancers, and for children who have had 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

Many of the symptoms of childhood leukemia can have other causes as well, and most often these symptoms are not caused by leukemia. Still, if your child has any of them, it’s important to have your child seen by a doctor so the cause can be found and treated, if needed.

The symptoms of leukemia are often caused by problems in the child's bone marrow, which is where the leukemia begins. As leukemia cells build up in the 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 might also invade other areas of the body, which can also cause symptoms.

Symptoms from low red blood cell counts (anemia): Red blood cells carry oxygen to all of the cells in the body. A shortage of red blood cells can cause:

- Tiredness (fatigue)
- Weakness
- Feeling cold
- Feeling dizzy or lightheaded
- Headaches
- Shortness of breath
- Pale skin

Symptoms from low white blood cell counts:

- Infections can occur because of a shortage of normal white blood cells. Children with leukemia can get infections that don't seem to go away or may get one infection after another. Although children with leukemia often have high white blood cell counts because they have so many leukemia cells, these cells don't protect against infection the way normal white blood cells do.
- Fever is often the main sign of infection. But some children might have a fever without having an infection.

Symptoms from low blood platelet counts: Platelets in the blood normally help stop bleeding. A shortage of platelets can lead to:

- Easy bruising and bleeding
- Frequent or severe nosebleeds
- Bleeding gums

Bone or joint pain: This pain is caused by the buildup of leukemia cells near the surface of the bone or inside the joint.

Swelling of the abdomen (belly): Leukemia cells can collect in the liver and spleen, making them bigger. This might 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 and weight loss: If the spleen and/or liver get big enough, they can press against other organs like the stomach. This can make the child feel full after eating only a small amount of food, leading to a loss of appetite and weight loss over time.

Swollen lymph nodes: Some leukemias spread to lymph nodes. Swollen nodes may be seen or felt 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 can also swell, but these can only be seen on imaging tests, such as CT or MRI scans.

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

Coughing or trouble breathing: Some types of leukemia can affect structures in the middle of the chest, such as lymph nodes or the thymus (a small organ in front of the trachea, the breathing tube that leads to the lungs). An enlarged thymus or lymph nodes in the chest can press on the trachea, causing coughing or trouble breathing. In some cases where the white blood cell count is very high, the leukemia cells can build up in the small blood vessels of the lungs, which can also cause 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. An enlarged thymus 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 brain and spinal cord when they are first diagnosed. This can lead to symptoms such as headache, trouble concentrating, weakness, seizures, vomiting, problems with balance, and blurred vision.

Rashes, gum problems: In children with acute myelogenous leukemia (AML), leukemia cells may spread to the gums, causing swelling, pain, and bleeding. If it spreads to the skin, it can cause small, dark 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: A 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.

Again, most of the symptoms above are more likely to be caused by something other than leukemia. Still, it's important to have these symptoms checked by a doctor so the cause can be found and treated, if needed.

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 find out what type it is and decide 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 might suggest leukemia, the doctor will want to get a thorough medical history to learn about the symptoms and how long your child has had them. The doctor may also ask about 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 (belly) will be felt for signs of an enlarged spleen or liver.

Tests to look for leukemia in children

If the doctor thinks your child might have leukemia, samples of 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 childhood cancers (including leukemias), to have some of these tests done. If leukemia is found, other body 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 leukemia 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 can't 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 sometimes they may be taken from the front of the pelvic bones or from other bones.

For a bone marrow *aspiration*, the skin over the hip bone is cleaned and numbed by injecting a local anesthetic or applying a numbing cream. In most cases, the child is also given other medicines to make them drowsy or even go to sleep 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 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, but they may also 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 applies a numbing cream in 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.

It is very important for this test 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 (where the child is asleep).

Lab tests to diagnose and classify leukemia

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. The samples might be exposed to chemical stains (dyes) that can cause color changes in some types of leukemia cells.

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*.

Flow cytometry and immunohistochemistry

These tests are used for *immunophenotyping* – classifying leukemia cells based on certain proteins in or on the cells. This kind of testing is very helpful in determining the exact type of leukemia. It is most often done on cells from bone marrow, but it can also be done on cells from the blood, lymph nodes, and other body fluids.

For both flow cytometry and immunohistochemistry, samples of cells are treated with antibodies that stick to certain proteins. For immunohistochemistry, the cells are then examined under a microscope to see if the antibodies stuck to them (meaning they have these proteins), while for flow cytometry a special machine is used.

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 more DNA than normal (a *DNA index* of 1.16 or higher) are often more sensitive to chemotherapy, and these leukemias have a better prognosis (outlook).

Flow cytometry 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.

Chromosome tests

Normal human cells have 23 pairs of chromosomes (strands of DNA), each of which is a certain size and looks a certain way under the microscope. But in some types of leukemia, the cells have changes in their chromosomes.

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. Other types of chromosome changes are also possible. 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, in ALL, chemotherapy is more likely to work if the cells have more than 50 chromosomes and is less likely to work if the cells have fewer than 46 chromosomes.

Finding these types of chromosome changes with lab tests can be very helpful in predicting a person's outlook and response to treatment.

Cytogenetics: For this test, leukemia cells are grown in a lab dish and the chromosomes are looked at under a microscope to detect any changes, including missing or extra 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 another way to look at chromosomes and genes. 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 test that can also find some chromosome changes too small to be seen under a microscope, even if there are very few leukemia cells 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 aren't 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 make sure the blood is clotting properly.

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

Imaging tests

Imaging tests use x-rays, sound waves, magnetic fields, or radioactive particles to make pictures of the inside of the body. Leukemia doesn't 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 *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 uses x-rays to make 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 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.

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 (especially to iodine or shellfish) 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 that slides in and out of the middle opening. Your child will need to lie still on the table 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: Some machines 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 grow rapidly, they absorb large amounts of the sugar. A special camera can then create a picture of areas of radioactivity in the body. The picture from the PET scan is not 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, makes detailed images of soft tissues in the body. It's most helpful in looking at the brain and spinal cord, so it's 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.

A contrast material called *gadolinium* is often injected into a vein before the scan to better show details. This 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 make pictures 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 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?

The type of leukemia a child has plays a major role in both treatment options and the child's outlook (prognosis). Determining the type (acute lymphocytic, acute myeloid, etc.) and subtype of the leukemia 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?"

For most types of cancer, determining the stage (extent) of the cancer is very important. The stage is 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's 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 these leukemia cells. 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

Newer types of lab tests can help determine 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

B-cell ALL: In about 80% to 85% of children with ALL, the leukemia starts in B cells. There are several subtypes of B-cell ALL:

- **Early precursor B (early pre-B) ALL** (also called *pro-B ALL*)
- **Common ALL**
- **Pre-B ALL**
- **Mature B-cell ALL** (also called *Burkitt leukemia*). This type is rare, accounting for only about 2% to 3% of childhood ALL. It is essentially the same as Burkitt lymphoma and is treated differently from most leukemias. It's discussed in detail in *Non-Hodgkin Lymphoma in Children*.

T-cell ALL: About 15% to 20% 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 the leukemia started in and how mature the cells are. In this system, the subtypes of AML are classified mainly based on their morphology (how they look under the microscope). There are 8 subtypes of AML: M0 to M7 (the M refers to myeloid).

- **M0:** Undifferentiated acute myeloblastic leukemia
- **M1:** Acute myeloblastic leukemia with minimal maturation
- **M2:** Acute myeloblastic leukemia with maturation (the most common subtype of AML in children)
- **M3:** Acute promyelocytic leukemia (APL)
- **M4:** Acute myelomonocytic leukemia (more common in children less than 2 years of age)
- **M5:** Acute monocytic leukemia (more common in children less than 2 years of age)
- **M6:** Acute erythroid leukemia
- **M7:** Acute megakaryoblastic leukemia

Subtypes M0 through M5 all start in immature forms of white blood cells. M6 AML starts in immature forms of red blood cells, while M7 AML starts in immature forms of cells that make platelets.

World Health Organization (WHO) classification of AML

The FAB classification system is still commonly used to group AML into subtypes. But it doesn't take into account many other factors that are now known to affect prognosis (outlook), such as chromosome changes in the leukemia cells. The newer WHO system includes some of these factors to help better classify AML based on a person's outlook.

The WHO system divides AML into several 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 a translocation between chromosomes 9 and 11
- APL (M3) with a translocation between chromosomes 15 and 17
- AML with a translocation between chromosomes 6 and 9
- AML with a translocation or inversion in chromosome 3
- AML (megakaryoblastic) with a translocation between chromosomes 1 and 22

AML with myelodysplasia-related changes

AML related to previous chemotherapy or radiation

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

- AML with minimal differentiation (M0)
- AML without 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)

Myeloid proliferations related to Down syndrome

Undifferentiated and biphenotypic acute leukemias (leukemias that have both lymphocytic and myeloid features). These are also known as *mixed phenotype* or *mixed lineage* leukemias. In children, these leukemias are generally treated like ALL and usually 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, night sweats, 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)

In this phase, bone marrow and/or blood samples 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 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 factors that can affect a child's outlook (prognosis) 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

Children with ALL are often divided into risk groups (such as standard-risk, high-risk, or very high-risk), with more intensive treatment given to 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 thought to be 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.

Initial white blood cell (WBC) count: Children with ALL who have very 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, common, 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 (the fluid around the brain and spinal cord), or to the testicles in boys, lowers the chance of being cured. 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 occur when chromosomes swap some of their genetic material (DNA). 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 guiding treatment for AML 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.

Initial 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.

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.

Chromosome changes: 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 are missing a copy of chromosome 7 (known as *monosomy* 7) have a poorer prognosis.

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.

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

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

Status of acute leukemia after treatment

How well ALL or AML responds to the initial (induction) treatment affects long-term prognosis.

Remission

A remission (or *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

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). In general, children with MRD during or after induction chemotherapy are more likely to have the leukemia relapse (come back) and therefore may need more intense treatment. Children with more MRD have a greater risk of relapse than those with less MRD.

Active disease

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 have 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 section "How is childhood leukemia treated?"

When discussing cancer survival statistics, doctors often use a number called the *5-year survival rate*. This 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's very rare for these cancers to return after this long.

Survival rates are often based on previous outcomes of large numbers of children who had the disease, but they can't predict what will happen in any 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 apply to your child, as he or she knows your situation best.

Current 5-year survival rates are based on children first diagnosed and treated more than 5 years ago. Improvements in treatment since then might result in a better outlook for children now being diagnosed.

Acute lymphocytic leukemia (ALL)

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

Acute myelogenous leukemia (AML)

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 vary depending on the subtype of AML and other factors. 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.

Other childhood leukemias

Accurate survival rates for less common forms of childhood leukemia are harder to find.

Juvenile myelomonocytic leukemia (JMML): For JMML, 5-year survival rates of about 50% have been reported.

Chronic leukemias: 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.

How is childhood leukemia treated?

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. These centers offer the advantage of being treated by 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 treats children's cancers. Many other specialists may be involved in your child's care as well, including other doctors, nurses, nurse practitioners (NPs), physician assistants (PAs), psychologists, social workers, rehabilitation specialists, and other health professionals.

Going through cancer treatment with a child often means meeting lots of specialists and learning about parts of the medical system you probably haven't had contact with before. You can find out more about this in our document *Children Diagnosed With Cancer: Understanding the Health Care System.*

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 discuss your child's treatment options as well as their possible side effects with the treatment team to help make the decision that's the best fit for your child. If there is anything you don't understand, ask to have it explained. (See the section "What should you ask your child's doctor about childhood leukemia?" for some questions to ask.)

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.

For more on how a specific type of childhood leukemia is treated, see the following sections:

- Treatment of acute lymphocytic (lymphoblastic) leukemia (ALL)
- Treatment of acute myelogenous leukemia (AML)
- Treatment of acute promyelocytic leukemia (APL)
- Treatment of juvenile myelomonocytic leukemia (JMML)
- Treatment of chronic myelogenous leukemia (CML)

Thinking about taking part in a clinical trial

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

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

Considering complementary and alternative methods

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

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

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

Help getting through cancer treatment

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

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

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

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 *A Guide to Cancer Surgery*.

Radiation therapy for childhood leukemia

Radiation therapy uses high-energy radiation to kill cancer cells. It is not always needed to treat leukemia, but it can be used in different situations:

- It is sometimes used to try to prevent or treat the spread of leukemia to the brain or treat the testicles if they are involved by leukemia cells.
- It can be used (rarely) to treat a tumor that is pressing on 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 Therapy section of our website, or in our document *Understanding Radiation Therapy: A Guide for Patients and Families.*

Chemotherapy for childhood leukemia

Chemotherapy (chemo) is the main treatment for nearly all childhood leukemias. This 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, chemo drugs enter the bloodstream and reach all areas of the body, making this treatment very 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 (usually less than a year), 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 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.

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 can also 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 treatment. These side effects can 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 usually 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. Too much of certain minerals can 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.

Chemo can also cause some long-term side effects. These are discussed in the section "What happens after treatment for childhood leukemia?"

For more information on chemotherapy, see the Chemotherapy section of our website, or our document *A Guide to Chemotherapy*.

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 can be useful in certain childhood leukemias.

For instance, nearly all children with chronic myeloid leukemia (CML) have an abnormal chromosome in their leukemia cells known as the *Philadelphia chromosome*. Targeted drugs such as imatinib (Gleevec) and dasatinib (Sprycel) specifically attack cells that have this chromosome. 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 their outcome is improved when these drugs are given along 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 *Targeted Therapy*.

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 intense chemotherapy. SCT lets doctors use even higher doses of chemotherapy than a child could normally tolerate.

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 blood-forming stem cells used for a transplant can come either from the blood or from the bone marrow. Sometimes stem cells from a baby's umbilical cord blood are used.

Allogeneic stem cell transplant

For childhood leukemias, the type of transplant used is known as an *allogeneic stem cell transplant*. In this type of transplant, the blood-forming stem cells are donated from another person.

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. 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.

To learn about how a stem cell transplant is done, see *Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants).*

When stem cell transplant (SCT) might be used

Acute lymphocytic leukemia (ALL): In ALL, SCT might be used for a child whose leukemia doesn't respond well to initial treatment or relapses (comes back) early after going into remission. It's 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.

Acute myelogenous leukemia (AML): 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 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.

Other leukemias: SCT might also offer the best chance to cure some less common types of childhood leukemia, such as juvenile myelomonocytic leukemia (JMML) and chronic myelogenous leukemia (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.

Practical points

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.

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

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), but they can be more 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 might 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 stem cell transplants. This happens when the donor immune system cells attack the patient's own cells. GVHD can be acute or chronic, based on how soon after the transplant it begins.

The parts of the body most often affected by GVHD include the skin, liver, and digestive tract. The most common symptoms 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.

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.

On the good side, GVHD can lead to graft-versus-leukemia activity, in which any remaining leukemia cells are 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 *Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants).*

Treatment of children with acute lymphocytic leukemia (ALL)

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 prolonged hospital stays for treatment and 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). For children in high-risk groups, a fourth drug in the anthracycline class (daunorubicin is the one most often used) is typically added. 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 (or more if the leukemia is high risk or leukemia cells have been found in the CSF) 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 treatment. 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 many leukemia cells 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, 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 treatment plans include 1 or 2 repeat intensified treatments similar to the initial induction. These 4-week intensifications are called *re-induction* or *delayed intensification*.

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

The total length 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 more intense or prolonged.

If the leukemia seems to have gone away by standard lab tests, the doctor may do more sensitive tests to look for even small numbers of remaining leukemia cells. 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, the same drugs might 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, or mitoxantrone), cyclophosphamide, cytarabine (ara-C), and epipodophyllotoxins (etoposide or 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 the child has 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.

If ALL doesn’t go away completely or if it comes back after a stem cell transplant, it can be very hard to treat. For some children, newer types of immunotherapy (treatments that boost the body’s immune response against the leukemia) might be helpful. For more on these treatments, see the section “What’s new in childhood leukemia research and treatment?”

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) might not be as effective. A stem cell transplant may be advised if induction treatment puts the leukemia in 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. Adding these drugs to chemotherapy seems to help improve outcomes, according to studies done so far.

Treatment of children with acute myelogenous leukemia (AML)

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 of AML (known as *acute promyelocytic leukemia*, or APL) is slightly different, and is described in the next section.

Induction

Treatment for AML uses different combinations of chemo 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 can be more effective in killing leukemia cells, but it can also cause more severe side effects.

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: Most children with AML will also get intrathecal chemotherapy (given directly into the cerebrospinal fluid, or CSF) 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 intense 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 the AML never went into remission, but this depends on how long the initial remission was. In more than half of cases of relapse, the leukemia can be put into a second remission 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 (APL), the M3 subtype of acute myeloid leukemia (AML), differs from the usual AML treatment. This leukemia usually responds well to treatment, which is given in 3 phases:

- Induction
- Consolidation (also called *intensification*)
- Maintenance

Induction

Many children with APL have bleeding and blood-clotting issues 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 these problems.

Children with APL get a non-chemotherapy drug similar to vitamin A called *all-trans retinoic acid* (ATRA). ATRA alone can often put APL into remission, 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 *differentiation syndrome* (formerly known as *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 get 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 often it 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. A 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 can't 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 cells. These drugs are usually very good 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 doesn't 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 *Leukemia--Chronic Myeloid*.

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?
- Do we need other tests 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? Can you recommend someone?
- What are our treatment choices?
- Should we consider a stem cell transplant? When?
- What do you recommend and why?
- How soon do we need to start treatment?
- What should we do to be ready for treatment?
- How long will treatment last? What will it be like?
- How much of the treatment will need to be done in the hospital?
- How will treatment affect our daily lives (school, work, etc.)?
- 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?

Along with these sample questions, be sure to write down your own. For instance, 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.

Also keep in mind that doctors are not the only ones who can give you information. Other health care professionals, such as nurses and social workers, may have the answers to some of your questions. You can find out more about speaking with your health care team in *Talking With Your Doctor*.

What happens after treatment for childhood leukemia?

During and after 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's certainly normal to want to put the 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 be 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 come back, it is most often while the child is still being treated or within a year or so after finishing treatment. It is unusual for an acute leukemia (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 go away soon after treatment, but others can last a long time, or might not even show up until years later. It's important to report any new symptoms to the doctor right away, so that the cause can be found and treated, if needed.

Keeping good medical records

As much as you might want to put the experience behind you once treatment is done, it's very important to keep good records of your child's medical care during this time. This

can be very helpful later on as your child changes doctors. Gathering the details during or soon after treatment may be easier than trying to get them at some point in the future. Be sure the doctors have the following information (and always keep copies for yourself):

- 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 the doctor wrote when your child was 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.
- The names and contact information of the doctors who treated your child's leukemia.

It's also very important to keep 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.

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 school re-entry programs that can help in these situations. In these programs, 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 *Children Diagnosed With Cancer: Returning to School*.)

Centers that treat many patients with leukemia may have programs to introduce new patients and their families to others who have finished their treatment. This can give them 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 and can include:

- 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's 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 the care and follow-up after 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 and doses of treatments they received, and the age of the child 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.

Second cancers: 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 getting 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.

Heart and lung problems: Certain chemotherapy drugs or radiation therapy to the chest can sometimes cause heart or lung problems later in life. The risks of heart disease and stroke 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.

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

Growth and development: Some cancer treatments may affect a child's growth, so 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.

Fertility issues: Cancer treatment may also affect sexual development and ability to have children later in life. 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 *Fertility and Women With Cancer* and *Fertility and Men With Cancer*.

Bone problems: 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.

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

Long-term follow-up guidelines

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

It's 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 read them on 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 your doctor.

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

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 these gene changes (such as translocations or extra chromosomes) can help explain why these cells may grow out of control, and why they don't 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 chromosome translocations or other 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?
- 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?
- 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)?

Immunotherapy to treat childhood leukemia

Immunotherapies are treatments that boost a child's own immune system to help fight leukemia. Some types of immunotherapy have shown a lot of promise in treating ALL, even when other treatments are no longer working.

Chimeric antigen receptor (CAR) T-cell therapy

In this treatment, immune cells called *T cells* are removed from the child's blood and genetically altered in the lab to have specific receptors (called *chimeric antigen receptors*, or CARs) on their surface. These receptors can attach to proteins on the surface of leukemia cells. The T cells are then multiplied in the lab and given back into the child's blood, where they can seek out the leukemia cells and launch a precise immune attack against them.

This technique has shown very encouraging results in early clinical trials against some advanced, hard-to-treat cases of ALL. In many children the leukemia could no longer be detected after treatment, although it's not yet clear if these children have been cured.

Some children have had serious side effects from this treatment, including very high fevers and dangerously low blood pressure in the days after it's given. Doctors are learning how to manage these side effects.

Doctors are still improving how they make the T cells and are learning the best ways to use them. CAR T-cell therapy is only available in clinical trials at a handful of major medical centers at this time.

Monoclonal antibody therapy

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

An example is blinatumomab (Blincyto), a special kind of monoclonal antibody that can attach to 2 different proteins at the same time. One part of blinatumomab attaches to a protein found on B cells (the cells that become leukemia cells in most cases of ALL). Another part of the antibody attaches to a protein on immune cells called *T cells*. By binding to both of these proteins, this drug brings the leukemia cells and immune cells together, which is thought to cause the immune system to attack the cancer cells. Early results with this drug against B-cell ALL have been promising, although so far it has been studied more in adults than in children.

Additional resources for childhood leukemia

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

National organizations and websites*

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

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.

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 and 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.

Websites for teens and children

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

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

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

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

Teens Living with Cancer
Website: www.teenslivingwithcancer.org

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

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

Supports, honors, and recognizes brothers and sisters of children diagnosed with cancer so they may face the future with strength, courage, and hope.

**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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