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# Acute Myeloid Leukemia in Children and Teens: In Detail

## A companion to AML: The Basics

**Revised 2025**

*Formerly titled Acute Myeloid Leukemia in Children and Adults*

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# Inside This Booklet




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# Introduction

This booklet provides information about acute myeloid leukemia (AML) in children and teens. The disease is also known as acute myelogenous leukemia. Although AML can occur at any age, adults age 60 years and older are more likely to develop the disease than younger people.

**For easy-to-read, general information about AML for yourself, family or friends, view LLS's *AML: The Basics*. For information about AML in adults, view LLS's *Acute Myeloid Leukemia in Adults: In Detail.* Both booklets are available at www.LLS.org/booklets.**

While AML is the second most common type of leukemia in children, it is a rare disease. Over the past several decades, advances in treatments for AML have resulted in improved remission and cure rates, but much work remains to be done. New therapies are being studied in clinical trials to find cures for all children with AML, including those with high-risk disease and those whose disease comes back after treatment.

This booklet provides medical information about AML as well as advice to help you, your child and your family cope. We trust that this information will provide you with a good working knowledge of AML and that it reinforces what you already know.

We hope that you will keep this booklet handy and, should you ever feel alone when confronting problems, that you will turn to it for information and guidance to find the support and resources you need.

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# Leukemia Basics

The human body is made up of trillions of cells. Normally these cells grow and multiply to form new cells as the body needs them. When cells become damaged or old, they usually die, and new cells take their place.

Sometimes cells start collecting mistakes in their DNA (deoxyribonucleic acid). DNA is like an instruction manual for your body, telling cells how to grow, function, and make you who you are. Genes are made up of DNA. A gene mutation is a change in the sequence of the DNA in a cell.

Cancer starts when a gene or several genes in a cell mutate and create a cancerous cell. This abnormal cancer cell grows and divides instead of dying. Cancer cells may spread into, or invade, other areas of the body, disrupting how the body works.

As cancer cells multiply, many types of cancers form solid tumors, but cancers of the blood, such as leukemia, generally do not. Instead leukemia cells affect the amount of blood cells in the body, and they may accumulate in organs such as the liver or spleen.

Cancer can happen in almost any cell anywhere in the body. Leukemia is a cancer of blood cells. It begins in the bone marrow, the spongy tissue in the center of most bones where most blood cells are formed. Blood cells begin as hematopoietic (blood) stem cells in the bone marrow. These stem cells develop into immature cells called “blasts” that go through many stages before they eventually develop into mature red blood cells, white blood cells and platelets.

Leukemia occurs when one of the blasts in the bone marrow mutates at some point in its development and becomes a leukemia cell. Leukemia cells do not mature into healthy functioning blood cells. They grow more quickly and live longer than normal blood cells. They divide and copy themselves to make more and more leukemia cells. Over time, the leukemia cells crowd out and stop the development of healthy blood cells in the bone marrow. When this happens, the body may not have enough red blood cells, white blood cells and/or platelets.

Red blood cells carry oxygen throughout the body. White blood cells help fight infections. Platelets help stop bleeding by clotting (clumping tougher) at the site of an injury. Without sufficient red blood cells, the body’s organs and tissues may not receive enough oxygen to work properly. Low white blood cell counts can lead to serious and frequent infections, and low platelet counts can cause excessive bleeding and bruising.

There are four major types of leukemia:

- Acute myeloid leukemia (AML)
- Chronic myeloid leukemia (CML)
- Acute lymphoblastic leukemia (ALL)
- Chronic lymphocytic leukemia (CLL)

Leukemia is classified as either "acute" or "chronic." These two terms describe how quickly the disease progresses without treatment. Acute leukemias progress rapidly and produce cells that are not fully developed. These immature white blood cells cannot perform their normal functions, putting patients at risk for infection. Chronic leukemias usually progress slowly, and patients have greater numbers of mature cells. In general, these more mature cells can carry out some or all of their normal functions.

Leukemia is further classified by the type of blood cell, either myeloid or lymphoid, that becomes cancerous. Blood cells begin as stem cells in the bone marrow. A blood stem cell may become a lymphoid stem cell or a myeloid stem cell. Lymphoid stem cells develop into white blood cells called lymphocytes. Myeloid stem cells can develop into red blood cells, platelets or certain other types of white blood cells. Leukemia is classified as "lymphocytic" or "lymphoblastic" if it originates in a lymphoid cell. It is classified as "myeloid" or "myelogenous" if the cancerous changes start in a myeloid cell. See **Figure 7** on page 59, for an illustration of blood cell development.

Acute lymphoblastic leukemia (ALL) is the most common type of leukemia in children, accounting for the majority of pediatric cases. AML is the second most common, though it occurs much less frequently than ALL. Chronic myeloid leukemia (CML) is rare in children but can occasionally be seen, often presenting in older pediatric patients. In contrast, Chronic lymphocytic leukemia (CLL) is almost exclusively an adult disease and is not typically found in children.

## Acute Myeloid Leukemia

AML is a type of cancer in which the bone marrow makes too many immature blood cells called myeloblasts. In AML, a mutation or a series of mutations in the DNA of a single myeloid stem cell results in the formation of an abnormal myeloblast. This abnormal myeloblast does not develop into a healthy, functioning myeloid cell. It becomes a leukemia cell (also referred to as an AML cell or a leukemia blast cell). Most cases of childhood AML do not seem to be caused by inherited mutations. Usually these DNA mutations develop after conception and are only found in the leukemia cells and not in other cells in the body.

Genetic errors in the mutated cell cause the leukemia cell to keep growing and dividing, whereas a healthy cell would stop dividing and eventually die. Every cell that arises from the initial leukemia blast cell also has the mutated DNA. As the leukemia cells multiply uncontrollably, they quickly accumulate in the bone marrow. This slows down or stops the production of normal, healthy red blood cells, white blood cells and platelets. As a result, there are too many leukemia blast cells (immature cells) and not enough mature, functional red and white blood cells and platelets.

Over time, the leukemia cells spill out of the bone marrow into the bloodstream. This can cause the number of white blood cells in the blood to increase, but most of these white blood cells are leukemia cells that do not protect against infection. Once they are in the bloodstream, the leukemia cells can spread to other parts of the body such as the cerebrospinal fluid, the fluid that surrounds the spinal cord and brain.

By the time AML is diagnosed, the number of healthy red blood cells, white blood cells and platelets in the blood is usually lower than normal. Low levels of blood cells may result in anemia, infections and excessive bleeding or bruising.

| Medical Term | Definition |
|---|---|
| Anemia | Low red blood cell count |
| Thrombocytopenia | Low platelet count (thrombocyte is another word for platelet) |
| Neutropenia | Low neutrophil count (a neutrophil is a type of white blood cell) |

In rare instances, AML cells collect outside the bone marrow and form a solid mass (a tumor). This type of tumor, called a myeloid sarcoma, can form in almost any part of the body. Other names for a myeloid sarcoma are extramedullary disease, chloroma, granulocytic sarcoma, myeloblastoma and monocytoma. It is important to note that a myeloid sarcoma is different from a true "sarcoma," which refers to a distinct group of cancers arising from connective tissues like muscle, fat or bone.

Surgery and radiation therapy are not effective ways of treating myeloid sarcomas. Myeloid sarcomas are generally treated with the same chemotherapy treatments used for AML in the bone marrow, even if the bone marrow and blood do not appear to be involved.

# Signs and Symptoms

Signs and symptoms are changes in the body that may indicate the presence of disease. A sign is a change that the doctor sees during an examination or in a laboratory test result. A symptom is a change that a patient can notice and/or feel.

Children who have signs and/or symptoms that suggest the possibility of leukemia are usually referred to a specialist, called a hematologist-oncologist. This is a doctor who has special training in diagnosing and treating blood disorders and blood cancers such as leukemia, lymphoma and myeloma. A pediatric hematologist-oncologist specializes in the care of children with blood cancers.

It is common for children with AML to feel unwell because they lack normal, healthy blood cells. This happens when the leukemia cells in the bone marrow crowd out the normal blood-forming cells. As a result, patients with AML may not have enough mature red blood cells, white blood cells and/or platelets, so they often have symptoms related to low blood cell counts.

Symptoms of anemia (a low red blood cell count) include:

- Fatigue
- Weakness
- Shortness of breath during normal physical activities
- Decreased activity/decreased play
- Increased sleep/increased naps
- Lightheadedness, dizziness or faintness
- Headaches
- Pale complexion

Symptoms of neutropenia (a low number of neutrophils, a type of white blood cell important in fighting infections) include:

- Frequent infections

Symptoms of thrombocytopenia (a low platelet count) include:

- Bruising easily
- Pinhead-sized red spots on the skin, called petechiae
- Bleeding that is hard to stop, even from a small cut
- Frequent or severe nosebleeds
- Bleeding gums
- Heavier or more frequent menstrual periods in females

Other general symptoms of AML include:

- Recurrent fevers
- Unexplained weight loss or loss of appetite
- Swollen lymph nodes, sometimes called glands
- Bone and joint pain
- Difficulty breathing
- Fullness or swelling in the abdomen, due to an enlarged spleen or liver
- Sore, red gums and oral ulcers (painful sores that appear in the mouth)

The symptoms of AML may be similar to those of other blood disorders or medical conditions. Speak with your doctor if your child has any of these symptoms to ensure proper diagnosis and treatment.

# Testing

While certain signs and symptoms may indicate that your child has AML, a series of tests are needed to confirm the diagnosis. It is important to have an accurate diagnosis, as it helps the doctor to:

- Estimate how the disease will progress
- Determine the appropriate treatment

**Talk to your child's doctor about:**

- The diagnostic tests that are being done
- What the results mean
- Getting copies of the results

Some tests may be repeated both during and after treatment to evaluate the effectiveness of treatment.

**Medical History.** Your child's doctor will take a thorough medical history. This may include information about past illnesses, injuries, medications and other treatments. Some illnesses run in families, so the doctor may also ask about the health of your child's blood relatives. The doctor should find out if there is a family history of blood cancer. Certain gene mutations present at birth may increase a person's risk of developing AML, creating an inherited predisposition to the disease. If your child has either a personal history of cancer or a family history of leukemia and/or other cancers in closely related relatives or recent generations, the doctor should evaluate your child for an inherited predisposition syndrome; this information will help the doctor to manage your child's treatment. For example, it may affect choice of chemotherapy or choice of a related donor for allogeneic stem cell transplantation.

**Physical Examination.** The doctor will want to know about your child's current symptoms and will conduct a physical examination. During the physical examination, the doctor may listen to your child's lungs and heart and carefully check their body for any signs of infection and disease. To check the internal organs, the doctor may feel different parts of your child's body. For example, the doctor may feel the abdomen to see if your child has an enlarged liver or spleen. The doctor may feel the lymph nodes in your child's neck, armpits and groin (the top inner part of the thigh) to see if they are enlarged.

**Complete Blood Count (CBC) With Differential (diff).** This test measures the number of red blood cells, white blood cells and platelets in a blood sample. It also measures the amount of hemoglobin in the red blood cells and the percentage of red blood cells in the sample. The CBC should include a differential, which measures the numbers of the different types of white blood cells in the sample.

People with AML often have a high number of white blood cells, but most of these are leukemia cells that do not protect against infection. These patients are immunocompromised, meaning they have a weakened immune system because they do not have enough mature white blood cells. They may also have low numbers of red blood cells and platelets.

**Bone Marrow Aspiration and Biopsy.** Leukemia starts in the bone marrow, the spongy tissue inside the center of most bones. When blood tests show cytopenias (low blood counts) or the presence of blast cells (immature blood cells), the doctor may recommend a test of the bone marrow to see whether your child's bone marrow is healthy and if it is making normal amounts of blood cells. Doctors use the findings from bone marrow aspiration and biopsy to diagnose and monitor blood and bone marrow diseases, including leukemia.

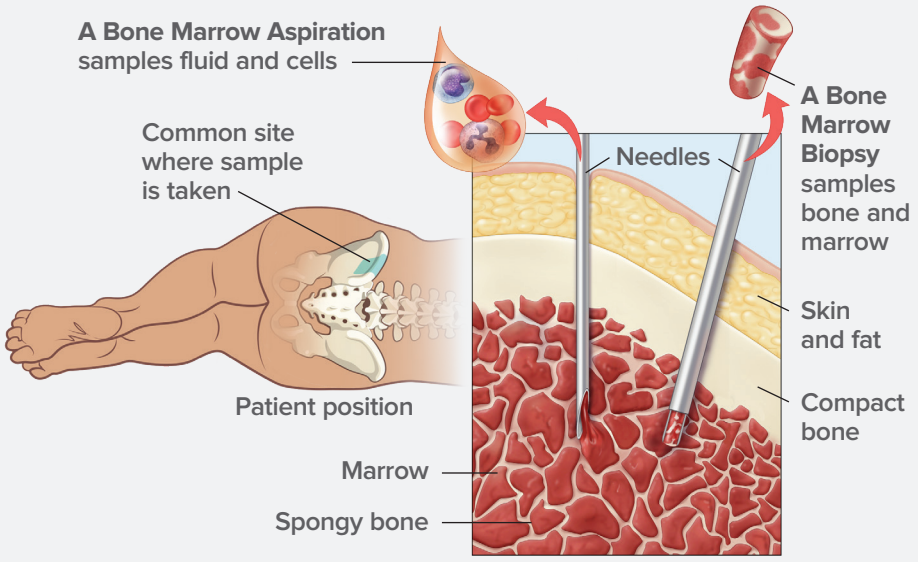
- A bone marrow aspiration is a test to remove a small sample of liquid bone marrow.
- A bone marrow biopsy is a test to remove a small sample of intact bone marrow.

Many children will have both tests done at the same time, but sometimes they just have a bone marrow aspiration. Bone marrow aspiration and bone marrow biopsy are generally done at the doctor's office or in a hospital. This can be a painful procedure, and most children undergoing bone marrow aspiration and biopsy are under sedation or general anesthesia. Adults and older teens may be given a local anesthetic and be awake during the procedure.

The samples are usually taken from the patient's pelvis or hip bone. Bone marrow has both a solid and a liquid component. For a bone marrow aspiration, a special, hollow needle is inserted through the hip bone and into the bone marrow to aspirate (remove) a liquid sample of cells. For a bone marrow biopsy,

a wider needle is used to remove a sample of solid bone that contains bone marrow. Both needles are inserted through the skin, generally in the same area. The bone marrow samples (the aspirate and the biopsy) are sent to the laboratory where they are examined under a microscope. See **Figure 1** below for an illustration of the bone marrow tests. Bone marrow tests are also done during and after treatment to see if the treatment worked.

### Figure 1. Bone Marrow Aspiration and Biopsy




**Left:** The place on the back of the patient's hip bone where a bone marrow aspiration or biopsy is done. **Right:** One needle goes into the bone marrow to get a liquid sample for aspiration (the needle on the left) and the other needle goes inside the bone for a bone marrow biopsy (the needle on the right). The needle for the aspiration is thinner than the one for the biopsy.

**Visit www.LLS.org/3D and click on "Bone Marrow Biopsy and Aspiration" to view an interactive 3D model that will help you visualize and better understand the bone marrow aspiration and biopsy procedures.**

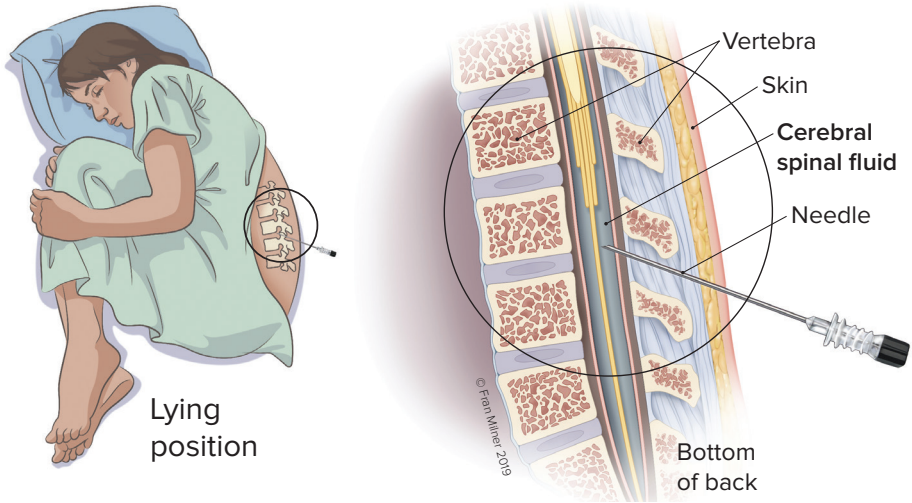
**Lumbar Puncture.** AML cells can spread to the cerebrospinal fluid (CSF), the fluid that flows around the brain and spinal cord. To determine if there are leukemia cells in this area, a sample of the CSF is tested. This may be done at the same time as the bone marrow aspiration and biopsy tests or, in some cases, shortly after treatment begins.

The procedure used to collect the CSF from the spinal column is called a lumbar puncture or spinal tap. After the area over the spine in the lower part of the back

has been numbed with local anesthesia, a thin needle is inserted between two vertebrae (back bones) and into the CSF space. A sample of the fluid is taken, sent to the laboratory and examined under a microscope to look for leukemia cells. See **Figure 2** below for an illustration of a lumbar puncture.

In many instances, a lumbar puncture is also used to inject chemotherapy medicine into the CSF to help prevent leukemia from spreading to the brain or spinal cord. This treatment is called intrathecal chemotherapy or IT chemotherapy. For more information on intrathecal chemotherapy see *Central Nervous System (CNS) Prophylaxis* on page 30.

### Figure 2. Lumbar Puncture



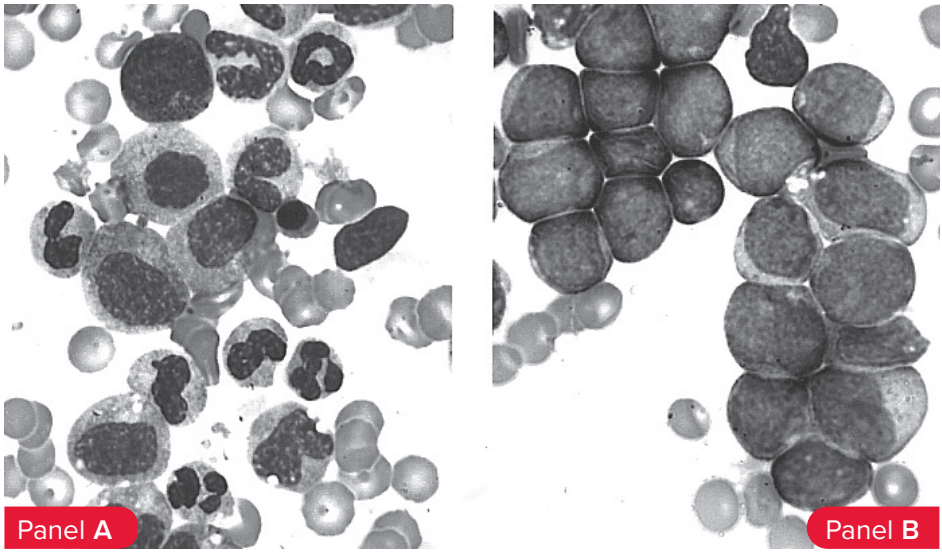

**Visit www.LLS.org/3D and click on "Lumbar Puncture" and "Intrathecal Therapy" to view interactive 3D models that will help you visualize and better understand these procedures.**

**Cell Assessment.** At the laboratory, a hematopathologist examines the blood, bone marrow and cerebrospinal fluid samples. A hematopathologist is a doctor who has special training in identifying blood diseases by examining cells under a microscope and performing other specialized tests on the blood and bone marrow samples.

The hematopathologist examines the cells under a microscope to determine their size, shape and type, and to identify other cell features (see **Figure 3** on page 12). The percentage of cells in the bone marrow and blood that are blast cells is another important finding. In individuals without leukemia, there are typically no blast cells in the blood, and no more than 5 percent of the cells in the bone marrow are (normal) blast cells.

In some types of AML, a diagnosis of AML requires finding at least 20 percent myeloblasts in the bone marrow. In certain cases, AML can also be diagnosed when the percentage of myeloblasts is less than 20 percent, if the myeloblasts have a chromosomal change or genetic mutation typically found in a specific type of AML.

### Figure 3. Normal Cells versus AML Cells




**Panel A** shows normal bone marrow cells seen through a microscope. The darker shapes are the nuclei of the cells. Some of the nuclei are circular and some are horseshoe shaped, reflecting the different developmental stages and the different types of cells. **Panel B** shows AML blast cells seen through a microscope. These cells are "arrested" in an early stage of development. In panel B, all the AML cells have a similar appearance, in contrast to the varied appearance of the normal cells in panel A.

Additional tests are done on the samples to determine the subtype of leukemia.

**Biomarker Testing.** These laboratory tests look for biomarkers, which are molecules found in the blood, other body fluids or tissues. Biomarkers are signs of a normal or abnormal process, or of a condition or disease. They provide information about a person's cancer. Each person's cancer has a unique pattern of biomarkers.

Biomarker testing is used to help diagnose some types of cancer. It may also be used to help plan treatment, make a prognosis or predict whether cancer will come back or spread to other parts of the body. It may also be used to monitor treatment. Important biomarker tests may include:

**Immunophenotyping (Flow Cytometry).** This laboratory test identifies cancer cells based on markers called antigens. Antigens are proteins found either on the surface of or within white blood cells. Finding (or not finding) certain antigens can help determine the type of leukemia.

Immunophenotyping is done with an instrument called a flow cytometer. Immunophenotyping measures the number of cells in a sample, as well as characteristics of the cells, including their size and shape, and identifies markers on the cell surface. A sample of cells from blood, bone marrow or other sample is tagged with a panel of antibodies that are specific to areas on the cell. The cells are stained with a light-sensitive dye and are passed through a laser beam in the flow cytometer. If they have an antibody-specific surface marker, the cells light up and are counted.

Leukemia cells can have different antigens on their surfaces, depending on the type of leukemia. Certain antigens, called "cluster of differentiation (CD)" proteins, are helpful in identifying leukemia cells. While the pattern of antigens varies among different AML subtypes, most AML cells express CD13, CD33 and/or CD34.

In addition to diagnosis, flow cytometry is also used following blocks of treatment for evaluating measurable residual disease (MRD), also called minimal residual disease. This term refers to the small number of cancer cells that may remain in the body after blocks of treatment. Flow cytometry can find one cancer cell among 10,000 to 100,000 normal bone marrow cells. Testing for MRD may help doctors to plan treatment, find out how well treatment is working and determine whether the cancer has come back.

**Karyotyping.** In this test, a hematopathologist uses a microscope to examine the chromosomes inside of cells. In patients with AML, karyotyping is used to look for abnormal changes in the chromosomes of the leukemia cells. Karyotyping is done with either a bone marrow sample or a blood sample.

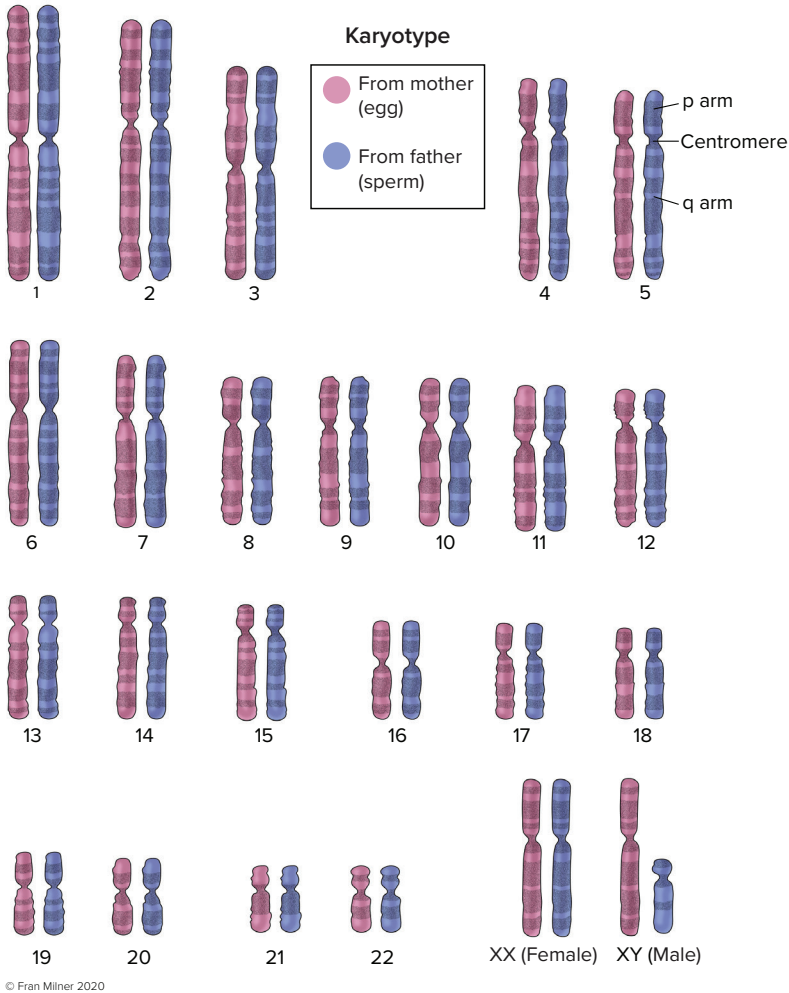
Normal human cells contain 23 pairs of chromosomes, for a total of 46 chromosomes. Each pair of chromosomes is a certain size, shape and structure. Each chromosome is divided into two sections or "arms." The short arm of the chromosome is labeled the "p arm." The long arm of the chromosome is labeled the "q arm." See **Figure 4** on page 14, for an illustration of human chromosomes lined up in pairs, an arrangement called a karyotype.

Chromosomal abnormalities in leukemia cells can be identified in approximately 70 percent to 80 percent of children and teens with AML. These abnormalities can be "numerical" or "structural." A numerical abnormality is when there is a different number of chromosomes in the cells than is usually found. For example, instead of the typical 46 chromosomes in each cell of the body, there may be 45 or 47 chromosomes. A structural abnormality occurs when the chromosome's structure has been altered in one of several ways including:

- Translocation, when a piece of one chromosome breaks off and attaches to another chromosome. Sometimes pieces from two different chromosomes trade places with each other.
- Inversion, when a part of a chromosome breaks off, turns upside down and then reattaches in that position.

- Deletion, when a part of the chromosome is missing.
- Duplication, when part of the chromosome is copied too many times, resulting in extra genetic material.

**Figure 4. Normal Karyotype**




In some cases, karyotyping analysis provides important information for the doctors who are determining your child's treatment options and prognosis. For example, a translocation between chromosomes 15 and 17, abbreviated t(15;17), is associated with a diagnosis of acute promyelocytic leukemia (APL). This AML subtype has a more favorable prognosis and requires a different treatment approach than that of other AML subtypes. For more information on APL, see page 33.

**Fluorescence In Situ Hybridization (FISH).** This very sensitive test is used to examine genes or chromosomes in cells and tissues. Doctors use FISH to detect certain abnormal changes in the chromosomes and genes of leukemia cells. Pieces of DNA that contain special fluorescent dyes are prepared in the laboratory and added to the leukemia cells on a glass slide. The pieces of DNA that bind to certain genes or areas of chromosomes light up when the slide is viewed under a specialized "fluorescence" microscope. Not only can FISH identify most abnormal changes that can be seen with karyotype testing under a microscope, but it can also detect some changes that are too small to be seen with karyotype testing. It is not, however, used as a general screening tool. Fluorescence in situ hybridization has one disadvantage—the doctor must select the specific chromosomes or genes that are going to be examined.

**Polymerase Chain Reaction (PCR).** This very sensitive test is used to detect and measure certain genetic mutations and chromosomal changes that cannot be seen with a microscope. PCR essentially amplifies (increases) small amounts of specific pieces of either RNA (ribonucleic acid) or DNA to make them easier to detect and measure in a cell sample. It can find a single leukemia cell among more than 100,000 to one million normal cells. It is used to measure MRD in patients because it can identify even a small amount of cancer cells that may remain in the body after treatment.

**Next-Generation Sequencing (NGS).** Next-generation sequencing, also called molecular testing or genomic testing refers to a number of different laboratory tests that examine the exact sequence (order) of DNA or RNA. These technologies allow for sequencing of DNA and RNA much more quickly and cheaply than sequencing methods that were used previously.

This makes it possible to identify a variety of genetic changes in a patient's cancer cells. These changes are important in guiding risk assessment and prognosis and may also inform treatment decisions. The information NGS provides can help doctors to determine which patients are at high risk and may need more intensive treatment or may benefit from treatment with novel therapies.

There are targeted sequencing tests (also called multigene panels) that look for specific mutations in the cancer cells. These tests focus on specific sets of genes or areas of DNA. There are also broad DNA sequencing tests (genomic screening tests) that analyze the sequence of large regions of DNA, rather than looking for mutations of specific genes. Doctors may also order sequencing of all the DNA in your entire genome. This test is known as whole genome sequencing.

NGS finds gene mutations in approximately 90 percent of people with AML. Standard protocols combine cytogenetic (chromosome) analysis with testing for mutations of a number of single genes, including *ASXL1, BCOR, EZH2, FLT3-ITD, FLT3-TKD, KIT, NPM1, CEBPA, IDH1, IDH2, RUNX1, SF3B1, SRSF2, STAG2, TP53, U2AF1, ZRSR2, BCR::ABL and PML::RARa*. These gene mutations are important

in guiding risk assessment and prognosis, and are also used to guide treatment decisions. For example, some patients may be eligible to receive drugs called inhibitors that target specific gene mutations expressed by leukemia cells, such as the *FLT3* mutation. Inhibitors may be taken alone or in combination with other chemotherapy drugs, but they only work against leukemia cells with these specific mutations.

Generally, NGS should be done when the cancer is first diagnosed and again after a relapse. This is because the leukemia cells may acquire additional mutations. If this is the case, it is important to know about these additional mutations because their presence or absence in leukemia cells affects treatment options both at the time of the initial diagnosis and again at the time of relapse.

**Visit www.LLS.org/booklets to view the free LLS booklets *Understanding Genetics* and *Biomarker Testing for Cancer Treatment* for more information about genetics and genetic testing**.

**Pre-treatment Tests.** Before your child starts treatment for AML, tests will be performed to learn more about your child's overall health and disease. Doctors use this information for treatment planning. Some of these tests are summarized below.

**Blood Chemistry Profile.** This blood test measures the levels of certain substances released into the blood by organs and tissues in the body. These substances include electrolytes (such as sodium, potassium and chloride), proteins, glucose (blood sugar), creatine, uric acid and liver enzymes. The test findings indicate how well a person's kidneys, liver and other organs are working. Although a blood chemistry profile is not used to diagnose leukemia, if the results show that there is an abnormal amount of a particular substance in the blood, it may be a sign of disease or some other health problem. A blood chemistry profile also provides helpful information about any potential organ damage caused by leukemia cells or cancer treatments.

**Human Leukocyte Antigen (HLA) Typing.** This blood test is done to identify certain proteins, called human leukocyte antigens (HLAs), found on the surface of most cells in the body. These proteins make up the body's tissue type, which varies from person to person. They also play an important role in the body's immune response to foreign substances by helping the body distinguish its own cells from foreign cells. An HLA test is done before allogeneic stem cell transplantation to find out if there is a tissue match between a potential donor and the patient receiving the transplant. While HLA typing is not used to diagnose leukemia, it is an important test for all newly diagnosed AML patients if allogeneic stem cell transplantation is being considered as a treatment option. See *Stem Cell Transplantation* on page 32 for more information.

**Echocardiogram.** Some chemotherapy drugs, such as the class of drugs called anthracyclines, can damage heart tissue. Because of this, the doctor may want to test your child's heart function before starting each new cycle of chemotherapy. An echocardiogram creates a computerized image of the heart by bouncing sound waves off internal tissues or organs in the chest. It shows the size, shape and position of the heart, as well as its internal structures. It also shows if the heart is beating and pumping blood normally.

**Coagulation Tests.** The body stops bleeding by turning blood into a gel-like form called a blood clot. Blood clots help control excessive bleeding when a person has a cut. Blood moving through blood vessels, however, should not clot. Thrombosis is the formation of a blood clot inside an artery or a vein. If clots form in blood vessels, they can travel through the bloodstream to the heart, lungs or brain. This can cause heart attack, stroke or even death. Clotting problems are common in AML, particularly in one subtype called acute promyelocytic leukemia (APL). Coagulation tests measure the blood's ability to clot and how long it takes to clot. This can help the doctor measure a patient's risk of excessive bleeding and thrombosis.

**Visit www.LLS.org/booklets to view the free LLS booklet *Understanding Lab and Imaging Tests*.**

# Diagnosis

AML is a diverse disease, meaning there are many subtypes of AML that are based on the different gene and chromosome changes in the leukemia cells. Knowing your child's AML subtype is very important, as it can affect both their prognosis (the likely outcome of a disease) and their best treatment plan. If you are not sure of your child's AML subtype, ask the doctor what it is and to explain how that subtype may affect your child's treatment.

The International Consensus Classification (ICC) has classified AML into subtypes (see **Table 1** on page 19). The subtypes of AML are based on the genetic abnormalities (gene or chromosome changes) in the myeloblasts (leukemia cells) and the percentage of myeloblasts in the bone marrow and blood.

In some types of AML, a diagnosis requires finding at least 20 percent myeloblasts in the bone marrow. In certain cases, AML can also be diagnosed when the percentage of myeloblasts is less than 20 percent if the myeloblasts have a chromosomal change or genetic mutation that is typically found in a specific type of AML. There is another group of blood cancers called myelodysplastic syndromes (MDS). People with MDS can also have increased myeloblasts in the bone marrow. MDS with 10 percent to 19 percent myeloblasts is called MDS/AML.

The ICC classification also has a list of diagnostic qualifiers that should be used after diagnosis to plan treatment. They include:

- **Therapy-related AML.** Certain treatments for other cancers such as prior chemotherapy and radiation can cause AML.
- **AML progressing from MDS.** Myelodysplastic syndromes (MDS) are a group of blood cancers in which the bone marrow does not make enough healthy blood cells. In some people, MDS can transform into AML.
- **AML progressing from MDS/MPN.** Myeloproliferative neoplasms (MPNs) are a group of blood cancers in which the bone marrow makes too many red blood cells, white blood cells and/or platelets. Certain MPNs may become AML.
- **AML with germline predisposition.** Germline mutations are DNA mutations that are inherited during conception. These mutations occur in a parent's reproductive cells (egg or sperm). These changes may be inherited directly from the parent or may occur spontaneously in the reproductive cells. Some people with AML have a germline mutation that increased their risk of developing AML.

Diagnostic qualifiers are not separate subtypes of AML, but doctors use them when planning treatment.

## Table 1. International Consensus Classification (ICC) of AML With Percentage of Blasts Required

| |
|---|
| APL with t(15;17)(q24.1;q21.2)*/PML::RARA* ≥10% |
| APL with other *RARA* rearrangements ≥10% |
| AML with t(8;21)(q22;q22.1)*/RUNX1::RUNX1T1* ≥10% |
| AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22)*/CBFB::MYH11* ≥10% |
| AML with t(9;11)(p21.3;q23.3)*/MLLT3::KMT2A* ≥10% |
| AML with other *KMT2A* rearrangements ≥10% |
| AML with t(6;9)(p22.3;q34.1)*/DEK::NUP214* ≥10% |
| AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)*/GATA2; MECOM(EVI1)* ≥10% |
| AML with other *MECOM* rearrangements ≥10% |
| AML with other rare recurring translocations ≥10% |
| AML with t(9;22)(q34.1;q11.2)*/BCR::ABL1* ≥20% |
| AML with mutated *NPM1* ≥10% |
| AML with in-frame bZIP *CEBPA* mutations ≥10% |
| AML with mutated *TP53* 10%–19% (MDS/AML) and ≥20% (AML) |
| AML with myelodysplasia-related gene mutations 10%–19% (MDS/AML) and ≥20% (AML)<br>Defined by mutations in *ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1* or *ZRSR2* |
| AML with myelodysplasia-related cytogenetic abnormalities 10%–19% (MDS/AML) and ≥20% (AML)<br>Defined by detecting a complex karyotype (≥3 unrelated clonal chromosomal abnormalities in the absence of other class-defining recurring genetic abnormalities), del(5q)/t(5q)/add(5q), −7/del(7q), +8, del(12p)/t(12p)/add(12p), i(17q), −17/add(17p) or del(17p), del(20q), and/or idic(X)(q13) clonal abnormalities |
| AML not otherwise specified (NOS) 10%–19% (MDS/AML) and ≥20% (AML) |
| Myeloid sarcoma |
| **Diagnostic qualifiers that should be used following AML diagnosis** |
| Therapy-related<br>• prior chemotherapy, radiotherapy, immune interventions |
| Progressing from MDS<br>• MDS should be confirmed by standard diagnostics |
| Progressing from MDS/MPN (specify)<br>• MDS/MPN should be confirmed by standard diagnostics |
| Germline predisposition |

**Key:** add, addition of genetic material; AML, acute myeloid leukemia; APL, acute promyelocytic leukemia; del, deletion of genetic material; i, isochromosome; inv, an inversion in a chromosome; MDS, myelodysplastic syndromes; MPN, myeloproliferative neoplasm; p, the short arm of a chromosome (the upper half); q, the long arm of a chromosome (the lower half); t, a translocation between chromosomes.

**Source:** Adapted from Arber DA, Orazi A, Hasserjian RP, et al. International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: integrating morphologic, clinical and genomic data. *Blood*. 2022;140(11):1200-1228.

**Learning About Your Child's Diagnosis.** You are likely to experience a wide range of emotions when your child is diagnosed with cancer, before, during and after treatment. These emotions may include shock, denial, fear, anger, guilt and sadness. You may feel that life for your child and family will never be the same. Allow yourself to feel sad. Understand that you are not to blame for your child's diagnosis.

Over time, you, your child and your family will find ways to adapt and gradually develop a new sense of normalcy. All of these feelings are to be expected, but if you feel consumed by negative feelings and emotions or if you feel as though you are unable to function, seek professional help. Psychologists, social workers and religious or spiritual advisers may be able to help you to come to terms with your child's diagnosis. It is important to work through your feelings so you can help your child cope, and you can continue to manage other aspects of family life and work.

**Talking to Your Child About the Diagnosis.** Regardless of age, children are usually aware when their health causes their parents concern. Your child may experience a variety of emotions, such as anger, guilt, fear, anxiety and sadness, possibly all in quick succession.

Sometimes parents wish to shield their child from information about the illness and its treatment. Keep in mind that children will use their imagination to fill in perceived gaps of information. Sharing information about the illness and its treatment helps your child build trust in both you and the members of the treatment team. Your child will feel more comfortable talking about fears and concerns with people they trust. Encourage your child to ask questions and let you know if they are anxious or fearful.

Introduce your child to treatment team members who can provide psychosocial support. Your child's treatment team will include psychologists, social workers, art or play therapists and child-life specialists. In addition to helping you explain the illness and its treatment to your child, they can also help your child to better understand their disease through play or other activities.

Keep the discussion age appropriate when you talk to your child about the diagnosis. Consider the following guidelines (organized by age).

**Baby/Toddler (0 to 3 Years)**

- When children are this young, they do not have an understanding of illness or cancer. However, they are aware of changes to routines and the feelings of people around them.
- Children in this age-group may be afraid of the medical staff and medical procedures.
- Babies and toddlers may be afraid of abandonment or being left at the hospital. Offer physical and verbal reassurance.

**Preschool/Kindergarten (4 to 6 Years)**

- Children may have some understanding of an illness such as a cold, but may not grasp the implications of a serious illness.
- Children's primary focus will be the symptoms they are experiencing in any specific moment.
- Children in this age-group may be afraid of pain, so explain tests or treatments to them in advance.
- Assure your child that they did nothing wrong to cause the cancer.

**Elementary/Middle School (7 to 12 Years)**

- Children in this age-group may have a better understanding of serious illness, but not specifically cancer.
- They may have heard things about cancer at school, from friends, on TV, or they may have found information online. Ask your child what they know and correct any misunderstandings, especially those that cause distress.
- Explain tests, treatments and other medical procedures in advance. Your child may be afraid of pain and resist some tests or procedures. Be honest. If a procedure may be painful, work with the healthcare team and decide how to explain what will be done to lessen their pain and why the procedure is important.
- Children may be very concerned about possible changes to their physical appearance, such as hair loss and losing or gaining weight, as well as worrying about how their peers will react to the changes. Talk to your child in advance about these possible changes.
- You may need to discuss fertility preservation with your child. Some cancer treatments can affect fertility. Fertility preservation, such as egg or sperm banking, may be an option for children who have begun puberty. Fertility preservation may need to be done before treatment begins. Enlist members of the healthcare team to help with this sensitive discussion.
- You may see signs of regression in a child's behavior, such as thumb sucking, bed-wetting or tantrums.
- At this age, a child may use play to process the information—play-acting doctor/patient scenarios, for example.
- If the cancer treatment will result in any changes to the child's daily routine, explain the changes ahead of time so they will know what to expect.

**High Schoolers/Teenagers (13 to 18 Years)**

- Teenagers are usually able to understand complex information about their cancer and may want to know more. You may still need to correct any misinformation your teenager has heard about cancer from school, friends, TV and movies, or has found online.
- Teenagers may want to participate in decisions about their treatment. Include them in discussions with members of the healthcare team, as appropriate.
- You may need to discuss fertility preservation with your child. Some cancer treatments can affect fertility. Fertility preservation, such as egg or sperm banking, needs to be done before treatment begins. Enlist members of the healthcare team to help with this sensitive discussion.
- Teenagers may also be very concerned about changes to their physical appearance, such as hair loss and losing or gaining weight, as well as worrying about how their peers will react to the changes.
- As teenagers struggle to find independence, a cancer diagnosis may feel like a setback that can lead to feelings of frustration and anger. They may try to test their boundaries or engage in risky behaviors, such as drinking, drug use or sex.

**Ways to Help Your Child Cope.** It will help your child cope with the diagnosis if you:

- Provide structure to increase your child's sense of control. Children crave structure in their environment. Make things as consistent as possible. For example, plan a regular routine that you and your child will follow during your time together in the hospital or clinic.
- Acknowledge and praise your child when they are doing difficult things. Intermittent praise is the best way to reinforce the desirable behaviors that you want to see in your child.
- Use the same consequences for unacceptable or inappropriate behavior as you did before your child was diagnosed with cancer. Consistency will maintain structure and normalcy.
- Show that you respect your child's anger, worry, sadness or fear. Give them appropriate outlets for expressing these feelings, such as drawing or keeping a journal.
- Keep your child busy with activities during treatment to take their mind off difficult and unpleasant experiences.

- Help your child stay connected with friends from home and school with phone calls, texts and emails, or visits if possible.
- Ask for professional assistance if your child is having an especially difficult time adjusting to the cancer diagnosis and its treatment.

**Siblings.** When a child is diagnosed with cancer, everyone in the family is affected by the experience. This includes their siblings, who may feel angry, anxious, lonely, sad, guilty or even resentful of the new attention their sibling is receiving. You can help your other children cope with the situation in some of the following ways:

- Give them the chance to talk about how the experience is affecting them.
- Be open and willing to answer questions about their brother's or sister's cancer and treatment.
- Reassure younger children that they cannot "catch" cancer from their brother or sister. Explain that their brother or sister did not do anything that caused the cancer.
- Let them know that their sibling with cancer may have less energy or lose their hair.
- Explain that other concerned family members and friends may ask them about their sibling's diagnosis. Talk about appropriate responses.
- Remember that brothers and sisters still have their own problems, unrelated to cancer. Their problems are real and require your attention.
- Provide consistent, fair discipline to all your children, even though it may be more difficult right now.
- Let all your children know that you love them and are proud of them.

Siblings of children with cancer need to continue to go to school and participate in their usual activities as much as possible. Ask friends, family, other parents and teachers for help. However, disruptions to routines are inevitable, and the other children in your family may feel lost or overlooked. Arrange for regular "alone time" with each child.

Make sure the school is aware of your child's diagnosis. Talk to your other children's teachers. Ask your hospital's social worker or psychologist, or your school psychologist, whether your community offers any programs for siblings of children who have cancer. For additional assistance finding programs and resources to help your other children, you can also call an LLS Information Specialist at (800) 955-4572.

SuperSibs, a program of Alex's Lemonade Stand Foundation, provides programs and support for the siblings of children with cancer. Visit www.alexslemonade.org/supersibs for more information.

**Visit www.LLS.org/ChildhoodYAresources for resources to help children and their families cope with a blood cancer. You can view the free LLS workbook *Caring for Kids and Adolescents with Blood Cancer* which includes practical guidance on how to support your child, other family members and yourself during your child's cancer treatment. You can also view *Stars Will Twinkle, The Sun Will Shine*, a three-book series that explains the cancer journey to young children and *A Teen's Guide To Everything Cancer*, a guide to self-advocacy and self-care during and after treatment.**

# Treatment Planning

**Choosing a Hospital and Doctor for Your Child's Cancer Treatment.** Once you learn that your child has AML, you need to decide where to go for treatment. Most children with cancer receive treatment at hospitals that specialize in treating children with cancer. The doctors and other healthcare providers at these centers have special training and expertise in giving comprehensive care to children and teens. These centers are often members of the Children's Oncology Group (COG). This is the world's largest organization devoted to clinical research to improve the care and treatment of children with cancer.

Going to a specialized children's cancer hospital helps ensure that your child gets the best available treatment. You can ask your child's pediatrician or family doctor for a referral, or you can call an LLS Information Specialist at (800) 955-4572 to find hospitals that specialize in treating children with AML.

Children who are diagnosed with AML usually need to start treatment as soon as possible after diagnosis. Some families may wish to seek a second opinion, right away, if they can, particularly if their child has a high-risk subtype of AML or the disease comes back (relapses) after their initial treatment. A second opinion may help you feel more confident about your child's treatment plan. The second opinion should come from a pediatric hematologist-oncologist, preferably one who specializes in childhood AML. This doctor will usually have the most knowledge and experience regarding the latest treatment options. Some pediatric AML specialists conduct telehealth visits, so you may have the opportunity to see an expert without traveling.

If you feel either unsure or uncomfortable about how you are going to tell your child's doctor that you are getting a second opinion, call our Information Specialists at (800) 955-4572, to discuss an approach that feels right to you. You may also want to check your child's health insurance coverage to be sure that the cost of getting a second opinion is covered.

**Visit www.LLS.org/booklets to view *Choosing a Specialist or Treatment Center.***

**Fertility.** Some cancer treatments can affect fertility (the ability to have children in the future). Before your child begins treatment, it is important to talk with the doctor about whether the treatment could affect their fertility. Not only should the doctor talk about fertility with you, the doctor should also discuss it with your child if they are old enough to understand.

You may also want to speak with a fertility specialist, a doctor who has special training helping people who have trouble conceiving or carrying a pregnancy to term. This specialist can talk to you about possible options for preserving your child's fertility. However, delaying treatment to address fertility options may not always be advisable. Many children with AML need to start treatment right away.

**Visit www.LLS.org/booklets to view the free LLS booklet *Fertility and Cancer*.**

**Prognostic Factors.** Certain factors can affect the prognosis of children with AML (prognosis means the likely outcome of their disease). Doctors use prognostic factors to help predict how a patient's disease is likely to respond to treatment. They also help doctors determine which patients need more intense treatment.

Children and teens with AML are often assigned to one of three risk groups—low risk, intermediate risk or high risk—based on prognostic factors. This is called risk stratification. Typically, children with AML who are in the low-risk group have a better prognosis and receive less-intensive treatment than those in the two higher-risk groups.

Doctors use the following prognostic factors to assign your child to a risk group:

**AML Subtype.** Chromosomal and genetic abnormalities are the most significant prognostic factors in children with AML. They help determine whether your child may benefit from treatment with more intensive therapies. **Table 2**, on page 26, lists some of the more common genetic abnormalities, and their risk categories, found in children with AML.

**Treatment Response.** Children who have a better response to the initial treatment have a lower risk of disease relapse. Treatment response is often evaluated based on testing for measurable residual disease (MRD). This refers to the small number of cancer cells that may remain in the body, even with a complete remission. This low level of residual cancer cells cannot be detected with basic tests that rely on examining cell samples with a microscope. So more sensitive tests are done to evaluate MRD.

Children who achieve remission after initial treatment but have MRD are at increased risk of disease relapse. Testing for MRD can help the doctor reevaluate your child's AML risk category and determine whether they may benefit from more intensive therapies.

**Table 2. Proposed Genetic Risk Stratification of Children With AML**

| High-risk Prognostic Markers | Low-risk Prognostic Markers |
|---|---|
| *MECOM/EVI1* (3q26.2) abnormality | t(8;21)(q22;q22) |
| t(6;9)(p23;q34.1) with *DEK::NUP214* fusion | Inv(16)/t(16;16)(p13.1;q22) |
| Monosomy 7 | *NPM1* mutation |
| Monosomy 5/5q- | *CEBPA* mutation |
| High-risk *KMT2A* (11q23) rearrangements | |
| ○ t(4;11) | |
| ○ t(6;11) | |
| ○ t(10;11)(p11.2;q23) | |
| ○ t(10;11)(p12;q23) | |
| ○ t(11;19)(q23;p13.3) | |
| t(11;17)(q23;q12) | |
| *NUP98* (11p15.5) fusions | |
| 12p abnormalities (*ETV6*) | |
| *ETS* fusions | |
| *FLT3*-ITD with AR >0.1 without *NPM1* or *CEBPA* mutation | |
| Inv(16) with *CBFA2T3::GLIS2* fusion | |
| RAM phenotype | |
| t(8;16)(p11;p13) with *KAT6A::CREBBP* fusion[a] | |
| t(10;11)(p12;q21) with *PICALM::MLLT10* fusion | |

**Abbreviations:** AR, allelic ratio; inv, an inversion in a chromosome; p, the short arm of a chromosome (the upper half); q, the long arm of a chromosome (the lower half); t, a translocation between chromosomes; v, variable.

[a]Possible inclusion as high-risk alteration.

**Source:** Lamble AJ, Tasian SK. Opportunities for immunotherapy in childhood acute myeloid leukemia. *Blood Advances.* 2019;3(22):3750-3758.

# Treatment

New treatments may have been approved since this booklet was printed.
Check www.LLS.org/DrugUpdates or call (800) 955-4572.

Before treatment begins, your child's doctor will discuss treatment options with you. Treatment options may include standard therapy or a clinical trial. Standard therapy is treatment that is accepted by medical experts as proper treatment for a certain type of disease. A clinical trial is a research study that tests how well a new medical treatment works in people. Participation in a clinical trial may be

your child's best treatment option, so it is important to discuss all your child's treatment options with the doctor.

A diagnosis of AML is associated with a wide range of outcomes. Not every child with AML receives the same type of treatment. The doctor will plan your child's treatment based on their AML subtype and other factors, such as age and overall health. For example, cases of acute promyelocytic leukemia (APL) are treated differently from other forms of AML. For more information on APL, see page 33.

AML progresses rapidly and should be treated aggressively and as soon as possible. The standard treatment for AML consists of intensive chemotherapy and is often divided into two phases: induction and consolidation. Some treatment plans may also include targeted therapies and stem cell transplantation.

**Talk to your doctor about:**

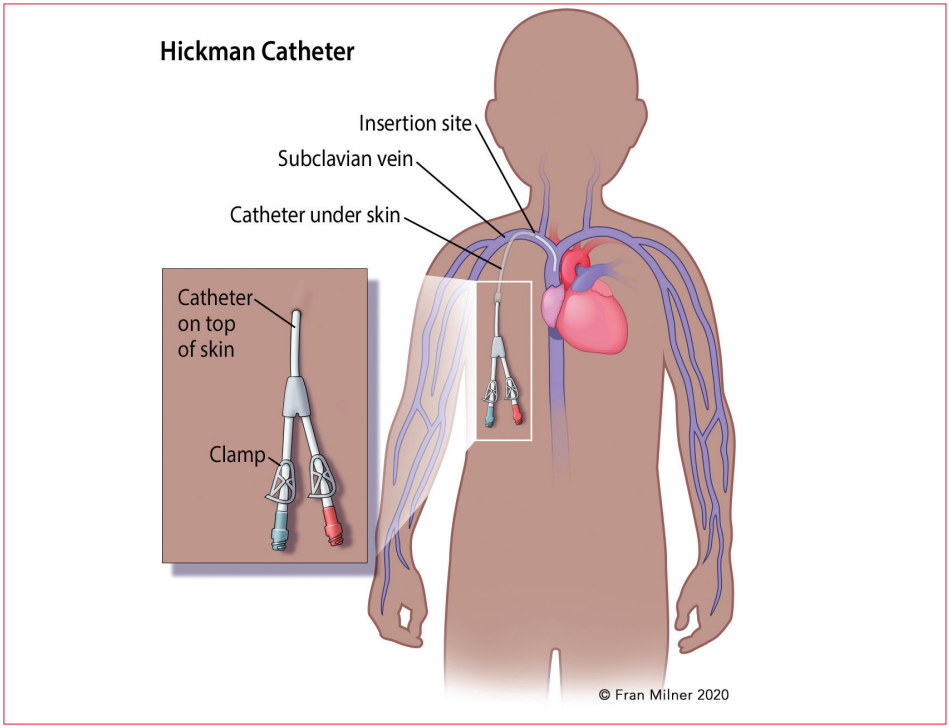
- Your child's treatment options and the results you can expect from the treatment
- The possibility of your child participating in a clinical trial

**Induction.** The first phase of chemotherapy is called induction. The goal of induction is to destroy as many cancer cells as possible to induce (achieve) a remission and to restore normal blood cell production. In patients with AML, remission means that there are less than 5 percent blasts in the bone marrow (when examined with a microscope) and that blood counts have returned to normal. Although obtaining a remission is the first step in controlling AML, it is also important for children to emerge from the induction phase physically fit enough to tolerate the intensive treatments given during the consolidation phase.

Chemotherapy is standard treatment for AML. It works by either stopping or slowing the growth of cancer cells. Different types of chemotherapy drugs work in different ways to either eliminate leukemia cells or stop new leukemia cells from forming. So, more than one chemotherapy drug is usually used.

Some chemotherapy drugs are given as an IV infusion. The drugs are infused slowly over the course of a few hours, or, in the case of a continuous infusion, over several days. Often, IV chemotherapy is given through a thin, soft tube called a central line (also called a central venous line or catheter). Many children with AML have a type of central line called a Hickman catheter. A Hickman catheter is a small, soft tube that is inserted into your child's chest or neck during surgery and then threaded under the skin into a large vein near the heart. The part of the catheter that is outside the body is taped to the chest and is used for taking and giving blood and giving medicines and other fluids. See **Figure 5** on page 28 for an illustration of a Hickman catheter.

## Figure 5. Placement of Hickman® Catheter




**Hickman® Catheter: An example of a type of central line.**

Children with AML often receive two rounds of induction chemotherapy. The most common chemotherapy regimen used during induction includes cytarabine (Ara-C, Cytosar-U®) and an anthracycline. Daunorubicin (Cerubidine®) is the anthracycline most often used for this regimen, although idarubicin (Idamycin®) and mitoxantrone (Novantrone®) are sometimes used. If an anthracycline is given, your doctor may administer another drug, dexrazoxane (Totect®, Zinecard®), around the same time as the anthracycline. This drug is not a chemotherapy agent, but it helps to minimize cardiac side effects that are associated with anthracyclines. Other chemotherapy drugs may be added to the cytarabine and the anthracycline regimen, such as etoposide (VP-16, Etopophos®, VePesid®) or thioguanine (Tabloid®).

For patients with therapy-related AML or AML with myelodysplasia-related changes, induction therapy may include CPX-351 (Vyxeos®), a liposomal formulation of cytarabine and daunorubicin. A liposomal medication contains the active drug inside small, fat-like particles. This special fatty preparation allows more medication to reach its target (the bone marrow) and stay in the bone marrow to kill leukemia cells.

In addition to the chemotherapy, children may receive targeted therapies. Targeted therapy is a treatment that uses drugs or other substances to identify and attack specific targets on cancer cells but cause less harm to normal cells. Not all cancers have the same targets. To find the most effective treatment for your child, the doctor will run tests to identify the genes, chromosomes, proteins and other factors in the cancer cells. This helps the doctor to choose the most effective treatment based on the specific factors of your child's disease. Targeted therapy for AML may include:

- One dose of the targeted therapy gemtuzumab ozogamicin (Mylotarg™) along with chemotherapy as part of their induction treatment. Gemtuzumab ozogamicin is a CD33-directed antibody linked to the chemotherapy drug calicheamicin. It binds to and then enters cells that have the CD33 protein on their surface. Once inside, it releases the toxin that kills the leukemia cells.
- A FLT3 inhibitor (for patients with *FLT3* mutations) such as sorafenib (Nexavar®) or midostaurin (Rydapt®).

See **Table 3**, *Drug Classes and Drug Mechanisms* on page 53; and **Table 4**, *Some Drugs Used in the Treatment of AML* on page 54 for each drug's prescribing information.

During the first round of induction therapy, children often stay in the hospital for at least 4 weeks until their blood cell counts recover. The large doses of chemotherapy given during induction destroys most of the leukemia cells, as well as healthy bone marrow cells. Most patients develop dangerously low blood cell counts and may become very ill. They often require transfusions of red blood cells and platelets. To reduce the risk of infection, antibiotics are given to prevent and treat bacterial and fungal infections. During this time, the doctor will order blood and bone marrow tests to see how well the treatment is working. After blood cell counts recover, children may go home for a few days or a week and then return to the hospital for the second round of induction, followed by another 4 weeks of recovery in the hospital. Some institutions will allow a subset of children to leave the hospital a week after chemotherapy with close outpatient follow-up. The second round of induction therapy may use the same drugs that were used in the first round, or it may be a new chemotherapy regimen.

For some children, the hospital stay is the first time they have been away from home for an extended period of time. Most hospitals allow a parent to stay with the child during hospitalization. Providing age-appropriate information about the illness and its treatment will help your child build trust in you and the members of the treatment team. Talking with your child about their fears and concerns will also help them to feel more comfortable.

**Visit www.LLS.org/FamilyWorkbook to view the free LLS workbook *Caring for Kids and Adolescents with Blood Cancer*.**

**Central Nervous System (CNS) Prophylaxis.** Pediatric AML regimens typically include treatment to prevent the spread of leukemia cells to the central nervous system (CNS) and to kill any leukemia cells that may already be there. It is uncommon for leukemia cells to be present in the cerebrospinal fluid (the fluid that flows in and around the hollow spaces of the brain and spinal cord) at the time of diagnosis; this occurs in only 5 to 10 percent of cases. However, without the routine administration of a therapy targeting the central nervous system (referred to as CNS prophylaxis), leukemia cells can eventually spread to the cerebrospinal fluid. The CNS-directed therapy begins during the induction phase and continues throughout the rest of treatment.

Some form of intrathecal chemotherapy is now incorporated into most protocols for the treatment of childhood AML. Intrathecal means that the chemotherapy drugs are injected into the fluid-filled space between the thin layers of tissue that cover the brain and spinal cord. Intrathecal chemotherapy can be combined with the other types of chemotherapy that are given during the induction phase of treatment.

Cytarabine, methotrexate and/or hydrocortisone (a corticosteroid) are the most common intrathecal chemotherapy drugs used in children with AML. If AML cells are found in the CNS at the time of diagnosis, more frequent intrathecal treatments may be used.

**Assessing Treatment Response.** After the second round of induction therapy, your child will have another bone marrow aspiration to see if a remission has been achieved. In children with AML, a complete remission is defined as:

- The bone marrow contains fewer than 5 percent blast cells when viewed under a microscope
- Blood cell counts return to normal
- There are no signs or symptoms of AML

Approximately 75 to 80 percent of children with AML achieve a remission by the end of induction. These patients will move on to the next phase of treatment, consolidation. They are, however, given a few weeks break to prepare for consolidation.

**Measurable Residual Disease (MRD).** Even when a complete remission is achieved, some leukemia cells that cannot be seen with a microscope may remain in the body. This is referred to as “measurable residual disease,” also called minimal residual disease. Children who have just a single AML cell among 1,000 normal bone marrow cells may be at greater risk of relapsing.

The tests used most often to detect MRD are flow cytometry, polymerase chain reaction (PCR) and next-generation sequencing (NGS). These tests usually use samples of bone marrow cells or blood samples. These tests can be done at various times, including after initial treatment, during therapy and after therapy completion.

Testing for MRD can help the doctor reevaluate your child's AML risk category and determine whether your child may benefit from more intensified therapies. Children and teens whose AML is not in remission after standard treatment should be considered as candidates for a clinical trial, allogeneic stem cell transplantation or drug regimens for relapsed or refractory AML.

Even in patients who test negative for MRD, undetectable cancer cells are believed to remain the body. Because of this, children with AML require additional treatment, called consolidation. Without this additional treatment, the leukemia is likely to relapse within months.

**Visit www.LLS.org/booklets to view the free LLS booklet *Measurable Residual Disease (MRD)* for more information.**

**Consolidation (Intensification).** Consolidation refers to treatments given to patients after their disease is in complete remission. Consolidation is designed to deepen the remission and eliminate any residual leukemia cells. Additionally, CNS prophylaxis usually continues during the consolidation phase.

There are two basic treatment options for consolidation:

- Additional intensive chemotherapy
- Stem cell transplantation (see page 32 for more information)

Patients with low-risk prognostic factors are often given 2 to 3 additional cycles of intensive chemotherapy with high-dose cytarabine and other drugs for consolidation therapy. The number of chemotherapy cycles varies from patient to patient. Children are often hospitalized during consolidation therapy. They may go home for a few days or a week between cycles.

Patients with high-risk AML, based on their prognostic factors, receive more intensive therapy that may include allogeneic stem cell transplantation. Allogeneic stem cell transplantation is a complex treatment and can cause serious side effects that can be life-threatening. It is important to discuss the benefits and risks of this procedure with your child's doctor.

For patients receiving an allogeneic stem cell transplantation, an important treatment decision is whether to have the stem cell transplantation after their first remission. Often, this is when transplantation offers the best chances of preventing AML from recurring. However, it is associated with higher treatment-related medical problems and death compared to other treatment options used during the consolidation phase. Patients who are candidates for an allogeneic stem cell transplant should begin a search for an HLA-matched stem cell donor while they are receiving induction therapy. If your child's doctor decides that stem cell transplantation should be part of your child's treatment, it is generally done after 2 to 3 cycles of chemotherapy.

**Stem Cell Transplantation.** For some patients, the doctor may recommend stem cell transplantation during the consolidation phase of chemotherapy. The goal of stem cell transplantation is to cure the patient's cancer. The process typically involves administering intensive chemotherapy, followed by an infusion of healthy stem cells. There are two main types of stem cell transplantation. They are:

- Allogeneic, in which a patient receives stem cells, either from a matched or a partially matched donor, who may be related or unrelated to the patient. This type of transplant, typically done for AML with higher-risk features, relies on the donor's immune system cells to fight off any residual leukemia within the recipient. Simply put, allogeneic stem cell transplant can be regarded as a form of immunotherapy.
- Autologous, in which the patient's own stem cells are collected before chemotherapy and stored. Then, after the patient has completed chemotherapy, these cells are reinfused into the patient's bloodstream. This type of transplant is not typically used for treating AML patients.

**Allogeneic Stem Cell Transplantation.** This is the most common type of stem cell transplantation used to treat AML. In preparation for the transplant, patients receive a conditioning therapy. This consists of intensive chemotherapy, either with or without radiation, to kill the leukemia cells remaining in their bodies. Importantly, it is also given to suppress their immune systems, so their bodies do not reject the donor stem cells.

After the conditioning therapy, patients receive donor stem cells by intravenous infusion. Allogeneic transplantation uses healthy blood-forming cells from an HLA-matched or partially matched donor. The cells can come from a family member, an unrelated person, or from a donated unit of umbilical cord blood. The donated stem cells restore the bone marrow's ability to form new blood cells.

Ideally, an allogeneic stem cell transplant will generate a new immune system for the patient, one that helps the body fight infections and other diseases. The new immune system also has the potential to recognize and attack any remaining cancer cells in the body. The transplanted immune cells (the graft) may perceive the leukemia cells in the body as foreign and destroy them. This is called the graft-versus-leukemia (GVL) effect.

Compared to other treatment options, allogeneic stem cell transplantation is associated with a higher rate of side effects and death. However, it may be considered for patients with higher-risk AML, based on their AML subtype and response to induction therapy. The decision to perform an allogeneic transplant also depends on the patient's age, physical fitness and the availability of an HLA-matched donor.

Though most children stay in the hospital for 4 to 6 weeks for the transplant process and recovery period, some children require very long hospitalizations

due to complications, or they may be readmitted with complications after their initial discharge. One possible serious side effect of allogeneic stem cell transplantation is graft-versus-host disease (GVHD). This occurs when the transplanted immune cells (the graft) from the donor identify healthy cells in the recipient's body (the host) as foreign and attack them. The parts of the body most commonly damaged by GVHD include the skin, liver, stomach, intestines and eyes. GVHD can develop within weeks after transplantation or much later. Your child's doctor can order medications to help prevent or minimize the complications of GVHD.

Research to determine which patients are most likely to benefit from stem cell transplantation after their first complete disease remission is evolving. Timing is one of the most important factors influencing transplant outcomes, so it is very important to start a donor search as soon as possible after an AML diagnosis in order to identify a suitably matched, related or unrelated donor.

**Talk to your doctor about:**

- Stem cell transplantation and ask whether it is a treatment option for your child.

**Visit www.LLS.org/booklets to view the free LLS booklets *Blood and Marrow Stem Cell Transplantation* and *Graft-Versus-Host Disease*.**

# Special Treatment Considerations

**Acute Promyelocytic Leukemia (APL).** This aggressive subtype of AML is associated with potentially life-threatening simultaneous bleeding and clotting complications. While APL usually occurs in middle-aged adults, it can happen at any age. It accounts for approximately 4 to 8 percent of all AML cases in children. While in the past APL was nearly always fatal, due to advances in its diagnosis and treatment, it is now one of the most curable subtypes of AML in children.

APL is due to a translocation between chromosome 15 and chromosome 17, abbreviated t(15;17), in a myeloid stem cell that is developing in the bone marrow. A translocation is a genetic change in which a piece of one chromosome breaks off and attaches to another chromosome. An abnormal fusion gene called *PML::RARa* forms as a result of the translocation. A diagnosis of APL depends upon confirmation of t(15;17) in the patient's AML cells.

The abnormal *PML::RARa* makes a protein that causes blood cells to get stuck in the immature promyelocytic stage, unable to develop into mature white blood cells. In people with APL, the promyelocytes build up in the bone marrow. Over time, the promyelocytes crowd out and suppress the development of healthy

blood cells. When this happens, the body may not have enough healthy red blood cells, white blood cells and/or platelets.

People with APL are particularly susceptible to severe bleeding and blood clots. This occurs, in part, due to the low number of platelets in the blood and to the leukemia cells releasing substances that alter the balance between bleeding and clotting. This may lead to symptoms of prolonged and excessive bleeding from cuts, nose bleeds, bleeding gums, blood in the urine and heavy menstrual bleeding. Serious bleeding events may occur including bleeding in the brain or lungs, which can be fatal. Thrombosis, the formation of a blood clot inside a blood vessel may also cause life-threatening conditions.

**Treatment.** APL treatment is divided into two phases: induction and consolidation. The drugs used to treat APL differ from the treatment of other AML subtypes described in this booklet. In addition, pediatric APL rarely spreads to the central nervous system (CNS) so routine CNS prophylaxis with intrathecal chemotherapy is usually not needed.

Children with lower-risk APL (those with a white blood cell count of $10X10^9$/L or less at diagnosis) are often treated with all-trans retinoic acid (ATRA, tretinoin, Vesanoid®) and arsenic trioxide (ATO, Trisonex®). Instead of working like traditional chemotherapy, these drugs help leukemia cells mature into normal blood cells and then die naturally. ATRA is a form of vitamin A that corrects the abnormal cell development in APL, while arsenic trioxide targets the faulty protein causing the disease. Together, they have transformed APL treatment, leading to high cure rates with fewer side effects than standard chemotherapy.

Some high-risk patients (those with a white blood cell count of more than $10X10^9$/L at diagnosis) may receive ATRA and ATO with a few doses of the chemotherapy drug idarubicin or a dose of gemtuzumab ozogamicin.

Despite high remission rates with APL, treatment resistance and relapse do occur in some children. ATRA and ATO are also used to treat relapsed/refractory APL. For children with relapsed or refractory APL, the doctor may discuss an allogeneic or autologous stem cell transplantation as a possible treatment option once a remission is achieved.

See **Table 3**, *Drug Classes and Drug Mechanisms* on page 53 and **Table 4**, *Some Drugs Used in the Treatment of AML* on page 54 for each drug's prescribing information.

**Treatment Complications.** APL treatment can cause unwanted and unpleasant side effects. If you have any concerns about your child's side effects, talk to their doctor to get help. Most side effects are temporary and resolve when treatment is completed.

**Bleeding.** The ability to form blood clots (a process called "coagulation") is impaired in APL patients because they have decreased numbers of platelets and clotting factors. When bleeding symptoms are present, patients are supported with transfusion therapy that contains platelets or fresh frozen plasma. Plasma is the liquid part of the blood that carries the blood cells. The proteins that form blood clots are found in the plasma. Plasma can be frozen and preserved after blood donation to help prevent and control bleeding disorders, which frequently occur in APL.

**Differentiation Syndrome.** See page 42 for more information.

**Pseudotumor cerebri.** This disorder, also known as intracranial hypertension, is related to high pressure in the brain that causes signs and symptoms of a brain tumor – hence the term "pseudo" (or false) tumor. It happens when the fluid that surrounds the spinal cord and the brain—called cerebrospinal fluid—accumulates abnormally in the brain, causing pressure and pain. Pseudotumor cerebri can be a rare side effect of ATRA therapy and is most often observed in children and adolescents. The main symptom of this disorder is headache. Pseudotumor cerebri can be treated with the use of painkillers, glaucoma drugs that might reduce production of cerebrospinal fluid, steroids to reduce inflammation, and/or diuretic medication to reduce fluid buildup. Sometimes the temporary discontinuation of ATRA is necessary.

**High White Blood Cell (WBC) Count.** Elevated WBC counts, also known as hyperleukocytosis, is a frequent side effect that occurs in APL patients receiving ATO and/or ATRA therapy. A WBC count higher than 10,000/microliter is considered elevated. This side effect is generally managed with medications such as hydroxyurea, gemtuzumab ozogamicin and anthracyclines (idarubicin and daunorubicin).

**Changes in Liver Function.** Liver enzymes can become elevated as a result of therapy with ATO, ATRA and/or gemtuzumab ozogamicin. Liver function should be routinely monitored during APL treatment. If needed, therapy can be temporarily discontinued until liver function returns to normal.

**QT Interval Prolongation.** The use of ATO can affect electrolyte levels. Electrolytes are essential minerals in the blood such as potassium, magnesium, and calcium. Electrolyte imbalance can cause a heart rhythm disorder known as QT interval prolongation. This disorder causes a fast heartbeat that may lead to sudden fainting or seizures. Electrolytes should be monitored before and during APL treatment to ensure that they stay within a normal reference range. The doctors on your treatment team may order routine blood work and electrocardiograms to monitor any negative effects of ATO or other drugs.

**Down Syndrome and AML.** Down syndrome occurs in people who have trisomy 21, meaning they have an extra copy of chromosome 21. Children with Down syndrome have a higher risk of developing AML during childhood than children without Down syndrome.

Children with Down syndrome who are diagnosed with AML younger than age 4 years have better overall survival with AML treatment when compared with children with AML who do not have Down syndrome. Their leukemia cells may be more sensitive to chemotherapy, and they can experience positive outcomes with less-intensive therapy. In fact, children with Down syndrome often have challenges tolerating the toxic effects of intensive pediatric AML regimens, and they can experience higher rates of complications, including infection and heart issues. Given these potential complications, the treatment approach for younger patients uses less-intensive chemotherapy. Research suggests that older patients with Down syndrome are at higher risk for recurrence and therefore should receive the same treatment as children without Down syndrome who are diagnosed with AML.

Children with Down syndrome who have AML require special care. They can benefit from being treated at a major children's hospital where the doctors have experience treating children with Down syndrome and are aware of the special care that these children need.

## Relapsed and Refractory AML

Some patients have high levels of residual leukemia cells in their bone marrow even after they have received intensive treatment for AML. In these cases, the disease is referred to as refractory (or refractory AML). Less than 15 percent of children treated have refractory AML.

Other patients achieve remission but later have a return of leukemia cells in their bone marrow. This is referred to as a relapse of the disease (or relapsed AML). Approximately 50 percent of children with AML will have disease relapse.

At the time of relapse, genetic testing of the leukemia cells is recommended. The mutational pattern at this time may be different from the pattern seen when the disease was first diagnosed. This can affect treatment decisions.

For children with relapsed AML, the length of first remission is an important factor affecting the ability to achieve a second remission. Children with a first remission that lasted less than a year have lower rates of second remissions than children whose first remission lasted longer than a year.

Relapsed and refractory cases of AML are more often difficult to cure. Treatment is typically more intensive than it is for newly diagnosed patients, and in most cases, it includes stem cell transplantation (for eligible patients). Treatment

options for patients with refractory or relapsed AML may include:

- **A clinical trial.** Participation in a clinical trial should be considered as a treatment option for all patients with refractory or relapsed AML. A clinical trial may offer new combinations of anti-cancer therapies or targeted therapies, or new approaches to stem cell transplantation. LLS offers help for a child's parents (or guardians) to understand, identify and access clinical trials appropriate for their child. The Clinical Trial Support Center provides Clinical Trial Nurse Navigators that will help a child's parents or guardians find these clinical trials and assist them throughout the entire clinical-trial process. Visit www.LLS.org/CTSC for more information. See *Clinical Trials for Blood Cancers* on page 37.
- **High-dose chemotherapy.** Due to overlapping resistance or concerns over cumulative doses of specific agents, your doctor will likely select a different chemotherapy regimen than what was given after initial diagnosis.
- **Gemtuzumab ozogamicin (Mylotarg™).** This CD33-directed antibody and cytotoxic drug conjugate is for the treatment of relapsed or refractory CD33-positive AML in adults and pediatric patients age 2 years and older. Many children now receive this drug as part of their initial treatment, but it may be repeated at time of recurrence.
- **Revumenib (Revuforj®).** This menin inhibitor is approved for the treatment of relapsed or refractory acute leukemia with a *KMT2A* translocation in adult and pediatric patients age 1 year and older.
- **Allogeneic stem cell transplantation.** The above treatments are used to induce a remission, so that stem cell transplantation can be considered for the patient. Not all patients whose disease relapses are eligible for transplant, particularly if they have already had a transplant and the AML relapsed less than 6 months from that first transplant. This consideration is nuanced. Ask your child's doctor if a stem cell transplant will be considered as part of the treatment for your child's relapsed disease. For more information, see *Stem Cell Transplantation* on page 32.

Research is ongoing to determine optimal drug combinations, doses and administration schedules for relapsed and refractory cases of AML.

# Clinical Trials for Blood Cancers

Every new cancer drug goes through a series of carefully controlled research studies before it can become part of standard cancer care. These research studies are called clinical trials. Researchers use them to find better ways to care for and treat people with cancer. In the United States, the FDA requires that all new drugs and other treatments be tested in clinical trials before they can be used. At any given time, there are thousands of cancer clinical trials taking place.

Doctors and researchers are always looking for new and better ways to treat cancer. Researchers use cancer clinical trials to study new ways to

- Treat cancer using:
  - A new drug
  - An approved drug to treat a different kind of cancer
  - A new combination of drugs
  - A new way of giving a drug (by mouth, intravenously (IV), etc)
- Manage cancer symptoms and treatment side effects
- Find and diagnose cancer
- Keep cancer from coming back after treatment
- Manage long-term treatment side effects

By taking part in a clinical trial, patients can see doctors who are experts in their disease, gain access to new, cutting-edge therapies, and provide helpful information for future patients. The treatments and information we have today are due in large part to patients who have been willing to join clinical trials. Anyone interested in participating in a clinical trial should talk to their hematologist-oncologist about whether a clinical trial might be right for them. During this conversation it may help to:

- Have a list of questions to ask about the risks and benefits of each trial (visit www.LLS.org/WhatToAsk for lists of suggested questions)
- Ask a family member or friend to go with you to your doctor visit—both for support and to take notes

Clinical trials can be difficult to navigate and figure out, but The Leukemia & Lymphoma Society is here to help. Patients and caregivers can work with **Clinical Trial Nurse Navigators** who will help find potential clinical trials, overcome the barriers to enrollment and provide support throughout the entire clinical-trial process.

Our Clinical Trial Nurse Navigators are registered nurses who are experts in adult and pediatric blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about your treatment goals
- Help you to understand the clinical-trial process, including your rights as a patient
- Ask you for details about your diagnosis (such as past treatments, treatment responses, and your cancer genetic profile), your current health and your medical history. This information is taken into account and may factor into your eligibility to participate in certain clinical trials

- Help you to understand how your finances, insurance coverage, and support network, as well as your ability and willingness to travel might impact your choice of a clinical trial
- Guide you and help you in your efforts to find and enroll in a clinical trial, including connecting you with trial sites
- Help deal with any problems you might have as you participate in a trial
- Support you throughout the clinical-trial process

**Call an LLS Information Specialist at (800) 955-4572 or visit www.LLS.org/CTSC for more information about clinical trials and the Clinical Trial Support Center at LLS.**

**Visit www.LLS.org/booklets to view *Understanding Clinical Trials for Blood Cancers* and *Knowing All Your Treatment Options.***

# Related Diseases

**Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN).** BPDCN is a very rare, fast-growing blood cancer. It is similar to AML. But, unlike AML, BPDCN can affect other organs such as the lymph nodes, spleen, central nervous system and skin in addition to the blood and bone marrow. In fact, many patients with BPDCN have skin lesions, and the disease is often diagnosed through a skin biopsy. It may also be diagnosed through a bone marrow or lymph node biopsy.

BPDCN is rare in children. Most patients with BPDCN are older adults, with a median age of 65 to 67 years at diagnosis, and it is more common in males than females. A diagnosis of BPDCN requires a finding of at least four of the following six antigens on the cancer cells: CD123, CD4, CD56, TCL-1, CD2AP and CD303/BDCA-2. In addition, recurrent mutations in the following genes have been described: *ASXL1, ETV6, IDH1, IDH2, IKZF1, IKZF2, IKZF3, NPM1, NRAS, TET1, TET2, SRSF2, TP53, U2AF, ZEB2* and *ZRSR2*.

Children with BPDCN should seek treatment at a cancer center with doctors who have experience treating children who have this disease. Children have better outcomes and higher rates of remission than adults. Treatment may include the drug tagraxofusp-erzs (Elzonris®). Tagraxofusp-erzs targets the CD123 protein on the surface of BPDCN cells and leads to cancer cell death.

Patients in first remission may undergo allogeneic stem cell transplantation, if appropriate. Other treatment options include induction regimens used for AML, acute lymphoblastic leukemia (ALL) or lymphoma.

See **Table 3**, *Drug Classes and Drug Mechanisms* on page 53; and **Table 4**, *Some Drugs Used in the Treatment of AML* on page 54 for each drug's prescribing information.

**Visit www.LLS.org/CTSC to work with LLS Clinical Trial Nurse Navigators to help search for clinical trials for children and teens with BPDCN.**

**Mixed Phenotype Acute Leukemia (MPAL).** MPAL is a subtype of acute leukemia, which is also known as biphenotypic leukemia, and has an ambiguous lineage. It has features of two forms of leukemia: acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). It accounts for 2 to 5 percent of all acute leukemia cases, affecting patients of all ages, and there are several different subtypes.

Since MPAL is rare, patients with MPAL should seek treatment at a cancer center that has experience treating patients who have this disease. The best treatment approach for MPAL has not yet been determined, and it is associated with a worse prognosis than other pediatric leukemias. This is due to the difficulty in correctly identifying this type of leukemia, its low incidence, the lack of experience in treating it and its tendency to be resistant to chemotherapy. The reasons for this resistance are not yet clear but may be related to the high percentage of high-risk chromosomal abnormalities found in patients with MPAL. Currently there is no standard therapy for MPAL, but clinical trials are underway. Some studies have shown that ALL therapy may be the preferred approach.

A variety of factors are involved in determining the best treatment for patients with MPAL. These include the patient's age, medical history and other relevant medical conditions, and the characteristics of the leukemia cells as determined by immunophenotyping and genetic tests. It is also important to determine whether the patient has the Philadelphia chromosome-positive (Ph+) subtype, which accounts for about 25 percent of all cases of MPAL. Treatment for Ph+ MPAL usually consists of a chemotherapy regimen for ALL, based on the patient's age, in combination with a tyrosine kinase inhibitor (TKI). This may be followed by allogeneic stem cell transplantation.

For patients with a Philadelphia chromosome-negative (Ph-) subtype of MPAL, treatment often consists of an ALL-treatment regimen. Some patients who are MRD positive after induction may be considered for allogeneic stem cell transplantation. For patients for whom an ALL regimen does not result in remission, treatment can be switched to an AML-like regimen followed by consolidation therapy with an allogeneic stem cell transplant.

**Visit www.LLS.org/CTSC to work with LLS Clinical Trial Nurse Navigators to help search for clinical trials for patients with MPAL.**

# Side Effects and Complications

Side effects occur when treatment affects healthy tissue and organs. Most children with AML are treated with intensive chemotherapy, which can cause severe side effects that may require supportive care. The goal of supportive care is to prevent or treat, as early as possible, the side effects caused by cancer or cancer treatment. Most side effects in patients with AML are temporary and subside once the body adjusts to therapy, or when therapy is completed. If side effects become severe, your child may need to be hospitalized.

**Low Blood Cell Counts.** Cancer and cancer treatments often cause drops in blood cell counts. This can result in a severe deficiency in the patient's number of red blood cells, white blood cells and platelets. While your child is in the hospital, their blood cell counts will be checked daily.

Children with severe or prolonged low red blood cell and platelet counts almost always need to receive transfusions of both red blood cells and platelets for several weeks during treatment for AML. After that, the blood cell counts usually return to normal levels.

During AML treatment, low white blood cell counts can lead to infections from bacteria, viruses and fungi that are normally present in the environment, on the skin, in the nose and mouth, on the gums or in the colon. The risk of infection may be increased because chemotherapy damages the cells lining the mouth and intestines, making it easier for bacteria to enter the bloodstream. When patients have a low white blood cell count, antibiotics are commonly given to prevent bacterial infection, and other drugs are given to prevent fungal and viral infections.

Because of the increased risk of infection during treatment, medical staff, family and friends need to practice frequent and vigorous handwashing and take other precautions to avoid exposing patients to bacteria, viruses and other infection-causing agents. Caregivers of children with central lines or ports need to be meticulous when cleaning insertion sites and catheters, as instructed by their medical team.

Seek medical attention immediately if any symptoms of infection develop in your child at home. A temperature of 100.4°F or higher or the onset of chills may be the only sign of infection. Other signs of infection may include persistent coughing, sore throat, pain during urination or diarrhea.

**Tumor Lysis Syndrome (TLS).** Children with AML may be at risk for developing a condition called TLS. This condition occurs when a large number of cancer cells die within a short period of time, releasing their contents into the blood. TLS can be severe during the early phases of treatment, especially for children who have very high white blood cell counts before they start induction therapy. As the leukemia cells die, they break apart and release their contents into

the bloodstream changing its normal balance of chemicals. The imbalance of chemicals can overwhelm the kidneys because they cannot get rid of the substances quickly enough.

Uric acid is one of the chemicals released by dying cancer cells. Very high levels of uric acid and other chemicals can cause severe damage to the kidneys and heart. If untreated, TLS can lead to heart arrhythmias, seizures, loss of muscle control, acute kidney failure and even death.

Supportive care should include hydration to reduce the risk of developing TLS. Intravenous fluids are usually started at the time of diagnosis and are continued throughout chemotherapy to prevent chemical imbalances in the blood and to support kidney function. Medicines used to treat high uric acid levels include allopurinol (Zyloprim®) or rasburicase (Elitek®), which prevent or lessen the effects of this condition.

**Differentiation Syndrome.** This is a potentially life-threatening complication of treatment with differentiating agents, such as all-trans retinoic acid (ATRA) for acute promyelocytic leukemia (APL) or revumenib for relapsed/refractory *KMT2A*-rearranged acute leukemia. It usually occurs within 1 to 2 weeks after the beginning of treatment, but it can occur later. It is caused by a large, fast release of cytokines (immune proteins) from leukemia cells that are affected by the anticancer drugs.

Symptoms of differentiation syndrome include fever, swelling in the limbs and trouble breathing. Patients may also experience a drop in blood pressure and have fluid build-up around the lungs or heart. Treatment must begin when the patient first experiences signs and/or symptoms of this side effect. Treatment consists of corticosteroid therapy or the administration of the antimetabolite drug hydroxyurea and other chemotherapy drugs to decrease the number of white blood cells, which are the source of differentiation effects. In severe cases, use of differentiating agents is stopped.

**Other Side Effects.** Cancer cells tend to divide more quickly than most normal cells. Chemotherapy drugs affect cells that divide quickly, which is why they work against cancer cells. But they also can affect healthy cells in the body that divide quickly, such as cells in the lining of the intestines, the skin and hair follicles. Common side effects of chemotherapy may include:

- Hair loss
- Rashes
- Itchy skin
- Mouth sores
- Diarrhea
- Nausea and vomiting

- Loss of appetite and weight loss
- Headaches
- Fatigue

These short-term side effects usually go away once a patient has completed treatment. Inform your child's doctor about any side effects that your child is experiencing. The doctor may prescribe drugs and other supportive therapies to help to either prevent or manage many side effects

**Helping Children and Teens Cope with Hair Loss**

For many children and teens, hair loss can be one of the most distressing side effects of cancer treatment. Children can be sensitive about how they look and how others perceive them. Unfortunately, most children treated for AML will begin to temporarily lose their hair 2 to 3 weeks after starting chemotherapy. The following information may be useful to help children cope with hair loss.

- Many children's hospitals work with organizations that help provide wigs and other head coverings to patients in need. A hospital social worker can help children explore their options, and help families understand what is or is not covered by insurance.
- If your child is planning on wearing a wig, take a picture of your child's hair (how it is usually worn) before hair loss occurs so a wig stylist can create a wig similar to your child's natural hair. In addition, you may want to snip and keep a lock of your child's hair to help match the color and texture for a wig.
- Some children cut their hair short or shave their head before their hair falls out. This may allow children to feel some control over their hair loss and make it somewhat less upsetting. Other children may want to wait and see what happens. They may also want to dye their hair a wild color or get a crazy hairstyle. However, it is important to check with your child's doctor before using any dyes or chemical products on the hair.
- Some children like to wear wigs, hats, caps, scarves or turbans. Consider different head coverings. Shopping for head coverings can give your child some sense of control.
- Some children, particularly younger ones, may decide not to cover their heads. It is a personal choice for children and their families. However, for children going outside in the sun, it is important to protect the very sensitive skin on their head with either a head covering or sunscreen.
- Hair loss can be very difficult for children going back to school. Hospital social workers can offer support and resources for children dealing with hair loss.

Sometimes drugs or drug combinations cause side effects that continue after treatment ends. Some of these effects may be long-lasting (see *Long-term and Late Effects of Treatment* on page 47 for more information).

**Visit www.LLS.org/booklets to view the free LLS series *Side Effects Management* (filter for Side Effect Management).**

# Nutrition and Cancer

Good nutrition is very important for children receiving cancer treatment. Cancer and cancer treatment, however, may cause side effects that make it difficult for children to eat enough food and to stay well-nourished. It is also important for children with weakened immune systems to follow all food safety guidelines to reduce the risk of foodborne illness. Speak to your child's healthcare team about food and nutrition and for a referral to an oncology registered dietitian (RD) for specific nutrition advice and guidance.

LLS offers free nutrition consultations with registered dietitians who have expertise in oncology nutrition. Consultations are available to patients and caregivers of all cancer types.

**LLS registered dietitians have expertise in oncology nutrition and provide patients, parents and caregivers with free nutrition consultations by phone. Call (877) 467-1936 or visit www.LLSnutrition.org/consult to schedule.**

**Visit www.LLS.org/booklets to view *Food and Nutrition During Cancer Treatment* and *Nutrition Handbook: Feeding your family from meal planning to meal time*.**

# Financial Concerns

Paying for healthcare is a major concern for families who are living with blood cancer. The high cost of cancer can lead to significant financial and emotional stress. Even if your child has health insurance, cancer can still take a toll on your finances. You may have new expenses such as co-payments or travel for treatment. You may also have less income if you need to take time off from work.

Speak with your healthcare team if you have any concerns about being able to afford your child's treatment. They may be able to provide information and resources that can help. Health insurance plans may not cover all the costs of cancer care, but there are many resources available to help with prescription

drug payment. In addition, several major drug manufacturers currently provide patient assistance or prescription assistance programs. These programs can provide both insured and uninsured patients free or reduced-cost medications.

**We offer financial assistance programs and medical debt case management for eligible patients. You can call our Information Specialists at (800) 955-4572 for more information.**

**Visit www.LLS.org/booklets to view *Cancer and Your Finances*.**

# Follow-Up Care

After your child completes treatment for AML and the disease is in remission, they will need follow-up care. Follow-up care involves regular medical checkups. These checkups may include blood work as well as other tests to check for signs of a possible relapse. The doctors will also test for other physical or emotional problems that may develop months or years after treatment. Even if your child is feeling entirely well, it is very important to keep the follow-up appointments.

Your child will undergo frequent follow-up tests during the first year after treatment, but the tests will be done less often during the second and third years. Testing and checkups may be required less frequently as time goes on, but scheduled follow-up visits should continue indefinitely.

Each patient has a different follow-up care schedule. How often your child has follow-up visits is based on your child's type of AML and the treatments given. The doctor will let you know the schedule that is right for your child. If your child participated in a clinical trial, the follow-up care and frequency of visits may be slightly different but should, likewise, be followed accordingly.

Some childhood vaccines may have been delayed during treatment. The doctor will advise you when to resume your child's vaccination schedule. Current COVID-19 vaccines are recommended even during treatment, as is the yearly influenza vaccine. Speak to your child's doctor for more information.

Your child's healthcare team may also recommend a schedule for evaluating your child's learning skills. If your child appears to be struggling with learning, special education methods may help. See *Returning to School* on page 49 for more information.

Your child will continue to need follow-up care even after becoming an adult. Young adult patients need to be educated about the importance of follow-up care. When teens reach adulthood, remind them that any new providers will need to know their detailed medical history and survivorship care plan. Work

with members of the cancer treatment team to coordinate care and transfer medical records to new providers.

It is important to keep a record of your child's cancer treatments so that during visits for follow-up care, the doctor can review them and monitor for specific late effects that may be associated with those treatments.

**Survivorship Care Plan.** Survivorship generally refers to the health and well-being of a person after cancer treatment. Your child's hematologist-oncologist will help create a survivorship care plan to guide your child's follow-up care. That way, as your child enters adulthood, they will have a clear, written history of the diagnosis, treatments and the schedule for follow-up care.

Share the survivorship care plan with any healthcare providers your child sees. The survivorship care plan should include the following information:

- A list of all your child's healthcare providers: pediatrician, hematologist-oncologist, radiation oncologist, etc.
- A diagnosis summary with specifics such as the AML subtype
- A treatment summary with specifics such as dates of treatment, names of chemotherapy or other drugs received, radiation dosage and site, responses to treatments and side effects
- A follow-up appointment schedule with the names of the medical providers and how often the appointments should occur
- A schedule for ongoing monitoring, with recommended tests and frequency
- A list of possible long-term and late effects
- Health and wellness lifestyle recommendations, such as nutrition, exercise, other cancer and disease screenings, and referrals to specialists (as needed) to assist with these recommendations

The Children's Oncology Group provides a downloadable Summary of Cancer Treatment template for you to fill out with the help of the members of your child's healthcare team. Visit www.survivorshipguidelines.org to download a template.

For additional survivorship information, visit www.LLS.org/survivorshipworkbook to view the free LLS booklet *Navigating Life During and After a Blood Cancer Diagnosis: A Workbook for Children and Adolescents.*

**Survivorship Clinics.** Childhood cancer survivors have special lifelong healthcare needs. Many hospitals and treatment centers offer survivorship clinics that specialize in long-term follow-up care for cancer survivors. Children often begin visiting a survivorship clinic 2 years after finishing cancer treatment. However,

the timeline can differ based on your child's unique needs and medical history. Additionally, coordination between members of your child's cancer survivorship healthcare team and primary care pediatrician is essential.

Your child should visit the survivorship clinic and primary care pediatrician at least once a year for a complete physical examination and any other necessary tests, even when your child feels well. Regular visits allow the doctor to:

- Assess the full effects of treatment
- Identify and manage long-term and late effects of treatment (see *Long-term and Late Effects of Treatment* below for more information)
- Detect and treat disease recurrence (relapse)

In preparation for your child's visits, keep a record of the physical or emotional symptoms that your child experiences so that you can discuss them with members of the healthcare team. For example, children may experience difficulties when they return to their daily routines after a long period of treatment. Getting support throughout this time, and for as long as needed, is important.

**Long-term and Late Effects of Treatment.** Cancer treatments can harm a child's organs, tissues or bones and may cause delayed growth and other health problems later in life. Childhood cancer survivors may have complex and long-term health issues due to the treatments they received. While treatments for AML have led to increased survival rates, some may cause significant long-term or late effects.

Long-term effects of cancer treatment are medical problems that last for months or years after treatment ends. Examples of long-term effects are infertility, growth problems and treatment-related fatigue. Late effects are medical problems that do not appear until years, or even decades, after treatment ends. Examples of late effects include the development of a treatment-related cancer or heart disease.

For survivors of childhood leukemia, long-term and late effects of treatment may involve:

- Cognition (the mental process of thinking, learning, remembering and using judgment)
- Physical development
- Psychological development

Factors that influence a child's risk for developing long-term or late effects include:

- Type and duration of treatment
- Sex

- Age at the time of treatment
- Overall health

The range and severity of these potential long-term and late effects vary. Some children have no significant long-term or late effects, or very mild effects, while others have serious complications. Some late effects become evident with the onset of puberty, growth and the normal aging process. Early intervention and healthy lifestyle practices (not smoking, good nutrition and exercise, regular screenings and follow-up care) may have a positive effect on the occurrence and/or severity of effects.

It is important for parents to discuss possible late effects with members of their child's healthcare team so that the proper planning, evaluation and follow-up care can take place.

**Types of Long-term and Late Effects of Treatment.** Long-term and late effects of AML treatment may include cognitive, physical and psychological effects.

**Cognitive (Learning) Effects.** Learning difficulties can range from mild to severe and can begin either during treatment or may become evident months or even years after treatment. Mathematics, spatial relationships, problem solving, attention span, reading and spelling, processing of information, planning and organizing, and concentration skills are all areas of learning that may be affected. Problems with fine motor coordination, which might cause poor handwriting, can also develop.

Treatments directed at the central nervous system, such as intrathecal chemotherapy with cytarabine, or total body radiation prior to stem cell transplantation, may increase the risk for cognitive effects. Receiving cancer treatment at a younger age also increases the risk.

Talk to your child's healthcare team about any educational or learning issues that cause concern. A pediatric psychologist can perform neuropsychological testing to evaluate your child for any signs of these potential late effects.

**Physical Effects.** Depending on the types of treatment received, children treated for AML may be at risk for growth delays, bone health issues, damage to the heart, thyroid gland or other organs, obesity, fatigue and secondary cancers. Cancer treatment may also affect fertility, the ability to conceive or father a biological child.

**Psychological Effects.** Most childhood survivors of cancer are psychologically healthy. However, some studies indicate that a small number of childhood leukemia survivors were more likely than healthy peers to report changes in behavior, feelings or mood, including depression or post-traumatic stress disorder (PTSD). Talk to your child's healthcare team if you notice any changes in

your child's mood or behavior, especially if these changes begin to interfere with your child's daily life.

**Cardiovascular System.** Children who receive intensive chemotherapy with anthracyclines, such as daunorubicin, are at increased risk of developing heart problems. They should receive ongoing monitoring of cardiac function for heart problems, including abnormal heartbeat, weakness of the heart muscle and congestive heart failure.

Talk to your child's doctor about whether tests are needed to check for signs of heart- and blood vessel-related late effects. If tests are recommended, find out how often they should be done.

**Second Cancer Risk.** Survivors of childhood AML are at an increased risk for developing a second cancer later in life. A second cancer may occur months or years after treatment is completed. Because of this risk, it is important for patients who have been treated for AML to get screened for second cancers on a regular basis.

**Visit www.LLS.org/FamilyWorkbook to find additional information about long-term and late effects (see the chapter *Beyond Treatment*).**

**Talk to your child's doctor about:**

- Possible long-term and late effects and follow-up care

**Returning to School.** School is a place for learning and fun, so children and teens benefit from returning to their classrooms as soon as medically possible. Most children who have cancer will attend school at least some of the time during their treatment. Yet returning to school after a diagnosis of cancer can be a tough adjustment. Your child may have reservations about returning to school, including fears about:

- The reaction of friends and other children at school
- Missed schoolwork and social activities
- Changes in abilities
- Changes in appearance

Discuss any fears your child may have before going back to school. Help your child develop strategies for coping with situations that may happen.

If your child has been out of the classroom for an extended time, it may be helpful to have them ease back into full-time school slowly. For example, your child may attend school for half days or every other day during the first weeks back. Talk to school administrators about adjustments to schedules and other options available.

Take the following steps to ensure that your child gets the support needed at school:

- Meet with school administrators, teachers, counselors and the school nurse as soon as you can after diagnosis to discuss your child's medical condition and address any special needs or concerns.
- Discuss any evaluations that may be needed to provide your child with extra support, such as neuropsychological testing. Ask the school staff to provide you with relevant information promptly when they identify any issues that arise.
- Work with the school nurse to make sure that a care plan is in place that addresses your child's medical needs during school hours. For example:
  - Your child may need to take medications at school. These may be daily medications or medications taken as needed (for example, when your child feels nauseated).
  - If your child has a catheter or some other medical device in place, make sure the school nurse knows how to care for the device properly.
  - The care plan should also include a list of issues that can come up, reasons to contact you and when to call for emergency care. Your child's healthcare team can help the school nurse develop a care plan and fill out any necessary paperwork.
- Ask your child's doctor to write a letter outlining your child's physical limitations or medical needs, such as the need for extra snacks or cool drinks, extra bathroom breaks and/or a safe place to rest, as needed. Modifications may also be needed for recess or physical education (PE) classes. Meet with school administrators and teachers to discuss these needs and how they will be accommodated. Ask your child's healthcare team for their expertise in explaining this information.
- To reduce your child's anxiety, arrange meetings with the teacher(s) before your child goes back to school.
- Ask about providing an age-appropriate class presentation, either before or after your child returns to school, to educate friends and classmates about cancer. Ask members of the healthcare team for assistance. Some treatment centers have healthcare professionals available to lead these presentations or have prepared versions of these presentations available for use. Ask your child if they would like to be present for the presentation. If so, your child can participate in ways that are comfortable for them.

**Visit www.LLS.org/booklets to view the free LLS booklet *A Parent's Guide to School and Childhood Cancer* for more information about returning to school after cancer treatment.**

**The Trish Greene Back to School Program.** This program offers free information and materials to parents and educators that can help ease a child back into school. The program was developed to encourage communication among parents, patients, healthcare professionals and school personnel to assure that children have a smooth transition from undergoing active treatment to settling back into school. Call our Information Specialists at (800) 955-4572 to learn more.

# Treatment Outcomes

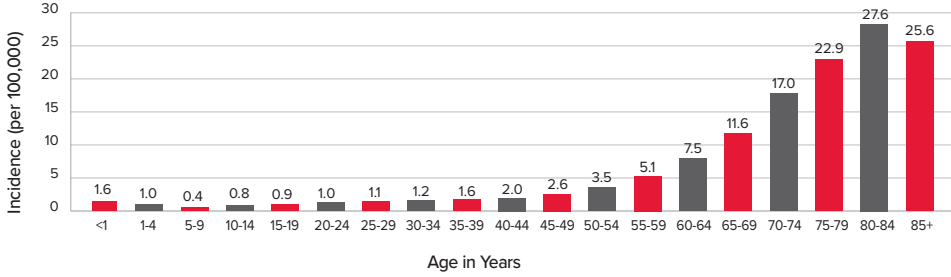
AML is a difficult disease to cure, but survival rates for childhood AML have improved over the past several decades. Today, up to 75 percent of children survive AML. However, there is a wide range of outcomes for different subtypes of AML.

It is also important to remember that survival statistics are only estimates and are based on patients diagnosed with AML some time ago. Since the statistics were collected, new treatments have been approved, and more are being studied in clinical trials. As a result, the outlook may be better for children diagnosed with AML today.

# Incidence, Causes and Risk Factors

**Incidence.** Older adults are more likely than younger adults or children to develop AML, but AML is the second most common childhood leukemia. In children, the incidence rate is highest before 1 year of age and decreases after that. The rate is lowest at approximately 9 years, followed by a slow increase during adolescence and young adulthood. See **Figure 6**.

### Figure 6. AML: Age-Specific Incidence Rates 2016-2020




The horizontal axis shows 5-year age intervals. The vertical axis shows the frequency of new cases of AML per 100,000 people, by age-group.

Source: SEER*Explorer: An interactive website for SEER cancer statistics [Internet] Surveillance Research Program, National Cancer Institute; 2023 Apr 19 [updated: 2023 Nov 16; cited 2024 Feb 21] Available from: https://seercancergov/statistics-network/explorer/ Data source(s): SEER Incidence Data, November 2022 Submission (1975-2020), SEER 22 registries.

**Causes and Risk Factors.** Although in most cases it is not clear what causes the genetic changes that lead to AML, there are some known risk factors. A risk factor is anything that increases a person's chance of developing a disease. However, having a risk factor does not mean that a person will develop the disease. Some people with several risk factors for a disease never develop it, while others with no known risk factors do. AML is not contagious.

The factors that are associated with an increased risk of developing AML as a child include:

- **Genetic disorders.** Certain genetic conditions, present at birth, seem to increase the risk of AML, including:
  - Down syndrome
  - Neurofibromatosis type 1
  - Bloom syndrome
  - Trisomy 8
  - Fanconi anemia
  - Klinefelter syndrome
  - Wiskott-Aldrich syndrome
  - Kostmann syndrome
  - Shwachman-Diamond syndrome
- **Familial risk.** Certain gene mutations present at birth may increase the risk of developing AML. This is also known as germline predisposition. Having a sibling with leukemia, especially a twin, is a risk factor for developing AML.
- **Previous treatment with chemotherapy or radiation.** Some people who received radiation therapy or certain types of chemotherapy have an increased risk of developing AML. When AML develops as a result of treatment for another disease in the past, it is often called "treatment-related" or "therapy-related" AML.
- **Other blood cancers.** People who have certain blood cancers are at greater risk of developing AML. These include myeloproliferative neoplasms (polycythemia vera, essential thrombocythemia and myelofibrosis), as well as myelodysplastic syndromes (MDS), which in some people can evolve, over time, into AML.
- **Chemical exposure.** Long-term exposure to high levels of certain chemicals, such as benzene, is linked to a greater risk of AML.

# Drug Information

**Table 3** below includes information on drug classifications and their functions and mechanisms of action. **Table 4** on page 54 lists some of the medications used to treat AML. For more information, see the package insert and/or the full prescribing information that accompanies each medication available on the internet.

### Table 3. Drug Classes and Drug Mechanisms

| | |
|---|---|
| **Anthracycline** | A chemotherapy drug that is derived from certain types of *Streptomyces* bacteria. Anthracyclines work by damaging the DNA of cancer cells, which causes them to die before they can multiply. |
| **Antimetabolite** | A chemotherapy drug that interferes with the normal division and function of cancer cells. Antimetabolites mimic the building blocks of DNA or RNA that cancer cells need to survive and grow. When the cancer cell uses an antimetabolite instead of the natural substances, it cannot produce normal DNA or RNA, and the cell dies. |
| **Antineoplastic Agent** | A type of chemotherapy drug that uses chemicals to kill cells that rapidly divide such as cancer cells. They interfere with the growth of cancer cells, which are eventually destroyed. |
| **CD33-Directed Antibody** | Most people with AML have leukemia cells that express a protein called CD33. CD33-directed antibodies target and kill cells with the CD33 protein. |
| **CD123-Directed Cytotoxin** | BPDCN cells have a high number of the protein CD123. By targeting the CD123 protein on the surface of BPDCN cells, the drugs can find and kill these cells. |
| **FLT3 Inhibitor** | Some people with AML have a mutation in the *FLT3* gene that can increase the growth and division of AML cells. FLT3 inhibitors are drugs that target these gene mutations to help reduce the growth of AML cells. |
| **Menin Inhibitor** | Menin is a protein that interacts with abnormal leukemia fusion proteins such as the fusion protein resulting from *KMT2A*-rearranged leukemia and plays a role in maintaining leukemic state in *NPM1*-mutated AML. This interaction is necessary for the leukemia cells to grow. When menin inhibitors block the interaction of the fusion protein with menin, it causes the leukemia cells to die. |

**Table 3. Drug Classes and Drug Mechanisms (continued)**

| | |
|---|---|
| **Retinoid** | Vitamin A or vitamin A-like compounds that may stop the growth of cancer cells. |
| **Topoisomerase inhibitor** | A substance that blocks topoisomerases (enzymes that break and rejoin DNA strands and are needed for cells to divide and grow). Blocking these enzymes may kill cancer cells. |

**Table 4** includes information about drug classifications and treatments for AML. For more information, see the Package Insert and/or the Full Prescribing Information for each medication on the internet.

**Table 4. Some Drugs Used in the Treatment of AML**

| Drug Name<br>Administration<br>Type of Drug | Indications |
|---|---|
| **All-trans retinoic acid (ATRA, Tretinoin, Vesanoid®)**<br>Oral<br>Retinoid | Approved for the induction of remission in adults and pediatric patients 1 year of age and older with acute promyelocytic leukemia (APL), characterized by the presence of the t(15;17) translocation or the presence of the *PML::RARα* gene expression, and who are refractory to or who have relapsed from anthracycline chemotherapy or for whom anthracycline-based chemotherapy is contraindicated. |
| **Arsenic trioxide (Trisenox®)**<br>Intravenous (IV)<br>Antineoplastic Agent | Approved:<br>○ In combination with tretinoin for treatment of adults with newly diagnosed low-risk acute promyelocytic leukemia (APL) whose APL is characterized by the presence of the t(15;17) translocation or *PML::RARα* gene expression.<br>○ For induction of remission and consolidation in patients with APL who are refractory to, or have relapsed from, retinoid and anthracycline chemotherapy, and whose APL is characterized by the presence of the t(15;17) translocation or *PML::RARα* gene expression. |

**Table 4. Some Drugs Used in the Treatment of AML (continued)**

| Drug Name<br>Administration<br>Type of Drug | Indications |
|---|---|
| **Cladribine (Leustatin®)**<br>Intravenous (IV)<br>Antimetabolite | For the treatment of hairy cell leukemia and is also being studied in the treatment of other types of cancer. |
| **Clofarabine (Clolar®)**<br>Intravenous (IV)<br>Antimetabolite | For the treatment of pediatric patients with relapsed or refractory acute lymphoblastic leukemia (ALL) and is also being studied in the treatment of other types of cancer. |
| **CPX-351 (Vyxeos®)**<br>Intravenous (IV)<br>Anthracycline and antimetabolite | Approved for the treatment of newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) in adults and pediatric patients 1 year and older. |
| **Cytarabine (Ara-C; Cytosar-U®)**<br>Intravenous (IV) or Subcutaneous Injection<br>Antimetabolite | Approved to be used either alone or with other chemotherapy drugs to treat certain types of leukemia including AML. |
| **Daunorubicin (Cerubidine®)**<br>Intravenous (IV)<br>Anthracycline | Approved to be used with other chemotherapy drugs to treat AML. |
| **Etoposide (Etopophos®, VePesid®, VP-16)**<br>Intravenous (IV)<br>Topoisomerase inhibitor | For the treatment of testicular cancer and small cell lung cancer, but is used as an off-label treatment for AML. |
| **Gemtuzumab ozogamicin (Mylotarg™)**<br>Intravenous (IV)<br>CD-33 Directed Antibody | Approved for the treatment of<br>○ Newly diagnosed CD33-positive AML in adults and pediatric patients 1 month and older.<br>○ Relapsed or refractory CD33-positive AML in adults and pediatric patients 2 years and older. |

**Table 4. Some Drugs Used in the Treatment of AML (continued)**

| Drug Name<br>Administration<br>Type of Drug | Indications |
|---|---|
| **Idarubicin (Idamycin®)**<br>Intravenous (IV)<br>Anthracycline | Approved for the treatment of AML in adults in combination with other approved antileukemia drugs but is also used to treat pediatric AML patients. |
| **Methotrexate (Trexall®)**<br>Intrathecal,<br>Intravenous (IV)<br>Oral<br>Antimetabolite | Approved for the prophylaxis and treatment of adult and pediatric patients with meningeal leukemia. |
| **Midostaurin (Rydapt®)**<br>Oral<br>FLT3 inhibitor | Indicated for the treatment of adult patients with newly diagnosed AML that is *FLT3* mutation-positive as detected by an FDA approved test, in combination with standard cytarabine and daunorubicin induction and high-dose cytarabine consolidation. |
| **Mitoxantrone (Novantrone®)**<br>Intravenous (IV)<br>Anthracycline | Approved for the treatment of AML. |
| **Revumenib (Revuforj®)**<br>Oral<br>Menin inhibitor | Approved for the treatment of relapsed or refractory acute leukemia with a lysine methyltransferase 2A gen (*KMT2A*) translocation in adult and pediatric patients 1 year and older. |
| **Sorafenib (Nexavar®)**<br>Oral<br>FLT3 inhibitor | Being studied in clinical trials in patients with AML with an *FLT3* mutation. |
| **Tagraxofusp-erzs (Elzonris®)**<br>Intravenous (IV)<br>CD123-Directed Cytotoxin | Approved for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPCDN) in adults and pediatric patients 2 years and older. |
| **Thioguanine (Tabloid®)**<br>Oral<br>Antimetabolite | Indicated for remission induction and remission consolidation of acute nonlymphocytic leukemias. |

# Normal Blood and Bone Marrow

**Blood.** Blood is the liquid that flows through a person's arteries and veins. It carries oxygen and nutrients throughout the body. It also carries away waste products. Blood is composed of plasma and cells.

**Plasma.** Plasma is largely made up of water in which many chemicals are dissolved. These chemicals each have a special role. They include:

- Proteins
  - Albumin. This is the most common blood protein.
  - Blood-clotting proteins (coagulation factors). They are made by the liver.
  - Erythropoietin. It is made by the kidneys and stimulates red blood cell production.
  - Immunoglobulins. These are cells that fight infection.
- Hormones, such as thyroid hormones and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin $B_{12}$
- Electrolytes, such as calcium, potassium and sodium

**Blood Cells.** Blood cells are formed in the bone marrow, a spongy tissue where blood cells grow and develop. Blood cells start as stem cells. The process of stem cells maturing into blood cells is called hematopoiesis (see **Figure 7** on page 59). The blood cells are suspended in the plasma.

Once the blood cell is created, it will develop into one of the three types of blood cells:

1. Red blood cells are the cells that carry oxygen; they
   - Make up a little less than half of the body's total blood volume
   - Are filled with hemoglobin, the protein that picks up oxygen from the lungs and takes it around the body. It binds with carbon dioxide ($CO_2$) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the $CO_2$ is removed from the lungs.
2. Platelets are cells that help blood clot; they
   - Are small cells (one-tenth the size of red blood cells)
   - Help stop bleeding from an injury or cut
   - Stick to the torn surface of the vessel, clump together, and plug up the bleeding site. They form a clot, with the help of proteins, such as fibrin, and electrolytes, such as calcium.

3. White blood cells (WBCs) are cells that fight infections. The several types of WBCs include:
    - Neutrophils and monocytes. These are phagocytes (eating cells) that ingest and destroy bacteria and fungi. Unlike red blood cells and platelets, monocytes can leave the bloodstream and enter tissues to attack invading organisms and fight off infection.
    - Eosinophils and basophils. These WBCs respond to allergens or parasites.
    - Lymphocytes. WBCs found mostly in the lymph nodes, spleen and lymphatic channels, lymphocytes are a key part of the immune system. Some enter the bloodstream. There are three major types of lymphocytes:
        - T lymphocytes (T cells)
        - B lymphocytes (B cells)
        - Natural killer (NK cells)

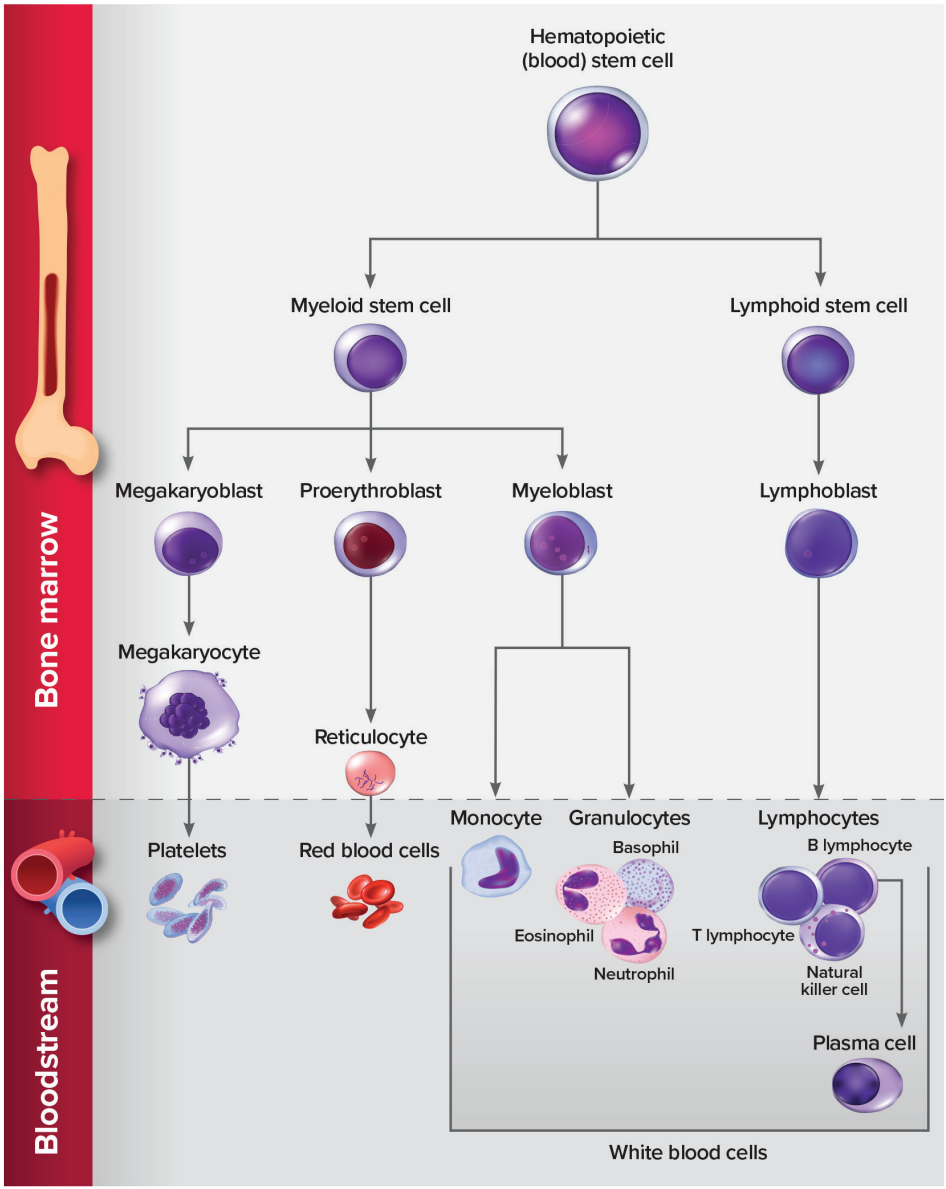
In healthy people, stem cells in the bone marrow produce new blood cells continuously. When blood cells are fully developed, they enter the bloodstream as it passes through the bone marrow and then circulates throughout the body.

In babies, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms and legs no longer have blood-forming marrow. In adults, bone marrow is only found in the spine (vertebrae), hip and shoulder bones, ribs, breastbone and skull.

Hematopoietic stem cells are found in the bone marrow. These stem cells are important because they can be transplanted. Some stem cells enter the bloodstream and circulate; there are not enough of them to be counted in standard blood tests. Doctors know how to stimulate the growth of these cells in the bone marrow and have them migrate into the bloodstream. Then a special technique called apheresis is used to separate them from the circulating blood so they can be collected and stored. In addition, stem cells from the placenta and the umbilical cord of a newborn infant can be collected and stored for future use in transplantation.

## Figure 7. Blood Cell and Lymphocyte Development

Most blood cells start as hematopoietic (blood) stem cells in the bone marrow. Hematopoietic stem cells are the most immature blood-forming cells. They must mature (go through many stages) to become a red blood cell, white blood cell or platelet. Some blood cells mature in the bone marrow. Other blood cells leave the bone marrow and travel to other parts of the body to develop into mature blood cells.



# Additional Resources

**Information for Firefighters.** Firefighters are at an increased risk of developing cancer. There are steps firefighters can take to reduce the risk. Please visit www.LLS.org/FireFighters for resources and information.

**Information for Veterans.** Veterans who were exposed to Agent Orange while serving in Vietnam; to airborne hazards and burn pits while serving in Iraq, Afghanistan and other areas of Southwest Asia; to contaminated water at Camp Lejeune between 1953-1987; or to ionizing radiation during service may be able to get help from the United States Department of Veterans Affairs (VA). For more information, please

- Call: the VA (800) 749-8387
- Visit: https://www.va.gov/disability/eligibility/hazardous-materials-exposure/

**Language Services.** Let members of your healthcare team know if you need translation or interpreting services because English is not your native language, or if you need other assistance, such as a sign language interpreter. Often these services are free.

**Mental Health.** Caring for your mental health has benefits for cancer patients. Seek medical advice if you are struggling. For more information, please

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov

If you or your loved one is experiencing a mental health crisis, call 988 to talk to a trained mental health professional. The 988 Suicide and Crisis Lifeline is free, confidential and always available. For the Crisis Text Line, text HOME to 741741.

**Other Helpful Organizations.** The Leukemia & Lymphoma Society (LLS) offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. For more information, visit www.LLS.org/ResourceDirectory to view the directory.

**World Trade Center Health Program.** People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be able to get help from the World Trade Center (WTC) Health Program. People eligible for help include:

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were in the NYC disaster area and those who lived, worked or were in school in that area
- Responders to the Pentagon and the Shanksville, PA crashes

For more information, please

- Call: WTC Health Program at (888) 982-4748
- Visit: www.cdc.gov/wtc/faq.html

# Health Terms

**Alkylating Agent.** A type of chemotherapy drug that is used in cancer treatment. It kills cancer cells by damaging their DNA, which prevents them from dividing (reproducing).

**Allogeneic Stem Cell Transplantation.** A treatment that uses stem cells from a healthy donor to restore a patient's bone marrow that is damaged or diseased after receiving high doses of chemotherapy and/or radiation therapy. **Visit www.LLS.org/booklets to view the free LLS booklet *Blood and Marrow Stem Cell Transplantation* for more information.**

**Anemia.** A condition in which the number of red blood cells is below normal. This results in reduced oxygen flow to the body's organs. Severe anemia can cause a pale complexion, weakness, fatigue and shortness of breath.

**Anthracycline.** A type of chemotherapy drug that is used to treat many types of cancer. It damages the DNA of cancer cells, causing them to die.

**Antibody.** A type of protein created by blood cells in response to an antigen (a substance that causes the body to mount a specific immune response). Antibodies help the body fight against invaders that make a person sick. They can also be made in the laboratory to help treat cancer.

**Antigen.** A substance that creates an immune response in the body, especially the production of antibodies. Examples include allergens, chemicals, bacteria, viruses and other substances outside the body. Cells in the body, including cancer cells, also have antigens on their surfaces that can cause an immune response.

**Antimetabolite.** A chemotherapy drug that interferes with the normal division and function of cancer cells.

**Autologous Stem Cell Transplantation.** A treatment in which stem cells are removed from a patient, stored and then returned to the patient's body after intensive cancer treatment. **Visit www.LLS.org/booklets to view the free LLS booklet *Blood and Marrow Stem Cell Transplantation* for more information.**

**Basophil.** A type of white blood cell that is involved in certain allergic reactions.

**Biopsy.** A procedure to remove a sample of cells or tissue from the body for examination by a pathologist. The pathologist may examine the specimen under a microscope or perform other tests on the cells or tissue.

**Blast Cell.** An immature blood cell.

**Blood Cells.** There are three major types of blood cells: 1) red blood cells, which carry oxygen; 2) white blood cells, which fight infections; and 3) platelets, which help stop bleeding.

**Bone Marrow.** A spongy tissue in the hollow central cavity of bones, where blood cells form.

**Bone Marrow Aspiration.** A procedure in which a liquid sample of bone marrow is removed for examination by a pathologist. The sample is usually taken from the patient's hip bone using a special needle, after a medication is given to numb the area. Bone marrow aspiration and bone marrow biopsy can be done in a doctor's office or in a hospital and are often done at the same time.

**Bone Marrow Biopsy.** A procedure in which a sample of bone containing bone marrow is removed for examination by a pathologist. The sample is usually taken from the hip bone, using a special hollow needle, after medication is given to numb the skin and tissue in that area. Bone marrow aspiration and bone marrow biopsy can be done in a doctor's office or in a hospital and are usually done at the same time.

**CBC.** See Complete Blood Cell Count.

**Central Line.** A flexible tube used to deliver medications, fluids or blood products into the body, or to withdraw blood samples from the body. Also called "central venous catheter" or simply "catheter." See Port.

**Central Nervous System (CNS) Prophylaxis.** Treatment given to lower the risk of leukemia cells spreading to the central nervous system (brain and spinal cord). It may include intrathecal chemotherapy (chemotherapy injected directly into the cerebrospinal fluid, the space between the layers of tissue that cover the brain and spinal cord), high-dose chemotherapy injected into a vein, or radiation therapy.

**Chemotherapy.** Treatment that stops the growth of cancer cells, either by killing them or by stopping them from dividing.

**Chromosome.** Part of a cell that contains genes in a linear order. Human cells have 23 pairs of chromosomes. **Visit www.LLS.org/booklets to view the free LLS booklet *Understanding Genetics* for more information.**

**Clinical Trial.** A research study that is carefully planned and monitored to evaluate how well new medical approaches work in patients. The goal of clinical trials for blood cancers is to develop new treatments, improve quality of life and increase survival time.

**Cluster of Differentiation (CD).** A term used along with a number to identify a specific protein found on the surface of cells that helps differentiate one cell type from another. It is commonly used in its abbreviated form, for example, "CD20." Also referred to as cluster of designation.

**Complete Blood Count (CBC).** A laboratory test that measures the number of red blood cells, white blood cells and platelets in the blood. It also measures the amount of hemoglobin (the substance in the blood that carries oxygen) and the hematocrit (the amount of whole blood that is made up of red blood cells).

**Cord Blood Stem Cells.** Stem cells collected from the placenta and umbilical cord after a baby is born. These stem cells can be infused into a patient's bloodstream to replace damaged or diseased stem cells in patients who undergo stem cell transplantation.

**Corticosteroid.** A class of drugs that is used to reduce inflammation, swelling and pain. In high doses, it can kill leukemia and lymphoma cells.

**Cytogenetic Analysis.** The process of analyzing the number and size of the chromosomes in cells. It detects chromosome alterations and, in some cases, may identify the actual genes that have been affected. These findings help doctors diagnose specific types of blood cancer, determine which treatment approaches to use and monitor a patient's response to treatment.

**Cytotoxic Drug.** An anticancer drug that kills cancer cells or prevents them from dividing.

**Deletion.** In genetics, this refers to a portion of a chromosome that is missing.

**DNA.** Abbreviation for deoxyribonucleic acid, the molecules found inside cells that carry genetic information. DNA is passed to new cells during the process of cell division. A change or mutation in the DNA can lead to cell death, changes in cell function and, in some cases, cancer.

**Eosinophil.** A type of white blood cell that is released during infections and allergic reactions.

**Erythrocyte.** See Red Blood Cell.

**Extramedullary Disease.** Leukemia cells that form tumors outside the bone marrow. See Myeloid Sarcoma.

**FDA.** The abbreviation used to refer to the United States Food and Drug Administration. The FDA is responsible for assuring the safety, effectiveness and security of drugs, medical devices and the nation's food supply.

**FISH.** See Fluorescence In Situ Hybridization (FISH).

**Flow Cytometry.** A test that measures certain characteristics of cells in a sample, including size, shape and the presence of tumor markers on the cell's surface. During this test, cells flow through an instrument called a "flow cytometer." When the cells pass through its laser beam, those with the antibody-specific features light up and can be counted.

***FLT3.*** A gene that makes a protein, FMS-like tyrosine kinase 3, which regulates blood cell development. Mutations of this gene can cause overproduction of the FLT3 protein, which may cause the body to make too many immature white blood cells.

**Fluorescence In Situ Hybridization (FISH).** A technique for studying abnormal chromosomes in cells and tissues. Pieces of DNA that contain fluorescent molecules are added to cells or tissues on a slide. When the pieces of DNA bind to specific genes or chromosomes, they light up when viewed under a specialized "fluorescence" microscope. This test can help to diagnose some types of cancer, plan treatment and monitor the effectiveness of treatment.

**Fungal.** Referring to a fungus, a single-celled or multicellular organism that is neither a plant nor an animal. Examples of fungi are molds, yeasts and mushrooms. Cancer treatments can weaken the immune system, which can increase a patient's chance of getting a fungal infection.

**Fusion Gene.** A gene made by joining parts of two different genes. Fusion genes can happen in the body when part of the DNA from one chromosome moves to another chromosome.

**Graft-Versus-Host Disease (GVHD).** A disease that occurs when stem cells transplanted from a donor (the graft) attack the tissues of the recipient (the host). Most often, GVHD affects a patient's skin, liver, stomach and gastrointestinal tract. **Visit www.LLS.org/booklets to view the free LLS booklet *Graft-Versus-Host Disease* for more information.**

**Graft-Versus-Leukemia (GVL) Effect.** When transplanted blood stem cells from a donor (the graft) perceive leukemia cells in the patient's body as foreign and attack them.

**Granulocyte.** A type of white blood cell that has many particles (granules). Neutrophils, eosinophils and basophils are types of granulocytes.

**Hematologist.** A doctor who specializes in treating blood diseases.

**Hematopathologist.** A doctor who has special training in identifying blood diseases by examining blood, bone marrow, lymph and other tissue samples under a microscope and performing tests to determine if the blood cells are normal or not.

**Hematopoietic Stem Cell.** An immature cell that can develop into any type of blood cell, including red blood cells, white blood cells and platelets. Also called a blood stem cell.

**Hemoglobin.** The iron-containing substance in red blood cells that carries oxygen around the body. Hemoglobin concentration decreases when there is a drop in the number of red blood cells. This condition is called anemia.

**Human Leukocyte Antigen (HLA).** A type of protein on cells that helps the body to distinguish its own cells from foreign cells. HLA factors are inherited from a person's mother and father. They make up a person's tissue type, which varies from person to person, and are a critically important factor in allogeneic (donor) stem cell transplantation. Before transplantation takes place, tissue typing is performed to determine if the donor's and the recipient's cells are compatible.

**Immune System.** A complex network of cells, tissues and organs that work together to defend the body against infections.

**Immunophenotyping.** A process that uses antibodies to identify specific types of cells based on the antigens (markers) on their surfaces.

**Immunotherapy.** A type of therapy that uses a person's immune system to help fight cancer.

**Incidence.** The number of new cases of a disease diagnosed each year.

**Induction.** The first phase of treatment, given to quickly and significantly reduce the number of leukemia cells in the body.

**Inherited Predisposition.** An increased risk that a person will develop a disease based on genes that they have inherited.

**Intrathecal.** The term for the fluid-filled space between the thin layers of tissue that cover the brain and the spinal cord. In some situations (for example, when leukemia cells are in the central nervous system), drugs are administered directly into the spinal canal. This treatment is called intrathecal therapy.

**Inversion.** A genetic abnormality that occurs when a section of a chromosome breaks off, turns upside down and then reattaches. As a result, the genetic material is inverted and is now in a different order. **Visit www.LLS.org/booklets to view the free LLS booklet *Understanding Genetics* for more information.**

**Karyotype.** An organized profile of a person's chromosomes. It shows the size, shape and number of chromosomes in a sample of cells.

**Late Effect.** A medical problem that either does not appear or is not noticed until years after treatment ends. Treatment-related cancer and heart disease are examples of late effects.

**Leukocyte.** See White Blood Cell.

**Lumbar Puncture.** A procedure in which a thin needle is inserted into the spinal column to collect spinal fluid or to administer anticancer drugs to the central nervous system (CNS). Also called spinal tap.

**Lymph Node.** A bean-sized structure that is part of the body's immune system. There are hundreds of lymph nodes throughout the body that contain large numbers of lymphocytes, white blood cells that help fight infection and disease.

**Lymphocyte.** A type of white blood cell that is important to the body's immune system. There are three major types of lymphocytes: 1) B lymphocytes (B cells), which produce antibodies to help combat infections; 2) T lymphocytes (T cells), which have several functions, including assisting B lymphocytes in making antibodies; and 3) natural killer (NK) cells, which can attack virus-infected cells or tumor cells.

**Macrophage.** A type of white blood cell that surrounds and kills microorganisms, eats dead cells and helps lymphocytes with their immune system functions.

**Marrow.** See Bone Marrow.

**Measurable Residual Disease (MRD).** The small amount of cancer cells that may remain in the body after treatment, even when the patient's blood and bone marrow appear to be normal. These residual cancer cells can only be identified by very sensitive tests. **Visit www.LLS.org/booklets to view the free LLS booklet *Measurable Residual Disease (MRD)* for more information.**

**Monocyte/Macrophage.** A type of white blood cell that forms in the bone marrow. Some monocytes travel through the blood to tissues in the body, where they become macrophages. Macrophages can combat infection in the body's tissues, ingest dead cells and assist lymphocytes in immune functions.

**Mutation.** A change in the DNA sequence of a cell. A mutation may be caused by an error in cell division or by contact with DNA-damaging substances in the environment.

**Myeloblast.** A type of immature white blood cell that develops in the bone marrow. Myeloblasts become mature white blood cells called granulocytes (neutrophils, basophils and eosinophils).

**Myelodysplastic Syndromes (MDS).** A group of blood cancers in which the bone marrow does not make enough healthy blood cells and there are abnormal cells in the blood and/or bone marrow. Sometimes MDS becomes AML.

**Myeloid Sarcoma.** A mass of myeloid leukemia cells that develops outside the bone marrow. It may occur beneath the skin or in other areas of the body and may be the first sign of leukemia. Also called chloroma, granulocytic sarcoma and extramedullary disease.

**Neutropenia.** A condition in which the number of neutrophils, a type of white blood cell, is below normal. People with low neutrophil counts are susceptible to infections.

**Neutrophil.** A type of white blood cell, and the principal type of phagocyte (microbe-eating cell), in the blood. It is the main type of cell that combats infection. People with low neutrophil counts are very susceptible to infections.

**Next-Generation Sequencing (NGS).** This refers to a number of different gene sequencing technologies that can rapidly examine stretches of DNA or RNA.

***NPM1*-Mutated AML.** A mutation that is present in some children with AML. *NPM1*-mutated AML can be used a biomarker for treatment. Patients with this gene mutation may be eligible for specific clinical trials or targeted therapies.

**Oncologist.** A doctor who has special training in diagnosing and treating cancer.

**Pathologist.** A doctor who has special training in identifying diseases by examining cells and tissue samples under a microscope.

**Petechiae.** Pinhead-sized red or purple spots under the skin caused by bleeding. Petechiae may be a sign of a low platelet count.

**Phagocyte.** A type of white blood cell that protects the body from infection by eating and killing microorganisms, such as bacteria and fungi. Neutrophils and monocytes are the two main types of phagocytes. Once an infection occurs, phagocytes enter the infected tissue from the bloodstream.

**Plasma.** The liquid portion of the blood, in which blood cells, platelets, proteins and various other blood components are suspended. Also called blood plasma.

**Platelet.** A small, colorless piece of cell that helps control bleeding. Platelets are pieces of large cells in the bone marrow called megakaryocytes. Platelets travel to and then collect at the site of a wound. The platelets' sticky surface helps them form clots at the site of the wound and stop bleeding. Also called thrombocyte.

**Polymerase Chain Reaction (PCR)**. A very sensitive genetic laboratory test that is used to detect and measure some genetic mutations and chromosomal changes that cannot be seen with a microscope. It essentially amplifies (increases) small amounts of specific pieces of either DNA or RNA so that they are easier to detect and measure. This test can find a single cancer cell among more than 100,000 to 1 million healthy blood cells.

**Port.** A small device that facilitates access to a central line (catheter). It is used to withdraw blood and to administer treatments such as intravenous fluids, drugs and blood transfusions. The port is placed under the skin, usually in the chest. It is attached to a catheter, which is a thin flexible tube that is inserted into a large vein.

**Prognosis.** The probable outcome or expected course of a disease; the likelihood of recovery or recurrence of the disease.

**Radiation Therapy.** The use of x-rays and other forms of radiation to treat cancer and other diseases.

**Recurrence.** The return of a disease after it has been in remission following treatment.

**Red Blood Cell.** A type of blood cell that contains a protein called hemoglobin. Hemoglobin carries oxygen from the lungs to the tissues of the body. Red blood cells make up about 40 to 45 percent of blood volume in healthy people. Also called erythrocyte.

**Refractory.** The term used to describe a disease that does not go into remission or improve substantially after treatment.

**Relapse.** The return of a disease after a period of improvement.

**Remission.** When signs and/or symptoms of a disease disappear, usually following treatment.

**Resistance/Resistant (to Treatment).** When cancer cells continue to grow even after intensive treatment. The cancer cells may be resistant to the drug at the beginning of treatment or may become resistant after being exposed to the drug over time. Also called drug resistance.

**Risk Factor.** A scientifically established factor that increases a person's chance of getting a disease. Risk factors can be classified as either genetic (inherited), lifestyle-related or environmental.

**RNA.** Abbreviation for ribonucleic acid, a molecule in cells that carries out the DNA instructions for making proteins.

**Spinal Tap.** See Lumbar Puncture.

**Spleen.** An organ in the left upper portion of the abdomen, just under the left side of the diaphragm. The spleen filters blood, stores blood cells and destroys old blood cells. Enlargement of the spleen is called splenomegaly.

**Stem Cell.** A cell from which other types of cells develop. In the bone marrow, blood-forming stem cells mature into red blood cells, white blood cells and platelets. Stem cells can be collected, preserved and used for stem cell therapy. See Hematopoietic Stem Cell.

**Stem Cell Transplantation.** See Allogeneic Stem Cell Transplantation and Autologous Stem Cell Transplantation.

**Therapy-Related AML.** A type of AML that is caused by previous treatment with chemotherapy or radiation therapy. Therapy-related AML is an aggressive cancer and usually occurs within 7 years after treatment. It is more common in adults than children.

**Thrombocytopenia.** A condition in which the number of platelets in the blood is below normal.

**Toxin.** A naturally derived substance that is poisonous to cells. A toxin can be attached to antibodies that then attach to and kill cancer cells.

**Transfusion.** A procedure in which whole blood or blood components are infused into a patient's bloodstream.

**Translocation.** A genetic abnormality in which a piece of one chromosome breaks off and attaches to another chromosome. Nearby genes in the location at which the break occurs may be affected, and this may lead to medical problems. See Mutation. **Also, visit www.LLS.org/booklets to view the free LLS booklet *Understanding Genetics* for more information.**

**White Blood Cell.** A type of blood cell that is part of the body's immune system. The five major types of white blood cells are neutrophils, eosinophils, basophils, monocytes and lymphocytes. Also called leukocyte.

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## A six-word narrative about living with blood cancer from patients in our LLS Community

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