LEUKEMIA & LYMPHOMA SOCIETY®

PROVIDING THE LATEST INFORMATION
FOR PATIENTS & CAREGIVERS

Acute Myeloid Leukemia

Revised **2019**

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

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

Discover what thousands already have at **www.LLS.org/Community**

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**

Inside This Booklet

Acknowledgement

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Introduction

This booklet provides information about acute myeloid leukemia (AML) for patients and their families. You may hear other terms that are sometimes used to refer to AML, including “acute myelogenous leukemia,” “acute myelocytic leukemia,” “acute myeloblastic leukemia” and “acute granulocytic leukemia.”

AML is the most common form of acute leukemia in adults. An estimated 21,450 new AML cases were expected to be diagnosed in the United States in 2019. As of January 2015, an estimated 53,491 people were either living with or in remission from AML. Although AML can occur at any age, adults age 60 years and older are more likely to develop the disease than younger people.[1]

Advances in diagnostic tests and treatment options for AML are resulting in improved remission and cure rates, but much work remains to be done. A number of new therapies for AML patients of all ages and in all stages of treatment are under study in clinical trials.

At LLS, we know that the more you understand about your disease, the better you can take care of yourself: your mind, body and health. This booklet provides information about AML, defines complicated terms, provides information about normal blood and bone marrow, explains tests and treatments for AML and lists new treatment options available through research and clinical trials.

We trust that the information in this booklet will provide you with a good working knowledge base or that it will reinforce what you already know. We hope you keep this booklet handy and, should you ever feel alone in confronting problems, we hope that you will turn to it for information and guidance and to find the support and resources you need. We are here to help.

1. Source: *Facts 2018-2019*. The Leukemia and Lymphoma Society. March 2019.

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Leukemia

Leukemia is a cancer of the blood and bone marrow. Bone marrow is the sponge-like tissue in the center of most bones, where blood cells form. Leukemia begins in an immature stem cell (a “hematopoietic” stem cell) in the bone marrow. The immature cell undergoes a change, called a “mutation,” and becomes a type of leukemia cell.

Leukemia cells do not mature into healthy, functioning blood cells. They grow quickly and live longer than healthy blood cells. They divide and copy themselves to make more and more leukemia cells. Over time, the leukemia cells either crowd out or suppress the development of healthy blood cells in the bone marrow. The leukemia cells can also leave the bone marrow and enter the bloodstream.

The four major types of leukemia are:

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

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

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

Visit www.LLS.org/booklets to view the free LLS booklet *The AML Guide: Information for Patients and Caregivers* for general information about AML. Also visit www.LLS.org/DiseaseInformation and click on the link to view the illustrational chart called *Where do Blood Cancers Develop?*

Acute Myeloid Leukemia (AML)

How AML Develops. In healthy bone marrow, stem cells become mature blood cells through the process of differentiation. In people with AML, however, a series of mutations in the genetic material (DNA) of the myeloid stem cell result in the formation of leukemic cells—the immature blast cells that are stuck in the earliest stages of cell development. These cells, also referred to as "AML cells," cannot mature into fully functional blood cells, and they multiply uncontrollably. The leukemic "blasts" quickly build up in the bone marrow and crowd out or suppress the development of healthy blood cells. As a result, there are too many blast cells that cannot function and too few mature, functioning blood cells.

By the time a person is diagnosed with AML, the number of healthy red blood cells, white blood cells and platelets is usually lower than normal. The person may have anemia, infections or frequent bleeding at this point.

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

Signs and Symptoms

Signs and symptoms are changes in the body that may indicate the presence of disease. A sign is a change that the doctor sees in an examination or a lab test result. A symptom is a change that a patient can see or feel. A person who has signs or symptoms that suggest the possibility of leukemia is usually referred to a doctor, called a hematologist-oncologist, who specializes in both blood diseases and cancer. Hematologist-oncologists have specialized training in diagnosing and treating blood cancers such as leukemia, lymphoma and myeloma.

The signs and symptoms of AML are also associated with a number of other, less serious diseases. Therefore, the doctor will order tests to make a diagnosis (see *Diagnostic Testing* on *page 6*).

It is common for people with AML to feel a loss of well-being because of the underproduction of healthy blood cells. Many signs and symptoms of AML occur because there is a shortage of healthy blood cells.

Having a low red blood cell count results in a condition called anemia, with the following symptoms:

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

Symptoms caused by a low white blood cell count include:

- Frequent infections
- Fever

Symptoms caused by a low platelet count include:

- Bruising easily
- Pinhead-sized red spots on the skin (called “petechiae”)
- Prolonged bleeding from minor cuts
- Frequent or severe nosebleeds
- Bleeding from the gums

Other general symptoms of AML include:

- Mild fever
- Swollen gums
- Loss of appetite
- Unexplained weight loss
- Discomfort in bones or joints
- Fullness or swelling in the abdomen due to an enlarged spleen or liver

In rare instances, an accumulation of AML cells called a “myeloid sarcoma” forms outside the bone marrow (a sarcoma is a tumor). A myeloid sarcoma may occur in almost any part of the body. If AML cells spread to the skin, they can cause lumps or spots that may look like a rash. Other signs of AML may not appear in the blood and marrow until weeks or even months after the initial myeloid sarcoma diagnosis. A myeloid sarcoma diagnosis is equivalent to a diagnosis of AML and is treated with chemotherapy. The treatment may also include allogeneic or autologous stem cell transplantation. Other names for a myeloid sarcoma are “chloroma,” “granulocytic sarcoma,” “myeloblastoma,” “monocytoma” and “extramedullary disease.”

Diagnostic Testing

A person may have certain signs and symptoms of AML, but laboratory tests are needed to confirm the diagnosis. It is important to have an accurate diagnosis of the type of leukemia. The exact diagnosis helps the doctor:

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

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

Medical History, Physical Examination and Tests. If a person has signs or symptoms of leukemia, the doctor will take a thorough medical history. The history may include information about past illnesses, injuries, treatments and medications.

Some illnesses run in families, so the doctor may also ask about the health of the patient's blood relatives. The doctor will want to know about the patient's current symptoms and conduct a physical examination. During the examination, the doctor may listen to the patient's lungs and heart and carefully examine the body for signs of infection and disease. To check the internal organs, the doctor may also palpate (feel) different parts of the patient's body. For example, the doctor may palpate the abdomen to see if the patient has an enlarged spleen.

Blood and Bone Marrow Samples. If the signs and symptoms suggest that the person may have leukemia, the doctor will order blood and bone marrow tests. The findings from blood and bone marrow tests are used for making a diagnosis and treatment decisions.

Blood samples are generally taken from a vein in the patient's arm. Two related procedures are used to examine bone marrow cells for abnormalities: bone marrow aspiration and bone marrow biopsy. The bone marrow samples are usually taken from the patient's hip bone. Bone marrow has both a solid and liquid part. For a bone marrow aspiration, after medicine has been given to numb the skin, a specialized, hollow biopsy needle is inserted through the hip bone and into the marrow to remove (aspirate) a liquid sample of cells. The procedure for a bone marrow biopsy is similar, but a wider needle is used to remove a sample of solid bone that contains marrow. Often these two procedures are done at the same time.

At the lab, a hematopathologist will examine the blood and bone marrow samples. A hematopathologist is a doctor who has special training in identifying blood diseases by studying cells under a microscope.

Complete Blood Count (CBC) with Differential. This test is used to measure the number of red blood cells, white blood cells and platelets in a sample of blood. 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 may have:

- A low red blood cell count
- A low platelet count
- Either a high or low white blood cell count
- Blasts, which are immature white blood cells (leukemic cells), in the blood (normally, there are no blast cells in a healthy person's blood)

These CBC findings may suggest leukemia, but usually a diagnosis of AML is made only after a hematopathologist has examined the bone marrow sample.

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

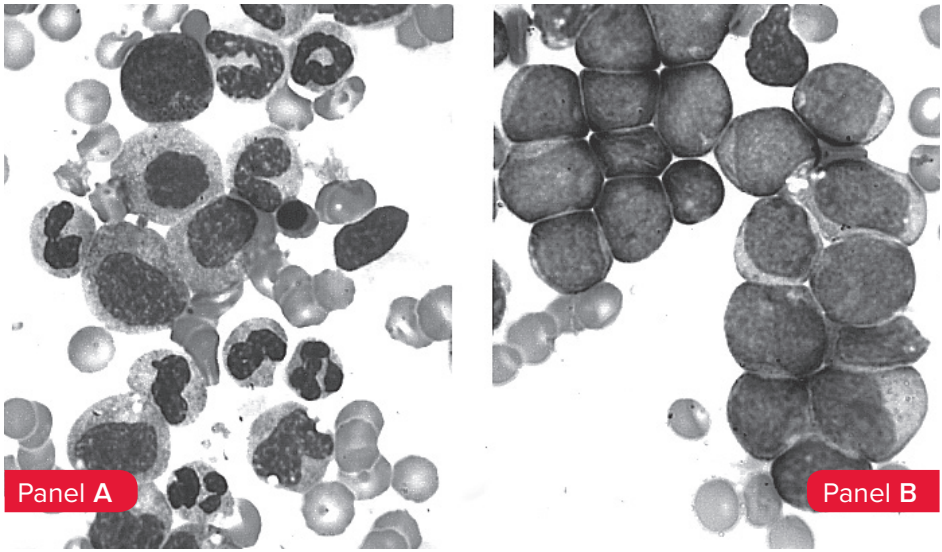
Blood Chemistry Profile. This is a test done on a sample of blood to measure the levels of certain substances released into the blood by organs and tissues in the body. These substances include electrolytes (such as sodium, potassium and chloride), fats, proteins, glucose (blood sugar), uric acid and enzymes. Blood chemistry tests provide important information about how well a person's kidneys, liver and other organs are working. These tests are not used to diagnose leukemia, but an abnormal amount of a particular substance in the blood may be a sign of another disease or health problem.

HLA Typing. This consists of a blood test to identify a person's HLA type. Human leukocyte antigens (HLAs) are proteins found on the surface of most cells in the body. These proteins make up a person's tissue type, which varies from person to person. HLAs play an important role in the body's immune response to foreign substances by helping the body distinguish its own cells from foreign cells. HLA matching is done before donor stem cell transplantation to find out if there is a tissue match between the donor and the person receiving the transplant.

HLA typing is not used to diagnose leukemia. It is, however, an important test for newly diagnosed AML patients if allogeneic stem cell transplantation is being considered as a treatment option.

Bone Marrow Cell Assessment. A hematopathologist will examine a sample of bone marrow cells under the microscope to determine the size, shape and type of cells, and to identify other features of the cells. A significant finding is whether the cells look more like normal, mature blood cells or abnormal, immature blood cells (blast cells). The percentage of blast cells in the sample is very important. Generally, the identification of 20 percent or more blasts in the peripheral blood and/or bone marrow sample is required to confirm a diagnosis of AML (see **Figure 1** *below*).

Figure 1. Normal Cells vs. AML Cells



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

Immunophenotyping (Flow Cytometry). This test is used to classify cells in a sample based on the type of antigens (markers) on the surface of the cells. The sample of cells is treated with special antibodies that only bind to cells that have a specific antigen on them. The cells are then passed through a laser beam. If the cells have the antibodies attached to them, they will give off light. Leukemia cells can have different antigens on their surfaces depending on their stage of development and whether they are myeloid or lymphoid. There are certain antigens, called cluster designation (CD) proteins, that are helpful in identifying blast cells as myeloblasts: CD13, CD14, CD33 and CD34. In addition to its use as

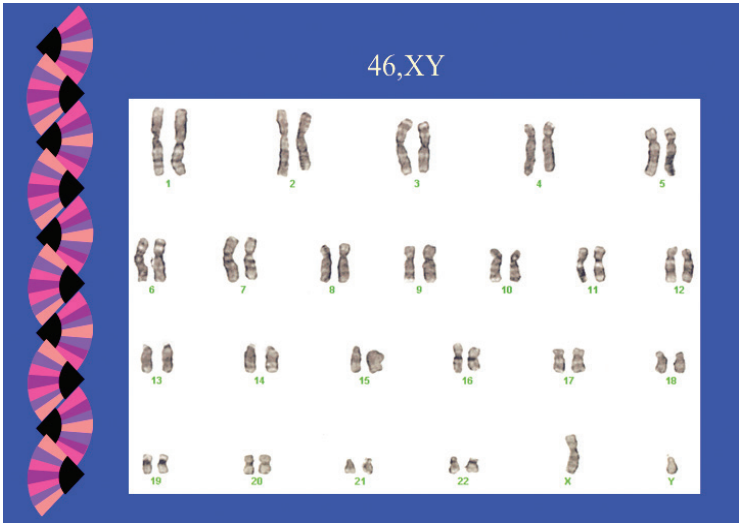
a diagnostic test, flow cytometry is also used for evaluating minimal residual disease (MRD), the small number of cancer cells that may remain in the body after treatment. (See *Minimal Residual Disease* on *page 38*.)

Genetic Tests. The following tests are done to examine the genes in a patient's leukemia cells.

Cytogenetic Analysis (Karyotyping). This test uses a microscope to examine the chromosomes inside of cells. For people with AML, karotyping is used to look for abnormal changes in the chromosomes of the leukemia cells.

Normal human cells contain 23 pairs of chromosomes, each of which are a certain size, shape and structure. In some cases of AML, the chromosomes of leukemia cells have abnormal changes, such as deletions, translocations and extra chromosomes, that can be seen under a microscope. Cytogenetic testing is done with either a bone marrow 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 will show if there are any abnormal changes in the size, shape, structure or number of chromosomes in the leukemia cells. See **Figure 2** *below*.

Figure 2. Normal Karyotype



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

Cytogenetic analysis provides information that is important when determining a patient's treatment options and prognosis. This information can predict how the disease will respond to therapy. For example, a translocation between chromosomes 15 and 17, abbreviated as t(15;17), is associated with a diagnosis of acute promyelocytic leukemia (APL). This is a subtype of AML that has a better-than-average prognosis and requires a different treatment approach than other AML subtypes.

Fluorescence In Situ Hybridization (FISH). This is a very sensitive test used to examine genes or chromosomes in cells and tissues. In cases of AML, 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. When the pieces of DNA bind to specific genes or areas of chromosomes, they light up when the slide is viewed under a fluorescent microscope. Not only can FISH identify most abnormal changes that can be seen with a microscope, but it can also detect some changes that are too small to be seen with basic cytogenetic testing. However, it is not used as a general screening tool. FISH has one disadvantage—the doctor must select specific chromosomes or genes to examine before the test is performed.

Molecular Testing. Molecular tests are very sensitive DNA tests that examine specific genetic characteristics of cancer cells and show abnormalities (mutations) in the chromosomes. Genetic mutations play an important role in the prognosis and treatment of patients with AML. Molecular testing does not replace cytogenetic testing, but together these tests help refine the prognosis and treatment options for AML patients, especially those who have no detectable chromosomal abnormalities.

DNA sequencing is a type of molecular test that checks for specific gene mutations in cells. 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 *FLT3, NPM1, CEBPA, KIT, IDH1* and *IDH2*. These markers are important in guiding risk assessment and prognosis and may also guide treatment decisions. Recent advances in genetic technologies are increasing the utilization of multi-gene panel diagnostics that can simultaneously test for mutations in numerous genes and for chromosomal abnormalities. Molecular testing should occur when the cancer is first diagnosed and also after a relapse because it is possible for patients to acquire additional genetic abnormalities after the completion of first-line treatment.

Understanding AML mutations. In patients with leukemia, specific mutations may only be present in a subset (rather than all) of the leukemic cells. This is called allelic ratio. Some patients have mutations with a "low-allelic ratio," meaning the mutation is present in only a minority of the leukemic blast cells, while others have mutations with a "high-allelic ratio" that could be present in most or all of the leukemic blast cells. This information can help guide prognosis and treatment options.

Polymerase Chain Reaction (PCR). This is a very sensitive test that detects and measures some genetic mutations and chromosomal changes that are too small to be seen with a microscope. PCR essentially increases or "amplifies" small amounts of specific pieces of either RNA or DNA to make them easier to detect and measure. This test can find a single leukemia cell among more than 500,000 to 1,000,000 normal cells. PCR is one method used to determine the amount of cancer cells that are still present after treatment. Doctors use this test for assessment of minimal residual disease (MRD).

Key Questions to Ask Your Treatment Team:

- What tests are necessary before I start treatment?
- When will the tests take place?
- Where will the tests take place? How long will the tests take?
- Will my insurance pay for all of my tests? If not, is there someone who can assist me with getting my tests covered?
- What are my options if my insurance plan does not cover the tests that are needed?
- Will the tests need to be repeated after the end of first-line (initial) treatment?

Heart Tests. Some chemotherapy drugs, such as the type called "anthracyclines," can damage heart tissue. Your doctor may want to test your heart function before starting treatment. Examples of heart tests that may be given to AML patients include:

- **Echocardiogram.** This test uses sound waves to make a picture of the beating heart, which is displayed on a monitor. The images are recorded for future review.
- **MUGA.** A multigated acquisition (MUGA) scan also makes pictures of the heart. Patients receive a shot containing a radiotracer into a vein. Pictures of the heart are taken with a special camera and they show the radiation being released by the radiotracer, making it possible to see how much blood the heart pumps with each beat.

Diagnosis

Generally, the identification of 20 percent or more leukemic blasts of myeloid origin in the peripheral blood and/or bone marrow sample is required to confirm an AML diagnosis. AML does not have a single cause, rather it is heterogeneous (diverse in character or content), characterized by many chromosomal abnormalities and gene mutations. AML is classified into subtypes that are based on lab test results.

AML Subtypes. Information about a person's AML subtype helps the doctor recommend a specific treatment plan. The World Health Organization (WHO) classification is the main system used to classify AML into subtypes.

WHO developed a classification system to include prognostic (predictive) factors, such as chromosomal abnormalities and genetic mutations that are known to affect the future outcome of the disease. These genetic factors help provide patients and their doctors with more reliable information regarding their probable outcome (prognosis), as well as their probable response to treatment.

The WHO classification is usually revised every eight years. The revised 2016 classification incorporates new scientific and clinical information. The 2016 classification of myeloid and lymphoid neoplasms was updated to include the category "myeloid neoplasms with germline predisposition." (See **Table 1** on *pages 13-14*). This inclusion reflects the increasing recognition that some cases of myeloid cancers, including myelodysplastic syndromes and AML, are associated with inherited mutations. Recognizing cases that run in families requires that doctors take a complete family history of the patient.

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

Type of AML	Inversion and/or Translocation	Gene Mutation
AML with recurrent genetic abnormalities		
AML with	t(8;21)(q22;q22.1)	*RUNX1-RUNX1T1*
AML with	inv(16)(p13.1q22) or t(16;16)(p13.1;q22)	*CBFB-MYH11*
APL (acute promyelocytic leukemia)	t(15:17)	*PML-RARA*
AML with	t(9;11)(p21.3;q23.3)	*MLLT3-KMT2A*
AML with	t(6;9)(p23;q34.1)	*DEK-NUP214*
AML with	inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)	*GATA2, MECOM(EV11)*
AML (megakaryoblastic) with	t(1;22)(p13.3;q13.3)	*RBM15-MKL1*
AML with		*NPM1*
AML with		Biallelic mutations of *CEBPA*
AML with myelodysplasia-related changes		
Therapy-related myeloid neoplasms		
AML, *not otherwise specified* (NOS)		
AML with minimal differentiation		
AML without maturation		
AML with maturation		
Acute myelomonocytic leukemia		
Pure erythroid leukemia		
Acute megakaryoblastic leukemia		
Acute basophilic leukemia		
Acute panmyelosis with myelofibrosis		
Myeloid sarcoma		
Myeloid proliferations related to Down syndrome		
Blastic plasmacytoid dendritic cell neoplasm		
Acute leukemias of ambiguous lineage		
Acute undifferentiated leukemia		
Mixed phenotype acute leukemia (MPAL) with	t(9;22)(q34.1;q11.2)	*BCR-ABL1*
MPAL with	t(v;11q23.3)	*KMT2A* rearranged
MPAL, B cell/myeloid lineage, NOS		
MPAL, T cell/myeloid lineage, NOS		

Table 1. AML and Related Neoplasms (cont.)

Type of AML	Inversion and/or Translocation	Gene Mutation
Myeloid neoplasms with germline predisposition without a preexisting disorder or organ dysfunction		
AML with germline *CEBPA* mutation		
Myeloid neoplasms with germline *DDX41* mutation		
Myeloid neoplasms with germline predisposition and preexisting platelet disorders		
Myeloid neoplasms with germline predisposition and other organ dysfunction		

Based on the World Health Organization (WHO) classification.
Abbreviations: t, a translocation between chromosomes; inv, an inversion in a chromosome; q, the long arm of a chromosome (the lower half); p, the short arm of a chromosome (the upper half).

Prognostic Factors. Various factors affect treatment options and the patient's likely outcome or disease course (the prognosis). A characteristic or attribute that helps predict prognosis is called a "prognostic factor." Doctors use prognostic factors to help predict how a disease will likely progress and respond to treatment. Some prognostic factors are called "favorable risk factors" because they are associated with a lower risk of relapse after treatment. Others are called "unfavorable risk factors" because they are associated with a higher risk of relapse after treatment. Doctors evaluate a variety of factors to classify AML, which are summarized in the remainder of this section.

Cytogenetics (Chromosomal Abnormalities). Chromosomal changes represent an important prognostic factor for predicting remission rates, relapse risks and survival outcomes. However, not all patients have a chromosomal abnormality. Patients without a chromosomal abnormality are usually classified as "intermediate risk." **Table 2**, on *page 15*, lists some of the more common chromosomal abnormalities.

Table 2. Common Chromosome Abnormalities and Associated Risk Status

Risk Category	Chromosome Abnormalities (Cytogenetic Analysis)
Favorable (low risk)	○ Translocation between chromosomes 8 and 21: t(8;21) ○ Inversion of chromosome 16: inv(16) ○ Translocation within chromosome 16 itself: t(16;16) ○ Translocation between chromosomes 15 and 17: t(15;17) (acute promyelocytic leukemia [APL])
Intermediate (intermediate risk)	○ Normal cytogenetics ○ Trisomy 8 ○ Translocation between chromosome 9 and 11: t(9;11) ○ Chromosome abnormalities not classified as favorable or adverse
Adverse (high risk)	○ Complex changes involving 3 or more chromosomal abnormalities ○ Monosomal karyotype (having a single copy of a chromosome pair instead of the usual two copies, plus at least 1 additional monosomy or structural chromosomal abnormality) ○ Deletion of part of chromosome 5 or 7: 5q– or 7q–; or monosomy of chromosomes 5 or 7: –5 or –7 ○ Deletion of part of chromosome 17: 17p–; or monosomy of chromosome 17 with an abnormality of 17p: –17/abn(17p) ○ Abnormalities of chromosome 11 (at the spot q23): 11q23 ○ Translocation or inversion of chromosome 3, inv(3): t(3;3) ○ Translocation between chromosomes 6 and 9: t(6;9) ○ Translocation between chromosome 9 and 22: t(9;22)

Based on *NCCN Clinical Practice Guidelines in Oncology*. Acute Myeloid Leukemia. 2018. and Dohner H, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. *Blood*. 2017;129:424-447.
Abbreviations: t, a translocation between chromosomes; inv, an inversion in a chromosome; q, the long arm of a chromosome (the lower half); p, the short arm of a chromosome (the upper half).

Molecular Abnormalities (Gene Mutations). AML patients whose leukemia cells have certain genetic mutations are assigned a specific risk status (see **Table 3** on *page 16*). For example, patients who have an *NPM1* gene mutation but no *FLT3*-ITD gene mutation seem to have a better prognosis than people without the *NPM1* mutation.

Some patients have mutations with a “low-allelic ratio,” meaning the mutation is present in only a minority of the leukemic blast cells, while others have mutations with a “high-allelic ratio” that could be present in most or all of the leukemic blast cells. Talk to your doctor about treatments available to target specific genetic mutations.

Table 3. Common Molecular Abnormalities and Associated Risk Status

Risk Category	Molecular Abnormalities
Favorable (low risk)	○ *NPM1* mutation without *FLT3*-ITD mutation or with *FLT3*-ITD^{low} ○ Biallelic (double) *CEBPA* mutation
Intermediate (intermediate risk)	○ Mutated *NPM1* and *FLT3*-ITD^{high} ○ Non-mutated *NPM1* without *FLT3*-ITD or with *FLT3*-ITD^{low} (without adverse-risk genetic abnormalities)
Adverse (high risk)	○ *TP53* mutation ○ Mutated *RUNX1* ○ Mutated *ASXL1* ○ Non-mutated *NPM1* and *FLT3*-ITD^{high}

Based on *NCCN Clinical Practice Guidelines in Oncology*. Acute Myeloid Leukemia. 2018. and Dohner H, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. *Blood*. 2017;129:424-447.
Superscripts: low = low allelic ratio (< 0.5); high = high allelic ratio (≥ 0.5).

Other Risk Factors

Age of the Patient. Usually, the older the patient, the poorer the prognosis. Unfavorable chromosomal abnormalities increase with age. Additionally, older patients sometimes have other medical conditions (comorbidities) that can make it difficult for them to tolerate intense chemotherapy treatments.

Therapy-Related AML. AML may develop in people who received chemotherapy in the past to treat a different type of cancer. Therapy-related AML is more resistant to treatment and is associated with a poorer prognosis.

Prior Blood Cancer. In patients who have had a prior blood cancer, such as a myelodysplastic syndrome or a myeloproliferative neoplasm, AML is associated with a poorer prognosis.

Central Nervous System Involvement. When leukemia cells have spread to the area around the brain and spine, AML can be more difficult to treat and is associated with a poorer prognosis.

Relapsed AML. Patients with AML that has been treated before and relapsed (come back) have a poorer prognosis.

Refractory AML. Patients with AML that failed to respond to the current standard treatment have a poorer prognosis.

High White Blood Cell Count. Some AML patients develop signs or symptoms attributable to a very high white blood cell count. A white blood cell count greater than 100,000 cells per microliter (100,000 cells/µL) at the time of diagnosis is associated with higher likelihood of complications.

Treatment Options for AML

New treatments may have been approved since this book was printed.
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Patients have two main treatment options: standard therapies or treatment in a clinical trial. It is important to talk to your healthcare team about the best treatment option in your case.

A diagnosis of AML is associated with a wide range of outcomes. Patients with different subtypes of AML may have varying responses to treatment. The main treatment for AML is chemotherapy, sometimes followed by a stem cell transplant. Other drugs, including all trans-retinoic acid (ATRA) and arsenic trioxide, may be used to treat patients with acute promyelocytic leukemia (APL).

Chemotherapy. The current standard treatment for AML consists of induction chemotherapy with a combination of **cytarabine and an anthracycline**, followed by either one to four cycles of consolidation (postremission) chemotherapy or a stem cell transplant. However, participation in a carefully conducted clinical trial may be the best available treatment option.

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

Chemotherapy is often given in treatment cycles. Each cycle is made up of a number of days of treatment followed by a 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 may be injected into a vein. An intravenous (IV) treatment is a slow injection into a vein that may take several minutes, a few hours or even several days (a continuous infusion). Often, doctors give IV chemotherapy through a thin, soft tube called a central venous line, catheter or central line. When a patient has a central line in place, doctors administer IV chemotherapy treatments through the line and do not have to inject a needle into the patient's vein each time a treatment is administered. Doctors can also access the central line to give other medicines and take blood samples. A central line can be left in place for weeks or months.

Treating AML. AML progresses rapidly and should be treated aggressively and as soon as possible. Standard treatment of AML is often divided into two phases: induction chemotherapy (to induce remission) and consolidation (postremission) therapy. Patients should also consider the option of participating in a clinical trial, as it may be a better treatment option in their case.

Induction Therapy. The initial (first) phase of chemotherapy is called "induction therapy." The goal of induction therapy is a complete remission. A complete remission is achieved when there are less than 5 percent blast cells in the bone marrow; the patient's red blood cell, white blood cell and platelet counts have returned to normal or close to normal levels; and there are no signs or symptoms of the disease. Although obtaining a remission is the first step in controlling AML, it is also important for patients to emerge from the induction phase physically fit enough to tolerate the intensive treatments given during the consolidation phase (see *page 21*).

The intensity of a patient's treatment depends on the person's age and health. Doctors often give the most intensive chemotherapy to people younger than age 60. Some older patients in good health may benefit from similar or slightly less intensive treatments. People who are older or in poor health may not do as well with intensive chemotherapy treatments. Treatment options for older patients are discussed on *pages 26-28*.

The most common induction regimen for AML includes **cytarabine** and an anthracycline drug such as **daunorubicin** or **idarubicin**. The drug cytarabine is most often given continuously for 7 days intravenously (IV infusion), while the anthracycline drug is given by IV infusion in a single dose for 3 days during the first week of treatment. This is called the "7 + 3" regimen. The induction therapy is usually given in the hospital and lasts about a week. Other drugs may be added or substituted for higher-risk patients.

- **Midostaurin (Rydapt®)** is FDA-approved for the treatment of adult patients with newly diagnosed AML that is *FLT3* mutation-positive, per an FDA-approved test, in combination with standard therapy: cytarabine and daunorubicin for induction and cytarabine for consolidation. Midostaurin is not indicated as a single-agent induction therapy. Midostaurin is taken twice a day in pill form.
- **Gemtuzumab ozogamicin (GO)** (**Mylotarg™**) is FDA-approved for the treatment of adults with newly diagnosed AML and relapsed or refractory AML whose leukemia cells express the CD33 antigen (CD33-positive AML). GO is a monoclonal antibody attached to the toxin calicheamicin. Gemtuzumab binds to CD33 and then enters the cell. Once inside, it releases the toxin. This medication is slowly injected into a vein through a needle. It is given in cycles consisting of treatment days followed by days of rest.
- **Daunorubicin and cytarabine (Vyxeos®)**, a liposomal combination, is FDA-approved for the treatment of adults with newly-diagnosed, therapy-related acute myeloid leukemia (t-AML), or AML with myelodysplasia-related changes (AML-MRC). A liposomal medication contains the active drug inside small, fat-like particles. This type of preparation allows more medication to get to its target (the bone marrow). The liposomal daunorubicin and cytarabine combination is slowly injected into a vein for 90 minutes. It is given in cycles consisting of treatment days followed by days of rest.

- **Glasdegib (Daurismo™)**, in combination with low-dose cytarabine, is FDA-approved for the treatment of newly-diagnosed AML in adult patients age 75 years and older or who have comorbidities that preclude use of intensive induction chemotherapy. Glasdegib is taken once daily in pill form. Limitation of use: glasdegib has not been studied in patients with the comorbidities of severe renal impairment or moderate-to-severe hepatic impairment.
- **Venetoclax (Venclexta®)**, in combination with azacitidine, decitabine or low-dose cytarabine, is FDA-approved for the treatment of newly-diagnosed AML in adults who are age 75 years and older, or who have comorbidities that preclude use of intensive induction chemotherapy. Venetoclax is taken once daily in pill form. This indication has a special designation, called "accelerated FDA approval," based on treatment response rates. Continued approval for this indication may be contingent upon verification and description of its clinical benefit in confirmatory trials.

Induction therapy destroys most of the leukemia cells as well as the healthy bone marrow cells. Most patients develop dangerously low blood counts and may become very ill. Typically, the severity of the disease and the side effects of this initial therapy result in a hospital stay of 4 to 6 weeks because of the need for supportive (palliative) care with IV antibiotics and frequent blood transfusions. The amount of time before the patient can be discharged home depends on the patient's condition, whether the patient lives near the medical facility with a caregiver, and if the patient can comply with the policies of the treatment center.

About 1 to 2 weeks after the completion of induction therapy, the doctor will take a bone marrow sample to evaluate the effectiveness of the treatment. (For example, if therapy is given for one week, this would be day 14 after the start of treatment, or day 21 if given for two weeks.) For patients who have a high percentage of leukemic blast cells, induction therapy can be repeated, either with the same drugs or with a new chemotherapy regimen. About 3 to 4 weeks after the completion of induction therapy, normal bone marrow cells should form and start making new blood cells. When that happens, the patient is considered to be in "complete remission." Patients who are unable to achieve a remission with standard treatment should be considered as a candidate for a clinical trial, allogeneic stem cell transplantation or drug regimens for relapsed or refractory AML.

Table 4, on *page 20*, lists some of the standard drugs used to treat AML, as well as some of the drugs under study in AML clinical trials. It is possible for patients to be treated with drugs that are not listed in this table and still receive appropriate and effective treatment for AML. For more information, please visit www.LLS.org/drugs or call our Information Specialists at (800) 955-4572.

Table 4. Some Drugs Approved or in Clinical Trials for the Treatment of AML

Anthracyclines (antitumor antibiotics)	○ daunorubicin (Cerubidine®) ○ doxorubicin (Adriamycin®) ○ idarubicin (Idamycin®) ○ mitoxantrone (Novantrone®)
Antimetabolites	○ cladribine (2-CdA; Leustatin®) ○ clofarabine (Clolar®) ○ cytarabine (cytosine arabinoside, ara-C; Cytosar-U®) ○ fludarabine (Fludara®) ○ methotrexate ○ 6-mercaptopurine (Purinethol®) ○ 6-thioguanine (Thioguanine Tabloid®)
Anthracycline and antimetabolite combination	○ Liposomal combination of daunorubicin and cytarabine (Vyxeos™)
Topoisomerase inhibitors	○ etoposide (VP-16; VePesid®, Etopophos®) ○ topotecan (Hycamtin®)
DNA-Damaging (alkylating) agents	○ cyclophosphamide (Cytoxan®) ○ carboplatin (Paraplatin®) ○ temozolomide (Temodar®)
Cell-maturing agents	○ all-trans retinoic acid (ATRA, tretinoin; Vesanoid®) ○ arsenic trioxide (Trisenox®)
Hypomethylating agents	○ azacitidine (Vidaza®) ○ decitabine (Dacogen®)
Immunomodulator	○ lenalidomide (Revlimid®)
Histone deacetylase inhibitors	○ pracinostat ○ panobinostat (Farydak®) ○ vorinostat (Zolinza®)
Antibody conjugate	○ gemtuzumab ozogamicin (Mylotarg®)
FLT3 inhibitors	○ sorafenib (Nexavar®) ○ midostaurin (Rydapt®) ○ gilteritinib (Xospata®) ○ quizartinib (AC-220)
IDH1 inhibitor	○ ivosidenib (Tibsovo®)
IDH2 inhibitor	○ enasidenib (Idhifa®)
Hedgehog inhibitor	○ glasdegib (Daurismo™)
BCL-2 inhibitor	○ venetoclax (Venclexta®)

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

Postremission Therapy (Consolidation Therapy). Blood cell production should return to normal in many patients several weeks after induction therapy is completed. Blood cell counts gradually approach acceptable levels, well-being returns and AML cells cannot be detected in the blood or bone marrow. The cancer is now "in remission." If there are a small number of residual AML cells, they will not interfere with normal blood cell development, but they do have the potential to multiply and cause a relapse. The term "minimal residual disease" (MRD) is used after treatment to refer to the leukemia cells that may still be present in the patient's body but cannot be detected in the bone marrow with standard tests (such as examining a bone marrow sample under a microscope). However, these residual cancer cells can be detected with more sensitive tests, such as flow cytometry and polymerase chain reaction (PCR).

Even when a patient achieves a complete remission, more treatment is usually needed to destroy any residual leukemia cells in the body. Without additional therapy, the leukemia is likely to relapse within months. To prevent a recurrence, intensive consolidation therapy is given after the patient recovers from induction therapy. Consolidation therapy is treatment that is given after cancer is in remission following the initial therapy. The goal of consolidation therapy is to lower the number of residual leukemia cells in the body, or eliminate them entirely.

There are two basic treatment choices for postremission therapy:

- Intensive chemotherapy
- Stem cell transplantation (see *pages 22-24* for more information about the three types of stem cell transplantation)

Patients with favorable risk outcomes are often given intensive chemotherapy with high-dose cytarabine and other drugs for their consolidation therapy. In the consolidation phase, patients generally receive multiple cycles of chemotherapy. The number of chemotherapy cycles varies from patient to patient. Patients are often hospitalized during postremission therapy. The length of stay varies depending on the treatment type and other factors.

Patients with high-risk AML, based on their prognostic factors, are rarely cured with chemotherapy alone. The treatment options that may be offered to these patients are allogeneic stem cell transplantation and/or participation in a clinical trial. An important treatment decision in AML is based on an evaluation of the benefits and risks associated with allogeneic stem cell transplantation after a patient's first remission. This is when transplantation offers the best means of preventing AML from recurring; however, it is associated with higher treatment-related morbidity and death, especially in older patients. Patients who are candidates for an allogeneic stem cell transplant should begin a search for an HLA-matched stem cell donor during the time that they are receiving induction therapy.

Stem Cell Transplantation. While treatment with chemotherapy alone is appropriate for some patients, others may benefit from stem cell transplantation.

Chemotherapy can cause very serious side effects. Even though administering higher doses of chemotherapy drugs may kill more leukemia cells, it is not possible to do so unless the patient will be receiving a stem cell transplant. This is because the higher doses would severely damage the bone marrow and result in anemia, serious infections and uncontrolled bleeding. Stem cell transplantation allows doctors to give higher doses of chemotherapy than can typically be given, either with or without radiation therapy. After the chemotherapy, the patient receives an infusion of stem cells to replace the stem cells destroyed by the intensive therapy. These new stem cells restore healthy stem cells in the bone marrow that can form new red blood cells, white blood cells and platelets. The three types of stem cell transplantation are described below.

- Allogeneic stem cell transplantation using stems cells from:
  - A healthy HLA-matched donor (sibling or unrelated donor)
  - A unit of umbilical cord blood
  - A parent, child or "half-matched" sibling of the patient (these are known as haploidentical stem cells)
- Reduced-intensity allogeneic stem cell transplantation
- Autologous stem cell transplantation

Research to determine which patients are most likely to benefit from transplantation after their first complete remission is evolving. Studies show that allogeneic stem cell transplantation may benefit high-risk and intermediate-risk patients who are younger than 60 and have an HLA-matched sibling donor. Timing of an allogeneic transplantation is one of the most important factors influencing transplant outcomes, so it is very important to start a donor search as soon as possible in order to identify a suitably matched related or unrelated donor.

Allogeneic Stem Cell Transplantation. This is the most common type of stem cell transplantation used to treat AML. In preparation for the transplant, patients are given strong doses of chemotherapy, either with or without radiation, to kill the remaining leukemic cells in their bodies and suppress their own immune system (this is called the "conditioning therapy"). Then patients receive infusions of the donor stem cells. Allogeneic transplantation uses healthy blood-forming cells from an HLA-matched family member, an unrelated donor, or from 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. The immune system helps the body fight infections and other diseases. The new immune system also has the potential to recognize and attack

any remaining cancer cells. The transplanted immune cells (the graft) perceive the leukemia cells in the body as foreign and destroy them. This is called the "graft-versus-leukemia (GVL)" effect.

Allogeneic stem cell transplantation, compared to other treatment approaches, is associated with a higher rate of side effects and mortality in patients. However, it may be considered for patients with higher-risk AML, based on cytogenetic and molecular test results and currently available therapies. The decision to perform an allogeneic transplant also depends on the patient's age, physical fitness, comorbidities (other coexisting medical conditions), social support (from family members, caregivers, friends, etc.) and the patient's understanding of the potential benefits and risks. The age limit for transplantation varies by treatment center; as "upper age limits," many centers use age 60 or 65 years for standard allogeneic transplantation and 70 years for reduced-intensity allogeneic transplantation.

After transplantation of the stem cells, one possible serious side effect is graft versus-host disease (GVHD). GVHD occurs when the transplanted donor immune cells (the graft) identify the cells in the recipient's body (the host) as foreign and attack them. The parts of the body most commonly damaged by GVHD include the skin, liver, stomach, intestines and eyes. GVHD can develop within weeks after transplantation or much later. A doctor can order medications to help prevent or minimize the complications of GVHD.

Reduced-Intensity Stem Cell Transplantation (also called "Nonmyeloablative" Transplantation or "Mini" Transplant). Lower doses of chemotherapy and/or radiation are used in the conditioning therapy for this type of allogeneic transplant. Therefore, it may be a treatment option for older patients who cannot tolerate the high doses of chemotherapy used for a standard allogeneic stem cell transplant. The therapy reduces the number of cancer cells, but it does not completely destroy the patient's bone marrow. As in a standard allogeneic transplant, the white blood cells (immune cells) from the donor may recognize any remaining leukemia cells as foreign and destroy them. Over time, if the transplant is successful, the donor's stem cells replace the patient's immune cells. The engrafted donor immune cells recognize minor tissue antigens on the patient's leukemia cells and continue to suppress their growth.

As is the case with standard allogeneic stem cell transplantation, the risk of graft-versus-host disease (GVHD) is an important consideration and a potentially disabling side effect.

Autologous Stem Cell Transplantation. This is a procedure in which bone marrow is removed from a patient after achieving a remission during induction therapy, and then frozen and stored. Once the stem cells are collected from the bone marrow, the patient receives additional high doses of chemotherapy and/or radiation. Before the stem cells are infused back into the patient's body, they undergo a

process called “purging” to try to eliminate any leukemic cells. Even after purging, there is the risk of returning some leukemia cells back to the patient.

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

For more information, visit www.LLS.org/booklets to view the free LLS booklets *Blood and Marrow Stem Cell Transplantation*, *Cord Blood Stem Cell Transplantation* and *Graft-Versus-Host Disease*.

Central Nervous System (CNS) Involvement. AML cells can spread to the cerebrospinal fluid, the fluid around the brain and spinal cord. This is uncommon, occurring in less than 3 percent of AML patients. Because CNS involvement is rare in cases of AML, doctors often do not test for it at the time of diagnosis unless the patient is experiencing neurologic symptoms, such as headache or confusion. If neurologic symptoms are present, the doctor may order an imaging test, such as a computed tomography (CT) scan or a magnetic resonance imaging (MRI) scan to evaluate the symptoms further. The doctor will also obtain a sample of the patient’s cerebrospinal fluid (CSF) by lumbar puncture, and the sample will be examined for leukemia cells.

A lumbar puncture (also called a “spinal tap”) is a procedure that is used to collect CSF from the spinal column. A thin needle is inserted between two bones in the spine and into the fluid. A sample of the fluid is removed and examined under a microscope to look for leukemia cells that may have spread to the brain and spinal cord.

If leukemia cells are found in the spinal fluid, “intrathecal chemotherapy” is administered, a treatment in which chemotherapy drugs are injected directly into the spinal fluid. Intrathecal chemotherapy can be given in combination with other chemotherapy drugs during induction therapy.

Acute Promyelocytic Leukemia (APL) Treatment. APL is due to a translocation (a genetic change in which a piece of one chromosome breaks off and attaches to another chromosome) between chromosomes 15 and 17, abbreviated as t(15;17). APL is a particularly aggressive subtype of AML. While in the past it was nearly always fatal, it is now one of the most curable subtypes of AML in adults.

APL accounts for approximately 10 percent of all AML cases and occurs primarily in middle-aged adults. APL treatment differs from the other AML treatments described in this booklet.

Visit www.LLS.org/booklets to view the free booklet *Acute Promyelocytic Leukemia Facts* for more information.

Treatments for Relapsed and Refractory AML

Most patients who receive treatment for AML achieve an initial remission. However, some patients have residual leukemic cells in their bone marrow, even after intensive treatment. This is referred to as "refractory AML." Between 10 and 40 percent of newly diagnosed AML patients do not achieve a complete remission with intensive induction therapy. Patients who have not achieved complete remission after two cycles of induction chemotherapy are usually diagnosed as having refractory AML. In other patients, leukemia cells reappear in the bone marrow and normal blood cell production decreases again at some point after achieving a remission. This is referred to as "relapsed AML."

Treatment options for patients with refractory or relapsed AML include:

- **A clinical trial** (see page 30)—LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. When appropriate, patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist them throughout the entire clinical trial process. Visit www.LLS.org/CTSC for more information.
- **Enasidenib (Idhifa®)**—This drug is FDA-approved for the treatment of adult patients with relapsed or refractory AML who have an *IDH2* mutation, as detected by an FDA-approved test. Enasidenib is an oral medication taken once a day.
- **Ivosidenib (Tibsovo®)**—This drug is FDA-approved for adult patients with relapsed or refractory AML who have an *IDH1* mutation, as detected by an FDA-approved test. This medication is taken orally once a day.
- **Gilteritinib (Xospata®)**—This drug is taken by mouth once a day. It is FDA-approved for the treatment of adult patients who have relapsed or refractory AML with an *FLT3* mutation, as detected by an FDA-approved test.
- **Palliative Care**—This term refers to specialized medical care focused on providing relief from symptoms and the stresses of a serious illness. The goal is to improve quality of life for both the patient and the family. With a palliative approach, less toxic treatments are administered to keep the disease under control for as long as possible. The emphasis is on improving the patient's quality of life. Palliative care is also referred to as "supportive care."

- **Intensive chemotherapy and targeted therapy**—These treatments are used for patients younger than 60 (and patients older than 60 who are physically fit) to induce a remission in order to prepare patients for an allogeneic stem cell transplant.
- **Re-treatment with the same induction regimen that produced the patient's first remission**—This is an option if relapse occurs 12 months or more after remission.

Research is ongoing to determine optimal drug combinations, doses and administration schedules. The following combinations are commonly used aggressive and less aggressive treatment regimens for refractory and relapsed AML.

Aggressive treatments for fit patients:

- Cladribine, cytarabine and granulocyte colony-stimulating factor (G-CSF), with or without mitoxantrone or idarubicin
- High-dose cytarabine, with or without an anthracycline
- Fludarabine, cytarabine and G-CSF, with or without idarubicin
- Etoposide and cytarabine, with or without mitoxantrone
- Clofarabine with or without cytarabine and G-CSF, with or without idarubicin

Less aggressive treatments:

- Low-dose cytarabine
- Hypomethylating agents (5-azacitidine or decitabine)

AML Treatment in Older Adults

AML occurs more frequently in older adults: at least half of patients are older than 65 years of age when the disease is diagnosed. The treatment of AML in older patients is a challenge; however, options include clinical trials, intensive or lower intensity chemotherapies and, in certain circumstances, supportive care only. Older patients are more likely to have other medical problems (comorbidities), including diabetes, high blood pressure, high cholesterol levels, heart disease and a history of stroke or lung disease. These comorbidities can limit treatment options.

Older patients may also need to take multiple medications to control their various medical conditions, and these medications may interact with their cancer treatments. Additionally, older adults may have poor performance status (meaning they may be unable to perform ordinary tasks and daily activities). Many older patients are not offered standard treatment options because they are considered unlikely to survive the rigors of intensive chemotherapy due

to their comorbidities and poor performance status. In some cases, intensive chemotherapy can actually shorten their lives.

It is also more difficult to treat AML successfully in older patients. There is a higher occurrence of unfavorable cytogenetic and molecular abnormalities in the leukemic cells of many older patients that make them more resistant to standard chemotherapy. The disease is also more likely to be resistant to standard therapy if it evolved from a prior blood cancer or was induced by a prior cancer treatment.

However, there are curative options available for some older patients with certain subtypes of AML, such as APL. For AML patients older than 60 years, rather than considering patient age only, other factors such as the patient's performance status, other health issues and AML risk features are all considered. Age alone does not determine treatment options, and physically fit patients in their 70s who have no serious health problems may benefit from intensive treatment.

For patients who are not candidates for a standard, intensive induction therapy with an anthracycline and cytarabine, treatment options include lower-intensity therapy with epigenetic agents, such as the hypomethylating drugs **5-azacitidine (Vidaza®)** and **decitabine (Dacogen®)**, or **low-dose cytarabine**.

Additional options that been approved for AML treatment in older patients are summarized below.

- **Glasdegib (Daurismo™)**, in combination with low-dose cytarabine, is FDA-approved for the treatment of newly-diagnosed AML in adult patients age 75 years and older or who have comorbidities that preclude use of intensive induction chemotherapy. Limitation of use: glasdegib has not been studied in patients with the comorbidities of severe renal impairment or moderate-to-severe hepatic impairment.
- **Venetoclax (Venclexta®)**, in combination with azacitidine, decitabine or low-dose cytarabine, is FDA-approved for the treatment of newly-diagnosed AML in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy. This indication is approved under the "accelerated FDA approval" designation based on treatment response rates. Continued approval for this indication may be contingent upon verification and description of its clinical benefit in confirmatory trials.
- **Ivosidenib (Tibsovo®)** is FDA approved for adult patients with newly diagnosed AML with an *IDH1* mutation, as detected by an FDA-approved test, who are age 75 years or older or have comorbidities that preclude use of intensive induction chemotherapy.
- The FDA granted breakthrough therapy designation for the oral HDAC inhibitor **pracinostat**, in combination with azacitidine, for patients with newly diagnosed AML who are older than 75 and are not candidates for intensive chemotherapy.

Diverse clinical trials are evaluating novel drugs and drug combinations, including non-chemotherapy agents that target genetic markers of the leukemia cells. Visit www.LLS.org/CTSC to find out more about clinical trials.

AML Treatment in Children and Adolescents

AML only accounts for approximately 20 percent of childhood leukemia cases. Most children who are diagnosed with leukemia have acute lymphoblastic leukemia (ALL), also called acute lymphocytic leukemia. The overall survival rate has increased for children with AML, but is still much lower than that of childhood ALL. From 2008 to 2014, the 5-year relative survival rate for children and adolescents younger than 15 years was 68.8 percent. However, there is a wide range in outcomes for different subtypes of AML, based on genetic factors.

As with adults, treatment decisions for children with AML should be based on cytogenetic and molecular factors to avoid overtreatment in patients with favorable prognoses and improve outcomes in those with unfavorable prognoses. The goal of treatment should be to cure the child by killing the leukemia cells while avoiding side effects and late effects of treatment as much as possible. Late effects are medical problems that do not manifest in the early stages of the disease, or do not become apparent until years after treatment ends.

Like AML treatment for adults, the treatment for children usually has two phases, induction therapy and consolidation therapy, which may consist of intensive chemotherapy and/or allogeneic stem cell transplantation. Children are usually treated with an induction therapy similar to that used for adults: **cytarabine** and an anthracycline, such as **daunorubicin**; or **idarubicin** or **mitoxantrone** in combination with other agents, such as **etoposide** or **thioguanine**. Maintenance therapy is not part of most pediatric AML treatment protocols, except in cases of acute promyelocytic leukemia (APL).

An option in cases of relapsed and refractory AML is **gemtuzumab ozogamicin (GO) (Mylotarg™)**, which is FDA-approved for use in patients age 2 years and older with relapsed or refractory, CD33-positive AML. Gemtuzumab ozogamicin is injected slowly into a vein (IV infusion) and is given in cycles consisting of treatment days followed by periods of rest.

Unlike adults with AML, children usually receive central nervous system (CNS) prophylaxis to prevent the spread of leukemia cells to the central nervous system. This is called intrathecal chemotherapy, a treatment in which anticancer drugs are injected directly into the spinal fluid. It is given to kill any AML cells that may be in the brain and spinal cord, even though no cancer cells have been detected in that area. The use of some form of intrathecal chemotherapy is now incorporated into most protocols for the treatment of childhood AML. Intrathecal chemotherapy can be given in combination with other chemotherapy drugs during induction therapy.

The following two subtypes of childhood AML are treated differently:

- AML in children with Down syndrome—Children with Down syndrome are at increased risk for developing AML, but in these children, the disease is more sensitive to chemotherapy. As a result, very good cure rates have been achieved with less intensive chemotherapy. Children with Down syndrome who develop AML tend to have a good prognosis, especially if the disease is diagnosed before the age of 4 years.
- Acute promyelocytic leukemia (APL)—This subtype accounts for approximately 7 percent of pediatric AML cases. APL is due to a translocation (a genetic change in which a piece of one chromosome breaks off and attaches to another chromosome) between chromosomes 15 and 17, abbreviated as t(15;17). Children with APL have a high cure rate.

Visit www.LLS.org/booklets to view the free LLS booklet *Acute Promyelocytic Leukemia Facts*.

Cancer treatments may cause health problems in children years after treatment is completed. They may damage organs, tissues or bones and may cause delayed growth and other health problems later in life. The potential late effects depend on the type and dose of therapy and the age at which it is received, as well as many other factors. Childhood and adolescent cancer survivors require close follow-up care because cancer treatment side effects may develop months or even years after treatment.

Children who receive intensive chemotherapy with anthracyclines, such as doxorubicin, daunorubicin and idarubicin, are at increased risk of developing heart problems and should receive ongoing monitoring of cardiac function. Anthracyclines may cause heart problems, including abnormal heart beat, weakness of the heart muscle and congestive heart failure.

The chemotherapy drugs cytarabine and high-dose methotrexate can cross the blood-brain barrier (the protective lining around the brain) and increase the risk of health problems that affect the brain and spinal cord after treatment. Learning difficulties ranging from mild to severe may become evident soon after treatment or years later. Common learning difficulties include issues with memory, processing speed and multitasking.

Survivors of childhood AML are also at an increased risk for developing a second cancer later in life. A second cancer may occur months or years after treatment is completed. It is important for patients who have been treated for cancer to be screened for a second cancer.

Children and adolescents with cancer should be referred to medical centers that have doctors who specialize in treating pediatric cancer. This will ensure they receive treatment, supportive care and rehabilitation that will help them achieve

optimal survival rates and quality of life. Most children with leukemia take part in clinical trials. These clinical trials give children the opportunity to obtain the very latest treatments being studied, options that may not be offered at all treatment centers.

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. Also see the free LLS booklet *Long-Term and Late Effects of Treatment for Childhood Leukemia or Lymphoma Facts*.

Research and Clinical Trials

New approaches to AML treatment are being studied in clinical trials that hold the promise of increasing the rate of remission and eventually finding a cure for the disease. Many of these clinical trials are being supported by LLS research programs.

Clinical Trials. Every new drug or treatment regimen goes through a series of studies called "clinical trials" before it becomes part of standard therapy. Clinical trials are carefully designed and reviewed by expert clinicians, researchers and patient advocates to ensure safety and scientific accuracy. Participation in a carefully conducted clinical trial may be the best available treatment option and should be considered each time treatment is discussed with the doctor. Patient participation in past clinical trials has resulted in the therapies we have today.

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

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

Genetics of Leukemia. The many chromosomal and genetic abnormalities in AML make treating this particular disease challenging. There is a need to identify these genetic variations and customize treatment options based on the genetic characteristics of the leukemia cells. Newer techniques in gene sequencing have revealed previously unknown mutations that may be involved in the development of AML. This information will help researchers develop new targeted therapies, tailored to specific disease characteristics in each patient. There are several ongoing multi-center studies around the world in which

patients are asked to donate samples of blood and bone marrow so these can be analyzed and stored for future study.

New Drugs and Treatment Regimens. Researchers are trying to find more effective and safer treatments for AML. They are studying new drugs, as well as existing drugs given in different doses and with different methods of delivery (such as liposomal encapsulation). In the last 10 years, improvements in overall survival of AML patients has been driven by advances in the understanding of the genetics of the disease, as well as finding new ways to use existing medications. Researchers are continuing to modify and reformulate traditional chemotherapy drugs to improve overall survival. They are also evaluating combinations of chemotherapy drugs with newer targeted therapies. Treatment approaches under investigation include:

- **Targeted therapy.** This is a type of treatment that uses drugs or other substances to block the action of certain enzymes, proteins or other molecules involved in the growth and survival of cancer cells, while causing less harm to healthy cells.
  - **FLT3 inhibitors.** Approximately one-third of AML patients have a mutation in the *FLT3* gene that can increase the growth and division of AML cells. Patients with *FLT3* mutations have a poor prognosis. Sorafenib (Nexavar®), gilteritinib (Xospata®), midostaurin (Rydapt®), quizartinib (AC-220) and crenolanib are FLT3 inhibitors that target this gene mutation.
  - **IDH1 and IDH2 inhibitors.** Mutations in the *IDH1* and *IDH2* genes cause cells to remain immature and grow too quickly. Several IDH inhibitors are being studied in patients with such genetic markers in their leukemia cells, including enasidenib (Idhifa®), which is already FDA approved.
  - **BCL-2 inhibitor.** Overexpression of the BCL2 protein allows cancer cells to evade "programmed cell death." One promising drug under research is venetoclax (Venclexta®), a BCL-2 inhibitor that binds to the leukemia cell and triggers apoptosis, a process that causes the cell to die.
  - **HDAC inhibitors.** Histone deacetylase (HDAC) inhibitors are substances that cause a chemical change that stops cancer cells from dividing. Pracinostat (SB 939) and panobinostat (Farydak®) are examples of HDAC inhibitors under study in clinical trials.
  - **PLK inhibitors.** Volasertib is a potent Polo-like kinase (PLK) inhibitor that is being studied. Volasertib is designed to inhibit the activity of PLK1, an enzyme that regulates cell division. This inhibition ultimately results in cell death.
- **Immunotherapy.** This is a type of biological therapy designed to either boost or suppress the immune system, as needed, to help the body fight cancer. It uses substances made naturally by the body or synthetically in a laboratory to improve, target or restore immune system function.

- **Monoclonal antibody therapy.** This is a type of targeted therapy being studied to treat AML. Antibodies are part of the immune system. Normally, the body creates antibodies in response to antigens, such as bacteria, viruses and even cancer cells. The antibodies attach to the antigens in order to help destroy them. Researchers are analyzing specific antigens, including CD33, a marker that is found on most AML cells.
  - Gemtuzumab ozogamicin (Mylotarg®) is a monoclonal antibody that has the toxin calicheamicin attached to it. When gemtuzumab ozogamicin binds to the CD33 antigen, it releases the toxin, resulting in the death of the myeloid cell. Gemtuzumab ozogamicin is FDA-approved for CD33+ AML patients.
  - Researchers are also studying vadastuximab (SGN-CD33A), another anti-CD33 monoclonal antibody designed to deliver the cytotoxic agent pyrrolobenzodiazepine (PBD) to myeloid leukemia cells. Another approach under study uses the bispecific T-cell engager (BiTE) antibody AMG 330 to harness T cells to target cells with the CD33 antigen.
- **Vaccine therapy.** Researchers are developing vaccines that can be personalized to individual patients to stimulate a strong immune response against their cancer. For instance, a recent study evaluated the efficacy of giving a peptide vaccine together with GM-CSF therapy to stimulate the immune system in different ways in order to build an effective response against AML, myelodysplastic syndromes (MDS) and other types of cancer.
- **CAR T-cell therapy.** This is a promising new way to harness the immune system to fight leukemia. In this approach, immune cells called "T cells" are collected from the patient's blood. The T cells are altered in the lab so they have specific substances, called "chimeric antigen receptors" (CARs), that will help them attach to leukemia cells. The T cells are then multiplied in the lab and later infused back into the patient's blood, where they can now seek out the leukemia cells and attack them.

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

Related Diseases

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN). This is a highly aggressive type of blood cancer. Most patients with BPDCN have skin lesions with or without bone marrow and/or multiple organ involvement. It is more common in the elderly; the median age is around 70 years.

BPDCN can be diagnosed by flow cytometry or immunohistochemistry of appropriate tissue by identifying surface markers (CD123, CD4, CD56) on the malignant cells. Skin is the most frequently involved site of this disease

(80 percent of cases). However, BPDCN usually progresses with bone marrow involvement and a decrease in red blood cell, white blood cell and platelet counts. Other organs may be involved, including the lymph nodes, spleen and liver. Most patients have a poor prognosis and aggressive disease course.

In the past, treatment has included therapies that are used for AML, acute lymphoblastic leukemia (ALL) or lymphoma. The drug **tagraxofusp-erzs (Elzonris™)** is a targeted therapy directed at CD123 that is FDA-approved for BPDCN in adults and in pediatric patients ages 2 and older. Patients in first remission may undergo allogeneic stem cell transplantation, if appropriate. Clinical trials in centers that have experience in treating BPDCN are the best option for patients. Recent clinical trials with agents targeting some of the BPDCN cell surface markers have shown great promise.

Visit www.LLS.org/booklets to view the free LLS booklet *Facts About Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN).*

Mixed Phenotype Acute Leukemia (MPAL). This subtype of acute leukemia of ambiguous lineage is also known as mixed lineage leukemia. It represents a group of rare acute leukemias that have characteristics of both lymphoid and myeloid precursor cells, so the leukemic cells of this disease rememble those of both acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). MPAL encompasses leukemias that contain both ALL blasts and AML blasts at the same time, or leukemia cells that have features of both ALL and AML on the same cell.

MPAL accounts for 2 to 5 percent of all acute leukemias affecting patients of all ages and it has several different subtypes. The best approach to treatment has not been defined. Currently, there is no standard therapy for MPAL and, in general, the disease is associated with a poor prognosis. This is due to difficulty in correctly identifying this type of leukemia, as well as its rare incidence, the lack of experience in treating it and its resistance to therapies for both ALL and AML. The reasons underlying this resistance are not yet clear, but may be related to the high proportion of patients with cytogenetic abnormalities. Developing the best treatment approach involves considering a variety of factors, including the patient's age and medical history, the presence of other relevant medical conditions and the characteristics of the leukemic cells, as determined by immunophenotyping and cytogenetic and molecular studies.

It is also important to determine if the patient has the Philadelphia chromosome positive (Ph+) subtype of MPAL. This subtype accounts for about 25 percent of all cases of MPAL. Patients with Ph+ MPAL are treated with an ALL chemotherapy regimen (determined based on the patient's age) in combination with a tyrosine kinase inhibitor (TKI), followed by autologous stem cell transplantation, if possible. For patients with a subtype that is Ph chromosome negative (Ph- MPAL), the treatment consists of an ALL regimen or a combination of ALL and

AML therapies, followed by consolidation with an allogeneic stem cell transplant, when a donor is available.

Side Effects and Complications

Most side effects in patients with AML are temporary and subside once the body adjusts to therapy, or when therapy is completed. Chemotherapy drugs attack rapidly dividing cells throughout the body, including both cancer cells and normal, healthy cells. Cells in the bone marrow, hair follicles and lining of the mouth and intestines divide quickly and may be affected by chemotherapy. The side effects of chemotherapy may vary, depending on the drugs used.

Low Blood Cell Counts. AML decreases the production of normal blood cells. In addition, chemotherapy is toxic to the healthy cells in the bone marrow.

For the patient, this may result in a severe deficiency of:

- Red blood cells, resulting in a condition called anemia
- Platelets, resulting in a condition called thrombocytopenia
- White blood cells
  - Neutrophil deficiency results in a condition called neutropenia.
  - Monocyte deficiency results in a condition called monocytopenia.

Patients may need red blood cell and platelet transfusions for a period of several weeks during treatment. After that, blood cell counts usually return to normal.

Infection. During treatment for AML, the deficiency of neutrophils and monocytes can lead to infection from bacteria and fungi that are normally present in the environment, on the skin and in the nose, mouth or colon. The risk of infection may increase because chemotherapy damages the lining of the mouth and intestines, making it easier for bacteria to enter the blood. When the white blood cell count is low and there is an increased risk of infection, antibiotics are given to prevent or treat infection.

White blood cell transfusions are not generally used for AML patients, so doctors sometimes use growth factors to help increase a patient's white blood cell count. Growth factors stimulate the bone marrow to make new white blood cells. Granulocyte colony-stimulating factors (G-CSF), such as filgrastim (Neupogen®) and pegfilgrastim (Neulasta®), stimulate the production and release of neutrophils into the bloodstream. Granulocyte-macrophage colony-stimulating factors (GM-CSF), such as sargramostim (Leukine®), stimulate the production of three types of white blood cells: neutrophils, macrophages and dendritic cells.

However, growth factors are used only in special circumstances, and routine use of these agents is not recommended. Growth factors are also not

recommended during induction therapy for patients with acute promyelocytic leukemia (APL) because they can increase the risk of differentiation syndrome. This is a condition with symptoms that include unexplained fever, weight gain, labored breathing, pleuropericardial effusion (fluid around the lungs and heart), hypotension (low blood pressure) and renal (kidney) failure. See *below* for more information.

Because the patient has an increased risk of developing an infection, the medical staff, family and friends of the patient need to wash their hands frequently and vigorously and take other precautions to avoid exposing the patient to bacteria, viruses and other infection-causing agents. Caregivers of patients with central lines or ports need to be meticulous in the cleaning of catheters.

Patients at home should seek medical attention right away if any signs of infection develop. A rise in temperature to 100.4°F or higher or the onset of chills may be the only sign of infection in a patient with a very low white blood cell count. Other signs of infection may include persistent coughing, tenderness at a site prone to infection (such as the area surrounding the anus or the facial sinuses), sore throat, pain on urination, or frequent loose stools.

Tumor Lysis Syndrome. Tumor lysis syndrome is another potential side effect of chemotherapy. It can occur in patients who have large numbers of leukemic cells in their body during the induction phase of chemotherapy. As the leukemia cells die, they break apart and release their contents into the blood. This causes a change in certain blood chemicals that may damage the kidneys and other organs. Tumor lysis can be prevented by giving the patient extra fluids to increase urination to flush the body of these substances. A medication called **allopurinol (Zyloprim®)** may be given to decrease levels of uric acid during treatment. The medication **rasburicase (Elitek®)** should be considered as initial treatment in patients with rapidly increasing blast counts, high uric acid levels or evidence of impaired kidney function.

Differentiation Syndrome. This is a potentially life-threatening complication of treatment with differentiating agents, such as **all-trans retinoic acid (ATRA)**, **enasidenib (Idhifa®)** and **ivosidenib (Tibsovo®)**. Symptoms include fever, swelling in the limbs and trouble breathing. Patients may also experience a drop in blood pressure and have fluid buildup around the lungs or heart. Treatment must begin at the first signs or symptoms. Treatment consists of steroid therapy or the administration of the antimetabolite drug hydroxyurea.

Other Side Effects. Chemotherapy affects tissues that normally have a high rate of cell turnover. The skin, hair follicles and the lining of the mouth and intestines may therefore be affected. Common side effects may include:

- Mouth ulcers
- Diarrhea

- Temporary hair loss
- Rashes
- Nausea and vomiting
- Fatigue

Patients should inform their doctors about any side effects they experience. The doctors may be able to prescribe medication to prevent or relieve side effects, suggest ways to prevent or minimize side effects, or change dosage or treatment schedules to prevent side effects from getting worse.

Chemotherapy may also affect fertility (the ability to have a child in the future). Patients concerned about this potential side effect should talk with a fertility specialist before beginning treatment.

There are drugs and other supportive therapies to prevent or manage many side effects.

Visit www.LLS.org/booklets to view the free LLS booklets *Blood Transfusion, Cancer-Related Fatigue Facts*, *Managing Low Blood Cell Counts* and *Reducing Your Risk of Infection*.

Sometimes, a drug or a drug combination causes effects that continue for a period of time after treatment ends. Some effects may be long-lasting (see *Long-Term and Late Effects of Treatment* in the section *below*).

Follow-Up Care

Some of the tests done to diagnose AML may be repeated to:

- Monitor the effects of treatment
- Make decisions about whether to continue, intensify, change or stop treatment

After treatment, patients who are in remission and have completed post-remission therapy continue to be examined regularly by their doctors. Careful periodic assessment of the patient's health, blood cell counts and, if indicated, bone marrow, are required. The length of time between these assessments may increase over time, but they should continue indefinitely.

Long-Term and Late Effects of Treatment. Children and young adults who have been treated for AML may be at increased risk for heart damage, other cancers and neurologic or cognitive problems. Patients should be seen by a primary care doctor for general health examinations at least once a year. They should also be examined regularly by an oncologist.

It is important to know about the potential for long-term effects of treatment so that any problems can be identified early and managed. Treatment for AML sometimes causes effects that continue after treatment ends (long-term effects) or that develop much later in life (late effects). Various factors can influence the patient's risk of developing long-term or late effects, including their:

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

Most AML patients are treated with an anthracycline, such as daunorubicin. Anthracyclines have been associated with increased risk for heart muscle injury or chronic heart failure. However, heart disease may not become apparent until many years after therapy ends.

Stem cell transplantation has been associated with long-term and late effects, including infertility, thyroid dysfunction, chronic fatigue and risk for developing a secondary cancer (although the number of patients who develop a secondary cancer is small).

These and other possible long-term and late effects can be managed. **Visit www.LLS.org/booklets to view the free LLS booklets *Long-Term and Late Effects of Treatment in Childhood Leukemia* or *Lymphoma Facts and Long-Term and Late Effects of Treatment in Adults Facts*.**

For more information about follow-up care, contact an LLS Information Specialist at (800) 955-4572.

Treatment Outcomes

AML is a difficult disease to cure. A few decades ago almost no adults with AML were cured. However, today, advances in understanding of the genetic features of the disease and utilization of targeted therapies have resulted in improved remission and cure rates for AML patients. **Table 5**, on *page 38*, describes some of the medical terms related to AML treatment outcomes.

Table 5. Terms Related to AML Treatment Outcomes

Treatment Outcomes	
Active disease	○ Refractory AML, meaning the disease does not respond to treatment. ○ Relapsed AML, meaning the disease responds to treatment but then returns. A patient with AML that has relapsed usually has more than 5 percent blast cells present in the bone marrow.
Remission	○ No evidence of disease after treatment is completed ○ Less than 5 percent blast cells in the bone marrow ○ Blood cell counts within normal limits ○ No signs or symptoms of the disease
Minimal residual disease (MRD)	○ No AML cells can be detected in bone marrow with sensitive tests, such as flow cytometry, or very sensitive tests, such as polymerase chain reaction (PCR).
Complete molecular remission	○ No evidence of AML cells in the bone marrow with very sensitive tests, such as PCR.

Minimal Residual Disease. Sensitive molecular techniques permit the identification of small amounts of cancerous cells, referred to as minimal residual disease (MRD), that cannot be detected by standard tests of blood and bone marrow samples. This can permit more sensitive follow-up of patients who are in remission and can help determine whether additional treatment is necessary. Measurement of MRD after induction and consolidation chemotherapy using PCR or flow cytometry has greater capacity to predict long-term survival than any other patient or disease characteristic that is evaluated at diagnosis, including cytogenetics or mutational analyses.

MRD measurements can be useful for classifying patients who enter clinical trials. These measurements are helpful for interpreting and comparing trial results, and for providing patients with valuable prognostic information.

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

Incidence, Causes and Risk Factors

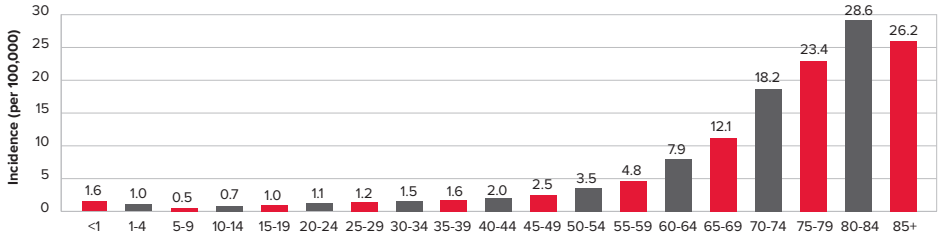
AML is the most common type of acute leukemia affecting adults. Older people are more likely than younger adults or children to develop AML.

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

While the cause of AML is unknown, several factors are associated with an increased risk of developing AML, including:

- Age. The risk of developing AML increases with age. While AML can occur at any age, it typically affects older adults. The risk for developing AML increases about 8-fold from ages 30 to 34 years (about 1.5 cases per 100,000 people) to ages 65 to 69 years (about 12.1 cases per 100,000 people). For people over 70, the incidence rate continues to increase, peaking between the ages of 80 and 84 (see **Figure 3** on *page 40*).
- Gender. Men are more likely than women to develop AML.
- Exposure to dangerous chemicals. Long-term exposure to high levels of certain chemicals, such as benzene, are linked to a greater risk of AML. Benzene is found in certain industrial settings; however, the strict regulation of its use has decreased benzene exposure in the workplace.
- Smoking. AML is linked to exposure to tobacco smoke, which contains benzene and other cancer-causing substances. According to the Agency for Toxic Substances and Disease Registry, despite the fact that petroleum products contribute to most of the benzene in the atmosphere, half of the total national exposure to benzene in humans comes from cigarette smoke.
- Previous cancer treatment. Prior cancer treatment with chemotherapy—especially with alkylating agents (such as cyclophosphamide and busulfan), topoisomerase II inhibitors (such as etoposide and doxorubicin) or platinum drugs—or with radiation therapy may increase a person's risk of developing AML. This is often called "treatment-related" or "therapy-related" AML.
- Exposure to very high doses of radiation. People exposed to very high levels of radiation are at increased risk of developing AML (for example, survivors of an atomic bomb blast or a nuclear reactor accident).

Figure 3. Acute Myeloid Leukemia (AML): Age-Specific Incidence Rates 2011-2015.



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

- Other blood cancers. People who have certain blood disorders, including myeloproliferative neoplasms (such as polycythemia vera, essential thrombocythemia and myelofibrosis), are at greater risk of developing AML. In some people who have myelodysplastic syndrome (MDS), the disease can evolve over time into AML.
- 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/germline predisposition. Certain gene mutations present at birth may increase the risk of developing AML.

Feedback. Visit www.LLS.org/PublicationFeedback to give suggestions about this booklet.

Normal Blood and Bone Marrow

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

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

- Proteins
  - Albumin, the most common blood protein
  - Blood-clotting proteins (coagulation factors) made by the liver
  - Erythropoietin, a protein made by the kidneys that stimulates red blood cell production
  - Immunoglobulins, proteins that help the body fight infection
- Hormones, such as thyroid hormone and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin B_{12}
- Electrolytes, such as calcium, potassium and sodium

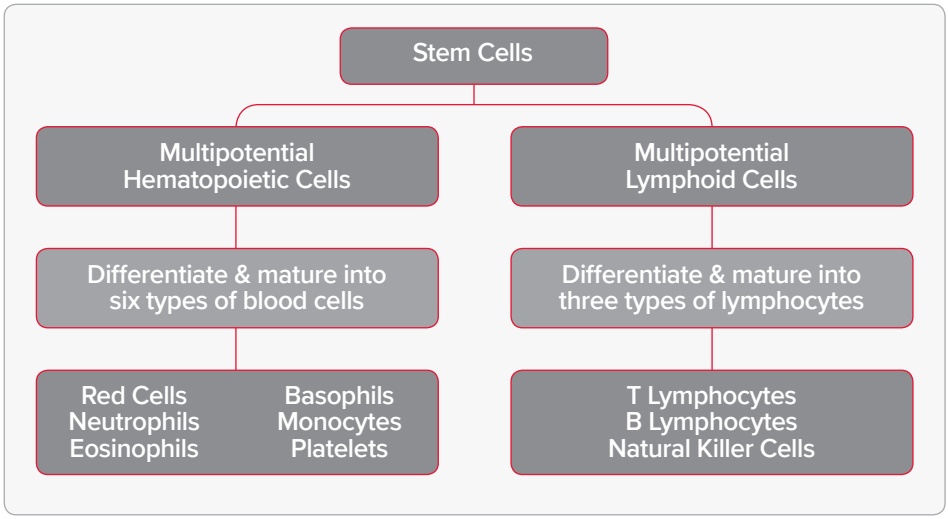
Blood cells. Blood cells are formed in the bone marrow, a spongy tissue where blood cells grow and develop. Blood cells start as stem cells. The process of stem cells maturing into blood cells is called "hematopoiesis." The blood cells are suspended in the plasma. See **Figure 4** on *page 42*.

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

1. Red blood cells (the cells that carry oxygen)
   - These make up a little less than half of the body's total blood volume.
   - They are filled with hemoglobin, the protein that picks up oxygen from the lungs and takes it around the body. It binds with carbon dioxide (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 (cells that help blood clot)
   - These are small cells (one-tenth the size of red blood cells).
   - They help stop bleeding from an injury or cut.
   - They stick to the torn surface of the vessel, clump together and plug up the bleeding site. They form a clot with the help of proteins, such as fibrin, and electrolytes, such as calcium.

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

Figure 4. Blood Cell & Lymphocyte Development



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

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

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

Hematopoietic stem cells are found in the marrow. These stem cells are important because they can be used for transplants. Some stem cells enter the bloodstream and circulate. Doctors know how to stimulate the growth of these cells in the marrow and make them migrate into the bloodstream. Then a special technique called "apheresis" is used to separate them from the circulating blood so they can be collected and stored. Stem cells from the placenta and the umbilical cord of a newborn infant can also be harvested and used for future transplantation.

Resources and Information

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

For Help and Information

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

- Call: (800) 955-4572 (Monday through Friday, from 9 am to 9 pm ET)
- Email: InfoCenter@LLS.org
- Live online chat: www.LLS.org/InformationSpecialists
- Visit: www.LLS.org/InformationSpecialists

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

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

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

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

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

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

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

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

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

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

Community Resources and Networking

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

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

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

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

Other Helpful Organizations. LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. For more information, please visit www.LLS.org/ResourceDirectory to obtain our directory.

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

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

Additional Help for Specific Populations

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

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

Children. AML occurs in a small number of children. A family that has a child diagnosed with AML is thrown into an unfamiliar world of treatment and follow-up care. The child, parents and siblings will all need support. Help is available. Do not hesitate to ask for assistance for your child, yourself or other family members, even if you are already working with a psychologist, social worker or child life specialist.

For practical guidance on how to support your child and other family members, deal with your own concerns, share the news with extended family and friends and make the transition to life after treatment, please call or visit our website.

- Call: (800) 955-4572 to ask about *The Trish Greene Back to School Program for Children with Cancer*
- Visit: www.LLS.org/booklets to see the free LLS booklet *Coping with Childhood Leukemia and Lymphoma*

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

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)

- Survivors who were either in the NYC disaster area, or who lived, worked or were in school in the area
- Responders to the Pentagon and the Shanksville, PA crashes

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

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

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

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

Health Terms

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

Allogeneic Stem Cell Transplantation. A treatment that uses stem cells from a healthy donor to replace a patient's damaged or diseased bone marrow after the patient has been treated with high doses of chemotherapy and radiation. See the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.

Anemia. A health condition in which the number of red blood cells is below normal. This results in a diminished ability of the blood to carry oxygen. Severe anemia can cause a pale complexion, weakness, fatigue and shortness of breath.

Anthracycline (Antitumor Antibiotic). A type of antibiotic that is used to treat many types of cancer. Anthracyclines damage 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 agents that cause illness. Antibodies can also be made in the lab and are used to help detect certain types of cancer and to help treat cancer.

Antigen. A foreign substance that creates an immune response, especially the production of antibodies. Antigens include allergens, chemicals, bacteria, viruses and other substances from outside the body.

Autologous Stem Cell Transplantation. A treatment in which bone marrow cells are collected from a patient, stored and then returned to the patient's body after an intensive "conditioning therapy". See the free LLS booklet *Blood and Marrow Stem Cell Transplantation.*

Basophil. A type of white blood cell that fights against 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 study 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: red blood cells that carry oxygen; white blood cells that fight infections; and platelets that help stop bleeding.

Bone Marrow. A spongy tissue in the hollow central cavity of bones, where blood cell formation occurs.

Bone Marrow Aspiration. A procedure done to obtain a bone marrow sample so the cells can be examined for abnormalities at a lab. After the patient is given a numbing agent, a liquid bone marrow sample is taken with a specialized needle, usually from the hip (pelvic) bone. Most often, this procedure is done at the same time as a bone marrow biopsy.

Bone Marrow Biopsy. A procedure done to obtain a bone marrow sample so the cells can be examined for abnormalities at a lab. It differs from a bone marrow aspiration in that a small amount of bone filled with marrow is removed, usually from the hip (pelvic) bone. After medication is given to numb the skin, a specialized, hollow needle is used to remove a piece of bone containing marrow. Bone marrow aspiration and bone marrow biopsy may be done in the doctor's office or in a hospital. The two procedures are almost always done together.

CBC. See Complete Blood Cell Count.

Central Line (Indwelling Catheter). A flexible tube used to deliver medications, fluids or blood products into the body, or to withdraw blood samples from the body. See Port.

Central Nervous System (CNS) Prophylaxis. Treatment in which chemotherapy drugs are injected in the fluid that surrounds the spinal cord and brain. In certain types of leukemia, particularly acute lymphocytic (lymphoblastic) leukemia and acute monocytic leukemia that often cause very high blood cell counts, the leukemic cells have a tendency to enter the covering of the spinal cord and brain. See Intrathecal.

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

Chloroma. See Myeloid Sarcoma.

Chromosome. Threadlike structures within cells that carry genes in a linear order. Human cells have 23 pairs of chromosomes.

Clinical Trial. Carefully planned and monitored research study that tests 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. A treatment that is proven 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, if it is either more effective or has fewer side effects than the current standard treatment.

Cluster of Designation (CD). A term used along with a number to identify a specific molecule on the surface of an immune cell. It is commonly used in its abbreviated form, for example, “CD20.”

Colony-Stimulating Factor. See Growth Factor.

Complete Blood Count (CBC). A lab 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 total body radiation.

Cord Blood Stem Cells. Stem cells collected from the placenta and umbilical cord after a baby is born. These stem cells have the capability to repopulate the bone marrow and produce healthy blood cells in patients undergoing stem cell transplantation.

CT (Computed Tomography) Scan. A procedure in which a computer is used to process a series of x-ray images to create 3-dimensional (3-D) views of tissues and organs in the body.

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

Cytogenetic Analysis. The process of analyzing the chromosomes in cells. It detects chromosome alterations and, in some cases, may identify the actual genes that have been affected. These findings help healthcare professionals diagnose specific types of blood cancer, determine treatment approaches and monitor a patient’s response to treatment. The individual who prepares and examines the chromosomes and interprets the results is called a “cytogeneticist.”

Cytopenia. A reduction in the number of cells circulating in the blood.

Cytotoxic Drugs. Anticancer drugs that kill cancer cells or prevent them from dividing. See Chemotherapy.

Deletion. A portion of a chromosome that is missing.

Differentiation. The process in which immature cells develop and mature into cells with specific functions. Stem cells mature into red blood cells, platelets or white blood cells. See Hematopoiesis.

DNA. Abbreviation of deoxyribonucleic acid, the genetic matter found in all cells. 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 promotes inflammation during allergic reactions and helps fight some parasitic infections.

Epigenetic Change. Any change that alters gene activity without changing the DNA sequence. Many types of epigenetic changes have been identified. Although epigenetic changes are natural and essential to many of the body's functions, certain epigenetic changes can cause major adverse health effects, including cancer.

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 Myeloblastoma. See Myeloid Sarcoma.

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

FISH. See Fluorescence In Situ Hybridization.

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

antibody-specific features light up and can be counted. This test may be used to examine blood cells, bone marrow cells or cells from other tissues.

FLT3. A gene that makes a protein, called FMS-like tyrosine kinase 3, which regulates blood cell development. *FLT3* gene mutations can make the FLT3 protein overactive, 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 microscope. FISH can be helpful in assessing risk and treatment needs and for monitoring treatment effectiveness.

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.

G-CSF (Granulocyte Colony-Stimulating Factor). See Growth Factor.

GM-CSF (Granulocyte-Macrophage Colony-Stimulating Factor). See Growth Factor.

Graft-Versus-Host Disease (GVHD). A disease that occurs when transplanted stem cells from a donor (the graft) attack the tissues of the recipient (the host). Most often, the patient's skin, liver, stomach and gastrointestinal tract are affected.

Graft-Versus-Tumor Effect (GVT), Graft-Versus-Leukemia (GVL) Effect. Transplanted blood stem cells (the graft cells) perceive the cancer cells (the tumor cells or leukemia cells) in the patient's body as foreign, and attack the cancer cells.

Granulocyte. A type of white blood cell with many particles (granules) in the cell body. Neutrophils, eosinophils and basophils are types of granulocytes.

Granulocytic Sarcoma. See Myeloid Sarcoma.

Growth Factor. A substance used to increase the numbers of neutrophils after chemotherapy. Granulocyte colony-stimulating factor (G-CSF) and granulocyte-macrophage colony-stimulating factor (GM-CSF) are growth factors that can be made in the lab.

Hematocrit. The percentage of whole blood that is made up of red blood cells. The normal hematocrit range is 40 to 54 percent in men and 35 to 47 percent in women. Anemia occurs when the hematocrit level is below this reference range.

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

Hematopathologist. A doctor who has special training in identifying diseases of the blood by examining blood cells, bone marrow, lymph and other tissues under a microscope.

Hematopoiesis. The formation of new blood cells. For the blood cell development process, see *Normal Blood and Bone Marrow* on *page 41*.

Hematopoietic Stem Cell. An immature cell that can develop into any of the types of mature blood cells, including red blood cells, white blood cells and platelets.

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

Human Leukocyte Antigen (HLA). HLA is a critically important factor in donor stem cell transplantation. HLA is a protein on the surface of cells that helps the body to distinguish its own cells from foreign cells. HLAs make up an individual's tissue type, which varies from person to person. HLA factors are inherited from a person's mother and father, and the greatest chance of having the same HLA type is between siblings. On average, one in four siblings share the same HLA type. HLA tests are done before a donor stem cell transplant to determine if there is a tissue match between the donor and the person receiving the transplant.

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 find specific types of cells based on the types of antigens or markers on the surface of the cells.

Indwelling Catheter. See Central Line.

Intrathecal. The term for the fluid-filled space between the thin layers of tissue that cover the brain and the spinal cord. This lining is called the "meninges." In some situations (when leukemia cells are in the meninges

of the spinal cord), drugs are administered directly into the spinal canal. This treatment is called “intrathecal therapy.”

Inversion. An abnormality of chromosomes that occurs when a section of a chromosome breaks off, turns upside down and then reattaches. As a result, the genetic material is inverted.

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 does not appear or is not noticed until a long time after treatment ends. Treatment-related cancer or heart disease may be examples of late effects.

Leukocyte. A white blood cell that is part of the body’s immune system. Leukocytes defend the body against infections and other diseases. Types of leukocytes include granulocytes (neutrophils, eosinophils and basophils), monocytes and lymphocytes (T cells and B cells). 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 a spinal tap.

Lymph Node. A bean-sized structure that is part of the body’s immune system. Throughout the body, there are hundreds of lymph nodes connected by lymph channels (lymphatics). Lymph nodes 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: B lymphocytes, which produce antibodies to help combat infections; T lymphocytes, which have several functions, including assisting B lymphocytes in making antibodies; and 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 and eats dead cells, and also helps lymphocytes with their immune functions.

Magnetic Resonance Imaging (MRI). A test that uses magnetic fields and radio waves to create images of the body’s organs and tissues.

Marrow. See Bone Marrow.

Microliter (µL). A measurement used for some blood test results. One microliter (µL) is an amount equal to one one-millionth of a liter. A liter is almost equal to a quart of blood.

Minimal Residual Disease (MRD). The term used to refer to the small amount of cancer cells that may remain in the body after treatment. These cells can only be identified by very sensitive molecular tests. See the free LLS booklet *Minimal Residual Disease*.

Molecular Remission. A response to treatment in which no leukemia cells can be detected in the bone marrow, even with very sensitive tests such as polymerase chain reaction (PCR).

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

Monoclonal Antibody Therapy. Treatment using proteins made in the laboratory that either react with or attach to targeted antigens on certain cancer cells. The antibodies are used in three ways: as "naked" antibodies (monoclonal antibodies); as antibodies to which radioactive isotopes are attached (radioimmunotherapies); and as antibodies to which toxins are attached (immunotoxins).

Monocyte/Macrophage. A type of white blood cell that is made in the bone marrow; monocytes comprise about 5 to 10 percent of the cells in normal human blood. Some monocytes travel through the blood to tissues in the body, where they become macrophages. Macrophages can combat infection in the tissues, ingest dead cells (in this function they are called "scavenger cells") and assist lymphocytes in their 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.

Myeloid Sarcoma. A mass of myeloid leukemia cells found outside the bone marrow. It may occur beneath the skin or other areas of the body and may be the first sign of leukemia. Other names for a myeloid sarcoma are "chloroma," "granulocytic sarcoma," "myeloblastoma," "monocytoma" and "extramedullary disease."

Neutropenia. An abnormal decrease in the number of neutrophils, a type of white blood cell, in the blood. See Neutrophil.

Neutrophil. A type of white blood cell and the principal phagocyte (microbe-eating cell) in the blood, the neutrophil is the main type of cell that combats infection. People with some blood cancers, or those who have received treatment (such as chemotherapy) for cancer, often have low neutrophil counts. People with low neutrophil counts are very susceptible to infections.

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

Pathologist. A doctor who diagnoses diseases by examining body tissues and fluids.

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

Peripheral Blood Smear. A procedure in which a sample of blood cells is stained (dyed) and examined under a microscope to check for unusual changes in the size, shape and appearance of various blood cells. The test also checks for the presence of blast cells in the blood. Blast cells are normally found in the bone marrow, but they are not typically found in the blood. Finding blast cells in the blood may suggest the presence of leukemia, but the disease is usually not diagnosed without looking at a sample of bone marrow cells.

Petechiae. Pinhead-sized red spots under the skin caused by bleeding. It may occur due to a low platelet count. (Pronounced puh tee' kee uh.)

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 that become macrophages are the two main types of phagocytes. Once an infection occurs, phagocytes migrate from the bloodstream and enter the infected tissue. Chemotherapy and radiation can decrease the numbers of these cells, making patients more susceptible to infection.

Plasma. The liquid portion of the blood, in which the blood cells, platelets, proteins and various other components are suspended. It is also referred to as “blood plasma.”

Platelet. A small colorless type of cell that helps control bleeding. Platelets are found in the blood and spleen. They help form blood clots to stop bleeding. Also known as “thrombocytes.”

Polymerase Chain Reaction (PCR). A technique used to expand trace amounts of DNA or RNA so that the specific type of DNA or RNA and

changes (mutations) can be studied. This technique has become useful in detecting a very low concentration of residual blood cancer cells, too few to be seen using a microscope. PCR can detect the presence of one blood cancer cell among 500,000 to 1,000,000 healthy blood cells.

Port. A small device placed under the skin (usually in the chest) and attached to a central line or a peripherally inserted central catheter (PICC or PIC line). A needle is inserted into the port to draw blood or to administer medications or fluids.

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

Radiation Therapy. The use of high-energy radiation from x-rays and other forms of radiation to kill cancer cells.

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

Red Blood Cell. A type of blood cell that contains hemoglobin, which carries oxygen 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."

Reduced-Intensity Stem Cell Transplantation. A type of allogeneic transplantation, also called "nonmyeloablative stem cell transplantation." Patients receive lower doses of chemotherapy drugs and/or radiation as preparation for the transplant. The chemotherapy and radiation do not completely kill all of the leukemia cells. But as with all donor stem cell transplants, the new immune cells that the patient receives in the transplant may attack the leukemia cells. This protocol may be safer than an allogeneic stem cell transplant, especially for older patients. See the free LLS booklet *Blood and Marrow Stem Cell Transplantation.*

Refractory. The term used to describe a disease that does not respond to treatment.

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

Remission. When signs and symptoms of a disease disappear, usually following treatment. The words "complete" and "partial" are sometimes used to further define the term "remission." Complete remission means that all evidence of the disease is gone. Partial remission means that the disease is markedly improved by treatment, but residual evidence of the disease is present.

Resistance to Treatment. When cancer cells do not respond to 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.

Risk Factor. Something that increases a person's chance of developing a disease. Risk factors can be genetic (inherited), lifestyle related or environmental.

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

Spinal Tap. See Lumbar Puncture.

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

Stem Cell. An immature 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 originate in the bone marrow, but some leave the bone marrow and circulate in the bloodstream. Stem cells can be collected, preserved and used for stem cell therapy. See Hematopoiesis.

Stem Cell Transplantation. See Allogeneic Stem Cell Transplantation; Autologous Stem Cell Transplantation; Reduced-Intensity Stem Cell Transplantation.

Thrombocythemia. A disorder characterized by having too many platelets in the blood.

Thrombocytopenia. A disorder characterized by having too few platelets in the blood.

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

Transfusion. A procedure in which whole blood or components of blood is/are placed into a patient's bloodstream.

Translocation. A chromosomal abnormality in which a piece of one chromosome breaks off and attaches to another chromosome. The

location at which the break occurs may affect nearby genes and lead to medical problems. See Mutation.

Transplantation. See Allogeneic Stem Cell Transplantation; Autologous Stem Cell Transplantation; Reduced-Intensity Stem Cell Transplantation.

White Blood Cell. A blood cell that is part of the body's immune system. The five types of infection-fighting cells in the blood are neutrophils, eosinophils, basophils, monocytes and lymphocytes. White blood cells are also called "leukocytes." See Leukocyte.

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