LEUKEMIA & LYMPHOMA SOCIETY®

PROVIDING THE LATEST INFORMATION
FOR PATIENTS & CAREGIVERS

Acute Myeloid Leukemia in Children and Teens

Revised 2023

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, and optimism. Finding 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.

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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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Support for this publication provided by Bristol Myers Squibb and Genentech, Inc. & Biogen

Introduction

This booklet provides information about acute myeloid leukemia (AML) in children and teens. The disease is also known as "acute myelogenous leukemia." Although AML can occur at any age, adults aged 60 years and older are more likely to develop the disease than younger people. **For more information about AML in adults, visit www.LLS.org/booklets to view the free LLS booklet *Acute Myeloid Leukemia in Adults*.**

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

We are here to help.

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Leukemia Basics

Leukemia is a type of cancer. “Cancer” is a term for diseases in which abnormal cells begin to grow uncontrollably. When the abnormal cells multiply, they may spread to other parts of the body. Cancer can start almost anywhere in the body. Leukemia is a cancer of blood cells. It starts in blood-forming tissue such as the bone marrow.

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 clotting (clumping together) at the site of an injury.

Blood cells are made in the bone marrow, the spongy tissue in the center of most bones. The bone marrow contains immature cells that eventually develop into blood cells. Leukemia begins in an immature cell in the bone marrow. When one or more mutations (changes) occur in the DNA (deoxyribonucleic acid) of the cell it becomes a type of cancer cell called a “leukemia cell.”

Leukemia cells do not mature into healthy functioning blood cells. They grow more quickly and live longer than normal blood cells. They divide and copy themselves to make more and more leukemia cells. Over time, the leukemia cells crowd out and suppress the development of normal healthy blood cells in the bone marrow. As a result, the body does not have enough healthy red blood cells, white blood cells and platelets. When this happens, the body’s organs and tissues may not receive enough oxygen to work properly. Also, the body may not be able to fight infections or form blood clots when they are needed.

There are four major types of leukemia. They are:

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

Doctors classify leukemia based on:

- **The type of blood cell.** Leukemia is classified by the type of blood cell that becomes cancerous. Blood cells begin as hematopoietic (blood) stem cells in the bone marrow. A blood stem cell may become a lymphoid stem cell or a myeloid stem cell. Lymphoid cells develop into white blood cells called “lymphocytes.” Myeloid cells can develop into red blood cells, platelets or certain other types of white blood cells (basophils, eosinophils, monocytes and neutrophils). Leukemia is classified as “lymphocytic” (“lymphoblastic”) if it originates in a lymphoid cell or “myeloid” (“myelogenous”) if the cancerous change originates in a myeloid cell. See **Figure 7** on page 51.

- **Disease progression (meaning how quickly or slowly the leukemia grows).** Leukemias can be "acute" or "chronic." Acute leukemias develop and progress rapidly and usually get worse quickly if they are not treated. Chronic leukemias usually progress more slowly.

Acute Myeloid Leukemia

AML is a type of cancer in which the bone marrow makes too many immature blood cells called "myeloblasts." In AML, a mutation or a series of mutations in the DNA (genetic material) of a single myeloid stem cell results in the formation of an abnormal myeloblast. This abnormal myeloblast does not develop into a healthy, functioning myeloid cell. It becomes a leukemia cell (also referred to as an "AML cell" or a "leukemia blast cell").

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

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

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

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

In some instances, AML cells spread to the cerebrospinal fluid (CSF), the fluid that surrounds the spinal cord and brain. In rare instances, AML cells collect outside the bone marrow and form a solid mass (a tumor). This type of tumor, called a

"myeloid sarcoma" can form in almost any part of the body. Other names for a myeloid sarcoma are "extramedullary disease," "chloroma," "granulocytic sarcoma," "myeloblastoma" and "monocytoma." Surgery and radiation therapy are not effective ways of treating myeloid sarcomas, so myeloid sarcomas are generally treated with the systemic chemotherapy regimens used for AML (even if the bone marrow and blood do not appear to be involved). "Systemic chemotherapy" is a treatment with anticancer drugs that travel through the bloodstream to cells all over the body. In some cases, treatment for myeloid sarcomas may also include allogeneic stem cell transplantation.

Visit www.LLS.org/booklets to see the free LLS booklet *The AML Guide: Information for Patients and Caregivers* for general information about AML.

Signs and Symptoms

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

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

Signs and symptoms of anemia (a low red blood cell count) include:

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

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

- Frequent infections
- Recurrent fevers

Signs and symptoms of thrombocytopenia (a low platelet count) include:

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

Other general symptoms of AML include:

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

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

Testing for AML

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

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

Talk to your child’s doctor about:

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

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

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

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

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

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

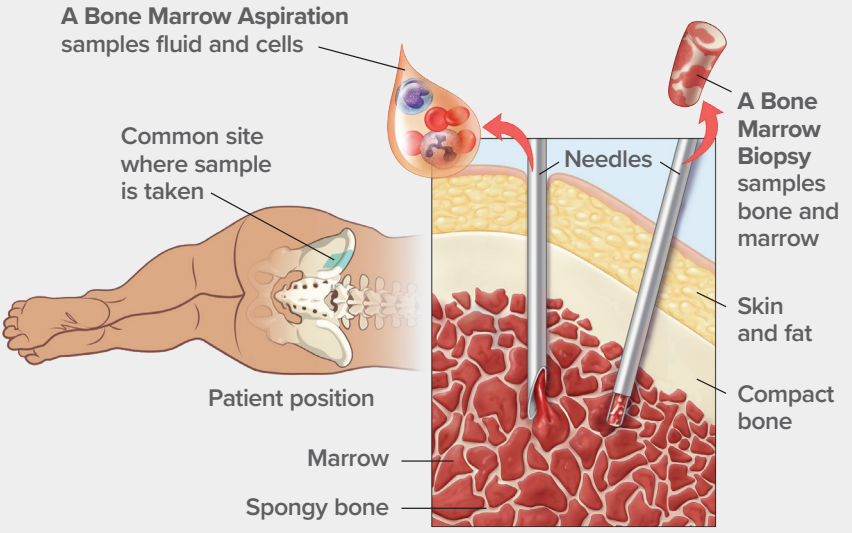
Bone Marrow Aspiration and Biopsy. Leukemia starts in the bone marrow, the spongy tissue inside the center of most bones. When blood tests show cytopenias (low blood counts) or the presence of blast cells (immature blood cells), the doctor may recommend a test of the bone marrow to see whether your child's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

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

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

The samples are usually taken from the patient's pelvis or hip bone. Bone marrow has both a solid and a liquid component. For a bone marrow aspiration, a special, hollow needle is inserted through the hip bone and into the marrow to aspirate (remove) a liquid sample of cells. For a bone marrow biopsy, a wider needle is used to remove a sample of solid bone that contains bone marrow. Both needles are inserted through the skin, generally in the same area. The bone marrow samples (the aspirate and the biopsy) are sent to the laboratory where they are examined under a microscope. See **Figure 1** below for an illustration of the bone marrow tests. Bone marrow tests are often done both during and after treatment to see if the treatment worked.

Figure 1. Bone Marrow Aspiration and Biopsy



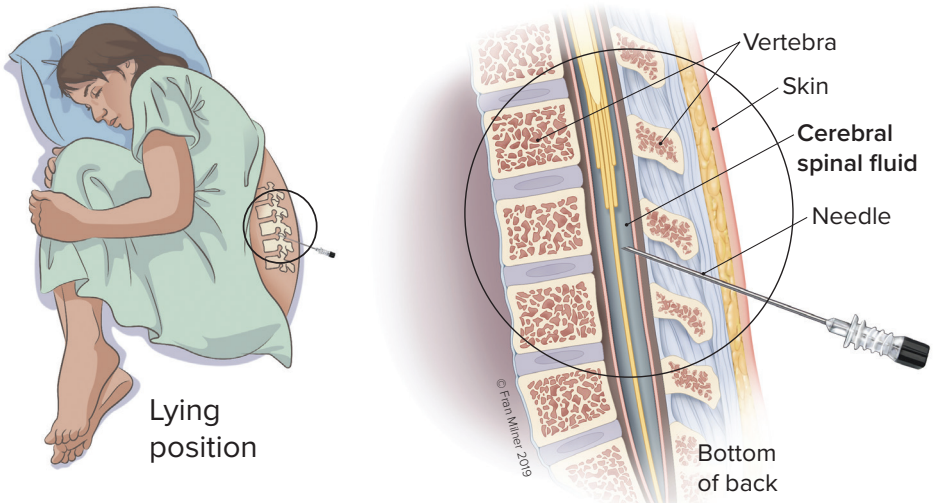
Left: The place on the back of the patient's pelvic bone where a bone marrow aspiration or biopsy is done. **Right:** Where the needles go inside the bone to collect the liquid sample for aspiration (the needle on the left) and the bone sample for biopsy (the needle on the right). The needles are different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

Lumbar Puncture. AML cells can spread to the cerebrospinal fluid (CSF), 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 begins.

The procedure used to collect the CSF from the spinal column is called a "lumbar puncture" or "spinal tap." After the area over the spine in the lower part of the back has been numbed with local anesthesia, a thin needle is inserted between two vertebrae (back bones) and into the cerebrospinal fluid. A sample of the fluid is taken, sent to the laboratory and examined under a microscope to look for leukemia cells. See **Figure 2** below for an illustration of a lumbar puncture.

In many instances, a lumbar puncture is also used to inject chemotherapy medicine into the cerebrospinal fluid to help prevent leukemia from spreading to the brain or spinal cord. This treatment is called "intrathecal chemotherapy" or "IT chemotherapy." For more information on intrathecal chemotherapy see *Central Nervous System (CNS) Prophylaxis* on page 29.

Figure 2. Lumbar Puncture



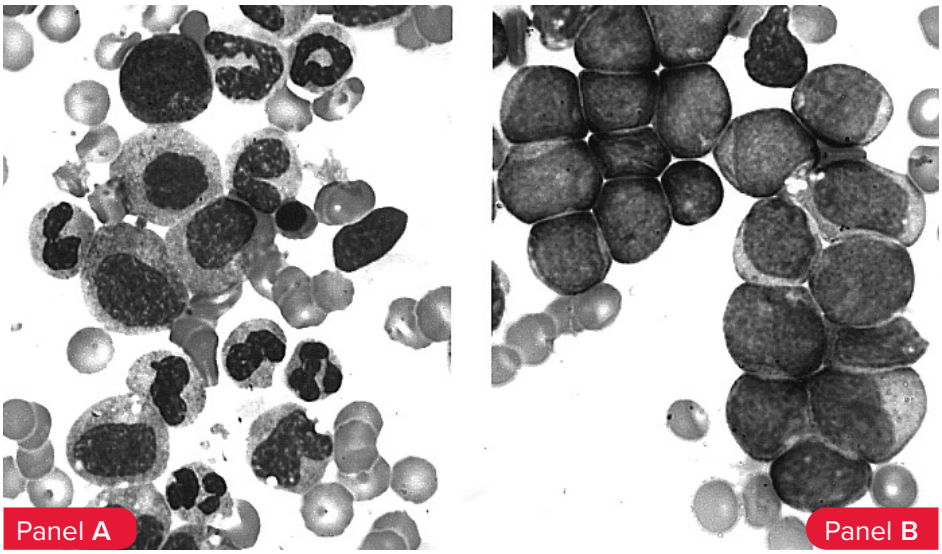
Cell Assessment. At the laboratory, a hematopathologist examines the blood, bone marrow and cerebrospinal fluid samples. A "hematopathologist" is a doctor who has special training in identifying blood diseases by examining cells under a microscope.

The hematopathologist examines the cells under a microscope to determine their size, shape and type, and to identify other cell features (see **Figure 3** on page 10). The percentage of blast cells in the bone marrow and blood is another important finding. In individuals without leukemia, there are typically no blast cells in the blood, and no more than 5 percent of the cells in the bone marrow are blast cells. In some types of AML, a diagnosis of AML requires a finding of at least 20 percent

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

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

Figure 3. Normal Cells versus 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. In panel B, all the AML cells have a similar appearance, in contrast to the varied appearance of the normal cells in panel A.

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

Immunophenotyping 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, bone marrow or other sample is tagged with a panel of antibodies that are specific to areas on the cell. The cells are stained with a light-sensitive dye and are passed through a laser beam in the flow cytometer. If they have an antibody-specific surface marker, the cells light up and are counted.

Leukemia cells can have different antigens on their surfaces, depending on the type of leukemia. Certain antigens, called "cluster of differentiation (CD)" proteins,

are helpful in identifying leukemia cells. While the specific pattern of antigens varies among different AML subtypes, most AML cells express CD13, CD33 and/or CD34.

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

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.

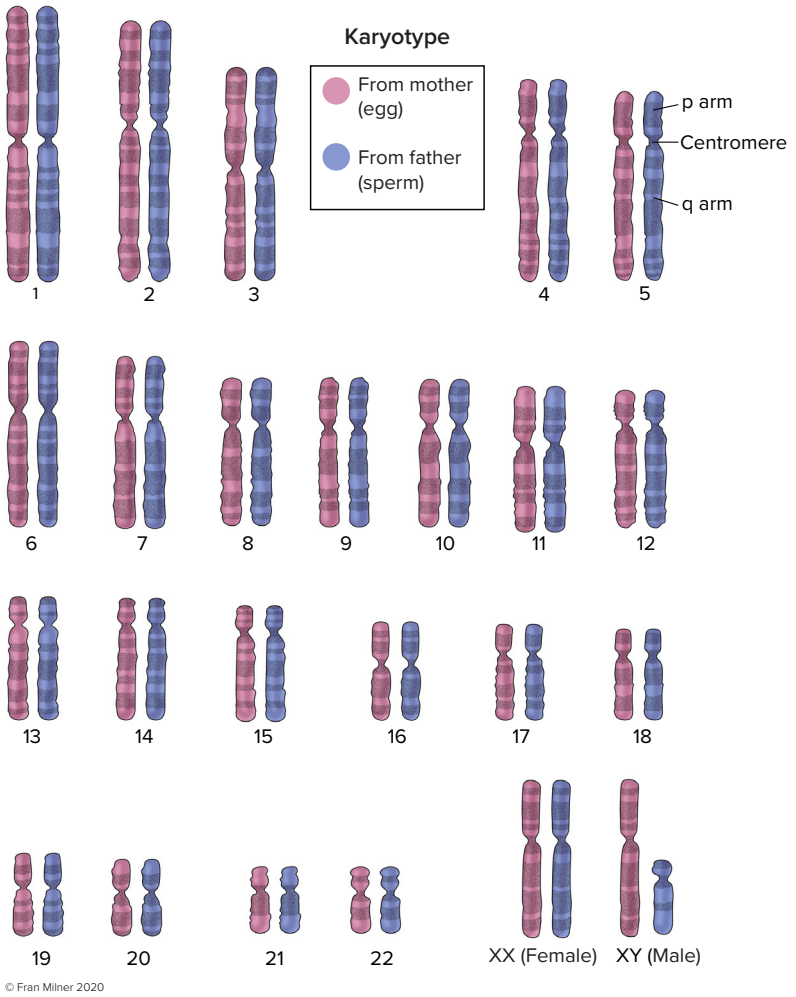
Normal human cells contain 23 pairs of chromosomes, for a total of 46 chromosomes. Each pair of chromosomes is a certain size, shape and structure. In some cases of AML, the chromosomes of leukemia cells have abnormal changes that can be seen under a microscope.

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 4** on page 12).

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

- Translocation, 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.

Figure 4. Normal Karyotype



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

Fluorescence In Situ Hybridization (FISH). This very sensitive test is used to examine genes or chromosomes in cells and tissues. Doctors use FISH to detect certain abnormal changes in the chromosomes and genes of leukemia cells. Pieces of DNA that contain special fluorescent dyes are prepared in the laboratory and added to the leukemia cells on a glass slide. The pieces of DNA that bind to certain genes or areas of chromosomes light up when the slide is viewed under a specialized "fluorescence" microscope. Not only can FISH

identify most abnormal changes that can be seen with karyotype testing under a microscope, but it can also detect some changes that are too small to be seen with karyotype testing. It is not, however, used as a general screening tool. Fluorescence in situ hybridization has one disadvantage—the doctor must select the specific chromosomes or genes that are going to be examined.

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

Biomarker Testing. Biomarker testing, also called "molecular testing" or "genomic testing" refers to a number of different laboratory tests that examine the exact sequence (order) of DNA or RNA. This makes it possible to identify a variety of genetic changes in a patient's cancer cells. These changes are important in guiding risk assessment and prognosis and may also inform treatment decisions. The information that it provices can help doctors to determine which patients are at high risk and may need more intensive treatment or may benefit from treatment with novel therapies.

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

The term "next-generation sequencing (NGS)" is a catch-all term used to describe a number of different modern sequencing technologies. These technologies allow for sequencing of DNA and RNA much more quickly and cheaply than sequencing methods that were used previously.

Since the introduction of DNA sequencing, the number of mutated genes that can be detected in AML patients has increased considerably. Standard protocols combine cytogenetic analysis with testing for mutations of a number of single genes, including *c-KIT, FLT3*-ITD, *FLT3*-TKD, *NPM1, CEBPA* (biallelic), *IDH1, IDH2, RUNX1, ASXL1, TP53, BCR-ABL* and *PML-RAR*. NGS testing, which includes both DNA and RNA testing, helps detect certain gene fusions that can be particularly high-risk like a *NUP98* fusion or *CBFA2T3-GLIS2* abnormality. These markers are important in guiding risk assessment and prognosis, and are also used to guide treatment decisions. For example, some patients may be eligible to receive drugs called "inhibitors" that target specific gene mutations expressed

by leukemia cells, such as *FLT3, IDH1* and *IDH2*. These inhibitors may be taken alone or in combination with other chemotherapy drugs, but they only work against leukemia cells with these specific mutations (See *Targeted Therapy* on page 25 for more information).

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

Visit www.LLS.org/booklets to view 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), proteins, glucose (blood sugar), creatine, uric acid and liver enzymes. The test findings indicate how well a person's kidneys, liver and other organs are working. Although a blood chemistry profile is not used to diagnose leukemia, if the results show that there is an abnormal amount of a particular substance in the blood, it may be a sign of disease or some other health problem. A blood chemistry profile also provides helpful information about any potential organ damage caused by leukemia cells or cancer treatments.

Human Leukocyte Antigen (HLA) Typing. This blood test is done to identify certain proteins, called "human leukocyte antigens (HLAs)," found on the surface of most cells in the body. These proteins make up the body's tissue type, which varies from person to person. They also play an important role in the body's immune response to foreign substances by helping the body distinguish its own cells from foreign cells. An HLA test is done before allogeneic stem cell transplantation to find out if there is a tissue match between a potential donor and the patient receiving the transplant. While HLA typing is not used to diagnose leukemia, it is an important test for newly diagnosed AML patients if allogeneic stem cell transplantation is being considered as a treatment option. See *Stem Cell Transplantation* on page 25 for more information.

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 each new cycle of chemotherapy. An echocardiogram creates a computerized image of the heart by bouncing

sound waves off internal tissues or organs in the chest. It shows the size, shape and position of the heart, as well as its internal structures. It also shows if the heart is beating and pumping blood normally.

Visit www.LLS.org/booklets to view the free LLS booklet *Understanding Lab and Imaging Tests* for more information about these tests.

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

Diagnosis

AML is a diverse group of diseases, and it is classified into many subtypes. Knowing your child's AML subtype is very important, as it can affect both their prognosis (outlook) and their best treatment plan. If you are not sure of your child's AML subtype, ask the doctor what it is and to explain how that subtype may affect your child's treatment.

The World Health Organization (WHO) classification is the main system used for classifying AML into subtypes (see **Table 1** on page 16). The subtypes of AML are based on the genetic abnormalities (gene or chromosome changes) in the myeloblasts (leukemia cells) and the percentage of myeloblasts in the bone marrow and blood.

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

The latest WHO classification also has a list of "diagnostic qualifiers" that should be used after diagnosis. They include:

- **Therapy-related AML.** Certain treatments for other cancers such as prior chemotherapy and radiation can cause AML.
- **AML progressing from MDS.** Myelodysplastic syndromes (MDS) can transform into AML.
- **AML progressing from MDS/MPN.** Myeloproliferative neoplasm (MPN) is a type of blood cancer in which the bone marrow makes too many red blood cells, white blood cells and/or platelets. Certain MPNs may become AML.
- **AML with germline predisposition.** Some people with AML inherited DNA mutations from a parent that increased their risk of developing AML.

These diagnostic qualifiers are not separate subtypes of AML, but doctors use these qualifiers when they are planning treatment.

Table 1. Classification of AML with Percentage of Blasts Required for Diagnosis

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

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

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

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

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

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

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

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

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

Baby/Toddler (0 to 3 Years)

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

Preschool/Kindergarten (4 to 6 Years)

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

Elementary/Middle School (7 to 12 Years)

- Children in this age-group may have a better understanding of serious illness, but not specifically cancer.
- They may have heard things about cancer at school, from friends, on TV, or they may have found information online. Ask your child what they know and correct any misunderstandings, especially those that cause distress.
- Explain tests, treatments and other medical procedures in advance. Your child may be afraid of pain and resist some tests or procedures. Be honest. If a procedure may be painful, work with the healthcare team and decide how to explain what will be done to lessen their pain and why the procedure is important.
- Children may be very concerned about possible changes to their physical appearance, such as hair loss and losing or gaining weight, as well as worrying about how their peers will react to the changes. Talk to your child in advance about these possible changes.
- You may need to discuss fertility preservation with your child. Some cancer treatments can affect fertility. Fertility preservation, such as egg or sperm banking, may be an option for children who have begun puberty. Fertility preservation 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 are usually able to understand complex information about their cancer and may want to know more. You may still need to correct any misinformation your teenager has heard about cancer from school, friends, TV and movies, or has found online.
- Teenagers may want to participate in decisions about their treatment. Include them in discussions with members of the healthcare team, as appropriate.
- You may need to discuss fertility preservation with your child. Some cancer treatments can affect fertility. Fertility preservation, such as egg or sperm banking, needs to be done before treatment begins. Enlist members of the healthcare team to help with this sensitive discussion.
- Teenagers may also be very concerned about changes to their physical appearance, such as hair loss and losing or gaining weight, as well as worrying about how their peers will react to the changes.
- As teenagers struggle to find independence, a cancer diagnosis may feel like a setback that can lead to feelings of frustration and anger. They may try to test their boundaries or engage in risky behaviors, such as drinking, drug use or sex.

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

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

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

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

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

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

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

Also, visit www.LLS.org/FamilyWorkbook and call an Information Specialist 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 and teens with cancer. The doctors and other healthcare providers at these centers have special training and expertise in giving comprehensive care to children and teens. These centers are often members of the Children's Oncology Group (COG). This is the world's largest organization devoted to clinical research to improve the care and treatment of children with cancer.

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

Children who are diagnosed with AML usually need to start treatment as soon as possible after diagnosis. Some families may wish to seek a second opinion, right away, if they can, particularly if their child has a high-risk subtype of AML or the disease comes back (relapses) after their initial treatment. A second opinion may help you feel more confident about your child's treatment plan. The second opinion should come from a pediatric hematologist-oncologist, preferably one who specializes in childhood AML. This doctor will usually have the most knowledge and experience regarding the latest treatment options.

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

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

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

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

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

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

AML Subtype. Chromosomal and genetic abnormalities are the most significant prognostic factors in children with AML. They help determine whether your child may benefit from treatment with more intensive therapies. **Table 2,** on page 23, lists some of the more common genetic abnormalities, and their risk categories, that are found in children with AML.

Treatment Response. Children who have a better response to the initial treatment have a lower risk of disease relapse. Treatment response is often evaluated based on testing for 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.

Children who achieve 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 more intensive therapies.

Treatment Options

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

Not all children or teens with AML receive the same type of treatment. The doctor will plan your child's treatment based on their AML subtype and other factors, such as age and overall health. Treatment may include chemotherapy, targeted therapy and/or stem cell transplantation. The treatment may be given in a hospital (inpatient treatment) or a clinic (outpatient treatment).

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

Table 2. Proposed Genetic Risk Stratification of Children with AML

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

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

[a]Possible inclusion as high-risk alteration.

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

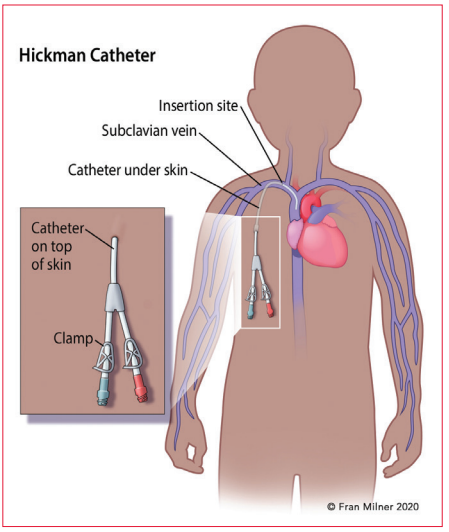
used. Chemotherapy may be given in different ways including intravenously (IV), (directly into a vein) or orally (in pills, capsules or liquids that are taken by mouth).

Cancer cells tend to grow and multiply much more quickly than most cells in the body. Chemotherapy drugs affect cells that divide quickly, which is why they work against cancer cells. But they also affect some of the fast-dividing healthy cells such as the cells in the skin, mouth, hair follicles and lining of the intestines. Chemotherapy drugs cause side effects when they damage these fast-dividing healthy cells along with the cancer cells.

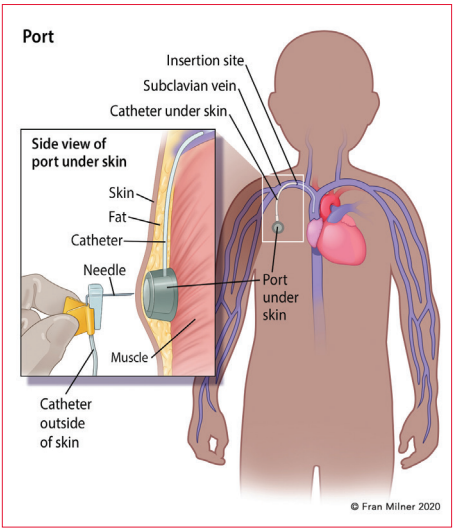
Chemotherapy is typically given in “cycles.” Each cycle is made up of a number of days of treatment, followed by a certain number of days of rest. The rest days allow the body time to recover before the next treatment cycle begins. Cycles vary in length, depending on which drugs are used.

Some chemotherapy drugs are given as an IV infusion. The drugs are infused slowly over the course of a few hours, or, in the case of a continuous infusion, over several days. Often, IV chemotherapy is given through a thin, soft tube called a "central line" (also called a "central venous line" or "catheter"). 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 5** below). Other centers rely on placement of a PICC (peripherally inserted central catheter) for administration of chemotherapy. This is similar to an IV but is more durable and less rigid. A PICC line is often placed in a vein near the elbow and can be removed without sedation.

Figure 5. Placement of Hickman® Catheter and Port



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



Port: A port used with a central line.

Antimetabolites. These chemotherapy drugs interfere with the normal division and function of cells. Some of the antimetabolites used to treat AML include:

- **Cladribine (Leustatin®)**
- **Clofarabine (Clolar®)**
- **Cytarabine (Ara-C, Cytosar-U)**
- **Methotrexate (Trexall®)**

Anthracyclines. These chemotherapy drugs damage and disrupt the making of DNA and cause cell death in both cancer cells and healthy cells. Some of the anthracyclines used to treat AML include:

- **Daunorubicin (Cerubidine®)**
- **Idarubicin (Idamycin®)**
- **Mitoxantrone (Novantrone®)**

Targeted Therapy. Targeted therapy is a treatment that uses drugs or other substances to identify and attack specific types of cancer cells but cause less harm to normal cells. Not all cancers have the same targets. Each type of targeted therapy works a little bit differently, but they all interfere with the growth and survival of cancer cells. To find the most effective treatment for your child, the doctor may run tests to identify the genes, proteins and other factors in the cancer cells. This helps the doctor to choose the most effective treatment based on the specific factors of your child's disease. Targeted therapy is usually combined with chemotherapy. Some types of targeted therapy include:

FLT3 Inhibitors. Some children with AML have a mutation in the *FLT3* gene that can increase the growth and division of AML cells. FLT3 inhibitors are drugs that target these gene mutations. For these patients, the following targeted treatments may be added to the chemotherapy regimen:

- **Gilteritinib (Xospata®)**
- **Midostaurin (Rydapt®)**
- **Sorafenib (Nexavar®)**

CD33 Targeted Therapy. Gemtuzumab ozogamicin (Mylotarg™) is a targeted therapy linked to the chemotherapy drug calicheamicin. It binds to and then enters cells that have the CD33 protein on their surface. Once inside, it releases the toxin that kills the cells. More than 90 percent of AML cells have CD33 on their surface, while mature blood cells do not (so these cells are not as affected by the treatment).

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

There are two main types of stem cell transplantation. They are:

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

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

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

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

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

Though most children stay in the hospital for 4 to 6 weeks for the transplant process and recovery period, some children require very long hospitalizations due to complications, or they may be readmitted with complications after their initial discharge. One possible serious side effect of allogeneic stem cell transplantation is graft-versus-host disease (GVHD). This occurs when the transplanted immune cells (the graft) from the donor identify healthy cells in the recipient's body (the host) as foreign and attack them. The parts of the body most commonly damaged by GVHD include the skin, liver, stomach, intestines and eyes. GVHD can develop within weeks after transplantation or much later. Your child's doctor can order medications to help prevent or minimize the complications of GVHD.

Research to determine which patients are most likely to benefit from stem cell transplantation after their first complete disease remission is evolving. 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 after an AML diagnosis in order to identify a suitably matched, related or unrelated donor.

Talk to your doctor about:

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

Visit www.LLS.org/booklets to view the free LLS booklets *Blood and Marrow Stem Cell Transplantation, Cord Blood Stem Cell Transplantation* Facts and *Graft-Versus-Host Disease* for more information about stem cell transplantation.

Treatment

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

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

A diagnosis of AML is associated with a wide range of outcomes. Not every child with AML receives the same type of treatment. The doctor will plan your child's treatment based on several factors, including the subtype of the disease. For example, cases of acute promyelocytic leukemia (APL) 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 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 induce (achieve) a remission. In patients with AML, remission means that there are less than 5 percent blasts in the bone marrow (when examined with a microscope) and that blood counts have returned to normal.

Children with AML often receive two rounds of chemotherapy. 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. If an anthracycline is given, your doctor may administer another drug, **dexrazoxane (Totect®, Zinecard®)**, around the same time as the anthracycline. This drug is not a chemotherapy agent, but it helps to minimize cardiac side effects that are associated with anthracyclines. Other chemotherapy drugs may be added to the cytarabine and the anthracycline regimen, such as **etoposide (Etopophos®, VePesid®, VP-16)** or **thioguanine (Tabloid®).**

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

In addition to the chemotherapy, children may receive targeted therapies during induction. This may include:

- One dose of the targeted therapy **gemtuzumab ozogamicin (Mylotarg™)** along with chemotherapy as part of their induction treatment. Gemtuzumab ozogamicin is a CD33-directed antibody treatment.
- An FLT3 inhibitor (for patients with *FLT3* mutations) such as **sorafenib (Nexavar®), gilteritinib (Xospata®)** or **midostaurin (Rydapt®)**.

For a full list of treatments and their indications, see **Table 3** starting on page 47.

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

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

of the treatment team. Talking with your child about their fears and concerns will also help them to feel more comfortable.

Visit www.LLS.org/FamilyWorkbook to view the free LLS workbook *Caring for Kids and Adolescents with Blood Cancer.* 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. You can also order *Stars Will Twinkle, The Sun Will Shine,* a 3-book series about a child's leukemia diagnosis.

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. **Cytarabine** is the most common intrathecal chemotherapy drug used in children with AML**.**

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

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

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

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 just a single AML cell among 1,000 normal bone marrow cells are at greater risk of relapsing and are often categorized as high-risk. Testing for MRD can help the doctor reevaluate your child's AML risk category and determine whether your child may benefit from more intensified therapies.

Children and teens who are unable to achieve a remission with standard treatment should be considered as candidates for a clinical trial, allogeneic stem cell transplantation or drug regimens for relapsed or refractory AML.

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

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

Consolidation (Intensification) Therapy. Consolidation therapy refers to treatments given to patients after their disease is in complete remission. Consolidation therapy is designed to deepen the remission and eliminate any residual leukemia cells.

There are two basic treatment options for consolidation therapy:

- Additional intensive chemotherapy
- Stem cell transplantation (see page 25 for more information on stem cell transportation)

Patients with low-risk factors are often given 2 to 3 additional cycles of intensive chemotherapy with **high-dose cytarabine** and other drugs for consolidation therapy. The number of chemotherapy cycles varies from patient to patient. Patients are often hospitalized during consolidation therapy. They may go home for a few days or a week between cycles. 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 their first remission. Often, this is when transplantation offers the best chances of preventing AML from recurring. However, it is associated with higher treatment-related medical problems and death compared to other treatment options used during the consolidation phase. Patients who are candidates for an allogeneic

stem cell transplant should begin a search for an HLA-matched stem cell donor while they are receiving induction therapy. If your child's doctor decides that stem cell transplantation should be part of your child's treatment, it is generally done after 2-3 cycles of chemotherapy.

Special Treatment Considerations

Acute Promyelocytic Leukemia (APL). APL is a unique subtype of AML. While APL usually occurs it middle-aged adults, it can happen at any age. It accounts for approximately 4 to 8 percent of all AML cases in children. While in the past 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. When there are too many promyelocytes in the bone marrow, they crowd out healthy blood cells, leading to low numbers of healthy white blood cells, red blood cells and platelets.

The mutation that causes 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/RARα* 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. These promyelocytes multiply abnormally, unable to develop into mature white blood cells.

Treatment for APL differs from the treatment of the other AML subtypes described in this booklet. Children with APL are often treated with a non-chemotherapy drug called **all-*trans*-retinoic acid (ATRA, Vesanoid®)** in combination with chemotherapy. In clinical trials, researchers have studied a combination of ATRA with another non-chemotherapy drug, **arsenic trioxide (Trisonex®)**. Select pediatric patients who received treatment with a chemotherapy-free ATRA and arsenic trioxide regimen experienced positive outcomes without the side effects of chemotherapy. APL rarely spreads to the central nervous system, so intrathecal chemotherapy is usually not needed.

For a full list of treatments and their indications, see **Table 3** starting on page 47.

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

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

Relapsed and Refractory AML

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

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

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

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

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

- **A clinical trial** (see *Clinical Trials for Blood Cancers* on page 33). Participation in a clinical trial should be considered as a treatment option for all patients with refractory or relapsed AML. A clinical trial may offer new combinations of anti-cancer therapies or targeted therapies, or new approaches to stem

cell transplantation. LLS offers help for a child's parents (or guardians) to understand, identify and access clinical trials appropriate for their child. The Clinical Trial Support Center provides **Clinical Trial Nurse Navigators** that will help a child's parents or guardians to find these clinical trials and assist them throughout the entire clinical-trial process. Visit www.LLS.org/CTSC for more information.

- **Re-treatment with the same induction regimen that produced the patient's first remission.** This is an option, particularly if a relapse occurs 12 months or more after remission.
- **Gemtuzumab ozogamicin (Mylotarg™).** This CD33-directed antibody and cytotoxic drug conjugate is for the treatment of relapsed or refractory CD33-positive AML in adults and pediatric patients aged 2 years and older. Many children now receive this drug as part of their initial treatment, but it may be repeated at time of recurrence.
- **Allogeneic stem cell transplantation.** Salvage chemotherapy can be used to induce a remission, so that stem cell transplantation can be considered for the patient. Not all patients whose disease relapses are eligible for transplant, particularly if they have already had a transplant and the AML relapsed less than 6 months from that first transplant. This consideration is nuanced. Ask your child's doctor if a stem cell transplant will be considered as part of the treatment for your child's relapsed disease.

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

Clinical Trials for Blood Cancers

Every new cancer drug goes through a series of carefully controlled research studies before it can become part of standard cancer care. These research studies are called "clinical trials" and they are used to find better ways to care for and treat people who have cancer.

In the United States, the FDA (US Food and Drug Administration) requires that all new drugs and other treatments be tested in clinical trials before they can be used. At any given time, there are thousands of cancer clinical trials taking place. Doctors and researchers are always looking for new and better ways to treat cancer.

Researchers use cancer clinical trials to study new ways to:

- Treat cancer using
  - A new drug
  - An approved drug to treat a different kind of cancer
  - A new combination of drugs
  - A new way of giving a drug—by mouth (pill), intravenously (IV)

- Manage cancer symptoms and ease treatment side effects
- Find and diagnose cancer
- Keep cancer from coming back after treatment
- Manage long-term side effects

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

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

Clinical trials can be difficult to navigate and figure out, but The Leukemia & Lymphoma Society is here to help. Parents, guardians and caregivers can work with **Clinical Trial Nurse Navigators** who will help find potential clinical trials, overcome barriers to enrollment and provide support throughout the entire clinical-trial process. Our Clinical Trial Nurse Navigators are registered nurses who are experts in blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about the treatment goals for your child
- Help you understand the clinical-trial process, including your child's rights as a patient
- Ask you for details about your child's diagnosis (for example, past treatments, treatment responses, and your child's cancer genetic profile [if you know it]). You will also be asked about your child's current health, and their medical history, because this is information that might affect whether or not your child can take part in certain clinical trials
- Help you understand your finances, your child's insurance coverage, and yours and your child's support networks. The Clinical Nurse Navigator will also be able to help you to assess your own ability and willingness to travel and how these considerations might influence your choice of whether or not to enroll your child in a clinical trial
- Guide you and help you in your efforts to find and enroll your child in a clinical trial, including connecting you with potential trial sites
- Help deal with any problems you might encounter when you are enrolling your child in a trial
- Support you and your child throughout the clinical-trial process

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

Also, visit www.LLS.org/booklets to view the free booklet *Understanding Clinical Trials for Blood Cancers* for more information.

Related Diseases

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

BPDCN is rare in children. Most patients with BPDCN are older adults, with a median age of 65 to 67 years at diagnosis, and it is more common in males than females. A diagnosis of BPDCN requires a finding of at least 4 of the following 6 antigens on the cancer cells: CD123, CD4, CD56, TCL-1, CD2AP and CD303/BDCA-2. In addition, recurrent mutations in the following genes have been described: *ASXL1, IDH1, IDH2, IKZF1, IKZF2, IKZF3, NPM1, NRAS, TET1, TET2, TP53, U2AF1* and *ZEB2*.

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

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

For a full list of treatments and their indications, see **Table 3** starting on page 47.

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

Mixed Phenotype Acute Leukemia (MPAL). MPAL is a subtype of acute leukemia, which is also known as “biphenotypic leukemia” or “mixed lineage leukemia,” and has an 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 leukemia cases, affecting patients of all ages, and there are several different subtypes.

Since MPAL is a rare form of blood cancer, patients with MPAL should seek treatment at a cancer center that has experience treating patients who have this disease. The best treatment approach for MPAL has not yet been determined. There is no standard therapy for the disease and, in general, it is associated with a poor prognosis. This is due to the difficulty in correctly identifying this type of leukemia, its low incidence, the lack of experience in treating it, and its tendency to be resistant to both ALL and AML therapies. The reasons for this resistance are not yet clear, but may be related to the high percentage of high-risk chromosomal abnormalities found in patients with MPAL.

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

For patients who do not have the Ph+ subtype, treatment typically consists of either an ALL-treatment regimen, or a combination of ALL and AML therapies. In many instances, this treatment is followed by consolidation therapy with an allogeneic stem cell transplant when a donor is available.

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

Side Effects and Complications

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

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

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

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

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

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

Tumor Lysis Syndrome (TLS). Children with AML may be at risk for developing a condition called TLS. This condition occurs when a large number of cancer cells die within a short period of time, releasing their contents into the blood. TLS can be severe during the early phases of treatment, especially for children who have very high white blood cell counts before they start induction therapy. As the leukemia cells die, they break apart and release their contents into the bloodstream changing its normal balance of chemicals. The imbalance of chemicals can overwhelm the kidneys because they cannot get rid of the substances quickly enough.

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

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

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

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

Other Side Effects. 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 also divide quickly, such as cells in the lining of the intestines, the skin and hair follicles. Common side effects of chemotherapy may include:

- Hair loss
- Rashes
- Itchy skin
- Mouth sores
- Diarrhea
- Nausea and vomiting
- Loss of appetite and weight loss
- Headaches
- Fatigue

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

Visit www.LLS.org/booklets to view the free LLS series *Side Effects Management* (filter for Side Effect 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 Treatmen*t on page 42 for more information).

Coping with Hair Loss in Children

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

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

Follow-up Care

After your child, or teen, completes treatment for AML and the disease 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 the tests will be done less often during the second and third years. Testing and checkups may be required less frequently as time goes on, but scheduled follow-up visits should continue indefinitely.

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

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

Your child's healthcare team may also recommend a schedule for evaluating your child's learning skills. If your child appears to be struggling with learning, special education methods may help. See *Returning to School* on page 44 for more information.

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

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

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

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

- A list of all your child's healthcare providers: pediatrician, hematologist-oncologist, radiation oncologist, etc
- A diagnosis summary with specifics such as the AML subtype

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

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

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

Survivorship Clinics. Childhood cancer survivors have special lifelong healthcare needs. Many hospitals and treatment centers offer survivorship clinics that specialize in long-term follow-up care for cancer survivors. Children often begin visiting a survivorship clinic 2 years after finishing cancer treatment. However, the timeline can differ based on your child's unique needs and medical history. Additionally, coordination between members of your child's cancer survivorship healthcare team and primary care pediatrician is essential.

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

- Assess the full effects of treatment
- Identify and manage long-term and late effects of treatment (see *Long-term and Late Effects of Treatment* on page 42 for more information)
- Detect and treat disease recurrence (relapse)

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

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

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

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

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

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

- Type and duration of treatment
- Sex
- Age at the time of treatment
- Overall health

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

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

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

Cognitive (Learning) Effects. Learning difficulties can range from mild to severe and can begin either during treatment or may become evident months or even

years after treatment. Mathematics, spatial relationships, problem solving, attention span, reading and spelling, processing of information, planning and organizing, and concentration skills are all areas of learning that may be affected. Problems with fine motor coordination, which might cause poor handwriting, can also develop.

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

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

Visit www.LLS.org/booklets to view 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 the members of your child's healthcare team if you notice any changes in your child's mood or behavior, especially if these changes begin to interfere with your child's daily life.

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

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

Second Cancer Risk. Survivors of childhood AML are at an increased risk for developing a second cancer later in life. A second cancer may occur months or years after treatment is completed. Because of this risk, it is important for

patients who have been treated for AML to get screened for a second cancer on a regular basis.

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

Talk to your child's doctor about:

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

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

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

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

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

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

- Meet with school administrators, teachers, counselors and the school nurse as soon as you can after diagnosis to discuss your child's medical condition and address any special needs or concerns.
- Discuss any evaluations that may be needed to provide your child with extra support, such as neuropsychological testing. Ask the school staff to 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 (PE) classes. Meet with school administrators and teachers to discuss these needs and how they will be accommodated. Ask your child's healthcare team for their expertise in explaining this information.
- To reduce your child's anxiety, arrange meetings with the teacher(s) before your child goes back to school.
- Ask about providing an age-appropriate class presentation, either before or after your child returns to school, to educate friends and classmates about the illness. Ask members of the healthcare team for assistance. Some treatment centers have healthcare professionals available to lead these presentations, or have prepared versions of these presentations available for use. Ask your child if they would like to be present for the presentation. If so, your child can participate in ways that are comfortable for them.

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

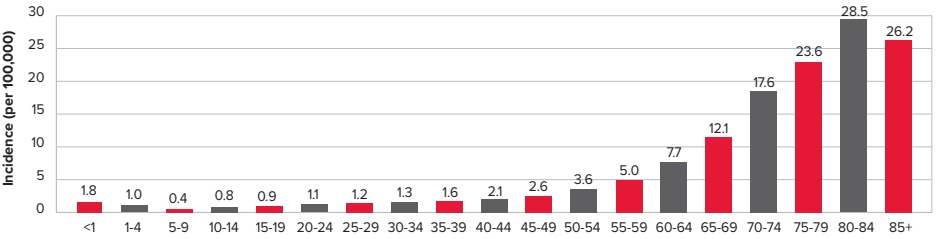
Treatment Outcomes

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

Figure 6. AML: Age-Specific Incidence Rates 2013-2018



The horizontal axis shows 5-year age intervals. The vertical axis shows the frequency of new cases of AML per 100,000 people, by age-group.
Source: Source: SEER (Surveillance, Epidemiology and End Results) Cancer Statistics Review, 1975-2018 National Cancer Institute; 2021.

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

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

- **Genetic disorders.** Certain genetic conditions, present at birth, seem to increase the risk of AML, including:
  - Down syndrome
  - Neurofibromatosis type 1
  - Bloom syndrome
  - Trisomy 8
  - Fanconi anemia
  - Klinefelter syndrome
  - Wiskott-Aldrich syndrome
  - Kostmann syndrome
  - Shwachman-Diamond syndrome

- **Familial risk.** Certain gene mutations present at birth may increase the risk of developing AML. This is also known as "germline predisposition." Having a sibling with leukemia, especially a twin, is a risk factor for developing AML.
- **Previous treatment with chemotherapy or radiation.** 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 cancers.** People who have certain blood cancers are at greater risk of developing AML. These include myeloproliferative neoplasms (polycythemia vera, essential thrombocythemia and myelofibrosis), as well as myelodysplastic syndromes (MDS), which in some people can evolve, over time, into AML.
- **Chemical exposure.** Long-term exposure to high levels of certain chemicals, such as benzene, is linked to a greater risk of AML.

Drug Information

Table 3 includes information about drug classifications and treatments for AML. For more information, see the Package Insert and/or the Full Prescribing Information for each medication on the internet.

Table. 3. Some Drugs Used in the Treatment of AML

Drug Name Type of Drug Administration	FDA-Approved Indications
All-*trans*-retinoic acid (ATRA, Tretinoin, Vesanoid®) Chemotherapy Oral	Is indicated for the induction of remission in patients with acute promyelocytic leukemia (APL), characterized by the presence of the t(15;17) translocation and/or the presence of the *PML/RARα* gene who are refractory to, or who have relapsed from, anthracycline chemotherapy, or for whom anthracycline-based chemotherapy is contraindicated.
Arsenic trioxide (Trisenox®) Chemotherapy Intravenous (IV)	Indicated • In combination with tretinoin for treatment of adults with newly-diagnosed low-risk acute promyelocytic leukemia (APL) whose APL is characterized by the presence of the t(15;17) translocation or *PML/RAR-alpha* gene expression. • For induction of remission and consolidation in patients with APL who are refractory to, or have relapsed from, retinoid and anthracycline chemotherapy, and whose APL is characterized by the presence of the t(15;17) translocation or *PML/RAR-alpha* gene expression.

Drug Name Type of Drug Administration	FDA-Approved Indications
Cladribine (Leustatin®) Chemotherapy Intravenous (IV)	Approved to treat hairy cell leukemia and is also being studied in the treatment of other types of cancer.
Clofarabine (Clolar®) Chemotherapy Intravenous (IV)	Approved for the treatment of pediatric patients with relapsed or refractory acute lymphoblastic leukemia (ALL) and is also being studied in the treatment of other types of cancer.
CPX-351 (Vyxeos®) Chemotherapy Intravenous (IV)	Indicated for the treatment of newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) in adults and pediatric patients 1 year and older.
Cytarabine (Ara-C; Cytosar-U®) Chemotherapy Intravenous (IV)	Indicated to be used alone or with other chemotherapy drugs to treat certain types of leukemia including AML.
Daunorubicin (Cerubidine®) Chemotherapy Intravenous (IV)	Approved for use with other chemotherapy drugs to treat AML.
Etoposide (Etopophos®, VePesid®, VP-16) Chemotherapy Intravenous (IV)	Approved for the treatment of testicular cancer and small cell lung cancer, but is used as an off-label treatment for AML.
Gemtuzumab ozogamicin (Mylotarg™) Targeted therapy Intravenous (IV)	Indicated for the treatment of • Newly diagnosed CD33-positive AML in adults and pediatric patients 1 month and older • Relapsed or refractory CD33-positive AML in adults and pediatric patients 2 years and older
Gilteritinib (Xospata®) Targeted therapy Oral	Indicated for the treatment of adult patients who have relapsed or refractory AML with a *FLT3* mutation as detected by an FDA-approved test.
Idarubicin (Idamycin®) Chemotherapy Intravenous (IV)	Indicated for the treatment of AML in adults in combination with other approved antileukemia drugs.
Methotrexate (Trexall®) Chemotherapy Intravenous (IV) Oral	Approved for the treatment of acute lymphoblastic leukemia (ALL), but is used as an off-label treatment for AML.
Midostaurin (Rydapt®) Targeted therapy Oral	Indicated for the treatment of adult patients with newly diagnosed AML that is *FLT3* mutation-positive as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation.

Drug Name Type of Drug Administration	FDA-Approved Indications
Mitoxantrone (Novantrone®) Chemotherapy Intravenous (IV)	Approved for the treatment of AML.
Sorafenib (Nexavar®) Targeted therapy Oral	Being studied in clinical trials in patients with AML with an *FLT3* mutation.
Tagraxofusp-erzs (Elzonris®) Targeted therapy Intravenous (IV)	Indicated for the treatment of blastic plasmacytoid dendric cell neoplasm (BPCN) in adults and pediatric patients 2 years and older.
Thioguanine (Tabloid®) Chemotherapy Oral	Indicated for remission induction and remission consolidation of acute nonlymphocytic leukemias.

Normal Blood and Bone Marrow

Blood. Blood is the liquid that flows through a person's arteries and veins. It carries oxygen and nutrients throughout the body. It also carries away waste products. Blood is composed of proteins within a liquid called "plasma," as well as cells such as red blood cells.

Plasma. Plasma is largely made up of water, in which many chemicals are dissolved. These chemicals each have a special role. Factors found in plasma 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 (B9) 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." The blood cells are suspended in the plasma. See **Figure 7** on page 51.

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

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

- These cells 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 (CO_2) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the CO_2 is removed from the lungs.

2. Platelets are the cells that help blood to clot.

- These are small cells (one-tenth the size of RBCs).
- 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 (WBCs) are the cells that fight infections. They include:

- Neutrophils and monocytes. These cells, called "phagocytes," ingest and destroy bacteria and fungi. Unlike RBCs and platelets, monocytes can leave the bloodstream and enter tissues to attack invading organisms and fight off infection.
- Eosinophils and basophils. These WBCs respond to allergens or parasites.
- Lymphocytes. These WBCs, found mostly in the lymph nodes, spleen and lymphatic channels, 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)

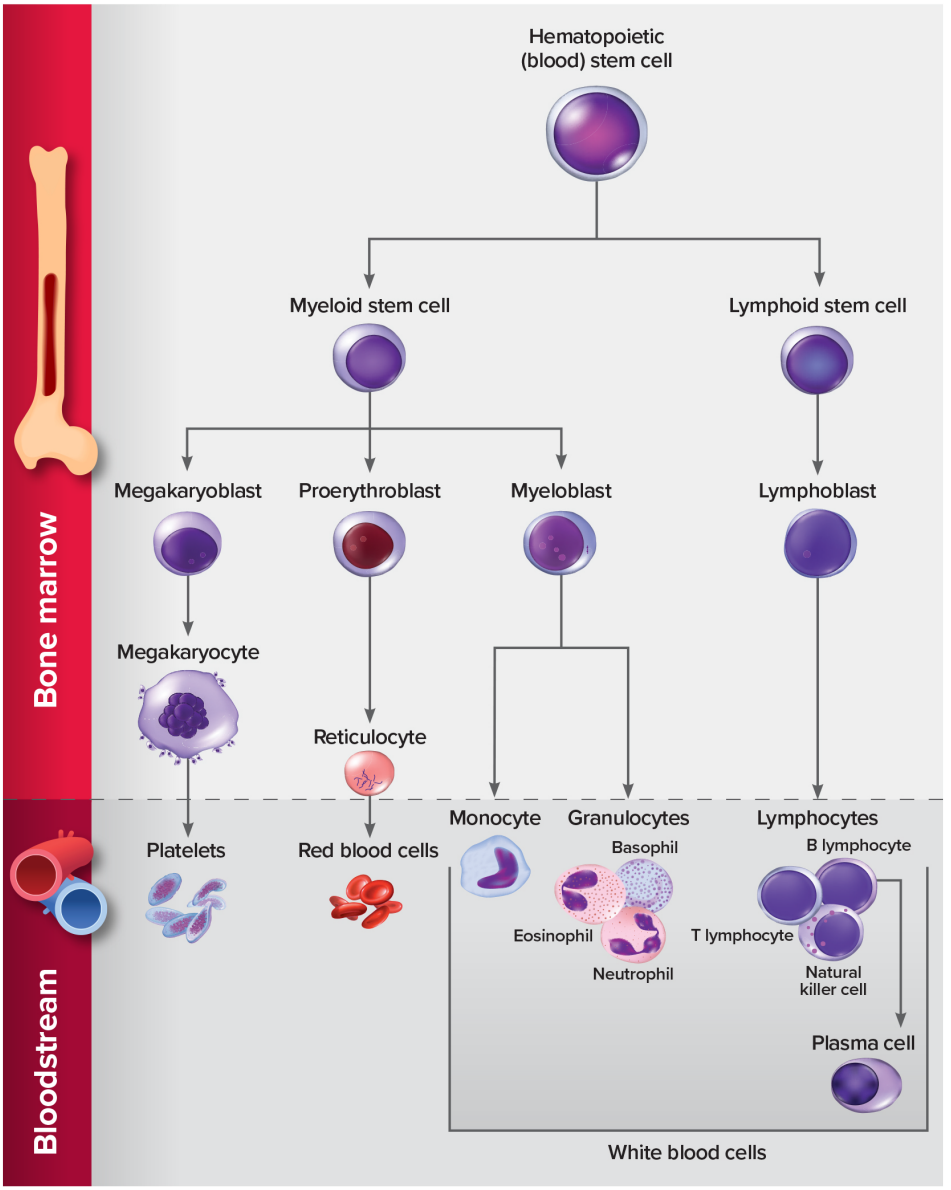
Bone Marrow. In healthy people, stem cells in the bone marrow produce new blood cells continuously. When blood cells are fully developed, they enter the bloodstream as it passes through the marrow and then circulates throughout the body.

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 stem cells are found in the marrow and have the ability to form the different mature blood cells found in circulation. 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.

Figure 7. Blood Cell & Lymphocyte Development

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



Resources and Information

LLS offers free information and services for patients and families affected by blood cancers. This section lists various resources you may find helpful.

For Help and Information

Consult with an Information Specialist. Information Specialists can assist you through cancer treatment, financial and social challenges and give accurate, up-to-date disease, treatment and support information. Our Information Specialists are highly trained oncology social workers and nurses. Language services are available. For more information, please:

- Call: (800) 955-4572 (Monday through Friday, 9 a.m. to 9 p.m. ET)
- Email and Live chat: www.LLS.org/InformationSpecialists

Clinical Trials (Research Studies). Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. Pediatric and adult patients and caregivers can work with our Clinical Trial Nurse Navigators who will help find clinical trials and provide personalized support throughout the entire clinical trial process. Visit www.LLS.org/CTSC for more information.

Nutrition Consultations. Schedule a free one-on-one nutrition consultation with one of our registered dietitians who have expertise in oncology nutrition. Consultations are available to patients of all cancer types and their caregivers. Dietitians can assist with information about healthy eating strategies, side effect management and more. Please visit www.LLS.org/nutrition for more information.

Free Information Booklets. LLS offers free education and support booklets for patients, caregivers and healthcare professionals that can either be 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 support to eligible individuals with blood cancer for insurance premiums, co-pays, and non-medical expenses like travel, food, utilities, housing, etc. For more information, please:

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

Resources for Families. Blood cancer occurs in a small number of children. Families face new challenges, and the child, parents and siblings may all need support. LLS has many materials for families including a caregiver workbook, children's book series, an emotion flipbook, dry erase calendar, coloring books

and a coloring app, a school reentry program, and other resources. For more information, please

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

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. Visit www.LLS.org/TheBloodline for more information and to subscribe to access exclusive content, submit ideas and topics, and connect with other listeners.

3D Models. LLS offers interactive 3D images to help visualize and better understand blood cell development, intrathecal therapy, leukemia, lymphoma, myeloma, MDS, MPNs and lab and imaging tests. Visit www.LLS.org/3D for more.

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.

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.

Connecting with Patients, Caregivers and Community Resources

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. Visit www.LLS.org/community to join.

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

Local Programs. 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 your region, please:

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

Advocacy and Public Policy. Working closely with dedicated volunteer advocates, LLS's Office of Public Policy elevates the voices of patients to state and federal elected officials, the White House, governors and even courts. Together, we advocate for safe and effective treatments. We pursue policies that would make care more accessible to all patients. And, most of all, we advocate for the hope for a cure. Want to join our work? Visit www.LLS.org/advocacy for more information.

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 view the directory.

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.

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) at (866) 615-6464
- Visit: NIMH at 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. **Visit www.LLS.org/booklets to view the free LLS booklet *Blood and Marrow Stem Cell Transplantation* for more information.**

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

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

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

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

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

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

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

Blast Cell. An immature blood cell.

Blood Cells. There are three major types of blood cells: 1) red blood cells 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.

Chloroma. See Myeloid Sarcoma.

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

Clinical Trial. A research study that is carefully planned and monitored to evaluate how well new medical approaches work in patients. The goal of clinical trials for blood cancers is to develop new treatments, improve quality of life and increase survival time. 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 protein found on the surface cells that help differentiate one cell type from another. It is commonly used in its abbreviated form, for example, "CD20." Also referred to as "cluster of designation."

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

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.

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

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 1 week followed by 3 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.

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 (FISH).

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

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

can help to diagnose some types of cancer, plan treatment and monitor the effectiveness of treatment.

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

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

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

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

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

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. They make up a person's tissue type, which varies from person to person, and are a critically

important factor in allogeneic (donor) stem cell transplantation. Before transplantation takes place, tissue typing is performed in order to determine if the donor's and the recipient's cells are compatible.

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

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

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

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

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

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

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

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

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

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

Leukocyte. See White Blood Cell.

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

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

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

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

Marrow. See Bone Marrow.

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

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

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

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

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

Myeloid Sarcoma. A mass of myeloid leukemia cells that develops outside the bone marrow. It may occur beneath the skin or 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.

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

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

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

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

Polymerase Chain Reaction (PCR). A very sensitive genetic laboratory test that is used to detect and measure some genetic mutations and

chromosomal changes that cannot be seen with a microscope. It essentially amplifies (increases) small amounts of specific pieces of either DNA or RNA so that they are easier to detect and measure. This test can find a single cancer cell among more than 100,000 healthy blood cells.

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

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

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

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

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

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

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

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

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

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

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

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. See Hematopoietic Stem Cell.

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

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

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

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

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

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

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

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.

References

Appelbaum FR, Meshinchi S. Measure for measure: measuring the impact of measuring residual disease in acute myeloid leukemia. American Society of Clinical Oncology. *Journal of Oncology Practice.* 2017;13(8):481-483.

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

Creutzig U, Kutny MA, Barr R, et al. Acute myelogenous leukemia in adolescents and young adults. *Pediatric Blood Cancer.* 2018;65(9):e27089.

Creutzig U, Zimmermann M, Reinhardt D, et al. Changes in cytogenetics and molecular genetics in acute myeloid leukemia from childhood to adult age groups. *Cancer.* 2016;122(24):3821-3830.

De Kouchkovsky I, Abdul-Hay M. Acute myeloid leukemia: a comprehensive review and 2016 update. *Blood Cancer Journal.* 2016;6(7):e441-e451.

Kadia TM, Ravandi F, Cortes J, et al. New drugs in acute myeloid leukemia. *Annals of Oncology.* 2016;(27):770-778.

Kavanagh S, Murphy T, Law A, et al. Emerging therapies for acute myeloid leukemia: translating biology into the clinic. *Journal of Clinical Investigation. JCI Insight* [online]. 2017;2(18):e95679. doi:10.1172/jci.insight.95679

Kim H. Treatments for children and adolescents with AML. *Blood Research.* 2020;55(suppl):S5-S13.

Kunty MA, Alonzo TA, Abla O, et al. Assessment of arsenic trioxide and all-trans retinoic acid for the treatment of pediatric acute promyelocytic leukemia: a report from the Children's Oncology Group AAML 1331 Trial. *JAMA Oncology.* 2022;8(1):79-87.

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

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). *Acute Myeloid Leukemia* Version 3.2022. January 13, 2023. https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed January 26, 2023.

Petronelli, M. Diagnosis, management challenging for pediatric BPDCN. Dermatology Times. Oct. 3, 2022. www.dermatologytimes.com/view/diagnosis-management-challenging-for-pediatric-bpdcn Accessed April 5, 2023.

Prada-Arismendy J, Arroyave JC, Rothlisberger S. Molecular biomarkers in acute myeloid leukemia. *Blood Reviews.* 2017;(31):63-76.

PDQ® Pediatric Treatment Editorial Board. Childhood Acute Myeloid Leukemia/Other Myeloid Malignancies Treatment. Bethesda, MD: National Cancer Institute. Updated August 11, 2022. https://www.cancer.gov/types/leukemia/patient/child-aml-treatment-pdq. [PMID: 26389454]. Accessed January 17, 2023.

Rubnitz JE, Kaspers GJL. How I treat pediatric acute myeloid leukemia. *Blood.* 2021;138(12):1009-1018.

Sexauer AN, Tasian SK. Targeting FLT3 signaling in childhood acute myeloid leukemia. *Frontiers in Pediatrics.* 2017;5:248.

Tarlock K, Cooper TM. Acute myeloid leukemia in children and adolescents. UpToDate [online healthcare news]. https://www.uptodate.com/contents/acute-myeloid-leukemia-in-children-and-adolescents. Accessed January 17, 2023.

Vujkovic M, Attiyeh EF, Ries RE, et al. Genomic architecture and treatment in pediatric acute myeloid leukemia: a Children's Oncology Group report. *Blood.* 2017;129(23):3051-3058.

NOTES

NOTES

LEUKEMIA & LYMPHOMA SOCIETY®

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

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