

Acute Myeloid Leukemia in Adults



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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

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The Leukemia & Lymphoma Society (LLS) appreciates the review of this material by:

Eunice S. Wang, MD

Chief, Leukemia Service
Professor of Oncology
Roswell Park Comprehensive Cancer Center
Buffalo, NY

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Introduction

This book provides information about acute myeloid leukemia (AML) in adults. This type of leukemia is also known as “acute myelogenous leukemia,” “acute myelocytic leukemia,” “acute myeloblastic leukemia” and “acute granulocytic leukemia.”

AML is the most common type of acute leukemia in adults. An estimated 20,240 new AML cases were expected to be diagnosed in the United States in 2021. As of January 2017, an estimated 55,548 people in the United States 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. **For more information about AML in children, see the free LLS book *Acute Myeloid Leukemia in Children and Teens*.**

Over the past several decades, advances in AML testing and treatment options have resulted in improved remission and cure rates, but much work remains to be done. Researchers continue to study and develop new therapies in clinical trials for AML patients.

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 book provides information about AML, explains tests and treatments for the disease, and lists new treatment options being studied in clinical trials. It also includes brief descriptions of normal blood and bone marrow, as well as definitions of health terms related to AML.

We trust that the information in this book will provide you with a good working knowledge about AML or that it reinforces what you already know. We hope you will keep this book handy and that, should you ever feel alone in confronting problems, you will turn to it for information and guidance to find the support and resources you need.

We are here to help.

* Source: Facts 2020-2021. The Leukemia and Lymphoma Society. April 2021.

All LLS publications mentioned in this book are free and can be viewed, downloaded or ordered online at www.LLS.org/booklets.

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Acute Myeloid Leukemia Basics

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

The four major types of leukemia are:

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

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

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

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

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

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

Blood cells begin as blood stem cells in the bone marrow. A blood stem cell may become a myeloid stem cell or a lymphoid stem cell. In healthy bone marrow, these blood-forming stem cells eventually develop into red blood cells, white blood cells and platelets.

In most cases of AML, a mutation or series of mutations in the DNA (genetic material) of a single myeloid stem cell results in the formation of an immature white blood cell called a myeloblast. In AML, the abnormal myeloblast does not develop into a healthy, functioning white blood cell. Instead, it becomes a leukemia cell (also referred to as an “AML cell” or “blast cell”).

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

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

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

In rare instances, a tumor made up of AML cells forms outside the bone marrow. This type of tumor, called a “myeloid sarcoma,” can form in almost any part of the body. Typically, surgery and radiation therapy are not sufficient to treat myeloid sarcomas. They are generally treated with systemic chemotherapy regimens used for AML, even if the bone marrow and blood do not appear to be involved. “Systemic chemotherapy” is a treatment with anticancer drugs that travel through the bloodstream to cells all over the body. Treatment for myeloid sarcomas may also include allogeneic stem cell transplantation. Other names for a myeloid sarcoma are “extramedullary disease,” “chloroma,” “granulocytic sarcoma,” “myeloblastoma” and “monocytoma.”

Signs and Symptoms

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

A person who has signs or symptoms that suggest the possibility of leukemia is referred to a specialist called a hematologist-oncologist. This is a doctor who has special training in diagnosing and treating blood disorders and blood cancers such as leukemia, lymphoma and myeloma. In some large medical centers, there are hematologist-oncologists who specialize in treating acute leukemias such as AML.

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

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

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

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

- Frequent infections
- Fever

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

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

Other general symptoms of AML include:

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

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

Medical Tests

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

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

Talk to your doctor about:

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

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

Medical History. Your doctor will take a thorough medical history. This may include information about past illnesses, injuries, medications and other treatments. Some illnesses run in families, so the doctor may also ask about the health of your blood relatives. Your doctor should find out if you have a family history of blood cancer. While AML cannot be inherited, certain gene mutations present at birth may increase a person's risk of developing AML. Patients with a family history of leukemia and/or other cancers occurring in two or more closely related relatives or generations should be evaluated for an inherited predisposition syndrome to help better manage their treatment.

Physical Examination. The doctor will want to know about your current symptoms and conduct a physical examination. During the exam, the doctor may listen to your lungs and heart and carefully examine your body for signs of infection and disease. To check your internal organs, the doctor may feel different parts of your body. For example, the doctor may feel your abdomen to see if you have an enlarged spleen or liver. Your doctor may also check your lymph nodes to see if any are enlarged.

Complete Blood Count (CBC) with Differential. This test is used to measure the number of red blood cells, white blood cells and platelets in a blood sample. A complete blood count (CBC) also measures the amount of hemoglobin in the red blood cells and the percentage of red blood cells in the sample. The CBC should include a differential, which measures the numbers of the different types of white blood cells in the sample.

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

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

Bone Marrow Aspiration and Biopsy. These two procedures are used to collect and examine bone marrow, the spongy tissue inside most bones. Doctors use these procedures to diagnose and monitor leukemia and other blood disorders. They are generally done at the same time, either at the doctor's office or in a hospital.

The samples are usually taken from the patient's pelvis or "hip bone," after medicine has been given to numb the skin and surface of the bone. Bone marrow has both a solid and a liquid component. For a bone marrow aspiration, a special, hollow needle is inserted through the hip bone and into the bone marrow to remove (aspirate) a liquid sample of cells. For a bone marrow biopsy, a wider needle is used to remove a sample of solid bone that contains bone marrow. Both samples are sent to the lab where they are examined under a microscope. See **Figure 1** on page 8 for more information on blood and bone marrow tests.

Cell Assessment. At the laboratory, a hematopathologist examines the blood and bone marrow samples. This is a type of doctor who has special training in identifying blood diseases by studying cells under a microscope and performing other specialized tests on these blood cells.

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

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

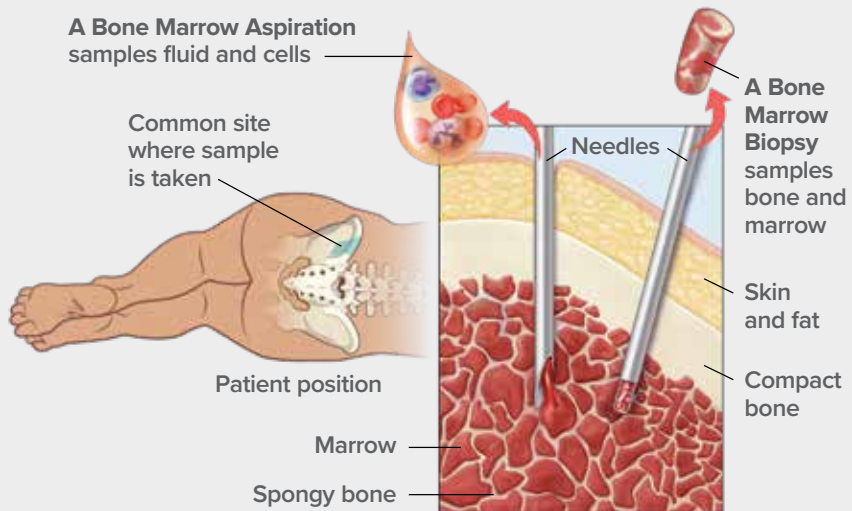
Bone Marrow Aspiration. A sample of fluid with cells is removed from the bone marrow and sent to a lab for testing.

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

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

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

Bone Marrow Aspiration and Biopsy

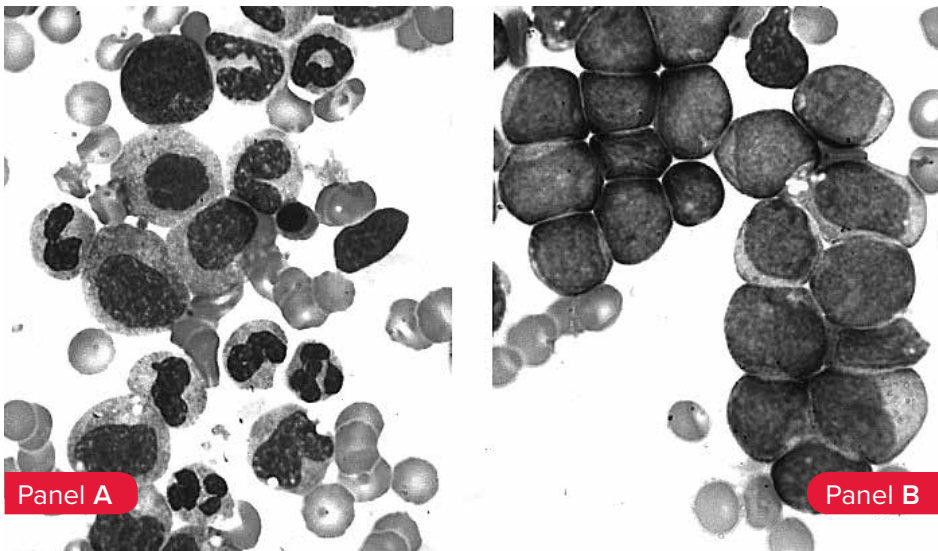


Left: The place on the back of the patient’s pelvic bone where a bone marrow aspiration or biopsy is done. **Right:** Where the needles go inside the bone to collect the liquid sample for aspiration (the needle on the left) and the bone sample for biopsy (the needle on the right). The needles are different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

The hematopathologist examines the blood and bone marrow cells under a microscope to determine their size, shape and type, and to identify other cell features. Whether the cells look like normal, mature blood cells or abnormal, immature blood cells (blast cells) is an important finding (see **Figure 2** below).

The percentage of blast cells identified in the samples is another important finding. Typically, there are no blast cells in the blood, and no more than 5 percent of the cells in the bone marrow are blast cells. A diagnosis of AML generally requires a finding that 20 percent or more of the cells in the bone marrow or blood are blasts.

Figure 2. Normal Cells vs AML Cells



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

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

Immunophenotyping (Flow Cytometry). This test is used to diagnose leukemia and lymphoma by comparing cancer cells to normal cells in either a bone marrow or blood sample. Immunophenotyping is done with an instrument called a “flow cytometer.” A flow cytometry test can measure the number of cells in a sample, as well as specific characteristics of the cells, including their size and shape, and identify specific markers on the cell surface. A sample of cells from blood or bone marrow is tagged with a panel of antibodies that are specific to areas on the cell surface. The cells are stained with a light-sensitive dye and are

passed through a laser beam in the flow cytometer. If they have an antibody-specific surface marker, the cells light up and are counted.

Leukemia cells can have different antigens on their surfaces, depending on the type of leukemia. Certain antigens, called “cluster of differentiation (CD) proteins,” help identify the type of leukemia cells. While the specific pattern of antigens varies among different AML subtypes, most AML blasts express CD13, CD14, CD33 and/or CD34.

In addition to its use for diagnosis, flow cytometry is also used after treatment for evaluating minimal residual disease (MRD), also called measurable residual disease. This refers to the small number of cancer cells that may remain in the body after treatment (for more information on minimal residual disease, see page 27).

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

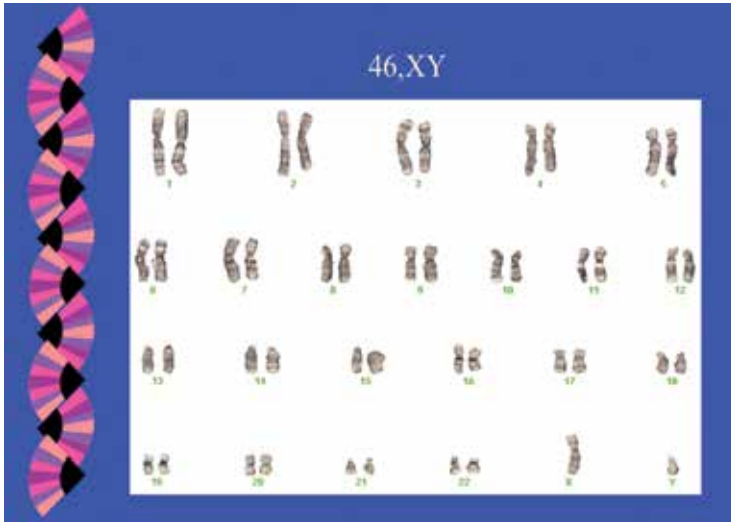
Cytogenetic Analysis (Karyotyping). In this test, a hematopathologist uses a microscope to examine the chromosomes inside of cells. In patients with AML, karyotyping is used to look for abnormal changes in the chromosomes of the leukemia cells.

Normal human cells contain 23 pairs of chromosomes, for a total of 46 chromosomes. Each pair of chromosomes is a certain size, shape and structure. In some cases of AML, the chromosomes of the leukemia cells have abnormal changes that can be seen under a microscope, such as an extra chromosome, a deletion or a translocation. A deletion occurs when part of a chromosome is missing; a translocation occurs when a piece of one chromosome breaks off and attaches to another chromosome; an inversion occurs when a part of a chromosome breaks off, turns upside down and reattaches; and a duplication occurs when part of the chromosome is duplicated, resulting in extra genetic material.

Cytogenetic testing is done using 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 shows if there are any abnormal changes in the size, shape, structure or number of chromosomes in the leukemia cells (see **Figure 3** on page 11).

In some cases, cytogenetic analysis can provide information that is important in determining a patient’s treatment options and prognosis (outcome). For example, a translocation between chromosomes 15 and 17, abbreviated t(15;17), is associated with a diagnosis of acute promyelocytic leukemia (APL). This subtype of AML has a more favorable prognosis and requires a different treatment approach than other AML subtypes.

Figure 3. Normal Karyotype



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

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

Polymerase Chain Reaction (PCR). This is a very sensitive test used to detect and measure certain genetic mutations and chromosomal changes that are too small to be seen with a microscope. Polymerase chain reaction (PCR) essentially amplifies (increases) small amounts of specific pieces of either RNA (ribonucleic acid) or DNA (deoxyribonucleic acid) to make them easier to detect and measure in a cell sample. This test can find a single leukemia cell among more than 500,000 to 1,000,000 normal cells. PCR is one method used to determine the amount of minimal residual disease (MRD) in patients, which refers to the small amount of cancer cells that may remain in the body after treatment (for more information on minimal residual disease, see page 27). A PCR test can be done with either a bone marrow sample or a blood sample.

DNA Sequencing. This refers to a number of different laboratory tests that examine the exact sequence (order) of DNA. By comparing the sequence of DNA in cancer cells with the DNA in normal cells, doctors can find genetic changes that are unique to the cancer cells and may be driving the growth of the patient's cancer.

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

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

Since the introduction of DNA sequencing, the number of mutated genes that can be detected in AML patients has increased considerably. Standard protocols combine cytogenetic analysis with testing for mutations of a number of single genes, including *c-KIT*, *FLT3-ITD*, *FLT3-TKD*, *NPM1*, *CEBPA*, *IDH1*, *IDH2*, *RUNX1*, *ASXL1*, *TP53* and *PML-RAR*. These markers are important in guiding risk assessment and prognosis, and are also used to guide treatment decisions. For example, some patients may be eligible to receive drugs called “inhibitors” that target specific gene mutations expressed by leukemia cells, such as *FLT3*, *IDH1* and *IDH2*. These inhibitors may be taken alone or in combination with other chemotherapy drugs, but they only work against leukemia cells with these specific mutations (for more information, see *Targeted Therapy* on page 21).

Genetic testing should be done when the cancer is first diagnosed and also after a relapse. This is because it is possible for patients to acquire additional genetic abnormalities after the completion of their initial, “first-line” treatment. Similar to when the disease is diagnosed, the presence or absence of these mutations in leukemia cells affects treatment options at the time of relapse as well.

See the free LLS book *Understanding Genetics* for more information about genetics and genetic testing.

Pre-Treatment Tests. Before you start treatment, your doctor will perform tests to learn more about your overall health and your disease. Doctors use this information for treatment planning. Some of these tests are summarized on page 13.

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

Human Leukocyte Antigen (HLA) Typing. This blood test is done to identify certain proteins, called human leukocyte antigens (HLAs), found on the surface of most cells in the body. These proteins make up the body's tissue type, which varies from person to person. They also play an important role in the body's immune response to foreign substances by helping the body distinguish its own cells from foreign cells. An HLA test is done before allogeneic stem cell transplantation to find out if there is a tissue match between a potential donor and the patient receiving the transplant. While HLA typing is not used to diagnose leukemia, it is an important test for newly diagnosed AML patients if allogeneic stem cell transplantation is being considered as a treatment option. See page 23 for more information on stem cell transplantation.

Heart Tests. Some chemotherapy drugs, such as the class of drugs called "anthracyclines," can damage heart tissue. Because of this, 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.** In this test, a computerized image of the heart is created by bouncing sound waves off internal tissues or organs in the chest. An echocardiogram shows the size, shape and position of the heart, as well as its internal structures. It also shows if the heart is beating and pumping blood normally.
- **Multigated Acquisition (MUGA) Scan.** For this test, patients receive a shot containing a radiotracer into a vein, and pictures of the heart are taken with a special camera. The pictures show the radiation being released by the radiotracer, making it possible to see how much blood the heart pumps with each beat.

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?

See the free LLS book *Understanding Lab and Imaging Tests* for more information about these tests. Visit www.LLS.org/3D to view interactive 3D illustrations of some lab and imaging tests.

Diagnosis and Cell Classification

For a person to be diagnosed with AML, generally 20 percent or more of the cells in the bone marrow or blood must be myeloblasts. AML is a diverse group of diseases that is classified into different subtypes based on chromosomal abnormalities, genetic mutations and other disease features. The AML subtype is determined based on the patient's laboratory test results.

AML Subtypes. The subtypes of AML are based on certain features of the leukemia cells. Determining the AML subtype is an important factor in treatment planning. Based on a patient's AML subtype, the doctor will decide which drugs, drug combinations and drug dosages are indicated, and will determine the appropriate duration of treatment.

The World Health Organization (WHO) classification is the main system used to classify AML into subtypes (see **Table 1** on pages 15-16). It includes prognostic (predictive) factors, such as chromosomal abnormalities and genetic mutations, which are known to affect the future outcome of the cancer. These genetic factors help provide patients and their doctors with more reliable information regarding their probable outcome (prognosis), as well as how they are likely to respond to treatment.

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

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

Table 1. AML and Related Neoplasms (cont.)

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

Based on the World Health Organization (WHO) classification.

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

Treatment Planning

Choosing a Hospital and Doctor. When you find out that you have cancer, you want to get the best possible medical care and treatment. AML is an aggressive blood cancer that can be difficult to treat, and a diagnosis of AML is associated with a wide range of possible outcomes. So, it is essential to seek treatment in a center with hematologists-oncologists who have significant experience in the care of patients with AML. A hematologist is a doctor who has special training in treating blood disorders, and an oncologist is a doctor who has special training in treating cancer. A hematologist-oncologist specializes in treating blood cancers.

Typically, AML patients need to start treatment as soon as possible after diagnosis. However, if time allows, you may want to seek a second opinion from another doctor, as it may help you feel more confident about the recommended treatment plan. The second opinion should come from another hematologist-oncologist, preferably one who treats AML. This type of doctor will usually have the most knowledge and experience about the latest treatment options for AML.

If you are unsure about getting a second opinion or feel uncomfortable about how to tell a doctor you are seeking one, call our Information Specialists at (800) 955-4572, to discuss a way to do so that makes you feel comfortable. You may also want to check with your insurance company to be sure that your plan covers the cost of getting a second opinion and to see if specific doctors or centers are recommended.

Fertility. If you are of child-bearing age, you should be aware that some cancer treatments can affect your fertility (the ability to have children in the future). Before you begin treatment, it is important to talk with your doctor about

whether your treatment could affect your fertility. You may also want to speak with a fertility specialist, a doctor who diagnoses and treats problems related to infertility. This specialist can talk to you about possible options for preserving your fertility. You may be able to take steps before treatment begins to preserve your fertility. However, delaying treatment to address fertility options may not always be recommended. You may need to start treatment right away.

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

Prognostic Factors. Certain factors can affect the prognosis of patients with AML, meaning the likely outcome of their disease. Doctors use “prognostic factors” to help predict how a patient’s disease is likely to respond to treatment. Prognostic factors also help doctors determine which patients need more intense treatment. Some prognostic factors are called “favorable risk factors” because they are associated with a lower risk of relapse after treatment. Others are called “poor/adverse risk factors” because they are associated with a higher risk of relapse after treatment.

The prognostic factors for adults with AML are listed below.

AML Subtype. Chromosomal and genetic abnormalities are the most significant prognostic factors in people with AML. **Table 2**, on page 18, lists some of the more common genetic abnormalities by their risk category.

Patient’s Age. AML occurs mostly in older adults; the median age at diagnosis is 67-70 years. AML patients are considered to be “young” if they are younger than age 60. Usually, the older the patient, the poorer the prognosis. Unfavorable genetic abnormalities increase with age. Additionally, older patients sometimes have comorbidities (other medical conditions) that can make it difficult for them to tolerate intense chemotherapy treatments.

Therapy-Related AML. People who received chemotherapy in the past to treat a different type of cancer may develop AML. This is known as therapy-related or treatment-related AML. In these cases, the disease 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 and/or Extramedullary Disease. AML can be more difficult to treat when leukemia cells have spread to the central nervous system (the area around the brain and spine) or other areas of the body outside of the bone marrow and blood. Intrathecal therapy and other potential interventions are needed to control the disease in these cases.

High White Blood Cell Count. A high white blood cell count $\geq 40,000/\text{mCL}$ at the time of diagnosis is an adverse risk factor for long-term remission.

Response to Induction Therapy. Patients who do not achieve a remission after one cycle of induction therapy have a poorer prognosis.

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

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

Table 2. Risk Stratification by Genetics in Non-APL AML

Risk Category	Chromosome Abnormalities (Cytogenetic Analysis)
Favorable	<ul style="list-style-type: none"> ○ t(8;21)(q22;q22.1); <i>RUNX1-RUNX1T1</i> ○ inv(16)(p13.1;q22) or t(16;16)(p13.1;q22); <i>CBFB-MYH11</i> ○ Biallelic mutated <i>CEBPA</i> ○ Mutated <i>NPM1</i> without <i>FLT3-ITD</i> or with <i>FLT3-ITD</i>^{low*}
Intermediate	<ul style="list-style-type: none"> ○ Mutated <i>NPM1</i> and <i>FLT3-ITD</i> high* ○ Wild-type <i>NPM1</i> without <i>FLT3-ITD</i> or with <i>FLT3-ITD</i>^{low*} (without adverse-risk genetic lesions) ○ t(9;11)(p21.3;q23.3); <i>MLL2-KMT2A</i> ○ Cytogenetic abnormalities not classified as favorable or adverse
Poor/Adverse	<ul style="list-style-type: none"> ○ t(6;9)(p23;q34.1); <i>DEK-NUP214</i> ○ t(v;11q23.3); <i>KMT2A</i> rearranged ○ t(9;22)(q34.1;q11.2); <i>BCR-ABL1</i> ○ inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); <i>GATA2, MECOM(EVI1)</i> ○ -5 or del(5q); -7; -17/abn(17p) ○ Complex karyotype, monosomal karyotype ○ Wild-type <i>NPM1</i> and <i>FLT3-ITD</i>^{high*} ○ Mutated <i>RUNX1</i> ○ Mutated <i>ASXL1</i> ○ Mutated <i>TP53</i>

Abbreviations: APL, acute promyelocytic leukemia; AML, acute myeloid leukemia; t, a translocation between chromosomes; inv, an inversion in a chromosome; q, the long arm of a chromosome (the lower half); p, the short arm of a chromosome (the upper half); v, variable; abn, abnormalities.

*Certain mutations may only be present in a subset (rather than all) of the leukemia cells. This is known as the allelic ratio. Some patients have mutations with a "low-allelic ratio," meaning the mutation is present in less than half of the leukemic blast cells. Others have mutations with a "high-allelic ratio" that could be present in most or all of the leukemic blast cells.

Adapted from NCCN (National Comprehensive Cancer Network) Clinical Practice Guidelines in Oncology. *Acute Myeloid Leukemia*. 2021.

Treatment

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

Before you begin treatment, you and your doctor will discuss your treatment options. One option may be a clinical trial. Like all treatment options, clinical trials have possible risks and benefits. By considering all your treatment options, including clinical trials, you will be taking an active role in a very important decision that affects you.

In the past, a diagnosis of AML was generally considered a medical emergency, and treatment usually started as soon as the diagnosis was made. This often did not allow time for doctors to obtain the specific genetic profile of a patient's leukemia prior to making treatment decisions. Preliminary research has recently found that waiting up to 7 days, in order to obtain genetic data and other laboratory test results on the AML cells, may be safe for the majority of patients. This is important in assigning patients to the best available treatment option for each patient before starting therapy.

Administration of Therapies. Treatments are given in different ways, including:

- Intravenous treatment. Some drugs are injected into a vein. During an intravenous (IV) infusion, the drugs are injected slowly into a vein over the course of several minutes, a few hours, or even several days (in the case of a continuous infusion). Often, doctors give IV treatment through a thin, soft tube called a central venous line (also called a central line or catheter), which is placed in a large blood vessel in the neck, chest or arm. When a patient has a central line in place, the drugs are administered through the line and doctors do not have to inject a needle into the patient's vein each time a treatment is administered. Doctors can also use the central line to give other medications and take blood samples. A central line can be left in place for weeks or months but must be carefully cleaned and maintained to minimize the risk of infections entering the bloodstream.
- Oral treatment. Oral medications are taken by mouth and come in a variety of forms, including pills, capsules and liquids. It is important to always follow directions carefully for oral medications, including the need for special handling (gloves), storage (room temperature or refrigerated) and disposal. Keeping a diary to track oral medication may be helpful.
- Intrathecal treatment. Treatment in which medicine is injected in the fluid-filled space that surrounds the brain and spinal cord, called the cerebrospinal fluid. This method of treatment may be used if there are signs that leukemia cells have spread to the brain or spinal cord. See *Central Nervous System (CNS) Involvement* on page 32.

- Subcutaneous injection. With subcutaneous injection, the needle goes under the skin into the space between the skin and muscle, but does not enter the muscle.

Types of Treatment. Not everyone with AML receives the same type of treatment. Your doctor will tailor your treatment based on your AML subtype and other factors, such as your age and overall health, as well as your preferences. Your treatment may include chemotherapy, targeted therapy and/or stem cell transplantation, and may be given in a hospital (inpatient treatment) or clinic (outpatient treatment).

Palliative Care. This refers to specialized medical care focused on providing relief from symptoms and the stresses of a serious illness. The goal is to prevent or treat disease symptoms, side effects caused by treatment, and psychological and social problems related to the disease or its treatment, in order to improve quality of life for both patients and families. Palliative care is also referred to as “supportive care.” For patients with AML, palliative care may include transfusions, non-toxic oral medications, growth factors, pain medications and specialized nursing care.

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

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

Below are some chemotherapy drugs that are often used to treat AML.

- **Cytarabine (cytosine arabinoside, ara-C; Cytosar-U®)** is FDA-approved to be used alone or with other chemotherapy drugs to treat certain types of leukemia including AML.
- **Daunorubicin (Cerubidine®)** is FDA-approved to be used with other chemotherapy drugs to treat AML.
- **Idarubicin (Idamycin®)** is FDA-approved to treat AML in combination with other chemotherapy drugs.
- **Daunorubicin and cytarabine (Vyxeos®)** is a liposomal formulation of daunorubicin and cytarabine, which is indicated for the treatment of newly-diagnosed therapy-related AML or AML with myelodysplasia-related changes in adults and pediatric patients 1 year and older. A liposomal medication contains the active drug inside small, fat-like particles. This special fatty

preparation allows more medication to reach its target (the bone marrow) and stay in the bone marrow to kill leukemia cells.

- **Azacitidine (Onureg®)** is given by mouth and used for continued treatment of adult patients with AML who achieved first complete remission or complete remission with incomplete blood count recovery following intensive induction chemotherapy and are not able to complete intensive curative therapy.
- **Azacitidine (Vidaza®) and decitabine (Dacogen®, Inqovi®)** are FDA-approved to treat myelodysplastic syndrome (MDS), another type of blood cancer. They are not FDA- approved to treat AML, but they are commonly used as an off-label treatment for AML.

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

- **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. FLT3 inhibitors are drugs that target these gene mutations. For these patients, the following targeted treatments are approved by the Food and Drug Administration (FDA):
 - **Midostaurin (Rydapt®)**, taken by mouth, is for the treatment of adult patients with newly diagnosed AML that is *FLT3* mutation-positive as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation.
 - **Gilteritinib (Xospata®)**, taken by mouth, is for the treatment of adult patients who have relapsed or refractory AML with an *FLT3* mutation as detected by an FDA-approved test.

Other FLT3 inhibitors being studied in clinical trials for the treatment of AML include **sorafenib (Nexavar®)**, **quizartinib (AC-220)** and **crenolanib**.

- **IDH Inhibitors.** In some people with AML, the leukemia cells have a mutation in the *IDH1* or *IDH2* gene. These mutations cause cells to remain immature and divide and multiply too quickly. For these patients, the following FDA-approved targeted therapy may be used:

- **Ivosidenib (Tibsovo®)**, taken by mouth, is an IDH1 inhibitor indicated for the treatment of AML with a susceptible *IDH1* mutation as detected by an FDA-approved test in:
 - Adult patients with newly-diagnosed AML who are age 75 and older or who have comorbidities that preclude the use of intensive induction chemotherapy.
 - Adult patients with relapsed or refractory AML.
- **Enasidenib (Idhifa®)**, a pill taken by mouth, is an IDH2 inhibitor indicated for the treatment of adult patients with relapsed or refractory AML with an *IDH2* mutation as detected by an FDA-approved test.
- **BCL2 Inhibitors.** Overexpression of the BCL2 protein allows cancer cells to evade “programmed cell death,” meaning it helps them live longer than they should. BCL2 inhibitors target the BCL2 protein. This helps restore what is called apoptosis, a process of natural cell death that is disrupted when you have cancer, restoring the body’s natural ability to tell cancer cells to die. Once this process is restored, your body can begin to kill cancer cells. With fewer cancer cells, there is room for healthy blood cells to grow in the bone marrow.

Venetoclax (Venclexta®) is an oral medicine taken by mouth each day. It is FDA-approved in combination with azacitidine, or decitabine, or low-dose cytarabine for the treatment of newly diagnosed AML in adults 75 years or older, or who have comorbidities that preclude the use of intensive induction chemotherapy. This drug binds to the leukemia cells and triggers apoptosis, a process that causes the cells to die.
- **CD33 Targeted Therapy. Gemtuzumab ozogamicin (Mylotarg™)** is a targeted therapy linked to the chemotherapy drug calicheamicin. It binds to and then enters cells that have the CD33 protein on their surface. Once inside, it releases the toxin that kills the cells. More than 90% of AML cells have CD33 on their surface, while mature blood cells do not (and so are not as affected by the treatment). Gemtuzumab ozogamicin is FDA-approved for the treatment of newly-diagnosed CD33-positive AML in adults, as well as relapsed or refractory CD33-positive AML in adults and pediatric patients 2 years and older. This medication is injected slowly into a vein through a needle. It is given in cycles, consisting of treatment days followed by days of rest.
- **Hedgehog Pathway Inhibitor.** The hedgehog pathway is essential for normal embryonic development. In adults, however, abnormal activation of this pathway is thought to contribute to the development and proliferation of cancer stem cells. Research studies have shown that disruption of this pathway can decrease the number of these cancer stem cells in the bone marrow. **Glasdegib (Daurismo™)**, given by mouth, is FDA approved in

combination with low-dose cytarabine, for the treatment of newly diagnosed AML in adult patients who are 75 and older, or who have comorbidities that preclude the use of intensive induction chemotherapy.

Stem Cell Transplantation. For some patients who are in remission and can tolerate intensive chemotherapy, the doctor may recommend stem cell transplantation during the consolidation phase of chemotherapy. The goal of stem cell transplantation is to cure the patient's cancer with very high doses of chemotherapy.

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

There are two main types of stem cell transplantation:

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

Research to determine which patients are most likely to benefit from stem cell transplantation after their first complete remission is evolving. Studies show that allogeneic stem cell transplantation may benefit patients with high-risk and intermediate-risk AML up to age 75 years and who have an HLA-matched donor.

Timing of is one of the most important factors influencing allogeneic transplant outcomes. In most cases, it is very important to start a donor search as soon as possible after an AML diagnosis. This is necessary in order to identify a suitably matched, related or unrelated donor and to plan for the best time to perform a transplant safely and successfully.

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

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

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

Compared to other treatment options, allogeneic stem cell transplantation is associated with a higher rate of side effects and mortality. However, it may be considered for patients with higher-risk AML, based on their cytogenetic and molecular test results and other prognostic factors. The decision to perform an allogeneic transplant also depends on other factors, including the patient's age, physical fitness, comorbidities (other co-existing medical conditions) and social supports (from family members, caregivers, friends, etc), as well as the patient's understanding of the potential benefits and risks.

One possible serious side effect of allogeneic stem cell transplantation is graft versus-host disease (GVHD). This occurs when the transplanted immune cells (the graft) from the donor identify the cells in the recipient's body (the host) as foreign and attack them. The parts of the body most commonly damaged by GVHD include the skin, liver, stomach, intestines and eyes. GVHD can develop within weeks after transplantation or much later. A doctor can order medications to help prevent or minimize the complications of GVHD. Most patients need to be closely monitored for GVHD for at least the first 100 days after the transplant.

Reduced-Intensity Allogeneic Stem Cell Transplantation. This type of transplantation may be a treatment option for older patients who cannot tolerate the high doses of chemotherapy used in preparation for a standard allogeneic stem cell transplant. The conditioning therapy in a reduced-intensity transplant uses lower doses of chemotherapy and/or radiation. With a reduced-intensity conditioning regimen, the patient's blood counts may not fall as low as they would with high-dose chemotherapy. Additionally, the less toxic regimens put less strain on the patient's organs, making this regimen safer and more tolerable.

The success of reduced-intensity transplantation depends on the graft-versus-leukemia effect of the donor stem cells, rather than on high-dose treatments to kill the cancer cells. This therapy reduces the number of cancer cells, but it does not completely destroy the patient's bone marrow. The goal is to have the donor stem cells become established in the patient's bone marrow and produce white blood cells that will attack the patient's remaining cancer cells. As 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 stem cells are collected from a cancer patient before they undergo intensive chemotherapy, either with or without radiation therapy. These stem cells are stored and then put back into the patient's blood stream after the conditioning therapy is completed.

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

Talk to your doctor about:

- Stem cell transplantation and ask whether it is a treatment option for you

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

Phases of Treatment. Treatment for AML is often divided into two phases:

- Induction Therapy. The first phase of treatment is called “induction.” The goal of induction is to destroy as many cancer cells as possible in order to achieve (induce) a remission.
- Consolidation (Post-remission) Therapy. This is the second phase of treatment, which begins after leukemia is in remission. The goal of consolidation therapy is to kill any remaining leukemia cells in the body.

Not everyone with AML receives the same treatment. The choice of initial induction therapy for AML depends on a series of factors, including:

- The status of the disease (best measured by the genetic profile of the leukemia cells and other prognostic factors)
- The patient's age, overall health and general level of fitness (called performance status)
- Consideration of the patient's goals for treatment and eligibility to undergo stem cell transplantation

Doctors often give the most intensive chemotherapy regimens to people younger than age 60. However, this age limit is just a guideline. Some older patients in good health may also benefit from intensive regimens or slightly less intensive treatments. For example, an AML patient age 63 with no other health issues may be treated as someone younger than age 60, while a person age 57 with serious health issues may be treated as someone age 60 years and older.

Therapy for Patients Younger Than Age 60 and “Fit” Patients Age 60 Years

and Older. For this group, the goal of treatment is to increase long-term survival with the possibility of a cure. Treatment is more intensive and may have more serious side effects. It typically consists of multidrug chemotherapy given in two phases: induction and consolidation. The specific drugs, the dosages used and timing of administration depend on several factors, including the genetics of the leukemia cells, the patient’s age and the overall health of the patient.

Induction. The first phase of therapy is called “induction.” The goal of induction is to destroy as many cancer cells as possible in order to achieve (induce) a complete remission. 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.

The most common induction regimen for AML includes **cytarabine** and an anthracycline drug, such as **daunorubicin** or **idarubicin**. This is called the “7 + 3” regimen, because cytarabine is most often given by continuous intravenous (IV) infusion over 7 days, while the anthracycline drug is given by an IV infusion in a single dose for 3 days during the first week of treatment. The induction therapy is usually given in the hospital and lasts about a week. However, patients typically remain in the hospital for an additional 3-5 weeks for a total of 4-6 weeks while their blood counts recover following “7+3” therapy. Other drugs may be added or substituted for these “7+3” drugs for higher-risk patients and targeted therapies, such as:

- **Midostaurin (Rydapt®)** for *FLT3*-mutated AML
- **Gemtuzumab ozogamicin (Mylotarg™)** for CD33-positive AML
- **Daunorubicin and cytarabine (Vyxeos®)** for the treatment of newly-diagnosed therapy-related AML or AML with myelodysplasia-related changes in adults

For approval information on these therapies see pages 20-23.

Table 3 on page 31 lists some of the drugs approved for use in the standard treatment of AML, as well as some of the drugs under study in AML clinical trials.

Induction therapy destroys most of the leukemia cells, as well as healthy bone marrow cells. Most patients develop dangerously low blood counts and may become very ill. 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 with a caregiver somewhere near the medical facility, and if the patient can comply with the policies of the treatment center.

Assessing Treatment Response. About 2 to 3 weeks after the completion of induction therapy, blood and bone marrow tests are done to see how well your treatment is working. If no leukemic blasts are found in the bone marrow, no treatment is given for 2 to 4 weeks to give your bone marrow time to recover and make new blood cells.

When blood cell counts return to normal, your doctor will test your bone marrow again to see whether you have achieved a complete remission. A complete remission is achieved when:

- No more than 5 percent of cells in the bone marrow are blast cells
- Blood cell counts are back to normal
- All signs and symptoms of AML are gone

If the initial treatment does not induce a remission, induction therapy can be repeated, either with the same drugs or with a new chemotherapy regimen. Patients who continue to have a high level of blasts should be considered as candidates for a clinical trial, allogeneic stem cell transplantation or drug regimens for relapsed or refractory AML.

Minimal/Measurable Residual Disease. Even when a complete remission is achieved, some leukemia cells that cannot be seen with a microscope may still remain in the bone marrow. This is referred to as minimal residual disease (MRD), also called measurable residual disease. Patients who achieve remission after initial treatment but have MRD are at increased risk of disease relapse. Testing for MRD can help doctors identify patients who may benefit from further treatment with intensified therapies, such as allogeneic stem cell transplantation.

It is important to get tested for MRD after achieving remission. The tests used most commonly to detect MRD are flow cytometry, polymerase chain reaction (PCR) and next-generation sequencing. These tests typically use samples of bone marrow cells, but in some cases blood samples can be used. They are much more sensitive and able to detect very low numbers of AML cells, compared to standard tests that can only detect AML cells that are visible with a microscope.

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

Consolidation (Post-remission) Therapy. In many patients, blood cell production should return to normal several weeks after induction therapy is completed. Blood cell counts gradually approach acceptable levels, and AML cells cannot be detected in the blood or bone marrow. The cancer is now said to be “in remission.” If there are a small number of residual AML cells, they will not interfere with normal blood cell development. However, they do have the potential to multiply and cause a relapse.

Even when a patient achieves a complete remission, more treatment is always needed to destroy any residual leukemia cells in the body. Without additional therapy, the leukemia will relapse within weeks or months. To prevent a relapse, intensive consolidation therapy is given after the patient recovers from induction therapy.

Consolidation therapy is treatment given after cancer is in remission following the initial therapy. The goal of consolidation therapy is to “consolidate” the remission by lowering the number of residual leukemia cells in the body or eliminating them entirely. There are three basic treatment options for post-remission therapy:

- Additional intensive chemotherapy
- Stem cell transplantation (see pages 23-25 for more information)
- Oral chemotherapy (as maintenance therapy)

Patients with favorable risk factors 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 may be hospitalized or receive post-remission therapy in an outpatient setting, depending on the clinical setting, the treatment type and other factors.

Patients with high-risk AML, based on their prognostic factors, receive more aggressive therapy, such as allogeneic stem cell transplantation (see page 23), during the consolidation phase of treatment. Allogeneic stem cell transplantation is a complex treatment that can cause serious, life-threatening side effects. So, it is important to discuss the benefits and risks of this procedure with your doctor.

An important treatment decision for a patient is whether to have the stem cell transplantation after their first remission. Often, this is when transplantation offers the best chance of preventing AML from recurring. However, it is associated with higher treatment-related morbidity and death compared to other treatment options, 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 as soon as possible, ideally while they are receiving induction therapy.

For patients 60 years of age or older who achieve a complete remission after induction therapy but who are not able to complete intensive chemotherapy or proceed to allogeneic stem cell transplantation, the doctor may prescribe an oral formulation of **azacitidine (Onureg®)** as maintenance therapy. For approval information, see page 21.

Therapy for Patients Aged 60 Years and Older. AML occurs more frequently in older adults; at least half of patients are older than 65 years of age when the disease is diagnosed. Treatment approaches for these patients range from standard intensive induction chemotherapy to less intensive therapies, or the best supportive care. Additionally, there are a growing number of new treatment options available for older adults.

The treatment of AML in older patients is a challenge. The higher occurrence of unfavorable cytogenetic and molecular abnormalities in the leukemia cells of many older patients makes the disease more resistant to standard chemotherapy than in younger patients. Also, as people age, they can have more difficulty tolerating more intense cancer treatments. Older patients are also more likely to have comorbidities (other medical problems), including diabetes, high blood pressure, high cholesterol, heart disease, and a history of stroke or lung disease. These comorbidities can limit treatment options. Many older patients are not offered standard treatment options with intensive chemotherapy because they are considered unlikely to survive the rigors of this treatment due to their advanced age, comorbidities and poor general level of fitness (called performance status). In some cases, intensive chemotherapy can actually shorten their lives.

The choice of therapy for older patients with AML also depends on the specific genetic profile of the leukemia cells; a patient's genetic profile is also the best way to predict how the disease will respond to chemotherapy as some specific genetic mutations may lead to poorer outcomes. In addition, consideration needs to be given to whether patients have available support from friends and family during treatment. You should discuss your treatment goals with your doctor. The doctor should explain the risks and benefits of your different treatment options and also provide realistic expectations about the likely results of each of them.

Older patients who are physically fit and have no serious health problems may benefit from intensive treatment (see page 26). Fit elderly patients may even be candidates for reduced-intensity allogeneic transplantation (see page 24).

Not all patients want or can tolerate intensive therapies. Patients whose comorbidities and performance status make them poor candidates for intensive chemotherapy may still be able to participate in clinical trials. Or they may benefit from lower-intensity therapies which may relieve symptoms, improve quality of life and potentially extend survival. **Table 3** on page 31 lists some of the drugs

approved for use in the standard treatment of AML, as well as some of the drugs under study in AML clinical trials.

Lower-intensity treatment strategies for induction as recommended by the NCCN Guidelines include:

- **Venetoclax (Venclexta®) and azacitidine (Vidaza®)**
- **Venetoclax and decitabine (Dacogen®)**
- **Venetoclax and low-dose cytarabine (Cytosar-U®)**
- **Azacitidine**
- **Decitabine**
- **Low-dose cytarabine**
- **Glasdegib (Daurismo™)**
- **Gemtuzumab ozogamicin (Mylotarg™)** for CD33-positive AML
- **Ivosidenib (Tibsovo®)** for AML with an *IDH1* mutation
- **Enasidenib (Idhifa®)** for AML with an *IDH2* mutation
- **Azacitidine or decitabine and sorafenib (Nexavar®)** for AML with an *FLT3*-ITD mutation

For approval information on these therapies see pages 20-23.

Assessing Treatment Response. After the completion of induction therapy, blood and bone marrow tests are done to check for a remission and to look for minimal/measurable residual disease (see page 27 for more information about minimal/measurable residual disease). A complete remission is still possible with lower-intensity treatments. A complete remission is achieved when:

- No more than 5 percent of cells in the bone marrow are blast cells
- Blood cell counts are back to normal
- All signs and symptoms of AML are gone

For patients who are tolerating and responding to treatment, the doctor will generally continue the treatment indefinitely as maintenance therapy. If there is no response or the cancer progresses, patients may want to consider a clinical trial or treatments for relapsed or refractory disease. Patients may also want to consider only palliative care to improve quality of life and alleviate discomfort.

Table 3. Some Drugs Approved or in Clinical Trials for the Treatment of AML

Anthracyclines (antitumor antibiotics)	<ul style="list-style-type: none"> ○ daunorubicin (Cerubidine®) ○ idarubicin (Idamycin®) ○ mitoxantrone (Novantrone®)
Antimetabolites	<ul style="list-style-type: none"> ○ cladribine (2-CdA; Leustatin®) ○ clofarabine (Clolar®) ○ cytarabine (cytosine arabinoside, ara-C; Cytosar-U®) ○ fludarabine (Fludara®) ○ methotrexate ○ 6-mercaptopurine (Purinethol®)
Anthracycline and antimetabolite combination	<ul style="list-style-type: none"> ○ liposomal combination of daunorubicin and cytarabine (Vyxeos®)
Topoisomerase inhibitors	<ul style="list-style-type: none"> ○ etoposide (VP-16; VePesid®, Etopophos®)
Cell-maturing agents	<ul style="list-style-type: none"> ○ all-trans retinoic acid (ATRA, tretinoin; Vesanoid®) ○ arsenic trioxide (Trisenox®)
Hypomethylating agents	<ul style="list-style-type: none"> ○ azacitidine (Vidaza®) ○ oral azacitidine (Onureg®, CC-486) ○ decitabine (Dacogen®) ○ oral decitabine (Inqovi®)
Immunomodulator	<ul style="list-style-type: none"> ○ cusatuzumab (Argx-110) ○ magrolimab
Antibody conjugate	<ul style="list-style-type: none"> ○ gemtuzumab ozogamicin (Mylotarg™)
FLT3 inhibitors	<ul style="list-style-type: none"> ○ crenolanib ○ gilteritinib (Xospata®) ○ midostaurin (Rydapt®) ○ quizartinib (AC-220) ○ sorafenib (Nexavar®)
IDH1 inhibitor	<ul style="list-style-type: none"> ○ ivosidenib (Tibsovo®)
IDH2 inhibitor	<ul style="list-style-type: none"> ○ enasidenib (Idhifa®)
Hedgehog inhibitor	<ul style="list-style-type: none"> ○ glasdegib (Daurismo™)
BCL2 inhibitor	<ul style="list-style-type: none"> ○ venetoclax (Venclexta®)

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

Special Treatment Considerations

Central Nervous System (CNS) Involvement. AML cells can spread to the cerebrospinal fluid (CSF), the fluid around the brain and spinal cord. This is uncommon, occurring in less than 3 percent of AML patients. Because central nervous system (CNS) involvement is rare in cases of AML, doctors usually 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) or magnetic resonance imaging (MRI) scan, to evaluate the symptoms further.

The doctor will also obtain a sample of the patient's cerebrospinal fluid by lumbar puncture. 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 CSF, the patient will be given "intrathecal chemotherapy." In this treatment, chemotherapy drugs are injected directly into the spinal fluid. Intrathecal chemotherapy needs to be administered 2-3 times per week until the leukemia cells are eliminated, followed by weekly or monthly treatments to prevent disease recurrence in the central nervous system. Treatments with intrathecal chemotherapy can be administered at the same time that the patient receives other chemotherapy treatments for AML.

Acute Promyelocytic Leukemia (APL). This aggressive subtype of AML is associated with potentially life-threatening simultaneous bleeding and clotting complications. While in the past acute promyelocytic leukemia (APL) was nearly always fatal, it is now one of the most curable subtypes of AML in adults, if it is diagnosed early and treated appropriately. APL accounts for approximately 10 percent of all AML cases and occurs primarily in middle-aged adults, although it can occur at any age. APL can also develop after receiving chemotherapy for another disease.

In people with APL, immature white blood cells called promyelocytes build up in the bone marrow. The overproduction of promyelocytes leads to a shortage of normal white blood cells, red blood cells and platelets. People with APL are particularly susceptible to bruising and excessive bleeding. This occurs in part because of the low number of platelets in the blood and also because the leukemia cells release substances that alter the balance between bleeding and clotting.

APL is due to a translocation between chromosomes 15 and 17, abbreviated t(15;17). A translocation is a genetic change in which a piece of one chromosome breaks off and attaches to another chromosome. In APL, an abnormal fusion

gene called *PML/RAR α* forms as a result of the translocation. This mutated gene leads to the production of a protein that causes blood cells to get stuck in the promyelocytic stage, unable to develop into mature white blood cells. A diagnosis of APL depends upon confirmation of t(15;17) in the patient's AML cells.

Treatment for APL differs from that of the other AML subtypes described in this book. Many people with APL are treated with a drug called **all-trans-retinoic acid (ATRA)** in combination with **arsenic trioxide (Trisenox[®])** or, in high-risk cases, chemotherapy.

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

Relapsed and Refractory AML

Most patients who receive treatment for AML achieve an initial remission. However, some patients have persistent and visibly present residual leukemia cells in the bone marrow at a level of 5% or higher, even after intensive treatment. In these cases, the disease is referred to as being “refractory” (or “refractory AML”). Approximately 30-50 percent of newly diagnosed AML patients do not achieve a complete remission with intensive induction therapy and may require additional chemotherapy. Patients who have not achieved complete remission after two cycles of intensive chemotherapy are considered to have refractory AML. For patients on targeted therapy, it may take 2 to 6 months to achieve a remission. So, it may be more difficult to define when a treatment has failed.

In other patients, despite achieving an initial remission, leukemia cells reappear in the bone marrow and normal blood cell production decreases again. This is referred to as a “relapse” of the disease (or “relapsed AML”). At the time of relapse, repeat genetic testing of the leukemia cells is considered “standard of care,” since the mutational pattern at the time of relapse may be different from when the disease was first diagnosed. This can affect treatment decisions.

Allogeneic stem cell transplantation remains the only potential curative option for patients with relapsed AML, and they must be considered fit enough to undergo the procedure. However, recent approval of several new treatments may help patients who cannot undergo a stem cell transplant to live longer with high quality of life.

Treatment options for patients with refractory or relapsed AML include:

- **A clinical trial** (see *Research and Clinical Trials* on 35). Treatment in a clinical trial should be considered first for all patients with refractory or relapsed AML. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. Patients and caregivers can work with Clinical Trial

Nurse Navigators who will help find clinical trials and personally assist them throughout the entire clinical trial process. Visit www.LLS.org/CTSC for more information.

- **Re-treatment with the same induction regimen that produced the patient's first remission.** This is an option if a relapse occurs 12 months or more after remission.
- **Allogeneic Stem Cell Transplantation.** In fit patients, salvage chemotherapy can be used to induce a remission before stem cell transplantation. This is an option for patients younger than age 60 and patients older than age 60 who are physically fit.
- **Targeted Therapy.** Some targeted therapies that may be used include:
 - **Gilteritinib (Xospata®)** for AML with an *FLT3* mutation
 - Low-intensity therapy (**azacytidine** or **decitabine**) plus **sorafenib (Nexavar®)** for AML with an *FLT3* mutation
 - **Enasidenib (Idhifa®)** for AML with an *IDH2* mutation
 - **Ivosidenib (Tibsovo®)** for AML with an *IDH1* mutation
 - **Gemtuzumab ozogamicin (Mylotarg™)** for CD33-positive AML

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

Aggressive treatments for fit patients, suggested by the National Comprehensive Care Network (NCCN) Guidelines, include:

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

Less aggressive treatments, suggested by the NCCN Guidelines, include:

- Hypomethylating agents (**azacitidine** or **decitabine**)
- Low-dose **cytarabine**
- **Venetoclax** plus hypomethylating agents (**azacitidine** or **decitabine**) or **low-dose cytarabine**

Research and Clinical Trials

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

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

LLS Information Specialists, available at (800) 955-4572, offer guidance on how 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. 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 on Treatment Approaches. Scientific research is being done to learn more about AML: how best to treat it and how to provide the best care to people diagnosed with this disease. A number of approaches are under study in clinical trials for the treatment of patients with AML.

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

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

- **Novel Targeted Therapies.** A targeted therapy 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.** Newer generation FLT3 inhibitors, including **quizaritinib** (formerly AC-220) and crenolanib, are being investigated in combination with chemotherapy to treat patients with newly diagnosed and relapsed AML with *FLT3* mutations.
 - **p53 Inhibitors.** Mutations in the *p53* gene deactivate processes (tumor suppressor genes) which prevent normal healthy cells from becoming cancerous. **APR-246 (eprenetapopt)**, a novel small molecular inhibitor, is being studied for the treatment of AML with *p53* mutations. APR-246 targets and restores the function of the mutated gene.
 - **Menin Inhibitors.** Research has shown that the menin protein plays a role in the development and growth of some leukemias with mutations in the *KMT2A* gene (formerly known as the mixed-lineage leukemia or *MLL* gene), as well as the *NPM-1* (nucleophosmin-1) gene. In the laboratory, menin inhibitors have been shown to produce anti-leukemic effects in AML with *KMT2A* and *NPM-1* mutations. Two menin inhibitors (**KO-539** and **SNDX-5613**) are being studied in clinical trials and may represent promising approaches to treat these specific genetic types of leukemia.
 - **Targeting Cancer Metabolism.** A new drug called **devimistat (CPI-613®)** targets enzymes involved in cancer cell energy metabolism and increases the sensitivity of cancer cells to a range of chemotherapies. Combining existing treatments with devimistat will potentially make them more effective and allow for the possibility of using lower doses of drugs that are generally toxic.
- **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 as potential targets, including CD123, which is found on most AML cells. A promising example is **magrolimab (an anti-CD47 antibody)**, which works by making leukemia cells recognizable to macrophage cells. These are the immune system cells whose job is to “eat” and remove infected and diseased cells from the body. Treatment with magrolimab combined with azacitidine appears to be effective in older patients with newly

diagnosed AML, even in those with mutations like *p53*. Another antibody called **cusatuzumab** targets CD70, which is expressed on leukemia cells, particularly leukemic stem cells—the specific population of cells responsible for disease relapse. Treatment with cusatuzumab combined with azacitidine is being explored in older patients with AML.

- **Bispecific T-Cell Engager (BiTE) Antibody Therapy.** Specialized antibodies have been designed to simultaneously target AML cells and activate the patient's immune system to attack these leukemia cells. One such agent, called **AMG-330**, is designed to harness T cells to target AML cells with the CD33 antigen. Another, called **flotetuzumab**, recruits T cells to target CD123, which is expressed on chemotherapy-resistant AML cells.
- **Vaccine Therapy.** Researchers are developing vaccines that can be personalized to individual patients to stimulate a strong immune response against their cancer. These vaccines are designed for patients who are in remission. They work by generating an immune response against the leukemia cells to hopefully prevent the disease from coming back in the future. Some of the targets of this vaccine approach include the **WT1 (Wilm's tumor 1) antigen** expressed on many AML cells.
- **Chimeric Antigen Receptor (CAR) T-Cell Therapy.** In this type of immunotherapy, the patient's own immune cells are genetically engineered to recognize and attack cancer cells. Scientists are conducting research to see whether these treatments are effective in patients with AML. They are also exploring whether it is possible to use someone else's engineered immune cells in an "off the shelf" approach, instead of the patient's own cells, to treat patients more quickly.

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

Related Diseases

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

Most patients with BPDCN are older, with a median age of 65 to 67 years at diagnosis. A diagnosis of BPDCN requires a finding of at least four of the following six antigens on the cancer cells: CD123, CD4, CD56, TCL-1, CD2AP, and CD303/BDCA-2.

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

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

Mixed Phenotype Acute Leukemia. Mixed phenotype acute leukemia (MPAL) is a subtype of acute leukemia, which is also known as “biphenotypic leukemia” or “mixed lineage leukemia,” and has an ambiguous lineage. It is a combination of two forms of leukemia: acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). It accounts for 2 to 5 percent of all acute leukemia cases, affecting patients of all ages, and there are several different subtypes. Since MPAL is rare, patients with MPAL should seek treatment at a cancer center that has experience treating patients with this disease.

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

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

For patients with a non-Ph+ subtype of MPAL, the treatment typically consists of either an ALL treatment regimen, or a combination of ALL and AML therapies. Ideally this is followed by consolidation therapy with an allogeneic stem cell transplant when a donor is available.

Side Effects and Complications

AML and its treatment often cause side effects. In addition to treating the cancer, an important part of care is relieving a person's symptoms and side effects resulting from treatment. Most side effects in patients with AML are temporary and subside once the body adjusts to therapy, or when therapy is completed. If side effects become severe, patients may need to be hospitalized.

Low Blood Cell Counts. Cancer and cancer treatments often cause drops in blood cell counts. This can result in a severe deficiency in the patient's number of red blood cells, white blood cells and platelets. Patients almost always need transfusions of red blood cells and platelets for several weeks during treatment. After that, the blood cell counts usually return to normal levels.

White blood cell transfusions are generally not 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. For patients with acute promyelocytic leukemia (APL), growth factors are also not recommended during induction therapy because they can increase the risk of differentiation syndrome. This is a condition with symptoms including unexplained fever, weight gain, labored breathing, pleuropericardial effusion (fluid around the lungs and heart), hypotension (low blood pressure) and renal (kidney) failure.

Infections. During treatment for AML, the deficiency of white blood cells can lead to infections from bacteria and fungi that are normally present in the environment, on the skin, in the nose and mouth, on the gums or in the colon. The risk of infection may be increased because chemotherapy damages the cells lining the mouth and intestines, making it easier for bacteria to enter the bloodstream. After starting a course of chemotherapy, patients commonly receive antibiotics to prevent bacterial infection, as well as other drugs that prevent fungal and viral infections.

Because of the increased risk of infection, medical staff and all family and friends need to practice frequent and vigorous handwashing and take other precautions to avoid exposing patients to bacteria, viruses and other infection-causing agents. Caregivers of patients who have central lines or ports need to be meticulous when cleaning insertion sites and catheters.

Patients at home should seek medical attention immediately if any signs of infection develop. A temperature of 100.4 °F or higher or the onset of chills may be the only sign of infection in a patient who has a very low white blood cell count. Other signs of infection may include persistent coughing, sore throat, pain during urination, or diarrhea.

Patients with AML are advised to receive certain vaccinations. For adult patients, these include vaccinations for influenza and pneumococcal pneumonia and the inactivated ("dead") vaccine for the herpes virus, called **Shingrix**. Vaccines using live organisms or high viral loads, such as the herpes zoster/shingles vaccine **zoster vaccine live (Zostavax®)**, should not be given to AML patients. If a family member or friend of the patient receives a live vaccine, they should not go near the recently vaccinated person for a period of time. COVID-19 vaccines are also recommended, but they have not been tested in patients with AML as of this printing. Talk to your doctor for more information.

Tumor Lysis Syndrome. Patients with AML may be at high risk of developing a condition called "tumor lysis syndrome" (TLS). This condition occurs when a large number of cancer cells die within a short period of time, releasing their contents into the blood. TLS can be severe during the early phases of treatment, especially for patients who have very high white blood cell counts before they start induction therapy.

As the leukemia cells die, they break apart and release their contents into the bloodstream, which changes the normal balance of chemicals in the blood. This can overwhelm the kidneys because they cannot get rid of the substances all at once. Uric acid is one of the chemicals released by the dying cancer cells. Very high levels of uric acid and other chemicals can cause severe damage to the kidneys and heart. If untreated, TLS can lead to heart arrhythmias, seizures, loss of muscle control, acute kidney failure and even death. Patients with leukemia who are at high risk for or have developed laboratory or clinical evidence of TLS are given drugs, such as **allopurinol (Zyloprim®)** or **rasburicase (Elitek®)**, which prevent or lessen TLS.

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 build-up 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** and other chemotherapy drugs to decrease the number of white blood cells, which are the source of differentiation effects. In severe cases, use of differentiating agents is stopped.

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

- Mouth ulcers
- Diarrhea
- Hair loss
- Rashes
- Nausea and vomiting
- Loss of appetite
- Fatigue
- Neuropathy (pain, numbness, tingling or muscle weakness, usually in the hands or feet)

You should inform your doctor about any side effects that you experience. Your doctor may be able to prescribe medications to prevent or relieve your side effects, change dosages or treatment schedules to prevent them from getting worse, or suggest ways to prevent or minimize them.

See the free LLS series *Side Effects Management (filter for Side Effect Management at www.LLS.org/booklets) for more information.*

Sometimes drugs or drug combinations cause side effects that continue for a period of time after treatment ends. Some of these effects may be long-lasting (see *Long-Term and Late Effects of Treatment* on page 42).

Follow-Up Care

Your medical care for AML does not stop once active treatment has finished. Your doctor will continue to check on you to make sure that your leukemia has not returned, manage side effects and monitor you for late effects of treatment. This is called follow-up care.

Monitoring for Recurrence of AML. After a patient completes treatment for AML and is in remission, follow-up tests are done to check how well the treatment worked and to look for signs of relapse. Tests are also done to check how well the patient's organs are working.

Patients undergo frequent follow-up tests during the first year after treatment, but tests are done less often during the second and third years. Testing and check-ups may be required less often as time goes on, but scheduled follow-up visits should continue indefinitely.

The National Comprehensive Cancer Network recommends that AML patients should have a complete blood count every 1 to 3 months for the first 2 years after completing consolidation therapy, then every 3 to 6 months thereafter for up to 5 years. Bone marrow tests should be performed only if blood test results are abnormal.

People who have been treated for AML are encouraged to:

- Maintain regular follow-up appointments with their hematologist-oncologists. Their doctors will monitor them for signs of relapse and also be able to detect any side effects from treatment or the onset of other medical problems.
- Keep a record of your cancer diagnosis, treatment, and follow-up care needs. This is often called a “survivorship care plan.” Ask your doctor for a written survivorship care plan. Share this information with any new healthcare providers you see. The plan should include the following information:
 - List of all healthcare providers
 - Diagnosis summary with specifics such as subtype and/or genetic markers
 - Treatment summary with specifics such as the names, dates, and dosages of chemotherapy or other drugs, site of radiation treatment, surgery and/or transplantation information, response to treatment, and side effects
 - Maintenance treatment information, if applicable
 - List of possible late effects
 - Schedule for ongoing monitoring with recommended tests, frequency and coordinating provider
 - Health and wellness recommendations such as nutrition, exercise or other disease screenings
- Receive periodic screening and monitoring for skin, gastrointestinal, kidney, blood, bladder, prostate, breast, lung, head and neck, and other types of cancer because of the increased risk of a second cancer associated with AML.
- Seek medical and psychosocial support for fatigue, depression and other long-term effects, if needed.
- Consider cancer risk-reduction strategies, such as smoking cessation, skin protection against prolonged sun exposure, healthy eating and exercising.

Long-Term and Late Effects of Treatment. Some treatments for AML can cause significant long-term or late effects. Long-term effects of cancer treatment are medical problems that last for months or years after treatment ends. Late effects are medical problems that do not appear until years, or even possibly decades, after treatment ends.

People who have been treated for AML may be at increased risk for heart damage, other cancers and neurologic or cognitive problems. They should be seen by a primary care doctor for general health examinations at least once a year and 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. 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

Many 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 treatment ends.

Certain long-term and late effects have been associated with stem cell transplantation. These include 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. **See the free LLS booklet *Long-Term and Late Effects of Treatment in Adults Facts*.**

Talk to your doctor about:

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

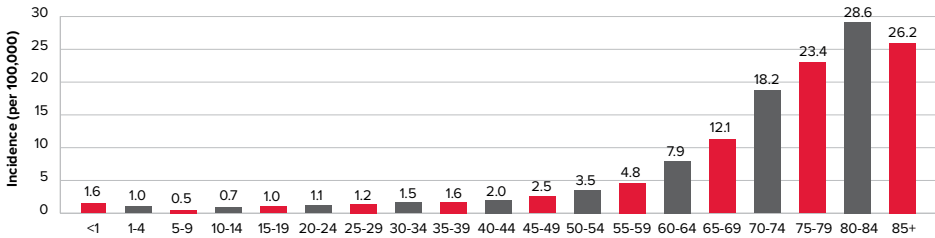
Treatment Outcomes

AML is a difficult disease to cure. Just a few decades ago, almost no adults with AML could be cured. But today, advances in understanding of the genetic features of the disease and the use of targeted therapies have resulted in improved remission and cure rates for AML patients.

Incidence, Causes and Risk Factors

Incidence. AML is the most common type of acute leukemia in adults. Older people are more likely than younger adults or children to develop AML. See **Figure 4** below. An estimated 20,240 new AML cases were expected to be diagnosed in the United States in 2021. As of January 2017, an estimated 55,548 people in the US were either living with or in remission from AML.

Figure 4. Acute Myeloid Leukemia (AML): Age-Specific Incidence Rates 2013-2017



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

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

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

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

- 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 (1.4 cases per 100,000 people) to ages 65 to 69 years (about 12.0 cases per 100,000 people). The incidence rate continues to increase in people over 70, peaking between the ages of 80 and 84 (28.4 cases per 100,000 people) (see **Figure 4** above).
- Sex. Males are more likely than females to develop AML.
- Exposure to dangerous chemicals. Long-term exposure to high levels of certain chemicals, such as benzene, is linked to a greater risk of AML. Although benzene is found in certain industrial settings, 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, half of the total exposure to benzene in humans in the United States comes from cigarette smoke. This is true despite the fact that petroleum products contribute to most of the benzene in the atmosphere.
- Previous cancer treatment. People who received radiation therapy or chemotherapy (especially with platinum drugs, alkylating agents such as cyclophosphamide and busulfan, or topoisomerase II inhibitors such as etoposide and doxorubicin) have an increased risk of developing AML. When AML develops as a result of treatment for another disease in the past, it is often called “treatment-related” or “therapy-related” AML.
- 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).
- Other blood cancers. People who have certain blood disorders are at greater risk of developing AML. These include myeloproliferative neoplasms (polycythemia vera, essential thrombocythemia and myelofibrosis), as well as myelodysplastic syndromes (MDS), which in some people can evolve over time into AML.
- 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.

Normal Blood and Bone Marrow

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

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

- Proteins
 - Albumin, the most common blood protein
 - Blood-clotting proteins (coagulation factors) made by the liver
 - Erythropoietin, a protein made by the kidneys that stimulates red blood cell production
 - Immunoglobulins, proteins that help the body fight infection
- Hormones, such as thyroid hormone and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin B₁₂
- Electrolytes, such as calcium, potassium and sodium

Blood cells. Blood cells are formed in the bone marrow, a spongy tissue where blood cells grow and develop. Blood cells start as stem cells. The process of stem cells maturing into blood cells is called "hematopoiesis." See **Figure 5** on page 47. The blood cells are suspended in the plasma.

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

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

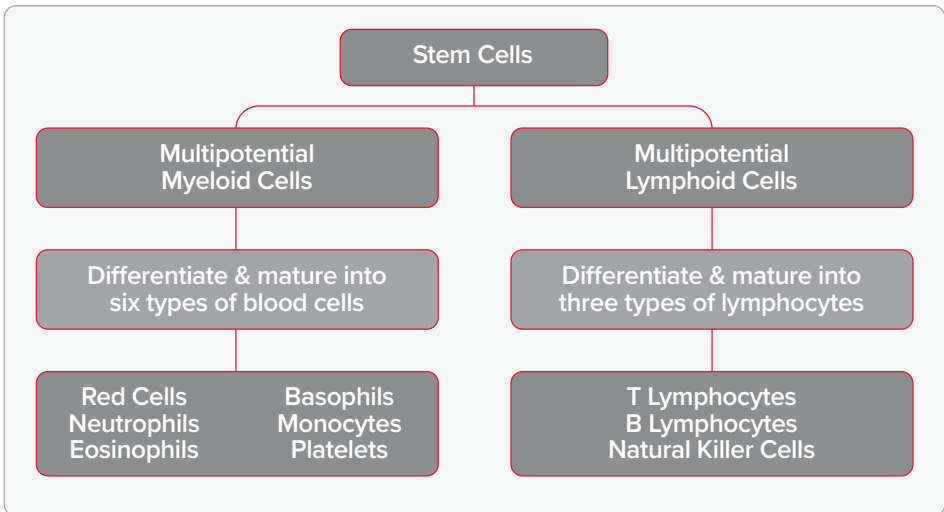
- These make up a little less than half of the body's total blood volume.
- They are filled with hemoglobin, the protein that picks up oxygen from the lungs and takes it around the body. It binds with carbon dioxide (CO₂) and removes it from the cells and then brings it back to the lungs. When a person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

2. Platelets (cells that help blood clot)

- These are small cells (one-tenth the size of red blood cells).
- They help stop bleeding from an injury or cut.
- They stick to the torn surface of the vessel, clump together and plug up the bleeding site. They form a clot with the help of proteins, such as fibrin, and electrolytes, such as calcium.

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

Figure 5. 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 book lists various resources available to you. Use this information to learn more, to ask questions and to make the most of the knowledge and skills of the members of your healthcare team.

For Help and Information

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

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

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

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

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

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

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

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

Free Mobile Apps

- LLS Coloring For Kids™ – Allows children (and adults) to express their creativity and offers activities to help them learn about blood cancer and its treatment. Visit www.LLS.org/ColoringApp to download for free.
- LLS Health Manager™ – Helps you track side effects, medication, food and hydration, questions for your doctor, and more. Visit www.LLS.org/HealthManager to download for free.

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

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

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

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

Community Resources and Networking

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

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

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

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

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

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

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

Additional Help for Specific Populations

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

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

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

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

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

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

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

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

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

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

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

Health Terms

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

Allogeneic Stem Cell Transplantation. A treatment that uses stem cells from a healthy donor to restore a patient's bone marrow that is damaged or diseased after receiving high doses of chemotherapy and/or radiation therapy. **See the free LLS book *Blood and Marrow Stem Cell Transplantation*.**

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

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

Antibody. A type of protein created by blood cells in response to an antigen (a substance that causes the body to mount a specific immune response). Antibodies help the body fight against invaders that make a person sick. They can also be made in the laboratory and are used to help identify certain types of cancer and also to help treat cancer, either alone or attached to toxic substances.

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

Autologous Stem Cell Transplantation. A treatment in which stem cells are removed from a patient, stored and then returned to the patient's body after intensive cancer treatment. **See the free LLS book *Blood and Marrow Stem Cell Transplantation*.**

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

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

Blast Cell. An immature blood cell.

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

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

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

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

CBC. See Complete Blood Cell Count.

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

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

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

Chloroma. See Myeloid Sarcoma.

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

Clinical Trial. A research study that is carefully planned and monitored to evaluate how well new medical approaches work in patients. The goal of clinical trials for blood cancers is to develop new treatments, improve quality of life and increase survival time. A treatment that is proven to be safe and effective in a clinical trial is often approved by the United States Food and Drug Administration (FDA) for use as a standard treatment for a disease, if it is either more effective or has fewer side effects than the current standard treatment for that disease.

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

Colony-Stimulating Factor. See Growth Factor.

Comorbidity. The condition of having two or more diseases at the same time.

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

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

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

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

Cycle of Treatment. A period of treatment (radiation, chemotherapy or other type of drug regimen) followed by a period of rest to allow

the body to recover. A cycle is the time from the start of one round of treatment until the start of the next round of treatment. For example, chemotherapy given daily for one week followed by three weeks of rest is one cycle of treatment.

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

Cytotoxic Chemotherapy. An anticancer drug that kills cancer cells or prevents them from dividing. See Chemotherapy.

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

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

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

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

Erythrocyte. See Red Blood Cell.

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

Extramedullary Disease. Occurs when leukemia cells form tumors outside the bone marrow. See Myeloid Sarcoma.

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

FISH. See Fluorescence In Situ Hybridization.

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

FLT3. A gene that makes a protein, called FMS-like tyrosine kinase 3, which regulates blood cell development. Mutations of this gene can cause overproduction of the FLT3 protein and contribute to the development of leukemia by causing 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 certain genes or chromosomes, they light up when viewed under a specialized “fluorescence” microscope. This test can help to diagnose some types of cancer, plan treatment and monitor the effectiveness of treatment.

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

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 stem cells transplanted from a donor (the graft) attack the healthy tissues of the transplant recipient (the host). Most often, GVHD affects a patient’s skin, liver, stomach and gastrointestinal tract. **See the free LLS booklet *Graft-Versus-Host Disease*.**

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

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

Granulocytic Sarcoma. See Myeloid Sarcoma.

Growth Factor. A substance made by the body that stimulates the growth of specific cells. Some growth factors are made in the laboratory for use in cancer treatment. For example, granulocyte-colony stimulating factor (G-CSF) is a substance used to increase the number of neutrophils after chemotherapy.

Hematologist. A doctor who specializes in treating blood diseases.

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

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

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

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

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

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

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

Inversion. A genetic abnormality that occurs when a section of a chromosome breaks off, turns upside down and then reattaches. As a result, the genetic material is inverted and is now in a different order.

See the free LLS book *Understanding Genetics*.

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

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

Leukocyte. See White Blood Cell.

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

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

Lymphocyte. A type of white blood cell that is important to the body's immune system. There are three major types of lymphocytes:

1) B lymphocytes (B cells), which produce antibodies to help combat infections; 2) T lymphocytes (T cells), which have several functions, including assisting B lymphocytes in making antibodies; and 3) natural killer (NK) cells, which can attack virus-infected cells or tumor cells.

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

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

Maintenance Therapy. Treatment that is given to help keep cancer from coming back after it has gone into remission following initial treatment.

Marrow. See Bone Marrow.

Minimal Residual Disease (MRD). The small amount of cancer cells that may remain in the body after treatment, even when the patient's blood and bone marrow may appear to be normal. These residual cancer cells

cannot be seen under a microscope and can only be identified by other very sensitive tests like polymerase chain reaction (PCR), next generation sequencing or flow cytometry. Also called “measurable residual disease.”

See the free LLS booklet *Minimal Residual Disease*.

Monoclonal Antibody. A type of synthetic protein that can bind to substances in the body, including cancer cells. Monoclonal antibodies are used in cancer treatment to target cancer cells; they can be used alone or modified to be attached to chemotherapy drugs.

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

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

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

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

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

Neutrophil. A type of white blood cell, and the principal type of phagocyte (microbe-eating cell), in the blood. It is the main type of cell that combats infection. People with some forms of blood cancer, or who have received treatment such as chemotherapy for cancer, often have low neutrophil counts. People with low neutrophil counts are very susceptible to infections and may be advised to take antibiotics daily to prevent potentially life-threatening infections.

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

Off-Label. The legal use of a prescription drug to treat a disease for which the drug has not been approved by the FDA.

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

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

Performance Status. A measure of how well a person is able to perform ordinary tasks and carry out daily activities.

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

Peripheral Blood Smear. A procedure in which a sample of blood cells is stained (dyed) and examined under a microscope to check for unusual changes in the size, shape and appearance of various types of blood cells and also for the presence of blast cells in the blood.

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

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

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

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

Polymerase Chain Reaction (PCR). A very sensitive genetic laboratory test that is used to detect and measure some genetic mutations and chromosomal changes that cannot be seen with a microscope. It essentially amplifies (increases) small amounts of specific pieces of either DNA or RNA so that they are easier to detect and measure. This test can find a single cancer cell among more than 500,000 to 1,000,000 healthy blood cells.

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

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

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

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

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

Reduced-Intensity Stem Cell Transplantation. A type of allogeneic stem cell transplantation in which patients receive lower doses of chemotherapy drugs and/or radiation in preparation for the transplant. The chemotherapy and radiation do not completely kill all the leukemia cells, but the new immune cells that the patient receives in the transplant may attack the leukemia cells. This protocol may be safer than a traditional high-dose conditioning or “myeloablative” allogeneic stem cell transplant, especially for older patients. **See the free LLS book *Blood and Marrow Stem Cell Transplantation*.**

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

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

Remission. When signs of a disease disappear, usually following treatment.

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

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

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

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

Spinal Tap. See Lumbar Puncture.

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

Standard of Care. Treatment that is accepted by medical experts as a proper treatment for a disease and that is widely used by healthcare professionals.

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

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

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

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

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

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

genes in the location at which the break occurs may be affected, which may lead to medical problems. See Mutation. **Also see the free LLS booklet *Understanding Genetics*.**

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

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

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NOTES



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