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Acute Myeloid Leukemia in Children and Teens



First Edition 2021

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

Stay strong and keep moving forward. Find the positive in every day. Be your own best patient advocate. Changed my life for the better. Accept, learn and focus on present. Learning to live a different life. Sudden and life changing—be positive. Waiting, worrying, anxiousness/happy I'm alive! Embrace a new normal each day. 5 years, 41 infusions, constant fatigue. Patience, positive attitude, hope and faith. Test to test, I will survive! Treatment, fatigue, treatment, fatigue and survival. Love life, live better every day. I don't look back only forward. So far, so good, live life. Meditation, mindfulness, wellness, faith, nutrition and optimism. Finding the joy while living with uncertainty. Watch, wait, treat, regroup, rest, re-energize. Blessed to be doing so well! Eye opening needed learning and healing. Feel great: uncertain travel plans annoying. Renewed faith, meditation, diet, mindfulness, gratitude. Watchful waiting can be watchful worrying. Scary, expensive, grateful, blessings, hope, faith. Thank god for stem cell transplants! Do not know what to expect. Extraordinarily grateful, I love my life. Diagnosed; frightened; tested; treating; waiting; hoping. I'm more generous, impatient less often. Embrace your treatment day after day. Live today, accept tomorrow, forget yesterday. Strength you never realized you had. Challenging to our hearts and minds. Life is what we make it. Live life in a beautiful way.



Discover what thousands already have at
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Join our online social network for people who are living with or supporting someone who has a blood cancer. Members will find:

- Thousands of patients and caregivers sharing experiences and information, with support from knowledgeable staff
- Accurate and cutting-edge disease updates
- The opportunity to participate in surveys that will help improve care

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Acknowledgement

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Introduction

This booklet provides information about acute myeloid leukemia (AML) in children and teens. AML is the second most common type of leukemia in this age group. It is also known as “acute myelogenous leukemia.” **For more information about AML in adults, see the free LLS booklet *Acute Myeloid Leukemia in Adults*.**

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 who relapse 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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Acute Myeloid Leukemia Basics

Leukemia. Leukemia is a cancer of the blood and bone marrow. Bone marrow is the sponge-like tissue in the center of most bones, where blood cells form. Leukemia begins in one of the immature cells in the bone marrow. One or more mutations (changes) occur in the DNA of the cell, and it becomes a type of cancer cell called a “leukemia cell.”

The four major types of leukemia are:

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

The different types of leukemia are identified based on the rate of disease progression, as well the type of cells that are involved in the disease.

Disease progression (meaning how quickly the disease gets worse) is one of the factors that doctors consider when they classify different types of leukemia. Leukemia can be either acute or chronic. “Acute” leukemias develop and progress rapidly and typically get worse quickly if not treated. “Chronic” leukemias usually progress more slowly.

Leukemia is also classified by the type of blood cell that becomes cancerous. Blood stem cells develop into two primary types: lymphoid and myeloid. Lymphoid stem cells develop into a type of white blood cells called “lymphocytes.” Myeloid stem cells eventually become red blood cells, platelets or certain types of white blood cells (basophils, eosinophils, monocytes and neutrophils). Leukemia is classified as “myeloid” (or “myelogenous”) if the cancerous change originates in a myeloid cell, or “lymphocytic” (or “lymphoblastic”) if it originates in a lymphoid cell.

See the free LLS booklet *The AML Guide: Information for Patients and Caregivers* for general information about this disease.

How AML develops. There are three main types of blood cells: red blood cells, white blood cells and platelets. Red blood cells carry oxygen throughout the body. White blood cells help fight infections. Platelets help stop bleeding by clumping together (clotting) at the site of an injury.

Blood cells begin as hematopoietic stem cells in the bone marrow. Hematopoietic stem cells, also referred to as blood stem cells, are immature (undeveloped) blood cells. In healthy bone marrow, these blood-forming stem cells eventually develop into red blood cells, white blood cells and platelets.

In people with AML, a mutation or series of mutations occurs in the DNA (genetic material) of a single, immature myeloid cell (or “myeloblast”). This results in the formation of a leukemia cell, which is an immature blood cell stuck in the early stages of development. The leukemia cell, also referred to as an “AML cell” or “blast cell,” cannot mature into a fully functioning white blood cell.

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

By the time AML is diagnosed, the number of healthy red blood cells, white blood cells and platelets is usually lower than normal. Having low levels of blood cells may result in infections, anemia 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)

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.

A person who has signs or symptoms that suggest the possibility of leukemia is 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 someone with AML to feel a loss of well-being because of the lack of 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, and they often have symptoms related to low blood cell counts.

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

- Fatigue
- Weakness
- Shortness of breath during normal physical activities
- Lightheadedness, dizziness or faintness
- Headaches
- Pale complexion

Symptoms of a low white blood cell count (called “neutropenia”) include:

- Frequent infections
- Recurrent fevers

Symptoms of a low platelet count (called “thrombocytopenia”) 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:

- Unexplained weight loss or loss of appetite
- Swollen glands
- Bone and joint pain
- Difficulty breathing
- Enlarged spleen or liver

In rare instances, a tumor made up of AML cells forms outside the bone marrow. This type of tumor, called a “myeloid sarcoma,” can form in almost any part of the body. If AML cells spread to the skin, they can cause lumps or spots that may look like a rash. Treatment for myeloid sarcomas generally consists of chemotherapy regimens used for AML and may also include allogeneic stem cell transplantation. Other names for a myeloid sarcoma are “extramedullary disease,” “chloroma” and “granulocytic sarcoma.”

Testing for AML

While certain signs and symptoms may indicate that a person 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:

- 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 of these 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 and ask about any health problems or treatments that your child has had. This may include questions 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.

Physical Examination. The doctor will evaluate your child's current symptoms and conduct a physical examination. During the exam, the doctor may listen to your child's lungs and heart and carefully examine the body for signs of infection and disease. To check the internal organs, the doctor may also 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. Because AML can cause enlarged lymph nodes, the doctor may check the lymph nodes in your child's neck and armpits.

Complete Blood Count (CBC) with Differential. This test is used to measure 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. The CBC should include a differential, which measures the numbers of the different types of white blood cells in the sample.

Children with AML often have a high number of white blood cells, but most of these are leukemia blast cells that do not protect against infection. Meanwhile, these children may not have enough mature white blood cells, red blood cells or platelets.

Peripheral Blood Smear. In this test, a single drop of blood is spread on a glass slide, dried and then stained with a special dye. The sample is viewed under a microscope to examine the number, shape and size of the red blood cells, white blood cells and platelets, and whether there are leukemia (blast) cells in it. In patients with AML, many of the white blood cells in the sample may be leukemia blast cells, which are not normally found in the blood.

Even if the blood test results suggest that your child has leukemia, an AML diagnosis is usually made only after the examination of the bone marrow cells.

Two Blood Tests Used to Diagnose AML	
Most patients with AML have:	Blood tests used:
Low red blood cell and platelet counts	Complete Blood Count (CBC) – Blood cell counts are determined by a blood test often abbreviated as a CBC.
Too many immature white blood cells (blasts) and too few mature white blood cells	Peripheral Blood Smear – A microscopic examination of the stained (dyed) blood cells usually shows the presence of leukemic blast cells called myeloblasts. These immature cells do not function like normal, mature white blood cells.

Bone Marrow Aspiration and Biopsy. These are two procedures that remove bone marrow cells and test them for abnormalities. They are generally done at the same time, either at the doctor’s office or in a hospital. Most children are under sedation or general anesthesia during these procedures.

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 marrow to remove (aspirate) 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 samples are sent to the lab where they are examined under a microscope. See **Figure 1** on page 8 for more information on blood and bone marrow tests.

Visit www.LLS.org/3D to view interactive 3D illustrations of some lab and imaging tests.

Figure 1. How Are the Blood and Bone Marrow Tests Done?

Blood Test. A small amount of blood is taken from the patient’s arm with a needle. The blood is collected in tubes and sent to a lab for testing.

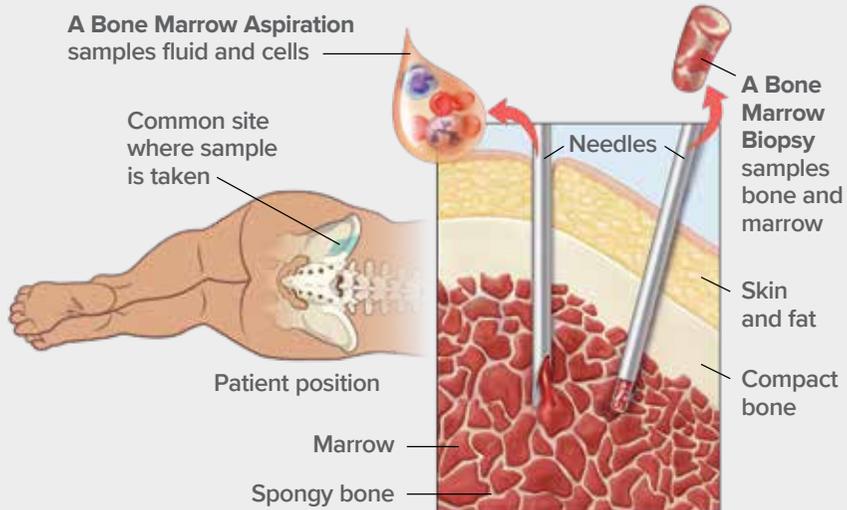
Bone Marrow Aspiration. A sample of fluid with cells is removed from the bone marrow and sent to a lab for testing.

Bone Marrow Biopsy. A very small amount of bone filled with bone marrow cells is taken from the body and sent to a lab for testing.

Both bone marrow tests are done with special needles. Adults and older teens may be given a local anesthetic and be awake during this procedure, but most children are under sedation or given general anesthesia, which makes them “sleep” briefly during the tests. The sample of cells is usually taken from the patient’s hip bone.

Blood and bone marrow tests may be done in the doctor’s office or in a hospital. A bone marrow aspiration and biopsy are almost always done at the same visit. Blood and bone marrow tests may be done both during and after treatment. The tests are repeated to see if treatment is working.

Bone Marrow Aspiration and Biopsy



Left: The place on the back of the patient’s pelvic bone where a bone marrow aspiration or biopsy is done. **Right:** Where the needles go inside the bone to collect the liquid sample for aspiration (the needle on the left) and the bone sample for biopsy (the needle on the right). The needles are different sizes for each of these tests.

Lumbar Puncture. AML cells can spread to the cerebrospinal fluid, the fluid that flows around the brain and spinal cord. In order to determine if there are leukemia cells in this area, a sample of the cerebrospinal fluid 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 starts.

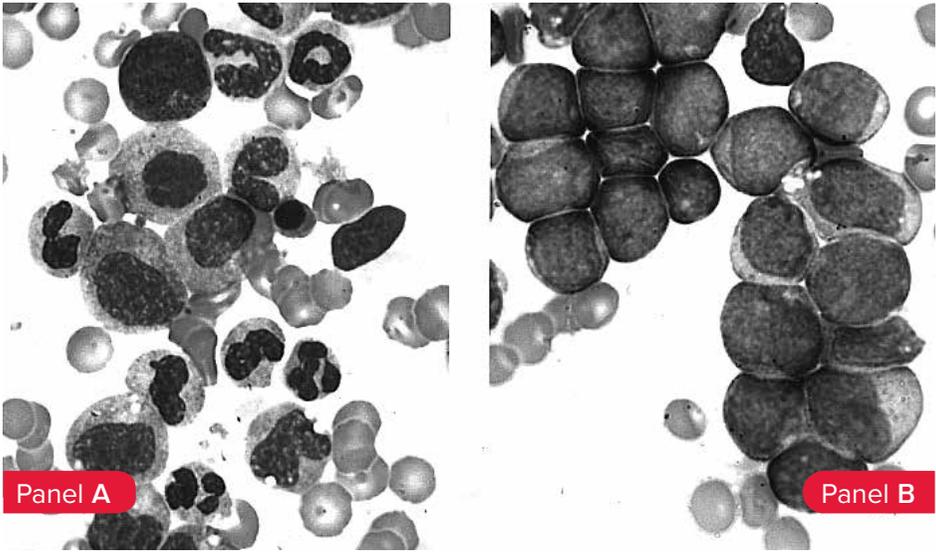
The procedure used to collect the cerebrospinal fluid from the spinal column is called a lumbar puncture or “spinal tap.” After the area over the spine in the lower part of the back has been numbed with local anesthesia, a thin needle is inserted between two vertebrae (back bones) and into the cerebrospinal fluid. A sample of the fluid is taken and examined under a microscope to look for leukemia cells.

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

The cells in the samples are examined under a microscope to determine their size, shape and type, and to identify other cell features. Whether the cells look like normal, mature blood cells or abnormal, immature blood cells (blast cells) is an important finding (see **Figure 2** on page 10).

The percentage of blast cells identified in the samples is another important finding. Typically, there are no blast cells in the blood, and no more than 5 percent of the cells in the bone marrow are blast cells. A diagnosis of AML generally requires a finding of 20 percent or more of the cells in the bone marrow sample to be myeloid blast cells. But AML can also be diagnosed if the blast cells have a chromosomal change or genetic mutation that occurs in a specific type of AML, even if the percentage of blast cells is less than 20 percent.

Figure 2. Normal Cells vs. AML Cells



Panel A shows normal 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. The AML cells in panel B all have a similar appearance, in contrast to the varied appearance of the normal cells in panel A.

If it is determined that your child has AML, additional tests are done on the blood and bone marrow samples to gather information about the subtype of AML.

Immunophenotyping (Flow Cytometry). This laboratory test is done with an instrument called a “flow cytometer.” A flow cytometry test can measure the number of cells in a sample, as well as specific characteristics of the cells, including their size and shape, and identify specific markers on the cell surface.

A sample of cells from blood or bone marrow is tagged with a panel of antibodies that are specific to areas on the cell surface. 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 specific pattern of antigens varies among different AML subtypes, most myeloblasts express CD33, CD13, CD14, CDw41, CD15, CD 11B and/or CD36.

In addition to its use as a diagnostic test, flow cytometry is also used after treatment for evaluating minimal/measurable residual disease (MRD). This refers to the small number of cancer cells that may remain in the body after treatment.

Genetic Tests. These are tests used to examine the chromosomes and genes in a patient's leukemia cells. They include:

Cytogenetic Analysis (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.

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. In some cases of AML, the chromosomes of leukemia cells have abnormal changes that can be seen under a microscope.

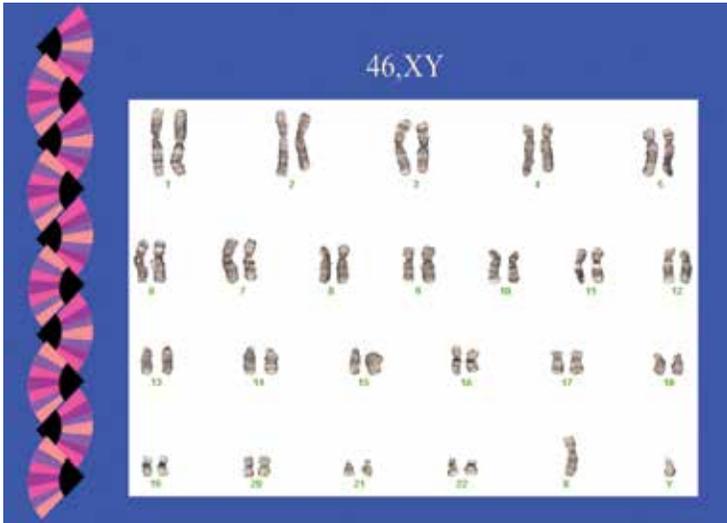
Cytogenetic testing is done with either a bone marrow sample or a blood sample. The leukemia cells in the sample are allowed to grow in the laboratory and then are stained prior to examination. The sample is then examined under a microscope and photographed to show the arrangement of the chromosomes. This is called a “karyotype.” The karyotype shows if there are any abnormal changes in the size, shape, structure or number of chromosomes in the leukemia cells (see **Figure 3** on page 12).

Chromosomal abnormalities in leukemia cells can be identified in approximately 70%-80% of children 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 means the chromosome's structure has been altered in one of several ways including:

- Translocation, which occurs 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, which occurs when a part of a chromosome breaks off, turns upside down and then reattaches in that position.
- Deletion, which occurs when a part of the chromosome is missing.
- Duplication, which occurs when part of the chromosome is copied too many times, resulting in extra genetic material.

In some cases, cytogenetic analysis can provide information that is important in determining a patient'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 subtype of AML has a more favorable prognosis and requires a treatment approach different from other AML subtypes.

Figure 3. Normal Karyotype



This figure shows a normal male karyotype. Courtesy of Dr. Dong Chen, hematopathologist, Mayo Clinic, Rochester, MN.

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 a microscope, but it can also detect some changes that are too small to be seen with basic cytogenetic testing. However, it is not used as a general screening tool. FISH has one disadvantage—the doctor must select the specific chromosomes or genes to examine before the test is performed.

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 (deoxyribonucleic acid) to make them easier to detect and measure in a cell sample. This test can find a single leukemia cell among more than 500,000 to 1,000,000 normal cells. PCR is one method used to measure minimal residual disease (MRD) in patients, which refers to the small amount of cancer cells that may remain in the body after treatment. A PCR test can be done with either a bone marrow sample or a blood sample.

Next-Generation Sequencing. This technique refers to several different laboratory tests that can rapidly examine the exact sequence (order) of DNA or RNA. This makes it possible to identify a variety of genetic alterations in a patient's cancer cells. These alterations are important in guiding risk assessment and prognosis and may also guide treatment decisions. It may help determine which patients are at high risk and may need more intensive treatment or may benefit from treatment with novel therapies.

The number of mutated genes that can be detected in AML patients has increased considerably with the availability of next-generation sequencing. Standard protocols combine cytogenetic analysis with testing for mutations of a number of single genes, including *c-KIT*, *FLT3-ITD*, *FLT3-TKD*, *NPM1*, *CEBPA*, *IDH1*, *IDH2*, *TP53* and *PML-RAR*.

Genetic testing should be done when the cancer is first diagnosed and may also be indicated after a relapse. This is because it is possible for patients to acquire additional genetic abnormalities after the completion of their initial, "first-line" treatment.

See the free LLS booklet *Understanding Genetics* 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), fats, proteins, glucose (blood sugar), uric acid and enzymes. The test findings indicate how well a person's kidneys, liver and other organs are working. Although this test 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.

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 newly diagnosed AML patients if allogeneic stem cell transplantation is

being considered as a treatment option. See page 30 for more information on stem cell transplantation.

Echocardiogram. Some chemotherapy drugs, such as the type called “anthracyclines,” can damage heart tissue. Because of this, the doctor may want to test your child’s heart function before starting treatment. 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.

Diagnosis and Cell Classification

For a child to be diagnosed with AML, generally 20 percent or more of the cells in their bone marrow must be found to be blast cells of myeloid origin, called “myeloblasts.” But AML can also be diagnosed if the blast cells have a chromosomal change or genetic mutation that occurs in a specific type of AML, even if the percentage of blast cells is less than 20 percent. Normal bone marrow typically has less than 5 percent blast cells. The subtype of AML is based on a patient’s laboratory test results.

AML Subtypes. Determining the AML subtype is an important factor in treatment planning for your child. This determination is made based on certain features of the leukemia cells identified with the diagnostic tests. The doctor will speak with you about the drugs and “treatment protocols” (detailed plans of treatments and procedures) that are indicated based on your child’s AML subtype. The doctor may also talk about whether a clinical trial may be an appropriate treatment option.

The World Health Organization (WHO) classification is the main system used to classify AML into subtypes. The revised 2016 classification incorporates new prognostic (predictive) factors, such as chromosomal abnormalities and genetic mutations (see **Table 1** on pages 15-16).

Table 1. Acute Myeloid Leukemia (AML) and Related Neoplasms

Type of AML	Inversion and/or Translocation	Gene Mutation
AML with recurrent genetic abnormalities		
AML with	t(8;21)(q22;q22.1)	<i>RUNX1-RUNX1T1</i>
AML with	inv(16)(p13.1;q22) or t(16;16)(p13.1;q22)	<i>CBFB-MYH11</i>
APL (acute promyelocytic leukemia)	t(15;17)	<i>PML-RARA</i>
AML with	t(9;11)(p21.3;q23.3)	<i>MLLT3-KMT2A</i>
AML with	t(6;9)(p23;q34.1)	<i>DEK-NUP214</i>
AML with	inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)	<i>GATA2, MECOM</i>
AML (megakaryoblastic) with	t(1;22)(p13.3;q13.3)	<i>RBM15-MKL1</i>
AML with		<i>NPM1</i>
AML with		Biallelic mutations of <i>CEBPA</i>
AML with myelodysplasia-related changes		
Therapy-related myeloid neoplasms		
AML, not otherwise specified (NOS)		
AML with minimal differentiation		
AML without maturation		
AML with maturation		
Acute myelomonocytic leukemia		
Acute monoblastic/monocytic leukemia		
Pure erythroid leukemia		
Acute megakaryoblastic leukemia		
Acute basophilic leukemia		
Acute panmyelosis with myelofibrosis		
Myeloid sarcoma		
Myeloid proliferations related to Down syndrome		
Blastic plasmacytoid dendritic cell neoplasm		
Acute leukemias of ambiguous lineage		
Acute undifferentiated leukemia		
Mixed phenotype acute leukemia (MPAL) with	t(9;22)(q34.1;q11.2)	<i>BCR-ABL1</i>
MPAL with	t(v;11q23.3)	<i>KMT2A</i> rearranged
MPAL, B cell/myeloid lineage, NOS		

Table 1. AML and Related Neoplasms (cont.)

Type of AML	Inversion and/or Translocation	Gene Mutation
MPAL, T cell/myeloid lineage, NOS		
Myeloid neoplasms with germline predisposition without a pre-existing disorder or organ dysfunction		
AML with germline <i>CEBPA</i> mutation		
Myeloid neoplasms with germline <i>DDX41</i> mutation		
Myeloid neoplasms with germline predisposition and pre-existing platelet disorders		
Myeloid neoplasms with germline predisposition and other organ dysfunction		

Based on the World Health Organization (WHO) classification.

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

Learning About Your Child’s Diagnosis. You are likely to experience a wide range of emotions when your child is diagnosed with cancer, as well as 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 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 are unable to function, seek professional help. Psychologists, social workers and religious or spiritual advisers may be able to help you 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 treatment helps your child build trust in both you and the members of the treatment team, so they can feel comfortable talking about fears and concerns. Encourage your child to talk about their concerns and ask questions.

Introduce your child to treatment team members who can provide psychosocial support. These 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 help your child 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, which are organized by age.

Baby/Toddler (0 to 3 Years)

- Children this young 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)

- At this age, 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 pain and why the procedure is important.
- Children in this age group 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 needs 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 understand more about cancer and may want to know even 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 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 for your child if they are having an especially difficult time adjusting to their 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 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 the 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.alexslimonade.org/supersibs to learn more.

Please call an Information Specialist or visit www.LLS.org/FamilyWorkbook to find additional support and information for caregivers.

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. 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.

Most children with AML are cared for by a pediatric hematologist-oncologist. A pediatric doctor (pediatrician) specializes in the treatment of children. A hematologist is a doctor who has special training in disorders of the blood, and an oncologist is a doctor who has special training in cancer. A pediatric hematologist-oncologist specializes in diagnosing and treating blood cancers in children.

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, if possible, 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.

If you are unsure or feel uncomfortable about how to tell your child's doctor you are getting a second opinion, call our Information Specialists to discuss a way that you feel comfortable with. You may also want to check with your health insurance company to be sure that a second opinion will be covered by your plan.

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. You may also want to speak with a fertility specialist, a doctor who diagnoses and treats problems related to infertility. 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 recommended. Many children with AML need to start treatment right away.

See the free LLS booklet *Fertility and Cancer* for more information about fertility preservation.

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. Some prognostic factors are called “favorable risk factors” because they are associated with a lower risk of disease relapse after treatment. Others are called “unfavorable risk factors” because they are associated with a higher risk of disease relapse after treatment.

Children with AML are often categorized into 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 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 23, lists some of the more common genetic abnormalities found in children with AML, and the risk category.

Table 2. Proposed Genetic Risk Stratification of Children with AML

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

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

^aPossible inclusion as high-risk alteration.

Source: Lamble AJ, Tasian SK. *Blood Advances*. 2019. (See References.)

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 minimal residual disease (MRD), also called measurable residual disease. This refers to the small number of cancer cells that may remain in the body, even when a complete remission is achieved. 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.

Patients who have achieved remission after initial treatment but have MRD are at increased risk of disease relapse. Testing for MRD can help the doctor re-evaluate your child's AML risk category and determine whether they may benefit from receiving further treatment with more intensive therapies.

Treatment Options

New treatments may have been approved since this book 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. 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 tailor your child's treatment based on several factors, including the subtype of the disease. For example, cases of acute promyelocytic leukemia (APL) and of AML related to Down syndrome are treated differently from other forms of AML in children.

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 results you can expect from standard treatment
- The possibility of your child participating in a clinical trial

Induction Therapy. The first phase of chemotherapy is called “induction therapy.” The goal of induction therapy is to destroy as many cancer cells as possible to achieve (induce) a remission. In patients with AML, remission means that leukemia cells are no longer found in bone marrow samples (when examined with a microscope) and that blood counts have returned to normal.

Induction therapy usually lasts for 4 weeks to 6 weeks. The chemotherapy regimen used most during the induction phase in children with AML includes **cytarabine** and an anthracycline. **Daunorubicin** is the anthracycline most often used for this regimen, although **idarubicin** and **mitoxantrone** are sometimes used. Other chemotherapy drugs may be added to the cytarabine + anthracycline, such as **etoposide** or **6-thioguanine**.

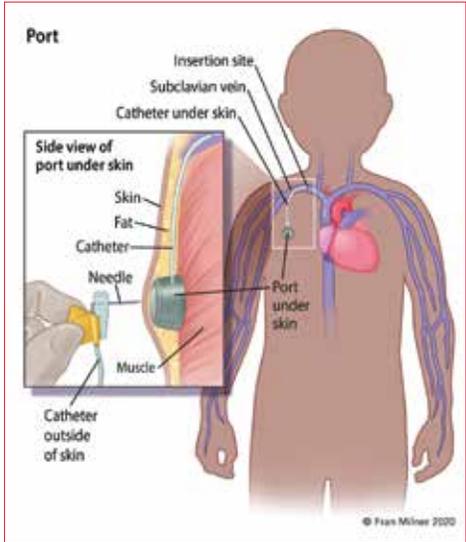
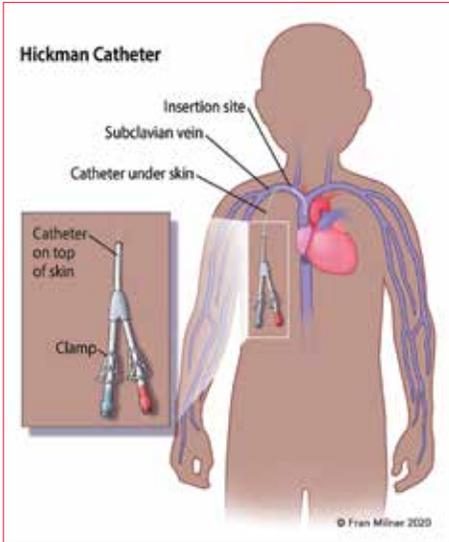
Vyxeos®, a combination of daunorubicin (an anthracycline) and cytarabine (a metabolic inhibitor), is FDA-approved for children 1 year and older with newly diagnosed therapy-related AML or AML with myelodysplasia-related changes. See page 65 for information about therapy-related AML and page 55 for information about AML with myelodysplasia-related changes in the *Health Terms* section.

Chemotherapy drugs kill fast-growing cells throughout the body, including both cancer cells and normal, healthy cells. Different types of chemotherapy drugs work in different ways to kill leukemia cells or stop new leukemia cells from forming. So more than one chemotherapy drug is usually used.

Chemotherapy is typically given in cycles. Each cycle is made up of a certain number of days of treatment, followed by a certain number of days of rest. The rest days allow the body time to recover before the next treatment cycle begins. Cycles vary in length, depending on which drugs are used.

Some chemotherapy drugs are given intravenously, meaning they are injected into a vein. During an intravenous (IV) infusion, the drugs are injected slowly over the course of a few hours, or several days in the case of a continuous infusion. Often, IV chemotherapy is given through a thin, soft tube called a “central line” (also called a central venous line or catheter). The central line is usually attached to a “port” that is surgically placed under the skin into the patient’s upper chest, to allow easy access to the central line. The port and central line can stay in place for months (see **Figure 4** on page 26).

Figure 4. Methods of Intravenous (IV) Injection: Hickman® Catheter and Port



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

Port: A port used with a central line.

Some children may also get 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 and cytotoxic drug conjugate indicated for the treatment of newly diagnosed CD33-positive AML in adults and pediatric patients 1 month and older. Gemtuzumab ozogamicin binds to a cell surface protein called CD33 that is found on most AML blast cells. Once the drug attaches to the blast cells, it releases chemotherapy into the cell.

Patients with *FLT3*-ITD mutations and some other *FLT3* mutations may receive an *FLT3* inhibitor drug. They may receive **sorafenib (Nexavar®)** or **midostaurin (Rydapt®)**.

Table 3, on page 27, lists some of the drugs approved for use in standard treatments for AML, as well as some of the drugs under study in clinical trials for AML. It is possible for patients to be treated with drugs that are not listed in this table and still receive appropriate and effective treatment for AML. Visit www.LLS.org/drugs or call our Information Specialists at (800) 955-4572 for more information.

Your child will receive chemotherapy until the disease is in remission. This usually occurs after 1 or 2 cycles of treatment.

Table 3. Some Drugs Approved for Standard Treatment and/or in Clinical Trials for Children with AML

Anthracyclines (antitumor antibiotics)	<ul style="list-style-type: none"> ○ daunorubicin (Cerubidine®) ○ idarubicin (Idamycin®) ○ mitoxantrone (Novantrone®)
Antimetabolites	<ul style="list-style-type: none"> ○ cladribine (2-CdA; Leustatin®) ○ clofarabine (Clolar®) ○ cytarabine (cytosine arabinoside, ara-C; Cytosar-U®) ○ fludarabine (Fludara®) ○ methotrexate ○ 6-mercaptopurine (Purinethol®) ○ 6-thioguanine (Thioguanine, Tabloid®)
Anthracycline and antimetabolite combination	<ul style="list-style-type: none"> ○ liposomal combination of daunorubicin and cytarabine (Vyxeos®)
Topoisomerase inhibitors	<ul style="list-style-type: none"> ○ etoposide (VP-16; VePesid®, Etopophos®)
Cell-maturing agents	<ul style="list-style-type: none"> ○ all-trans retinoic acid (ATRA, tretinoin; Vesanoid®) ○ arsenic trioxide (Trisenox®)
Hypomethylating agents	<ul style="list-style-type: none"> ○ azacitidine (Vidaza®) ○ decitabine (Dacogen®)
Antibody conjugate	<ul style="list-style-type: none"> ○ gemtuzumab ozogamicin (Mylotarg™)
FLT3 inhibitors	<ul style="list-style-type: none"> ○ crenolanib ○ gilteritinib (Xospata®) ○ midostaurin (Rydapt®) ○ quizartinib (AC-220) ○ sorafenib (Nexavar®)
IDH1 inhibitor	<ul style="list-style-type: none"> ○ ivosidenib (Tibsovo®)
IDH2 inhibitor	<ul style="list-style-type: none"> ○ enasidenib (Idhifa®)
Hedgehog inhibitor	<ul style="list-style-type: none"> ○ glasdegib (Daurismo™)
BCL-2 inhibitor	<ul style="list-style-type: none"> ○ venetoclax (Venclexta®)

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

Induction therapy destroys most of the leukemia cells, as well as healthy bone marrow cells. Most patients develop dangerously low blood counts and may become very ill during this time. The severity of the disease and the side effects of this initial therapy usually result in a hospital stay of 4 to 6 weeks. This is because of the need for supportive care with IV antibiotics and frequent blood transfusions. 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 for the free LLS workbook *Caring for Kids and Adolescents with Blood Cancer*. This workbook includes practical guidance on how to support your child and other family members, deal with your own concerns, share news about your child with relatives and friends, and make the transition to life after treatment.

Central Nervous System (CNS) Prophylaxis. Pediatric treatment regimens typically include treatment to prevent the spread of leukemia cells to the brain and spinal cord and kill any leukemia cells that may already be there. It is uncommon for leukemia cells to be present in the cerebrospinal fluid at the time of diagnosis, occurring 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. The most common intrathecal chemotherapy drug used in children with AML is **cytarabine**.

If AML cells are found in the CNS at the time of diagnosis, a more intensive CNS-directed therapy is used. In these cases, additional drugs are included in the intrathecal therapy, such as **methotrexate** and a corticosteroid.

Assessing Treatment Response. About 4 weeks from the start of the first course 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 achieved when:

- The bone marrow contains fewer than 5% 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 therapy. However, 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 minimal residual disease (MRD), also called measurable residual disease. Children who have 1 single AML cell among 1,000 normal bone marrow cells are at greater risk of relapsing and are often categorized into the high-risk group. Testing for MRD can help the doctor re-evaluate your child's AML risk category and determine whether your child may benefit from further treatment with more intensified therapies.

For patients who do not achieve remission after the first course of induction chemotherapy, additional courses of chemotherapy may be given, either with the same drugs or with a new chemotherapy regimen.

Patients who are unable to achieve a remission with standard treatment should be considered as a candidate 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 therapy, after they achieve remission (see page 30). Without this additional treatment, the leukemia is likely to relapse within months.

See the free LLS fact sheet *Minimal Residual Disease (MRD)* for more information.

Consolidation (Intensification) Therapy. Consolidation therapy refers to treatments given to patients after their disease is in complete remission. It is given to children with AML after they complete induction therapy. The goal of consolidation therapy is to eliminate the residual leukemia cells in the body.

There are two basic treatment options for consolidation therapy:

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

Patients with favorable risk factors are often given 2-4 cycles of intensive chemotherapy with **high-dose cytarabine** and other drugs for consolidation therapy. The number of chemotherapy cycles varies from patient to patient. They are often hospitalized during consolidation therapy. Additionally, CNS prophylaxis usually continues during the consolidation phase.

Patients with high-risk AML, based on their prognostic factors, receive more aggressive 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 the patient's first remission. Often, this is when transplantation offers the best chances of preventing AML from recurring. However, it is associated with higher treatment-related morbidity 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.

Stem Cell Transplantation. For some high-risk category patients who are in remission, 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 with very high doses of chemotherapy.

Although administering such high doses of chemotherapy drugs can kill more leukemia cells, it can severely damage the stem cells in the bone marrow. This can cause dangerously low blood cell counts and may result in anemia, serious infections and uncontrolled bleeding. Stem cell transplantation allows doctors to give higher doses of chemotherapy than can typically be given, either with or without radiation therapy. This is because, after the intensive chemotherapy, the patient receives an infusion of stem cells to replace those destroyed by the intensive chemotherapy. The healthy blood stem cells grow and multiply, forming new bone marrow and blood cells.

There are two main types of stem cell transplantation:

- Allogeneic, in which a patient receives stem cells from a matched or a partially matched donor, either related or unrelated to the patient
- Autologous, in which the patient's own stem cells are collected before chemotherapy, stored and then given back to the patient after completing chemotherapy

Research to determine which patients are most likely to benefit from stem cell transplantation after their first complete remission is evolving. Studies show that allogeneic stem cell transplantation may benefit high-risk and intermediate-risk AML patients who have an HLA-matched sibling donor.

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 in order to identify a suitably matched, related or unrelated donor.

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 very high doses of chemotherapy, either with or without radiation therapy, to kill the leukemia cells remaining in the body after induction therapy. It is also given to suppress the immune system, so that it does not reject the donor's stem cells.

After the conditioning therapy, patients receive the donor stem cells by IV infusion. Allogeneic transplantation uses healthy blood-forming cells from an HLA-matched donor. They can be from a family member or 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 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) 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 approaches, allogeneic stem cell transplantation is associated with a higher rate of side effects and mortality in patients. 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 availability of an HLA-matched donor.

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 the 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. A doctor can order medications to help prevent or minimize the complications of GVHD.

Autologous Stem Cell Transplantation. This is a procedure in which stem cells are removed from a cancer patient before undergoing intensive chemotherapy, either with or without radiation therapy. These stem cells are treated, stored and then returned to the patient's body after the chemotherapy is completed.

Autologous transplantation is sometimes used for patients who do not have an HLA-matched donor. Autologous transplants are usually easier for patients to tolerate than allogeneic transplants. This is because patients receive their own stem cells (which are specially prepared for the transplant), so the risk of some complications, such as graft-versus-host disease, is lower. The high doses of chemotherapy, however, can cause major side effects. Autologous transplants are done less frequently than allogeneic transplants for AML patients, mainly because of the lack of a graft-versus-leukemia effect and the risk of returning some leukemia cells back to the patient.

Talk to your doctor about:

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

See the free LLS booklets *Blood and Marrow Stem Cell Transplantation*, *Cord Blood Stem Cell Transplantation Facts* and *Graft-Versus-Host Disease* for more information about all types of stem cell transplantation.

Special Treatment Considerations

Acute Promyelocytic Leukemia. Acute promyelocytic leukemia (APL) is an aggressive subtype of AML. It accounts for approximately 7 percent of all AML cases in children. While in the past it 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.

In APL, immature white blood cells called promyelocytes build up in the bone marrow. The overproduction of promyelocytes leads to a shortage of normal white blood cells, red blood cells and platelets.

APL is caused by a translocation between chromosomes 15 and 17, abbreviated t(15;17). A translocation is a genetic change in which a piece of one chromosome breaks off and attaches to another chromosome. In APL, an abnormal "fusion gene" called *PML/RAR α* forms as a result of the translocation. This mutated gene

leads to the production of a protein that causes blood cells to stop developing and stay in the promyelocytic stage, unable to develop into mature white blood cells.

Treatment for APL differs from that of the other AML subtypes described in this booklet. Many people with APL are treated with a drug called all-*trans* retinoic acid (ATRA) in combination with either a chemotherapy regimen or arsenic trioxide.

Visit www.LLS.org/booklets to view the free booklet *Acute Promyelocytic Leukemia Facts* to learn more about this disease.

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 have better overall survival when compared with children with AML who do not have Down syndrome. Children with Down syndrome who develop AML tend to have a good prognosis, especially if the disease is diagnosed before the age of 4 years. 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 cannot tolerate the toxic effects of intensive pediatric AML regimens, and they can experience higher rates of complications, including infection and heart issues.

Children with Down syndrome who have AML require special care. They particularly need treatment protocols that are less toxic than traditional treatments used for childhood AML. They can benefit from being treated at a major children’s hospital where the doctors have experience treating other children with Down syndrome and are aware of the special care that they require.

Relapsed and Refractory AML

Some patients have residual leukemia cells in their bone marrow even after they receive intensive treatment for AML. In these cases, the disease is referred to as “refractory” (or “refractory AML”). Less than 15 percent of children 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 the time of relapse may be different from when the disease was first diagnosed, and 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 of less than 1 year have lower rates of second remissions than children whose first remission is longer than 1 year.

In relapsed and refractory cases of AML, the disease is often hard to cure. Treatment is typically more intensive than for newly diagnosed cases and may include stem cell transplantation (for eligible patients). Treatment options for patients with refractory or relapsed AML include:

- **A clinical trial** (see below). Treatment in a clinical trial should be considered for all patients with refractory or relapsed AML. A clinical trial may offer new combinations of anticancer therapies or targeted therapies, or new approaches to stem cell transplantation. LLS offers help for patients and caregivers to understand, identify and access clinical trials. Patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist them throughout the entire clinical trial process. Visit www.LLS.org/CTSC for more information.
- **Gemtuzumab ozogamicin (Mylotarg™)**. This CD33-directed antibody and cytotoxic drug conjugate is approved for the treatment of newly diagnosed CD33-positive AML in adults and pediatric patients 1 month and older and for the treatment of relapsed or refractory CD33-positive AML in adults and pediatric patients 2 years and older.
- **Allogeneic stem cell transplantation**. Salvage chemotherapy can be used to induce a remission, so that stem cell transplantation can be considered for the patient.

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

Research and Clinical Trials

New treatment approaches for AML are under study in clinical trials. Many of the trials are being supported by LLS research programs and hold the promise of increasing remission rates and finding a cure for AML.

Clinical Trials. Every new drug or treatment regimen goes through a series of studies called “clinical trials” before it becomes part of the standard treatment for a disease. Clinical trials are carefully designed and reviewed by expert clinicians and researchers as well as patient advocates to ensure safety and scientific accuracy. Participation in a carefully conducted clinical trial may be the best available treatment option and should be considered each time you discuss treatment with your child’s doctor. Patient participation in past clinical trials has resulted in the FDA-approved therapies we have today.

LLS Information Specialists, available at (800) 955-4572, offer guidance on how parents can work with their child's doctor to determine if a specific clinical trial is an appropriate treatment option. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. Patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist throughout the entire clinical trial process. Visit www.LLS.org/CTSC for more information.

Research on Treatment Approaches. A number of approaches are under study in clinical trials for the treatment of patients with AML.

Genetics of Leukemia. The many chromosomal and genetic abnormalities in AML make treating this disease particularly challenging. There is a need to identify these genetic variations and customize treatment options based on the specific, genetic characteristics of the leukemia cells. New gene sequencing techniques have revealed previously unknown mutations that may be involved in the development of AML. This information will help researchers develop new targeted therapies for specific subgroups of patients with AML.

New Drugs and Treatment Regimens. Researchers are working to develop safer and more effective treatments for AML. They are studying new drugs, as well as the use of different doses and delivery methods for existing drugs. During the last few decades, advances in the understanding of disease genetics has led to improvements in the overall survival of AML patients. Researchers are also continuing to modify and reformulate traditional chemotherapy drugs and are evaluating combinations of chemotherapy drugs with newer targeted therapies to improve overall survival. Treatment approaches being studied for use in AML patients include:

- **Targeted therapy.** This is a type of treatment uses drugs or other substances to block the action of certain enzymes, proteins or other molecules involved in the growth and survival of cancer cells, while causing less harm to healthy cells.
- **FLT3 inhibitors.** Approximately 25 percent of children with AML have a mutation in the *FLT3* gene that allows cancer cells to grow. Patients with *FLT3* mutations have a poor prognosis. FLT3 inhibitors have been approved for use in adults, but they are still being studied in children. Some of these drugs include **crenolanib**, **gilteritinib (Xospata®)**, **midostaurin (Rydapt®)**, **quizartinib (AC220)** and **sorafenib (Nexavar®)**.
- **BCL2 inhibitor.** Overexpression of the BCL2 protein allows cancer cells to evade “programmed cell death.” One promising drug being researched for use in AML treatment is **venetoclax (Venclexta®)**. This BCL2 inhibitor binds to the leukemia cells and triggers apoptosis, a process that causes them to die.

- **Immunotherapy.** This is a type of biological therapy designed to either boost or suppress the immune system, as needed, to help the body fight cancer. It uses substances made naturally by the body or synthetically in a laboratory to improve, target or restore immune system function.
- **Monoclonal antibody therapy.** This is a type of targeted immunotherapy being studied to treat AML. Antibodies are part of the immune system. Normally, the body creates antibodies in response to antigens, such as bacteria, viruses and even cancer cells. The antibodies attach to the antigens in order to help destroy them. Researchers are analyzing specific antigens that play a role in AML, including CD33, a marker found on most AML cells.
 - **Gemtuzumab ozogamicin (Mylotarg™)** is a monoclonal antibody that has the toxin calicheamicin attached to it. When gemtuzumab ozogamicin binds to the CD33 antigen, it releases the toxin, resulting in the death of the myeloid cell. Gemtuzumab ozogamicin is FDA-approved for CD33+ AML patients.
 - **Bispecific T-cell engager (BiTE)** antibody technology is an immunotherapy approach that helps the body's T cells target cancer cells. BiTEs are antibodies with two arms. One arm of the drug attaches to a specific protein on the cancer cell. The other arm of the drug activates T cells in the patient to kill the cancer cells. **AMG 330** is a BiTE antibody being studied to harness T cells against cancer cells with the CD33 antigen.
 - Researchers are studying the dual affinity re-targeting (DART) protein, called **flotetuzumab**, which targets AML cells that express the CD123 protein.
 - **CAR T-cell therapy** is a promising new way to harness the immune system to fight leukemia. CAR T cells can be engineered to attack specific proteins (antigens) on the surface of AML cells. In this approach, T cells are collected from the patient's blood. The T cells are altered in the laboratory to attack specific proteins (antigens) on the surface of leukemia cells. The T cells are then multiplied in the lab and later infused back into the patient's blood, where they attack and kill the leukemia cells. Researchers are focusing on identifying targets, such as CD33, for this type of therapy. This research may help to develop new CAR T-cell immunotherapies for children with AML. **See the free LLS booklet *Chimeric Antigen Receptor (CAR) T-Cell Therapy Facts* for more information on how this treatment works.**

Patients who want to learn more about clinical trials for AML can contact an LLS Information Specialist at (800) 955-4572.

Related Diseases

Blastic Plasmacytoid Dendritic Cell Neoplasm. Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a highly aggressive cancer of the blood and bone marrow that can affect other organs such as the lymph nodes, spleen, central nervous system and skin. In fact, most patients with BPDCN have skin lesions, and the disease is often diagnosed through a skin tissue biopsy. It may also be diagnosed through a bone marrow or lymph node biopsy.

BPDCN is rare in adults and even rarer in children. It mostly occurs in older adults, with a median age of 65 to 67 years at diagnosis. A diagnosis of BPDCN requires the presence of at least 4 of these 6 antigens on the cancer cells: CD123, CD4, CD56, TCL-1, CD2AP and CD303/BDCA-2.

Patients with BPDCN should seek treatment at a cancer center that has experience treating patients with this disease. The drug **tagraxofusp-erzs (Elzonris®)** is a targeted therapy directed at CD123 that is FDA-approved for BPDCN in adults and in pediatric patients 2 years and older.

Patients in first remission may undergo allogeneic stem cell transplantation, if appropriate. Other treatment options include induction therapy regimens used for AML, acute lymphoblastic leukemia (ALL) or lymphoma. Recent clinical trials with agents targeting some of the BPDCN cell surface markers have shown great promise.

Mixed Phenotype Acute Leukemia. Mixed phenotype acute leukemia (MPAL), also known as “biphenotypic leukemia” or “mixed lineage leukemia,” is a subtype of acute leukemia of ambiguous lineage. It is a combination of two forms of leukemia: acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). It accounts for 2 to 5 percent of all acute leukemias, affecting patients of all ages, and includes several different subtypes.

The best treatment approach for MPAL has not yet been determined. There is no standard therapy for the disease and, in general, it is associated with a poor prognosis. This is due to 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 both ALL and AML therapies. The reasons for this resistance are not yet clear, but it may be related to the high percentage of high-risk chromosomal abnormalities found in patients with MPAL.

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 is followed by allogeneic stem cell transplantation, if needed.

For patients with a Ph-negative subtype of MPAL, the treatment typically consists of either an ALL regimen, or a combination of ALL and AML therapies. This may be followed by an allogeneic stem cell transplantation when a donor is available.

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

Side Effects and Supportive Care

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 and that may require supportive care. The goal of supportive (palliative) 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.

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 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 who have 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 signs 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. Children with AML may be at risk for developing a condition called “tumor lysis syndrome” (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. 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. IV 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 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)**, **enasidenib (Idhifa®)** and **ivosidenib (Tibsovo®)**. Symptoms include fever, swelling in the limbs and trouble breathing. Patients may also experience a drop in blood pressure and have fluid buildup around the lungs or heart. Treatment consists of steroid therapy or administration of the antimetabolite drug **hydroxyurea**, and must begin when the first signs or symptoms appear.

Other Side Effects. Chemotherapy drugs affect cells that divide quickly, which is why they work against cancer cells. But they also 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
- Headaches
- Fatigue

These short-term side effects usually go away once a patient has completed treatment. There are drugs and other supportive therapies to either prevent or manage many side effects.

See the free LLS series *Side Effects Management* for more information.

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 43).

Coping with Hair Loss in Children

For many children, 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 head. 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.

Follow-Up Care

After your child completes treatment for AML and is in remission, your child will need to receive 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 they 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. 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.

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. Your doctor will let you know the schedule that is right for your child.

Some childhood vaccines may have been delayed during treatment. Your doctor will advise you when to resume your child's vaccination schedule. Current COVID-19 vaccines are also recommended for specific ages, although they have not been specifically tested in patients with AML as of this printing. Speak to your 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 45.

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 they reach adulthood, remind your child 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 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 oncologist will help create a survivorship care plan for your child to guide 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.
- Diagnosis summary with specifics such as the AML subtype
- 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
- Follow-up appointment schedule with the names of the medical providers and how often the appointments should occur
- Schedule for ongoing monitoring, with recommended tests and frequency
- 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 to fill out with your child's healthcare team. Visit www.survivorshipguidelines.org to download a template.

The Passport for Care Survivor Website offers free access to resources, education and tools for survivorship for childhood cancer survivors. Visit www.cancersurvivor.passportforcare.org to learn more.

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* on page 43)
- 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 receive. 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 possibly 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:

- Cognitive (learning) effects
- 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. 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.

See the free LLS booklet *Learning & Living with Cancer: Advocating for Your Child's Educational Needs* for information about planning for your child's entry or return to school following diagnosis and treatment.

Physical Effects. Depending on the specific types of treatment received, children treated for AML may be at risk for growth delays, bone health issues, heart, thyroid gland (or other organ damage), 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 posttraumatic 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 and should receive ongoing monitoring of cardiac function. Anthracyclines may cause 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 a second cancer.

Visit www.LLS.org/FamilyWorkbook to find additional information about long-term and late effects (in 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 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 coping strategies for situations that may happen.

If your child has been out of the classroom for an extended time, it may be helpful to 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 school staff members to promptly provide you with relevant information 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 recesses or physical education (P.E.) 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 the illness. Ask 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 they feel comfortable.

See the free LLS booklet *Learning and Living with Cancer* for more information about returning to school after cancer treatment.

The Trish Greene Back to School Program. This LLS 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 an LLS Information Specialist at **(800) 955-4572** to learn more.

Treatment Outcomes

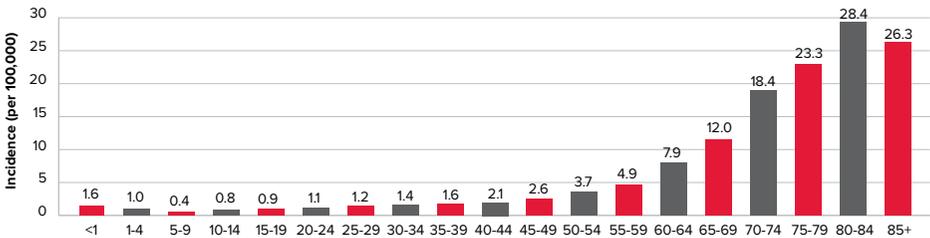
AML is a difficult disease to cure, but survival rates for childhood AML have improved over the past several decades. From 2010 to 2016, the 5-year relative survival rate was 70.6 percent for children and adolescents younger than 15 years. However, there is a wide range of outcomes for different subtypes of AML.

Incidence, Causes and Risk Factors

Incidence. AML is the most common type of acute leukemia in adults. Older people are more likely than younger adults or children to develop AML.

AML is the second most common leukemia in children. The incidence rate is highest before age 1 and decreases after that. The rate is lowest at approximately age 9, followed by a slow increase during adolescence and young adulthood. See **Figure 5** below.

Figure 5. Acute Myeloid Leukemia (AML): Age-Specific Incidence Rates 2013-2017.



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

Source: Source: SEER (Surveillance, Epidemiology and End Results) Cancer Statistics Review, 1975-2017. National Cancer Institute; 2020.

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.”
- Previous treatment with chemotherapy or radiation. When AML develops as a result of treatment for another disease in the past, it is often referred to as “treatment-related” or “therapy-related” AML.
- Other blood disorders. In some people who have myelodysplastic syndrome (MDS), the disease can evolve over time into AML.

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, the most common blood protein
 - Blood-clotting proteins (coagulation factors) made by the liver
 - Erythropoietin, a protein made by the kidneys that stimulates red blood cell production
 - Immunoglobulins, proteins that help the body fight infection
- Hormones, such as thyroid hormone and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin B₁₂
- 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 6** on page 50. The blood cells are suspended in the plasma.

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

1. Red blood cells (the cells that carry oxygen)

- These make up a little less than half of the body’s total blood volume.
- They are filled with hemoglobin, the protein that picks up oxygen from the lungs and takes it around the body. It binds with carbon dioxide (CO₂) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the CO₂ is removed from the lungs.

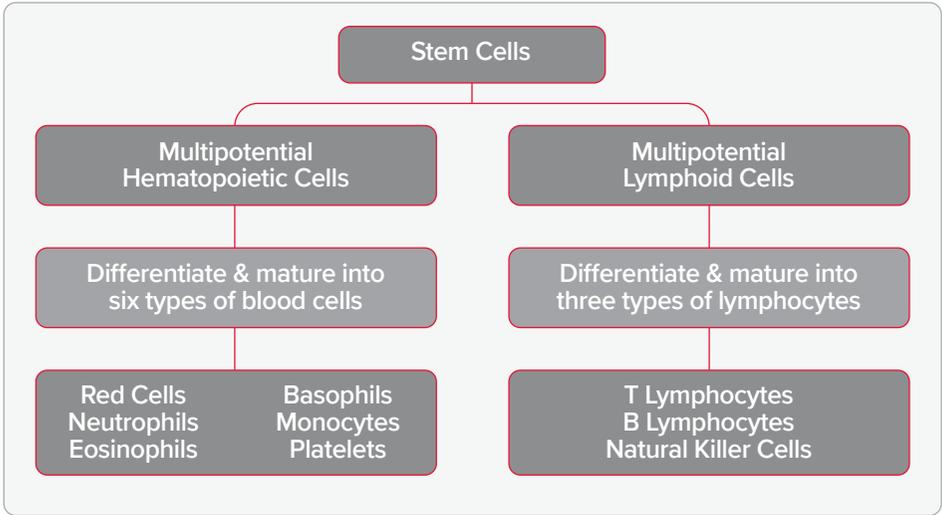
2. Platelets (cells that help blood clot)

- These are small cells (one-tenth the size of red blood cells).
- They help stop bleeding from an injury or cut.
- They 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 (or WBCs, the cells that fight infections), including:

- Neutrophils and monocytes. These are cells called “phagocytes” 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 are the WBCs that respond to allergens or parasites.
- Lymphocytes. These are the WBCs found mostly in the lymph nodes, spleen and lymphatic channels that 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 cells (NK cells)

Figure 6. Blood Cell & Lymphocyte Development



Stem cells develop into blood cells (hematopoiesis) and lymphocytic cells.

Bone Marrow. 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 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, marrow is only found in the spine (vertebrae), hip and shoulder bones, ribs, breastbone and skull.

Hematopoietic (blood) stem cells are found in the bone marrow. These stem cells are important because they can be used for transplants. Some stem cells enter the bloodstream and circulate. Doctors know how to stimulate the growth of these cells in the marrow and make 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. Stem cells from the placenta and the umbilical cord of a newborn infant can also be harvested and used for future transplantation.

Resources and Information

LLS offers free information and services to patients and families affected by blood cancers. This section of the booklet lists various resources available to you. Use this information to learn more, to ask questions and to make the most of the knowledge and skills of the members of your healthcare team.

For Help and Information

Consult With an Information Specialist. Information Specialists are highly trained oncology social workers, nurses and health educators. They offer up-to-date disease, treatment and support information. Language services (interpreting and translation) are available. Please contact our Information Specialists or visit our website for more information.

- Call: (800) 955-4572 (Monday through Friday, from 9 am to 9 pm ET)
- Email and Live Chat: www.LLS.org/InformationSpecialists

Clinical Trial Support Center. Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. Patients and caregivers can work with Clinical Trial Nurse Navigators who will help find a clinical trial according to their needs and personally assist them throughout the entire clinical-trial process. Please visit www.LLS.org/CTSC for more information.

Free Information Booklets. LLS offers free education and support booklets that can be either read online or ordered. Please visit www.LLS.org/booklets for more information.

Telephone/Web Education Programs. LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit www.LLS.org/programs for more information.

Financial Assistance. LLS offers financial assistance to individuals with blood cancer. Please visit www.LLS.org/finances for more information.

Co-Pay Assistance Program. LLS offers insurance premium and medication co-pay assistance for eligible patients. Please call or visit our website for more information.

- Call: (877) 557-2672
- Visit: www.LLS.org/copay

Free Mobile Apps

- LLS Coloring For Kids™ – Allows children (and adults) to express their creativity and offers activities to help them learn about blood cancer and its treatment. Visit www.LLS.org/ColoringApp to download for free.

- LLS Health Manager™ – Helps you track side effects, medication, food and hydration, questions for your doctor, and more. Visit www.LLS.org/HealthManager to download for free.

One-on-One Nutrition Consultations. Access free one-on-one nutrition consultations provided by a registered dietitian with experience in oncology nutrition. Dietitians assist callers with information about healthy eating strategies, side effect management and survivorship nutrition. They also provide additional nutrition resources. Please visit www.LLS.org/nutrition to schedule a consultation or for more information.

Podcast. *The Bloodline with LLS* is here to remind you that after a diagnosis comes hope. Listen in as patients, caregivers, advocates, doctors and other healthcare professionals discuss diagnosis, treatment options, quality-of-life concerns, treatment side effects, doctor-patient communication and other important survivorship topics. Please visit www.LLS.org/TheBloodline for more information and to subscribe.

Suggested Reading. LLS provides a list of selected books recommended for patients, caregivers, children and teens. Visit www.LLS.org/SuggestedReading to find out more.

Continuing Education. LLS offers free continuing education programs for healthcare professionals. Please visit www.LLS.org/ProfessionalEd for more information.

Community Resources and Networking

LLS Community. The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. Please visit www.LLS.org/community to join.

Weekly Online Chats. Moderated online chats can provide support and help cancer patients reach out and share information. Please visit www.LLS.org/chat to join.

LLS Chapters. LLS offers community support and services in the United States and Canada, including the *Patti Robinson Kaufmann First Connection® Program* (a peer-to-peer support program), local support groups and other great resources. For more information about these programs or to contact the nearest chapter, please call or visit our website.

- Call: (800) 955-4572
- Visit: www.LLS.org/ChapterFind

Other Helpful Organizations. 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, please visit www.LLS.org/ResourceDirectory to obtain our directory.

Advocacy. The LLS Office of Public Policy (OPP) engages volunteers in advocating for policies and laws that encourage the development of new treatments and improve access to quality medical care. Please call or visit our website for more information.

- Call: (800) 955-4572
- Visit: www.LLS.org/advocacy

Additional Help for Specific Populations

Información en Español (LLS Information in Spanish). Please visit www.LLS.org/espanol for more information.

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.

Information for Veterans. Veterans who were exposed to Agent Orange while serving in Vietnam may be able to get help from the United States Department of Veterans Affairs (VA). For more information, please call the VA or visit the website.

- Call: (800) 749-8387
- Visit: www.publichealth.va.gov/exposures/AgentOrange

World Trade Center (WTC) Survivors. People involved in the aftermath of the 9/11 attacks who were subsequently diagnosed with a blood cancer may be eligible for help from the 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 either in the NYC disaster area, or who lived, worked or were in school in the area
- Responders to the Pentagon and the Shanksville, PA, crashes

For more information, please call the WTC Health Program or visit their website.

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

People Suffering from Depression. Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time, for example, if you feel depressed every day for a 2-week period. For more information, please call the National Institute of Mental Health (NIMH) or visit their website.

- Call: (866) 615-6464
- Visit: www.nimh.nih.gov and enter “depression” in the search box

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. **See the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.**

AML with Myelodysplasia-Related Changes. A type of AML in which at least 20 percent of a patient's blood or bone marrow is myeloblasts and the patient has one of the following conditions: 1) has had myelodysplastic syndrome (MDS) or a myelodysplastic/myeloproliferative neoplasm (MDS/MPN) before, 2) cells that have changes in certain chromosomes that are similar to those found in MDS, or 3) at least half of the cells (of at least two types of blood cells) are abnormal.

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 and are used to help identify certain types of cancer and 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.

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. **See the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.**

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 that carry oxygen; 2) white blood cells that fight infections; and 3) platelets that 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 usually done at the same time. When this procedure is done in children, they are usually under sedation or general anesthesia.

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. When this procedure is done in children, they are usually under sedation or general anesthesia.

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 stopping them from dividing.

Chimeric Antigen Receptor (CAR) T-Cell Therapy. Treatment that uses a patient's own T cells (a type of white blood cell) to identify and attack cancer cells. The T cells are taken from the patient's blood and sent to a laboratory, where they are genetically modified to attack cancer cells. The engineered T cells are then multiplied and later re-infused into the patient's blood stream. **See the free LLS fact sheet *Chimeric Antigen Receptor (CAR) T-Cell Therapy Facts*.**

Chloroma. See Myeloid Sarcoma.

Chromosome. Part of a cell that contains genes in a linear order. Human cells have 23 pairs of chromosomes. **See the free LLS booklet *Understanding Genetics*.**

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. A treatment that is proven to be safe and effective in a clinical trial is often approved by the United States Food and Drug Administration (FDA) for use as a standard treatment for a disease, if it is either more effective or has fewer side effects than the current standard treatment for that disease.

Cluster of Differentiation (CD). A term used along with a number to identify a specific molecule found on the surface cells that help differentiate one cell type from another. It is commonly used in its abbreviated form, "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).

Conditioning Therapy. Intensive therapy used to prepare a patient for stem cell transplantation. It may include chemotherapy and/or total body radiation.

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.

Cycle of Treatment. A period of treatment (radiation, chemotherapy or other type of drug regimen) followed by a period of rest to allow the body to recover. A cycle is the time from the start of one round of treatment until the start of the next round of treatment. For example, chemotherapy given daily for one week followed by three weeks of rest is one cycle of treatment.

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. See Chemotherapy.

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

Differentiation. The process in which immature cells develop and become mature cells with specific functions. Blood stem cells mature into red blood cells, platelets or white blood cells.

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 the 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.

Erythropoietin (EPO). A hormone needed for normal production of red blood cells. It is made mainly by the kidneys and is released into the blood in response to decreased blood oxygen levels. Drugs with synthetic EPO, called erythropoietin-stimulating agents (ESAs), are available to help produce red blood cells.

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.

Flow Cytometry. A test that measures certain characteristics of cells in a sample, including the size, shape, and 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, called 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.

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.

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.

Granulocytic Sarcoma. See Myeloid Sarcoma.

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 “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. HLAs 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 in order to determine if the donor and recipient 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.

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.

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.

Minimal 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 may appear to be normal. These residual cancer cells can only be identified by very sensitive tests. Also called "measurable residual disease." **See the free LLS fact sheet *Minimal Residual Disease*.**

Monoclonal Antibody. A type of synthetic protein that can bind to substances in the body, including cancer cells. Monoclonal antibodies are used in cancer treatment to target cancer cells.

Monoclonal Antibody Therapy. Targeted treatment using proteins made in the laboratory that either react with or attach to antigens on cancer cells.

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).

Myeloid Sarcoma. A mass of myeloid leukemia cells that develops outside the bone marrow. It may occur beneath the skin or 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 some forms of blood cancer, or who have received treatment such as chemotherapy for cancer, often have low neutrophil counts. People with low neutrophil counts are very susceptible to infections.

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

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.

Peripheral Blood. The blood that circulates throughout the body in the arteries, capillaries and veins.

Peripheral Blood Smear. A procedure in which a sample of blood cells is stained (dyed) and examined under a microscope to check for unusual

changes in the size, shape and appearance of various types of blood cells and also for the presence of blast cells in the blood.

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 500,000 to 1,000,000 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 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 (deoxyribonucleic acid) instructions for making proteins.

Salvage Therapy. Treatment given when a person’s cancer has not responded to other treatments.

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.

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 placed 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 see the free LLS booklet *Understanding Genetics*.**

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."

World Health Organization (WHO). An agency of the United Nations that deals with major health issues around the world. The WHO sets standards for healthcare and medicines and publishes scientific papers and reports.

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Get support. Reach out to our **INFORMATION SPECIALISTS**

The Leukemia & Lymphoma Society team consists of highly trained oncology social workers, nurses and health educators who are available by phone Monday through Friday, 9 a.m. to 9 p.m. (ET).

- Get one-on-one personalized support and information about blood cancers
- Know the questions to ask your doctor
- Discuss financial resources
- Receive individualized clinical-trial searches

Contact us at
800-955-4572 or
**www.LLS.org/
InformationSpecialists**

(Language interpreters can be requested)





For more information, please
contact our Information Specialists
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