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Acute Myeloid Leukemia

Support for this publication provided by

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Support by an educational grant from Daiichi Sankyo, Inc.

Revised **2017**

A Message from Louis J. DeGennaro, PhD

President and CEO of The Leukemia & Lymphoma Society

The Leukemia & Lymphoma Society (LLS) is the world's largest voluntary health organization dedicated to finding cures for blood cancer patients. Our research grants have funded many of today's most promising advances; we are the leading source of free blood cancer information, education and support; and we advocate for blood cancer patients and their families, helping to ensure they have access to quality, affordable and coordinated care.

Since 1954, we have been a driving force behind almost every treatment breakthrough for blood cancer patients. We have invested more than $1 billion in research to advance therapies and save lives. Thanks to research and access to better treatments, survival rates for many blood cancer patients have doubled, tripled and even quadrupled.

Yet we are far from done.

Until there is a cure for cancer, we will continue to work hard—to fund new research, to create new patient programs and services, and to share information and resources about blood cancers.

This booklet has information that can help you understand acute myeloid leukemia, prepare your questions, find answers and resources, and communicate better with members of your healthcare team.

Our vision is that, one day, all people with acute myeloid leukemia will either be cured or will be able to manage their disease so that they can experience a great quality of life. Today, we hope our expertise, knowledge and resources will make a difference in your journey.

Louis J. DeGennaro, PhD
President and Chief Executive Officer
The Leukemia & Lymphoma Society

Inside this Booklet

Acknowledgement

The Leukemia & Lymphoma Society gratefully acknowledges, for his critical review and important contributions to the material presented in this booklet,

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Introduction

This booklet provides information about acute myeloid leukemia (AML) for patients and their families. AML may be called by other names, including "acute myelogenous leukemia," "acute myelocytic leukemia," "acute myeloblastic leukemia" and "acute granulocytic leukemia."

AML is the most common form of acute leukemia in adults. An estimated 21,380 new AML cases are expected to be diagnosed in the United States in 2017. As of January 2013, an estimated 48,615 people were either living with (or were in remission from) AML. Although AML can occur at any age, adults aged 60 years and older are more likely to develop the disease than younger people.[1]

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

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

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

We are here to help.

[1] *Facts 2016-2017*.

Resources and Information

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

For Help and Information

Consult with an Information Specialist. Information Specialists are master's level oncology social workers, nurses and health educators. They offer up-to-date disease and treatment information. Language services are available. For more information, please

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

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

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

Continuing Education. LLS offers free continuing education programs for healthcare professionals. For more information, please visit www.LLS.org/professionaled.

Co-Pay Assistance Program. LLS offers insurance premium and medication co-pay assistance for eligible patients. For more information, please

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

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. To join, visit www.LLS.org/community.

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

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

- 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.

Clinical Trials (Research Studies). New treatments for patients are under way. Patients can learn about clinical trials and how to access them. For more information, please call (800) 955-4572 to speak with an LLS Information Specialist who can help conduct clinical-trial searches. When appropriate, personalized clinical-trial navigation by trained nurses is also available.

Advocacy. The LLS Office of Public Policy (OPP) enlists volunteers to advocate for policies and laws to speed new treatments and improve access to quality medical care. For more information, please

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

Additional Help for Specific Populations

Información en Español (LLS information in Spanish). For more information, please visit www.LLS.org/espanol.

Language Services. Let your doctor know if you need a language interpreter or other resource, such as a sign language interpreter. Often, these services are free.

Children. AML occurs in a small number of children. Families face new and unfamiliar treatments and care protocols. The child, parents and siblings may all need support. For more information, please

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

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

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

For more information, please

- Call: WTC Health Program at (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) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov. Enter "depression" in the search box.

Feedback. To give suggestions about this booklet, visit www.LLS.org/publicationfeedback.

Leukemia

Leukemia is a cancer of the blood and bone marrow. Most blood cells form in the bone marrow, the spongelike tissue in the center of most bones. Leukemia begins in the hematopoietic stem cell (an immature blood cell) in the bone marrow. The cell undergoes a change (mutation) and becomes a type of leukemia cancer cell.

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

The four major types of leukemia are

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

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

Leukemia is also classified by the type of blood cell that becomes cancerous. Leukemia is called "myeloid" (or "myelogenous") if the cancerous cell change originates in cells in the myeloid cell line. Normally, cells start out as myeloid stem cells and eventually become red blood cells, platelets and most types of white blood cells. Leukemia is called "lymphocytic" (or "lymphoblastic") if the cancerous change starts in the lymphoid cell line. Normally, bone marrow cells become lymphocytes (a type of white blood cell).

More general information about AML is given in the free LLS booklet, *The AML Guide: Information for Patients and Caregivers.*

About Acute Myeloid Leukemia

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

By the time that AML is diagnosed, the number of healthy blood cells (red blood cells, white blood cells and platelets) is usually lower than normal. At this point, anemia, infection, or easy bleeding may happen.

The medical term for a	Is
Low red blood cell count	Anemia
Low platelet count	Thrombocytopenia ("thrombocyte" is another word for platelet)
Low neutrophil count (a neutrophil is a type of white blood cell)	Neutropenia

Incidence, Causes and Risk Factors. AML is the most common acute leukemia affecting adults. Older people are more likely than younger adults or children to develop AML.

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

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

- Age. The risk of developing AML increases with age. While AML can occur at any age, it typically affects older adults.

  The risk for developing AML increases about 8-fold from ages 30 to 34 years

(about 1.5 case per 100,000 people) to ages 65 to 69 years (about 11.9 cases per 100,000 people). For people over 70, the incidence rate continues to increase, peaking between the ages of 80 and 84 (see Figure 1).

Acute Myeloid Leukemia: Age-Specific Incidence Rates (2009 - 2013)

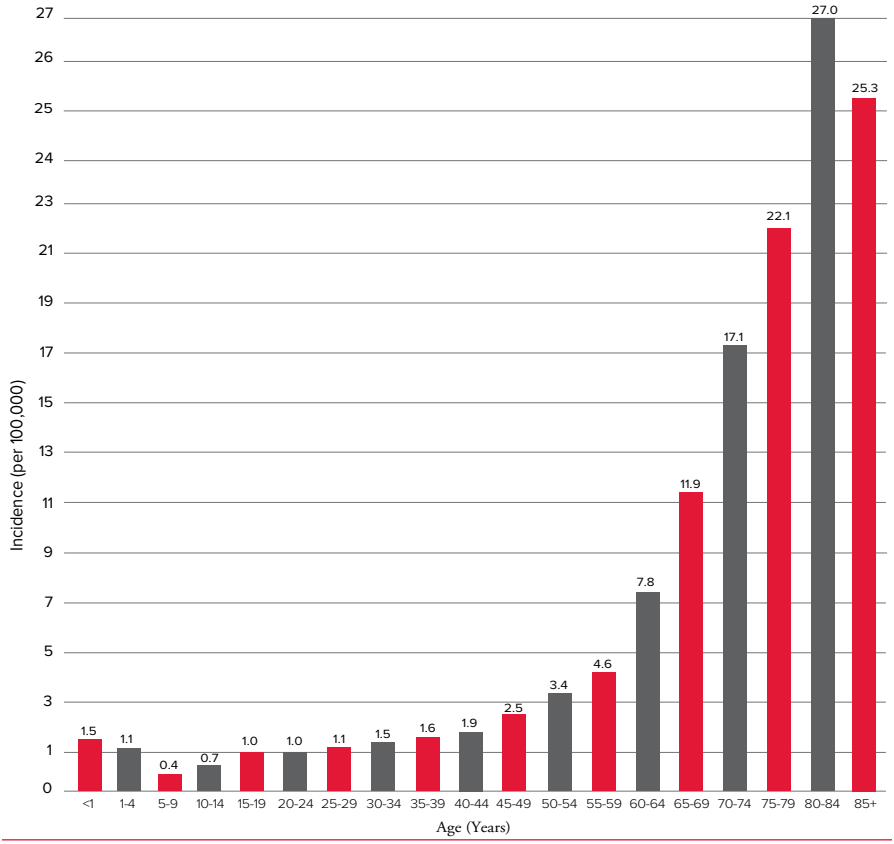

Figure 1. | The horizontal axis shows 5-year age intervals. The vertical axis shows the frequency of new cases of AML per 100,000 people, by age-group. Source: Surveillance, Epidemiology and End Results [SEER] Program; Cancer Statistics Review, 1975-2013.National Cancer Institute; 2016).

- Gender. Men are more likely than women to develop AML.
- Exposure to dangerous chemicals. Long-term exposure to high levels of certain chemicals, such as benzene, is linked to a greater risk of AML. Benzene is found in certain industrial settings; however, the strict regulation of its use has decreased benzene exposure in the workplace.
- Smoking. AML is linked to tobacco smoke, which contains benzene and other cancer-causing substances. According to the Agency for Toxic Substances and Disease Registry, despite the fact that petroleum products contribute to most of

the benzene in the atmosphere, half of the total national personal exposure to benzene comes from cigarette smoke.

- Previous cancer treatment. Prior cancer treatment with chemotherapy (especially with alkylating agents [such as cyclophosphamide and busulfan], platinum drugs or topoisomerase II inhibitors [such as etoposide and doxorubicin]) or radiation therapy may increase a person's risk of developing AML. This is often called "treatment-related" or "therapy-related" AML.
- Exposure to very high doses of radiation. People exposed to very high levels of radiation (for example, survivors of an atomic bomb blast or a nuclear reactor accident) are at increased risk of developing AML.
- Other blood disorders. People who have certain blood disorders including myeloproliferative disorders, such as polycythemia vera, essential thrombocythemia and myelofibrosis, are at greater risk of developing AML. For some people who have myelodysplastic syndromes (MDSs), their disease can evolve over time into AML.
- Genetic disorders. Certain genetic conditions present at birth seem to increase the risk of AML. These include
  - Down syndrome
  - Neurofibromatosis type 1
  - Bloom syndrome
  - Trisomy 8
  - Fanconi anemia
  - Klinefelter syndrome
  - Wiskott-Aldrich syndrome
  - Kostmann syndrome
  - Shwachman-Diamond syndrome.

Signs and Symptoms. Signs and symptoms are changes in the body that may indicate disease. A sign is a change that the doctor sees in an examination or a lab test result. A symptom is a change that a patient can see or feel. A person who has signs or symptoms that suggest the possibility of leukemia is usually referred to a specialist. This may be a hematologist-oncologist. A hematologist-oncologist is a doctor who has special training in diagnosing and treating blood cancers such as leukemia, lymphoma and myeloma.

The doctor will order tests to make a diagnosis (see *Diagnostic Testing* on page 11). The signs and symptoms of AML are also associated with a number of other, less serious diseases.

It is common for people with AML to feel a loss of well-being because of the underproduction of normal blood cells. Many signs and symptoms of AML occur because there is a shortage of normal blood cells. This happens when the leukemia cells in the bone marrow crowd out or suppress the normal blood-making cells. Consequently, people do not have sufficient numbers of red blood cells, white blood cells and platelets.

Symptoms due to low red blood cell counts (anemia) include

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

Symptoms due to low white blood cell counts include

- Frequent infections
- Fever.

Symptoms due to low platelet counts include

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

Other general symptoms of AML include

- Mild fever
- Swollen gums
- Loss of appetite
- Unexplained weight loss
- Discomfort in bones or joints
- Enlarged spleen
- Enlarged liver.

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

Diagnostic Testing

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

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

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

Medical History and Physical Examination. If a person has signs or symptoms of leukemia, the doctor will take a thorough medical history. The history may include information about past illnesses, injuries, treatments and medications. Some illnesses run in families, so the doctor may also ask about the health of the patient's blood relatives. The doctor will want to know about the patient's current symptoms and conduct a physical examination. During the examination, the doctor may listen to the patient's lungs and heart and carefully examine the body for signs of infection and disease. To check the internal organs, the doctor may also feel (palpate) different parts of the patient's body. For example, the doctor may feel the abdomen to see if the patient has an enlarged spleen.

Blood and Bone Marrow Samples. If the signs and symptoms suggest that the person may have leukemia, the doctor will test the blood and bone marrow. The findings from blood and bone marrow tests are used for making a diagnosis and treatment decisions. The doctor may also refer the patient to a hematologist-oncologist, a doctor who has special training in diagnosing and treating blood cancers.

Blood samples are generally taken from a vein in the patient's arm. Bone marrow aspiration and biopsy are two procedures used to examine bone marrow cells for

abnormalities and are generally done at the same time. The samples are usually taken from the patient's hip bone (after medicine has been given to numb the skin). Bone marrow has both a solid and liquid part. For a bone marrow aspiration, a special hollow biopsy needle is inserted through the hip bone and into the marrow to remove (aspirate) a liquid sample of cells. For a bone marrow biopsy, a specialized wider needle is used to remove a core sample of solid bone that contains marrow.

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

Complete Blood Count (CBC) with Differential. This test is used to measure the number of red blood cells, white blood cells and platelets in a sample of blood. It 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. The differential measures the numbers of the different types of white blood cells in the sample. People with AML may have

- A low red blood cell count
- A low platelet count
- A high white blood cell count (too many immature white blood cells that are not normally found in the peripheral blood)
- Blasts, leukemia cells, in the blood. Normally, there are no blast cells in a healthy person's blood.

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

Most patients with AML have	Blood tests used
Lower-than-expected red cell and platelet counts	**CBC** – Blood cell counts are determined by a blood test called a "complete blood count (CBC)."
Too many immature white cells and too few mature white cells	**Peripheral Blood Smear** – An examination of the stained (dyed) blood cells with a microscope usually shows the presence of leukemic blast cells (myeloblasts). These immature cells do not function like normal, mature white blood cells.

Blood Chemistry Profile. A test done on a sample of blood to measure the levels of certain substances released into the blood by organs and tissues in the body. These substances include electrolytes (such as sodium, potassium and chloride), fats, proteins, glucose (sugar), uric acid and enzymes. Blood chemistry tests give important information about how well a person's kidneys, liver and other organs are

working. These tests are not used to diagnose leukemia, but an abnormal amount of a particular substance in the blood may be a sign of disease or other health problems.

HLA Typing. HLA typing is a blood test that identifies a person's HLA type. Human leukocyte antigens (HLAs) are proteins found on the surface of most cells in the body. These proteins make up a person's tissue type, which varies from person to person. HLAs play an important role in the body's immune response to foreign substances by helping the body to distinguish its own cells from foreign cells. HLA matching is done before a donor stem cell transplantation to find out if there is a tissue match between the donor and the person receiving the transplant. HLA typing is not used to diagnose leukemia. It is, however, an important test for newly diagnosed AML patients if an allogeneic stem cell transplantation is being considered as a treatment option.

Cell Assessment. A hematopathologist will examine a sample of bone marrow cells under the microscope to determine the size, shape, type of cells and identify other features of the cells. A significant finding is whether the cells look more like normal, mature blood cells or more like abnormal, immature blood cells (blast cells). The percentage of blast cells in the sample is very important. Generally a diagnosis of AML requires 20 percent or more blasts in the bone marrow (see Figure 2).

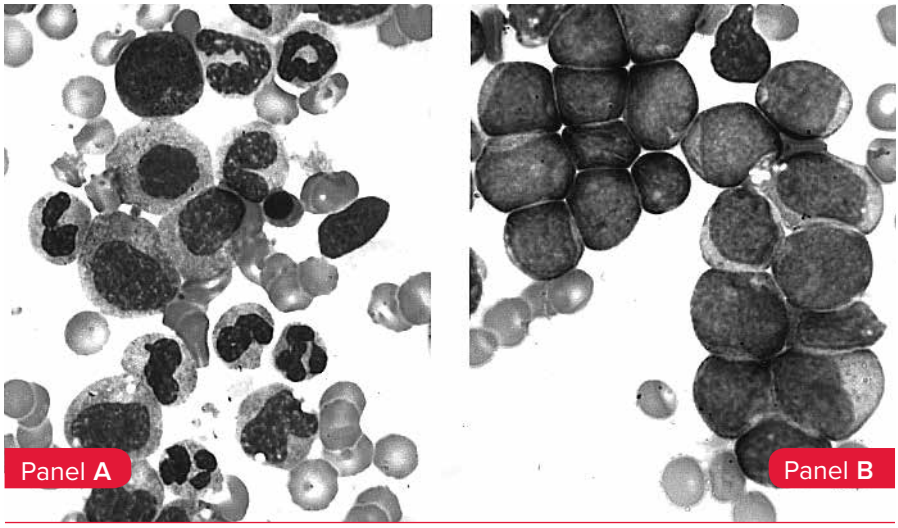

Figure 2. | **Panel A** shows normal marrow cells seen through a microscope. The darker shapes are the nuclei of the cells. Some of the nuclei are circular and some are horseshoe shaped, reflecting the different developmental stages and the different types of cells. **Panel B** shows AML blast cells seen through a microscope. These cells are "arrested" in an early stage of development. The AML cells in panel B all have a similar appearance, in contrast to the varied appearance of the normal cells in panel A.

Immunophenotyping (Flow Cytometry). A test used to classify cells in a sample based on the type of antigens, or markers, on the surface of the cells. A sample of cells is treated with special man-made antibodies that only stick to the

cells if the cells have a specific antigen on them. The cells are then passed through a laser beam. If the cells have the antibodies attached to them, they will give off light. Leukemia cells can have different antigens on their surface depending on whether they are myeloid or lymphoid and their stage of development. There are certain antigens called cluster designation (CD) proteins that are relatively specific to AML cells such as CD13, CD14, CD33 or CD34. This test in addition to making a diagnosis, is used for evaluating minimal residual disease (MRD).

Genetic Tests. The following tests are done to look at a patient's leukemia cell genes.

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

Normal human cells contain 23 pairs of chromosomes, each of which are a certain size, shape and structure. In some cases of AML, the chromosomes of leukemia cells have abnormal changes that can be seen under a microscope, such as deletions, translocations and extra chromosomes. 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 stained sample is examined under a microscope and then photographed to show the arrangement of the chromosomes. This is called a "karyotype." The karyotype will show if there are any abnormal changes in the size, shape, structure or number of chromosomes in the leukemia cells. See Figure 3, below.

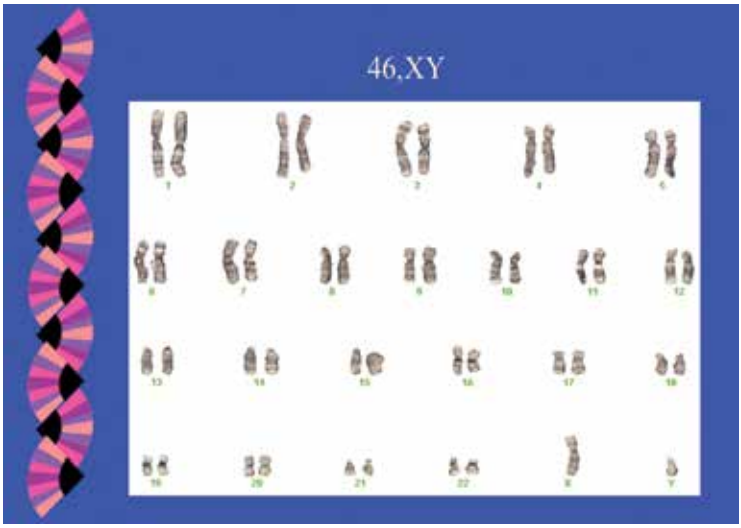

Figure 3. | This figure shows a normal male karyotype. (Courtesy of Dr. Dong Chen, hemato-pathologist, Mayo Clinic, Rochester, MN)

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

Fluorescence in situ Hybridization (FISH). FISH is a very sensitive test used to look at genes or chromosomes in cells and tissues. In cases of AML, doctors use FISH to detect certain abnormal changes in the chromosomes and genes of leukemia cells. Pieces of DNA that contain special fluorescent dyes are made in the laboratory and added to the leukemia cells on a glass slide. When the pieces of DNA bind to specific genes or areas of chromosomes on the slide, they light up when viewed under a fluorescent microscope. FISH can identify most abnormal changes that can be seen with a microscope, but it can also detect some changes that are too small to be seen with basic cytogenetic testing. It is not, however, a general screening tool. FISH has one disadvantage—the doctor must select specific chromosomes or genes to examine before running the test.

Molecular Testing. Molecular genetic tests are very sensitive DNA tests that examine specific genetic traits of cancer cells. In addition to chromosomal abnormalities, genetic mutations have been shown to play an increasingly important role in the prognosis and treatment of AML. Molecular testing does not replace cytogenetic testing, but together these tests help refine prognosis and treatment options especially for nearly half of all AML patients who have no detectable chromosomal abnormalities.

DNA sequencing is a type of molecular test that checks for specific gene mutations in cells. Since the introduction of DNA sequencing, the number of mutated genes found in AML patients has increased considerably. Next-generation sequencing of AML genomes has identified an average of 13 mutations per patient. Researchers and doctors, however, do not always agree on which mutations are good or bad indicators of prognosis to the current or "standard" treatment. Current standard of care combines cytogenetic analysis with testing for mutations of a number of single genes, *FLT3, NPM1, CEBPA,* and *KIT*. These markers are important in guiding treatment decisions for risk assessment, prognostication and may also guide treatment decision making.

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

Diagnosis

The diagnosis of AML generally requires the identification of 20 percent or more leukemic blasts of myeloid origin in the peripheral blood and/or bone marrow. AML is not one single disease but a heterogeneous disease that is characterized by many chromosomal abnormalities and gene mutations. AML is divided into subtypes that are based upon a patient's laboratory results.

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

WHO developed a classification system to include prognostic factors such as chromosomal abnormalities and genetic mutations that are known to affect prognosis. These genetic factors help provide patients and their doctors with more reliable information regarding their prognosis and their response to treatment.

The WHO classification is usually revised every eight years. The revised 2016 classification incorporates new scientific and clinical information (see Table 1).

Acute Myeloid Leukemia Classification

Acute myeloid leukemia (AML) and related neoplasms

	Inversion and/or Translocation	Gene
AML with recurrent genetic abnormalities		
AML with	t(8;21)(q22;q22.1)[1]	*RUNX1-RUNX1T1*
AML with	inv(16)(p13.1q22) or t(16;16)(p13.1;q22)	*CBFB-MYH11*
APL	t(15;17)	*PML-RARA*
AML with	t(9;11)(p21.3;q23.3)	*MLLT3-KMT2A*
AML with	t(6;9)(p23;q34.1)	*DEK-NUP214*
AML with	inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)	*GATA2, MECOM*
AML (megakaryoblastic) with	t(1;22)(p13.3;q13.3)	*RBM15-MKL1*
AML with		mutated *NPM1*
AML with		Biallelic mutations of *CEBPA*

AML with myelodysplasia-related changes		
Therapy-related myeloid neoplasms		
AML, Not Otherwise Specified (NOS)		
AML with minimal differentiation		
AML without maturation		
AML with maturation		
Acute myelomonocytic leukemia		
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)	*BCR-ABL1*
MPAL with	t(v;11q23.3)	*KMT2A* rearranged
MPAL, B/myeloid, NOS		
MPAL, T/myeloid, NOS		

Table 1. | Based on the World Health Organization (WHO) classification. This new classification categorizes AML into groups based on more recent discoveries about the cytogenetic and clinical features of AML.
[1]Cytogenetic changes are sometimes abbreviated. For example,

- t– a translocation beween chromosomes.
- inv– an inversion in a chromosome.
- q– the long arm of a chromosome (the lower half)
- p– the short arm of a chromosome (the upper half)

Prognostic Factors. Various factors affect treatment options and the patient's prognosis, the likely outcome or course of a disease. A characteristic or attribute that helps predict prognosis is called a "prognostic factor." Doctors use prognostic factors to help predict how AML will likely progress and respond to treatment. Some prognostic factors are associated with a lower risk that AML may not return after treatment. These are called "favorable-risk factors." Other factors are associated with a higher risk that AML may return after treatment. These are called "poor-risk factors." Doctors use a variety of factors to classify AML.

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

Common Chromosome Abnormalities

Risk Status	Chromosomes (Cytogenetic Analysis)
Most Favorable (low risk)	• Translocation between chromosomes 8 and 21 t(8;21)[1] • Inversion of chromosome 16 inv(16) • Translocation between chromosome 16 and itself t(16;16) • Translocation between chromosomes 15 and 17 t(15;17) (APL)
Intermediate (intermediate risk)	• Normal cytogenetics • Trisomy 8 • t(9;11). Translocation between chromosome 9 and 11.
Least Favorable (high risk)	• Complex changes involving 3 or more chromosomal abnormalities • Monosomal karyotype (having a single copy of a chromosome pair instead of the usual two copies) • Deletion of part of chromosome 5 or 7 or monosomy of chromosomes 5 or 7, -5, 5q-, -7, 7q- • 11q23. Abnormalities of chromosome 11 (at the spot q23) • Translocation or inversion of chromosome 3 inv(3), t(3;3) • Translocation between chromosomes 6 and 9 t(6;9) • Translocation between chromosomes 9 and 22 t(9;22)

Table 2. Based on National Comprehensive Cancer Network guidelines.
[1]Cytogenetic changes are sometimes abbreviated. For example,
- t– a translocation between chromosomes
- inv– an inversion in a chromosome
- del– a piece of the chromosome is missing (deleted).
- q– the long arm of a chromosome (the lower half)

Molecular Abnormalities (Gene Mutations). AML patients whose leukemia cells have certain genetic mutations are assigned a specific risk status (see Table 3). For example, patients with a *NPM1* gene mutation (without a *FLT3-ITD* gene mutation) seem to have a better prognosis than people without the *NPM1* mutation. Talk to your doctor about treatments available to target specific genetic mutations.

Common Molecular Abnormalities

Risk Status	Molecular Abnormalities
Favorable Risk	• Normal cytogenetics with *NPM1* mutation in the absence of *FLT3-ITD* mutation • Normal cytogenetics with *CEBPA* mutation in the absence of *FLT3-ITD* mutation.
Intermediate Risk	• Core binding factor leukemias t(8;21) and inv(16) or t(16;16) with *KIT* mutation • Associated with *NPM1* and *FLT3-ITD* mutations
Poor Risk	• Normal cytogenetics (karyotype) with *FLT3-ITD* mutation • *TP53* mutation

Table 3. Based on National Comprehensive Cancer Network guidelines.

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

Therapy-Related AML. Patients who have received chemotherapy in the past to treat a different cancer, may develop AML that is more resistant to treatment. Therapy-related AML is associated with a worse outcome.

Prior Blood Cancer. When a patient has had a prior blood cancer, such as myelodysplastic syndrome or a myeloproliferative neoplasm, AML is associated with a poorer outcome.

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

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

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

Systemic Infection at Diagnosis. An AML patient with a systemic infection, an infection affecting the entire body, at diagnosis is more likely to have a poorer outcome.

High White Blood Cell Count. About 5 percent of AML patients develop signs or symptoms attributable to a very high blast cell count. A white blood cell count greater than 100,000 cells per microliter (100,000 cells/μL) at the time of diagnosis is associated with unfavorable risk.

Treatment

A diagnosis of AML is associated with a wide range of outcomes. Patients with different subtypes of AML may have different responses to treatment. The main treatment for AML is chemotherapy, sometimes followed by a stem cell transplant. Other drugs may be used to treat patients with acute promyelocytic leukemia (APL).

Chemotherapy. The current "standard" treatment for AML includes induction chemotherapy with a cytarabine/anthracycline combination followed by either one to four cycles of consolidation (postremission) chemotherapy or a stem cell transplantation. However, participation in clinical trials is strongly encouraged or preferred.

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 eradicate leukemia cells or stop new leukemia cells from forming. Therefore, more than one chemotherapy drug is frequently used.

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

Some chemotherapy drugs may be injected into a vein. An intravenous (IV) infusion is a slow injection (infusion) into a vein that may take a few hours or, it may take several days (a continuous infusion). Often, doctors give IV chemotherapy through a thin soft tube called a "central venous line," "catheter," or "central line." When a patient has a central line in place (in situ), doctors administer IV chemotherapy treatments via the line and do not have to "stick" a patient's vein with a needle each time a treatment is administered. Doctors can also access the central line to give other medicines and take blood samples. A central line can be left in place for weeks or months.

See the free LLS booklet, *Understanding Side Effects of Drug Therapy* for additional information about drug administration.

Treating AML. In newly diagnosed, untreated AML, the patient has only received treatment to relieve symptoms such as fever, bleeding or pain. However, AML is an aggressive leukemia and should be treated as soon as possible. Often treatment of AML is divided into two phases, induction chemotherapy and consolidation therapy. Participation in a carefully conducted clinical trial may be the best available therapy.

Induction Therapy. The initial phase of chemotherapy is called "induction therapy." The goal of induction therapy is a complete remission. A complete remission is achieved when there are less than 5 percent blast cells in the bone marrow, blood counts (red blood cells, white blood cells and platelets) have returned to normal and there are no signs or symptoms of the disease. Although obtaining a remission is the first step in controlling AML, it is also important for patients to emerge from the induction phase physically fit enough to tolerate intensive treatments during the consolidation phase (see page 23).

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

The most common induction regimen for AML includes the drug cytarabine and an anthracycline drug such as daunorubicin or idarubicin. Cytarabine is most often given continuously for 7 days intravenously (IV) while the anthracycline drug is given IV in a single dose for 3 days during the first week of treatment. This is called the "7 + 3" regimen. The induction therapy is usually given in the hospital and lasts about a week. Other drugs may be added or substituted for higher-risk patients. For newly diagnosed adult patients that are *FLT3* mutation positive as detected by an FDA-approved test, the FDA has approved midostaurin (Rydapt®) in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation. Midostaurin is not indicated as a single-agent induction therapy. Gemtuzumab ozogamicin (Mylotarg™) is FDA approved for the treatment of adults with newly diagnosed AML whose tumors express the CD33 antigen (CD33-positive AML). Daunorubicin and cytarabine (Vyxeos™), a liposomal combination, is FDA approved for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC).

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

About 1 to 2 weeks after the completion of induction therapy (day 14 or 21 of treatment), the doctor will take bone marrow samples to evaluate the effectiveness of the treatment. For patients who have a higher percentage of leukemia or blast cells, induction therapy can be either repeated with the same drugs or a new chemotherapy regimen can be given. About 3 to 4 weeks after the completion of induction therapy, normal bone marrow cells should return and start making new blood cells. This state is called "complete remission." Patients who are unable to achieve a remission with standard care should be considered for a clinical trial, an allogeneic stem cell transplantation or drug regimens for relapsed/refractory disease.

Table 4, on page 22, lists some of the standard drugs used to treat AML patients, as well as some of the drugs under study in AML clinical trials. For more information, please visit www.LLS.org/drugs or call our Information Specialists at (800) 955-4572.

Some Drugs That are Used to Treat AML or are in Clinical Trials

Most antileukemic drugs affect the cell's genetic material (the DNA).

Anthracyclines (Antitumor Antibiotics)

- daunorubicin (Cerubidine®)
- doxorubicin (Adriamycin®)
- idarubicin (Idamycin®)
- mitoxantrone (Novantrone®)

Antimetabolites

- cladribine (2-CdA; Leustatin®)
- clofarabine (Clolar®)
- cytarabine (cytosine arabinoside, ara-C; Cytosar-U®)
- fludarabine (Fludara®)
- methotrexate
- 6-mercaptopurine (Purinethol®)
- 6-thioguanine (Thioguanine Tabloid®)

Anthracycline and Antimetabolite

- fixed combination of daunorubicin and cytarabine (Vyxeos™)

Topoisomerase Inhibitors

- etoposide (VP-16; VePesid®, Etopophos®)
- topotecan (Hycamtin®)

DNA Damaging (Alkylating) Agents

- cyclophosphamide (Cytoxan®)
- carboplatin (Paraplatin®)
- temozolomide (Temodar®)

Cell-Maturing Agents

- all-*trans* retinoic acid (ATRA, tretinoin; Vesanoid®)
- arsenic trioxide (Trisenox®)

Hypomethylating Agents

- azacitidine (Vidaza®)
- decitabine (Dacogen®)

Immunomodulator

- lenalidomide (Revlimid®)

Histone Deacetylase Inhibitors

- pracinostat
- panobinostat (Farydak®)
- vorinostat (Zolinza®)

Antibody Conjugate

- gemtuzumab ozogamicin (Mylotarg®)

FLT3 Inhibitors

- quizartinib (AC-220)
- sorafenib (Nexavar®)
- midostaurin (Rydapt®)

IDH2 Inhibitor

- enasidenib (Idhifa®)

Table 4. This table lists some drugs used in standard treatment for AML and some drugs under study in clinical trials. A patient may be treated with drugs that are not listed in this table and still be receiving appropriate and effective treatment.

Postremission Therapy (Consolidation Therapy). Normal blood cell production should return in many patients several weeks after induction therapy is completed. Blood cell counts gradually approach normal, well-being returns and AML cells cannot be detected in blood or bone marrow. This condition is called a "remission." A small number of residual AML cells will not interfere with normal blood cell development, but they do have the potential to grow and cause a relapse of the AML. "Minimal residual disease" is a term used after treatment when leukemia cells cannot be detected in the bone marrow using standard tests, such as examining a bone marrow sample under a microscope. These remaining cells, however, can be detected using more sensitive tests such as flow cytometry and PCR.

Once a patient achieves a complete remission, more treatment is usually needed to destroy any residual leukemia cells in the body. Without additional therapy, the leukemia is likely to return within months. To prevent a recurrence of leukemia, intensive consolidation therapy is given after the patient recovers from induction therapy. The goal of consolidation therapy is to either lower the number of, or eliminate, the residual leukemia cells in the body.

There are two basic treatment choices for postremission therapy. They are

- More intensive chemotherapy
- Stem cell transplantation (allogeneic, reduced-intensity allogeneic or autologous).

Favorable-risk patients are often offered intensive chemotherapy using high-dose cytarabine and other drugs for their consolidation therapy. Patients are generally given multiple cycles of chemotherapy. The number of chemotherapy cycles required during consolidation varies from patient to patient. Patients are often hospitalized for postremission therapy. The length of stay varies depending on the treatment and other factors.

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

Stem Cell Transplantation. Some patients may benefit from intensive chemotherapy alone. Others may benefit from stem cell transplantation. Stem cell transplantation is used to help patients recover from aggressive cancer treatments.

Chemotherapy can cause very serious side effects. Even though higher doses of these drugs may kill more leukemia cells, they cannot be prescribed because they would severely damage a patient's bone marrow resulting in anemia, serious infections and uncontrolled bleeding. Stem cell transplantation allows doctors to give higher doses of chemotherapy than cannot typically be given. Chemotherapy is sometimes given along with radiation therapy. After treatment, the patient receives an infusion of stem cells to replace the stem cells destroyed by the intensive therapy. These new stem cells restore the bone marrow so that there are healthy stem cells that can form new red blood cells, white blood cells and platelets. There are three types of stem cell transplantation. They are

- Allogeneic (from a healthy HLA-matched donor (siblings or unrelated), umbilical cord or haploidentical (parents to children and vice versa)
- Reduced-intensity allogeneic
- Autologous.

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

Allogeneic Stem Cell Transplantation. Allogeneic stem cell transplantation is the most common type of stem cell transplantation used to treat AML. In preparation for the transplant, patients are given strong doses of chemotherapy, either with or without radiation, to kill the remaining leukemic cells in their bodies ("conditioning therapy"). Then, patients receive infusions of the donor stem cells. Allogeneic transplantation uses healthy blood-forming cells from an HLA-matched family member, unrelated donor, or an umbilical cord blood unit. The donated stem cells restore the bone marrow's ability to form new blood cells.

An allogeneic stem cell transplantation creates a new immune system for the patient. The immune system helps the body fight infections and other diseases. The new immune system has the potential to recognize and attack any remaining cancer cells. The transplanted immune cells (the graft) see the leukemia cells in the body as foreign and destroy them. This is called the "graft-versus-leukemia (GVL) effect."

Allogeneic stem cell transplantation, compared to other treatment approaches, is associated with a higher rate of side effects and mortality. It may, however, be considered for patients with higher-risk AML, based on cytogenetic and

molecular test results and currently available therapy. The decision to perform an allogeneic transplantation also depends on the age of the patient and the patient's understanding of the potential benefits and risks. The upper age limit for transplantation varies by treatment center; many centers use age 60 or 65 years for allogeneic transplantation and 70 years for reduced-intensity allogeneic transplantation.

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

Reduced-Intensity Stem Cell Transplantation (also called "nonmyeloablative" transplantation or "mini" transplantation).
A reduced-intensity stem cell transplantation is a type of allogeneic transplantation. It 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 transplantation. The conditioning therapy in a reduced-intensity transplant uses lower doses of chemotherapy and/or radiation to prepare the patient for the donor cells. The therapy reduces the number of cancer cells, but it does not completely destroy the patient's bone marrow. As in a standard allogeneic transplantation, the white blood cells from the donor may also recognize any remaining leukemia cells as foreign and destroy them. Over time, if the transplant is successful, the donor's stem cells replace the patient's immune cells. The engrafted donor immune cells recognize minor tissue antigens on the patient's leukemia cells and continue to suppress their growth.

As is the case with 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. Autologous stem cell transplantation is a procedure in which a patient's own bone marrow is removed, frozen and stored after achieving a remission during induction therapy. Once the cells are removed, the patient receives additional high doses of chemotherapy and/or radiation. Before the stem cells are infused back into the patient's blood, they undergo a process called "purging" to try to eliminate any leukemic cells before the stem cells are returned to the patient's body. Even after purging, there is the risk of returning some leukemia cells back to the patient.

Autologous transplantation is sometimes used for patients who do not have an HLA-matched donor. Autologous transplantations are usually easier for patients to

tolerate than allogeneic transplantations. This is because patients receive their own stem cells so the risk of some complications, such as graft-versus-host disease, is lower. The high doses of chemotherapy, however, can still cause major side effects. Autologous transplants are used less frequently than allogeneic transplants for AML patients mainly because of the lack of a graft-versus-leukemia effect and the risk of returning some leukemia cells back to the patient.

For further information about all types of stem cell transplantation, see the free LLS booklets, *Blood and Marrow Stem Cell Transplantation* and *Cord Blood Stem Cell Transplantation.*

Central Nervous System (CNS) AML. AML leukemia cells can spread to the cerebrospinal fluid, the fluid around the brain and spinal cord. CNS disease is uncommon, occurring in less than 3 percent of AML patients. Because CNS AML is rare, doctors often do not test for it at the time of diagnosis unless the patient is experiencing neurological symptoms such as headache or confusion. If neurological symptoms are present, the doctor may order an imaging test, such as a computed tomography scan (CT) scan or a magnetic resonance imaging scan (MRI), to rule out a hemorrhage or a brain tumor. If no hemorrhage or tumor is seen, the doctor will test the patient's cerebrospinal fluid (CSF) by lumbar puncture, either at the time of complete remission or before consolidation therapy.

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 CSF. 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, intrathecal chemotherapy is recommended. Intrathecal chemotherapy is a treatment in which anticancer drugs are injected directly into the spinal fluid. Intrathecal chemotherapy can be given at the same time as other chemotherapy drugs during induction therapy.

Routine screening for CNS AML is not recommended in most AML patients in remission. The exceptions are patients with

- Monocytic differentiation
- Biphenotypic leukemia
- A white blood count greater than 40,000 cells per microliter (40,000/mcL) at diagnosis.
- Inversion 16 (inv[16]) CD7- and CD56-positive (neural-cell adhesion molecule) immunophenotypes.

Refractory and Relapsed AML. Most patients achieve an initial remission. However, some patients have residual leukemic cells in their marrow, even after intensive treatment. This is referred to as "refractory leukemia." Between 10 and 40 percent of newly diagnosed AML patients do not achieve a complete remission with intensive induction therapy. Refractory disease is usually diagnosed in patients who have not achieved complete remission after two cycles of induction chemotherapy. There are other patients who have a return of leukemia cells in the marrow and a decrease in the number of normal blood cells after achieving a remission. This is referred to as "relapsed leukemia."

Treatment options for patients with refractory or relapsed disease include

- A clinical trial
- Enasidenib (Idhifa®)—This drug is given by mouth. It is FDA approved for the treatment of adult patients with relapsed or refractory AML with an isocitrate dehydrogenase-2 *(IDH2)* mutation as detected by an FDA-approved test.
- Palliative care—Palliative care refers to specialized medical care focused on providing relief from symptoms and the stresses of a serious illness. The goal is to improve quality of life for both the patient and the family. With a palliative approach, less toxic treatments are administered to keep the disease under control as long as possible. In this approach, the emphasis is on improving the patient's quality of life. Supportive care is an option for patients who either cannot or do not wish to pursue further intensive treatment. Increasingly, hematologists use the palliative care team in the care of all patients with AML at different phases of their treatment.
- Intensive chemotherapy and targeted therapy for patients younger than 60 or patients who are older than 60 and physically fit to induce a remission to "bridge" patients to an allogeneic stem cell transplantation
- Re-treatment with the previously successful induction regimen if relapse occurs 12 months or more after remission.

Optimal drug combinations, drug doses and administration schedules remain under investigation. There are several commonly used aggressive and less aggressive treatment regimens for refractory/relapsed disease.

Aggressive treatments for appropriate patients

- Cladribine+cytarabine+granulocyte-colony stimulating factor (G-CSF)±mitoxantrone or idarubicin
- High-dose cytarabine (if not received previously in treatment)±anthracycline
- Fludarabine+cytarabine+G-CSF±idarubicin
- Etoposide+cytarabine±mitoxantrone
- Clofarabine±cytarabine+G-CSF± idarubicin.

Less aggressive treatments

- Low-dose cytarabine
- Hypomethylating agents (5-azacitidine or decitabine)
- Hypomethylating agents (5- azacitidine or decitabine)+sorafenib for *FLT3-ITD* mutations
- Hypomethylating agents (5-azacitidine or decitabine)+midostaurin (Rydapt).

The Information Specialists at LLS offer guidance on how patients can work with their doctors to find out if a specific clinical trial is an appropriate treatment option. Information Specialists conduct clinical-trial searches for patients, family members and healthcare professionals. When appropriate, personalized clinical-trial navigation by trained nurses, is also available.

Acute Promyelocytic Leukemia (APL) Treatment. APL is a particularly aggressive subtype of AML. While it was once considered to be fatal, it is now one of the most curable subtypes of AML in adults. APL comprises approximately 10 percent of all AML cases and occurs primarily in middle-aged adults.

APL treatment differs from the other AML treatments described in this booklet. For more information about acute promyelocytic leukemia, please see the free LLS booklet *Acute Promyelocytic Leukemia Facts*.

Acute Monocytic Leukemia Treatment. In some types of leukemia, including the subtype of acute monocytic leukemia (see Table 1 on page 16), the leukemic blast cells sometimes invade the lining of the spinal cord or brain, and other internal organs. When the lining of the spinal cord or brain is involved, chemotherapy is injected into the spinal fluid. A lumbar puncture is the commonly used medical procedure to administer this chemotherapy. It is performed either under local anesthesia or with heavy sedation. During a lumbar puncture, a needle is placed between the vertebrae and into the spinal canal. Spinal fluid is extracted and the fluid volume is then replaced with fluid containing appropriate drugs, usually cytarabine or methotrexate. The spinal fluid specimen is sent to the lab and examined for leukemia cells.

AML Treatment in Older Adults. AML occurs more frequently with advancing age. At least half of patients are older than 65 years of age when the disease is diagnosed. The treatment of AML in older patients is a challenge; however, options include clinical trials, intensive or less-intensive chemotherapies, and only supportive therapies (in certain circumstances). Older patients are more likely to have other medical problems (comorbidities) including diabetes, high blood pressure, high cholesterol levels, heart disease, and history of stroke or lung disease. Older patients may also be taking multiple medications to control their medical problems, and these medications may interact with their cancer treatments. Additionally, older adults may also have poor performance status (the measurement

of how well a person is able to perform ordinary tasks and daily activities). Many older patients are not offered intensive treatments because they are considered unlikely to survive the rigors of intensive chemotherapy due to their comorbidities and poor performance status. In fact, in some cases, intense chemotherapy can actually shorten their lives.

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

There are, however, curative options available for some older patients with some subtypes of AML, like APL. For AML patients older than 60 years, patient performance status, other health issues and AML risk features are all considered in developing a treatment plan rather than just relying on a patient's chronological age. Age alone does not determine treatment options, and physically fit patients in their 70s and 80s who have no serious health problems may benefit from intensive treatment.

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

Diverse clinical trials are looking at novel drugs and combinations, including non-chemotherapy targeted agents directed to genetic markers of the leukemia cells. Examples include, lenalidomide (Revlimid®), clofarabine (Clolar®), pracinostat either alone or with low-dose cytarabine. Another novel regimen is volasertib, a potent inhibitor of the Plk1 (polo-like kinase 1) protein that is being studied for the treatment of AML in patients who are aged 65 years or older.

AML Treatment in Children. AML only accounts for approximately 20 percent of childhood leukemia cases. Most children who are diagnosed with leukemia have acute lymphoblastic (lymphocytic) leukemia. The improvement in overall survival rates has increased for children with AML, but much lower than that of ALL. Approximately 70 percent of pediatric AML patients achieve a complete remission after intensive induction therapy, and 60 to 65 percent are cured after postremission therapy. There is, however, a wide range in outcomes for different subtypes of AML based on genetic factors.

As with adults, AML treatment in children should be based on cytogenetic and

molecular factors to avoid overtreatment in patients with favorable prognoses and improve outcomes in those with unfavorable prognoses. The goal of treatment should be to cure the child by killing the leukemia cells while avoiding side effects and late effects of treatment as much as possible. Late effects are medical problems that do not develop or become apparent until years after treatment ends.

Like the treatment for adults, AML treatment for children usually consists of two phases: induction therapy and consolidation therapy, which may consist of intensive chemotherapy and/or allogeneic stem cell transplantation. Children with AML are usually treated with an induction therapy similar to that used for adults with AML: cytarabine and an anthracycline such as daunorubicin, idarubicin or mitoxantrone in combination with other agents such as etoposide (VP-16), Etopophos®, VePesid® and thioguanine (Tabloid®). Maintenance therapy is not part of most pediatric AML protocols except in cases of acute promyelocytic leukemia (APL). An option for relapsed or refractory patients is gemtuzumab ozogamicin (Mylotarg™) which is FDA approved for the treatment of patients aged 2 years and older with CD33-positive AML.

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

Two subtypes of childhood AML are treated differently. They are

- AML in children with Down Syndrome—Children with Down syndrome are at increased risk for developing AML, but in these children AML is more sensitive to chemotherapy. As a result, less intense chemotherapy may be used with very good cure rates. Children with Down syndrome who develop AML tend to have a good outlook, especially if they are diagnosed before the age of 4 years.
- Acute Promyelocytic Leukemia (APL)—APL represents approximately 7 percent of pediatric AML cases. APL is due to a translocation (a genetic change in which a piece of one chromosome breaks off and attaches to another chromosome) between chromosomes 15 and 17 denoted as t(15;17). As in adults, this subtype of AML is generally treated differently than other types of AML. It is usually treated with all-*trans* retinoic acid (ATRA) in combination with chemotherapy or arsenic trioxide. The standard approach to treating children with APL begins with induction therapy followed by consolidation and maintenance

therapy. Pediatric APL rarely spreads to the brain or spinal cord so intrathecal chemotherapy is generally not needed. Children with APL have high cure rates.

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

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

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

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

Children and adolescents with cancer should be referred to medical centers that have cancer specialists with experience treating pediatric cancers to ensure that children receive treatment, supportive care and rehabilitation that will help them achieve optimal survival and quality of life. Most children with leukemia take part in clinical trials. These clinical trials give children the opportunity to obtain the very latest treatment options being studied, options that may not be offered at all treatment centers.

See the free LLS booklet *Learning & Living with Cancer: Advocating for your child's educational needs* for information about planning for the child's entry or return to school following diagnosis and treatment. Also see the free LLS booklet *Long-Term and Late Effects of Treatment for Childhood Leukemia or Lymphoma Facts.*

Research and Clinical Trials

Today, people who are diagnosed with AML are typically treated with the same chemotherapy treatments that have been used for the past 40 years. The proportion of patients with AML who enter remission, stay in remission for years or are cured has not increased during the last 30 years. AML is still one of the most difficult cancers to treat. The challenge remains to develop treatments that cure patients of all ages and with all subtypes of AML.

With current treatment regimens, only a minority of AML patients are cured. Outcomes are particularly poor for older patients with low complete remission rates and there are few long-term survivors compared with the number of long-term survivors of younger patients. Given that almost half of AML patients are more than 70 years of age, a great unmet need exists for effective therapies for older patients that are less toxic than the chemotherapy regimens in use now.

There are new approaches under study in clinical trials for AML treatment, many of which are being supported by LLS research programs. LLS is also leading the offensive against AML with the LLS Beat AML Master Trial. LLS has convened an unprecedented collaboration of renowned academic researchers, pharmaceutical companies and a genomic provider to test multiple experimental treatments at the same time. This collaborative clinical trial is designed to develop better individualized treatments for AML patients and to facilitate FDA approval of new drugs for AML patients over 60 years of age.

Clinical Trials. AML patients are encouraged to explore clinical trials. Clinical trials test new drugs and treatments, many of which are supported by LLS research programs, before they are approved by the FDA as standard treatments. Every new drug or treatment regimen goes through a series of phases of clinical trials before it becomes part of standard therapy. Clinical trials are carefully designed and rigorously reviewed by expert clinicians and researchers to ensure as much safety and scientific accuracy as possible. Participation in a carefully conducted clinical trial may be the best available therapy.

Clinical trials are designed to be accurate and very safe. There are clinical trials for newly diagnosed patients, for patients with advanced disease, and for patients who are intolerant or resistant to their medications. Sometimes, a clinical trial is the best option for a patient. Clinical trials hold great promise to increase remission rates and find a cure for AML.

LLS Information Specialists, at (800) 955-4572, can offer guidance on how patients can work with their doctors to determine if a specific clinical trial is an appropriate treatment option. Information Specialists will conduct individualized

clinical-trial searches for patients, family members and healthcare professionals. When appropriate, personalized clinical-trial navigation by trained nurses, is also available.

Research 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 AML. The following 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 AML challenging. There is a need to identify these genetic variations and customize treatment options based on the genetic characteristics of the leukemia cells. Newer techniques in gene sequencing have revealed novel mutations that may be involved in the development of AML. This information will help researchers develop new targeted therapies, tailored to each patient's disease. For example, two genes appear promising for guiding AML therapy in the future. AML patients with a *DNMT3A* gene mutation may respond better to high-dose anthracyclines, and patients with a *RUNX1* gene mutation may have better outcomes with an allogeneic stem cell transplantation. These findings demonstrate that testing for gene mutations may improve treatment options. Additional testing will be needed to confirm these findings.

New Drugs and Treatment Regimens. Researchers are trying to find more effective and safer treatments for AML. Researchers are studying new drugs, and they are also studying the use of existing drugs given in different doses and on different schedules. In the last 10 years, improvements in overall survival of AML patients has been driven by using older chemotherapy drugs more effectively. Researchers are continuing to modify and reformulate traditional chemotherapy drugs to improve overall survival. They are also looking at combining chemotherapy with newer types of drugs to see if this approach may work to increase patient survival. Researchers are studying many new drugs for use in AML including

- Targeted therapy. A 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 but cause less harm to healthy cells.
    - FLT3 inhibitor. Approximately one-third of AML patients have a mutation in the *FLT3* gene which can increase the growth and division of AML cells. Patients with *FLT3* mutations have a poor prognosis. Sorafenib, midostaurin (Rydapt), quizartinib and crenolanib are FLT3 inhibitors that target this gene mutation. Gilteritinib is a FLT3/AXL tyrosine kinase inhibitor for the treatment of relapsed or refractory AML patients. These drugs have shown activity against AML cells especially when combined with chemotherapy.

Thus far only midostaurin is approved by FDA in combination with chemotherapy.

- BCL-2 inhibitor. A mutation in the *BCL-2* gene allows cancer cells to evade "programmed cell death." One promising drug under research is venetoclax (Venclexta™), a BCL-2 inhibitor that binds to the leukemia cell and leads to apoptosis, cell death. The drug is being studied alone and also in combination with low-dose cytarabine and hypomethylating agents such as decitabine or azacitidine.

- IDH1 and IDH2 inhibitors. Mutations in *IDH1* and *IDH2* genes causes cells to remain immature and grow too quickly. Several IDH inhibitors are being studied including the approved enasidenib (Idhifa®) in patients with such genetic markers in their leukemia cells.

- PLK inhibitors. Volasertib is a potent PLK inhibitor that is being studied. Volasertib is designed to inhibit the activity of PLK1, an enzyme that regulates cell division. This inhibition ultimately results in cell death.

- HDAC inhibitor. Histone deacetylase (HDAC) inhibitor is a substance that causes a chemical change that stops cancer cells from dividing. HDAC inhibitors under study in clinical trials include vorinostat (Zolinza®), pracinostat (SB939) and panobinostat (Farydak®). Additionally, in August 2016, the FDA granted breakthrough therapy designation for the HDAC inhibitor pracinostat in combination with azacitidine for patients newly diagnosed with AML who are over the age of 75 and ineligible for intensive chemotherapy.

- Immunotherapy. A type of biological therapy that is designed to either boost or suppress the immune system to help the body fight cancer. It uses materials made either by the body or in a laboratory to improve, target, or restore immune system function.

  - Monoclonal antibody treatment. This treatment 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 an antigen such as bacteria, viruses and even cancer cells. The antibodies attach to the antigen in order to help destroy the antigen. Researchers are analyzing specific antigens, including CD33, a marker that is found on most AML cells. Gemtuzumab ozogamicin (Mylotarg®) is a monoclonal antibody with the toxin, calicheamicin, attached to it. When gemtuzumab ozogamicin binds to the CD33 antigen, it releases the toxin resulting in the death of the myeloid cell. Gemtuzumab ozogamicin is FDA approved for AML patients. It continues to be studied in other combinations. Researchers are also studying SGN-33A, another anti-CD33 monoclonal antibody designed to deliver the cytotoxic agent, pyrrolobenzodiazepine (PBD) dimer, to myeloid leukemia cells. SGN-33A is undergoing clinical investigation as a single agent and in combination with hypomethylating agents. Another approach is using the treatment AMG-330 to harness T cells, which are part of the body's immune system, to target cells with the CD33 antigen.

- Vaccine therapy. Researchers are developing vaccines that can be personalized to individual patients to stimulate a strong immune response against their cancer.
- CAR T-cell therapy. This is a promising new way to get the immune system to fight leukemia. For this technique, immune cells called "T cells" are removed from the patient's blood and altered in the lab so they have specific substances (called "chimeric antigen receptors" [CARs]) that will help them attach to leukemia cells. The T cells are then grown in the lab and infused back into the patient's blood, where they can now seek out the leukemia cells and attack them.

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

Related Diseases

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN). Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a highly aggressive hematologic malignancy. Most patients present with skin lesions with or without bone marrow and/or multiple organ involvement. It is more common in the elderly; the median age is around 70 years.

BPDCN can be diagnosed by flow cytometry or immunohistochemistry of appropriate tissue by identifying surface markers (CD123, CD4, CD56) on the malignant cells. Skin is the most frequently involved site of disease (80 percent of cases). However, BPDCN usually progresses with bone marrow involvement and with a decrease in red blood cell, white blood cell, and platelet counts. Other organs including lymph nodes, spleen, and liver may be involved. Most patients have poor prognosis and aggressive disease course.

In the past, treatment has included therapies that are used for AML, acute lymphoblastic leukemia (ALL), or lymphoma. A patient in first remission may be treated with an allogenic hematopoietic stem cell transplantation (allo-HCT) if appropriate. Given there are no approved or recommended therapies for BPDCN, clinical trials in centers that have experience in treating BPDCN are the best option for patients. Recent clinical trials with agents targeting some of the BPDCN cell surface markers have shown great promise. SL-401 is an experimental targeted therapy directed to CD123, one of the surface markers found on BPDCN cells. Clinical trials with this experimental agent and others are ongoing.

See the free booklet *Blastic Plasmacytoid Dendritic Cell Neoplasm*.

Mixed Phenotype Acute Leukemia (MPAL). Mixed phenotype acute leukemia,

also known as mixed lineage leukemia, is a subtype of acute leukemia of ambiguous lineage. It represents a group of rare acute leukemias which have characteristics of both lymphoid and myeloid precursor cells, hence they resemble both ALL and AML. MPAL encompasses leukemias containing separate populations of blasts (immature cells) of more than one lineage or a single population of blasts co-expressing antigens of more than one lineage.

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

It is also important to define if a patient has a Philadelphia chromosome positive (Ph+) subtype. This subtype accounts for about 25 percent of all cases of MPAL. Patients with Ph+ MPAL are treated with age-specific ALL chemotherapy in combination with a tyrosine kinase inhibitor (TKI), followed by autologous stem cell transplantation (ASCT) if possible. For patients with a non-Ph+ MPAL subtype, the treatment consists of an ALL regimen or a combination of ALL and AML therapy, followed by consolidation with ASCT, when a donor is available.

Disease and Treatment Side Effects

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

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

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

- Red blood cells (anemia)
- Platelets (thrombocytopenia)
- White blood cells including neutrophils and monocytes (neutropenia and monocytopenia).

Transfusion of red blood cells and platelets may be needed for a period of several weeks during treatment. After that, the blood cell counts usually return to normal.

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

White blood cell transfusions are not generally used for AML patients. Instead of white blood cell transfusions, 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. Routine use of growth factors is not recommended. These agents are used only in special circumstances. Growth factors are also not recommended during induction therapy for patients with acute promyelocytic leukemia (APL), as they can increase the risk of differentiation syndrome (a condition that consists of unexplained fever, weight gain, labored breathing with pulmonary infiltrates, pleuropericardial effusion, hypotension, and renal failure).

Because the patient has an increased risk of developing an infection, the medical staff, family and friends of the patient need to practice frequent and vigorous hand washing and take other precautions to avoid exposing the patient to bacteria, viruses and other infection-causing agents. Caregivers for patients with central lines or ports need to be meticulous in the cleaning of catheters.

Patients at home should not delay in seeking medical attention if any signs of infection develop. A rise in temperature to 101°F or higher, or the onset of chills, may be the only sign of infection in a patient with a very low white blood cell count. Other signs of infection may include persistent coughing; tenderness at a site prone to infection, such as the area surrounding the anus or the facial sinuses; sore

throat; pain on urination; or frequent, loose stools.

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

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

- Mouth ulcers
- Diarrhea
- Temporary hair loss
- Rashes
- Nausea and vomiting
- Fatigue.

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

Chemotherapy may also affect a patient's fertility. Patients concerned about the ability to have a child in the future should talk with a fertility specialist before beginning treatment.

There are drugs and other supportive therapies to prevent or manage many side effects. For more information see the free LLS booklets, *Blood Transfusion, Cancer-Related Fatigue Facts* and *Understanding Side Effects of Drug Therapy*.

Sometimes, a drug or a drug combination causes effects that continue for a period of time after treatment ends. Some effects may be long-lasting (see *Long-Term Effects of Treatment* on page 39).

Follow-Up Care

Some of the tests that were done to diagnose AML may be repeated to

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

After treatment, patients who are in remission and have completed postremission therapy continue to be examined regularly by their doctors. Careful periodic assessment of the patient's health, blood cell counts and, if indicated, bone marrow is required. As time progresses, the length of time between assessments may grow, but assessments should continue indefinitely.

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

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

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

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

Stem cell transplantation is used to treat some patients with AML. It has been associated with long-term or late effects, including infertility, thyroid dysfunction, chronic fatigue and risk for developing a secondary cancer. The number of patients who develop secondary cancers, however, is small.

These and other possible long-term and late effects can be managed. For more information see the free LLS booklets, *Long-Term and Late Effects of Treatment in Childhood Leukemia or Lymphoma Facts* and *Long-Term and Late Effects of Treatment in Adults Facts.*

Treatment Outcomes

AML is a difficult disease to cure. However, a few decades ago almost no adults with AML were cured. Today, advances in AML treatment have resulted in improved remission and cure rates.

Terms for AML Treatment Outcomes

Active disease	AML is still present during treatment or after treatment (refractory) or AML has come back after treatment (relapsed). A patient with AML that has relapsed has more than 5 percent blast cells present in the marrow.
Minimal residual disease	No AML cells are detected in bone marrow using standard tests, such as looking at cells under a microscope. But more sensitive tests, such as flow cytometry, or very sensitive tests, such as polymerase chain reaction (PCR), detect remaining AML cells in the marrow.
Remission	No evidence of disease after treatment, (complete based on remission) ○ Less than 5 percent blast cells in the marrow ○ Blood cell counts within normal limits ○ No signs or symptoms of the disease
Complete molecular remission	No evidence of AML cells in the marrow when using very sensitive tests such as PCR

Sensitive molecular techniques permit the identification of small amounts of cells (minimal residual disease [MRD]) that cannot be detected by standard tests of the patient's blood and marrow. This can permit more sensitive follow-up of patients who are in remission and can help determine whether additional treatment is necessary. It is worth noting that, after treatment, finding 1 to 5 percent of the white blood cells in a patient's marrow are blast cells is not an indication of MRD. This percentage of blast cells may be found in persons who do not have leukemia. The timing and means of evaluating MRD in AML is an evolving concept.

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

Normal Blood and Bone Marrow

Blood. Blood is the liquid that flows through a person's arteries and veins. It carries oxygen and nutrients to living cells and carries away the cells' waste products. It also contains immune cells to fight infections and platelets that can stop bleeding in damaged blood vessels.

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) that are 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 insulin and corticosteroids
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin B_{12}
- Electrolytes, such as calcium, potassium and sodium.

Blood cells. There are three types of blood cells suspended in the plasma.

- Red blood cells (the cells that carry oxygen); they
  - Make up a little less than half of the body's total blood volume.
  - Are filled with hemoglobin, which is a protein that picks up oxygen from the lungs and delivers it to the cells throughout the body. Hemoglobin then picks up carbon dioxide from the cells and delivers it to the lungs where it is removed when a person exhales.
- Platelets
  - Are fragments of cells (one-tenth the size of red blood cells)
  - Help stop bleeding from an injury. For example, when a person has a cut, the vessels that carry blood are torn open. Platelets stick to the torn surface of the blood vessel, clump together and plug up the bleeding site with the help of blood-clotting proteins, such as fibrin and electrolytes such as calcium.

- White blood cells (cells that fight infections). There are several types of white blood cells, including
  - Neutrophils. A type of immune cell that is a "phagocyte" (eating cell). It helps fight infection by ingesting microorganisms and releasing enzymes that kill the microorganisms. It is a type of granulocyte, a white blood cell that has small particles.
  - Eosinophils. A type of immune cell that has granules (small particles). It plays an important role in the body's response to allergic reactions and infection with parasites.
  - Basophils. A type of immune cell that has granules (small particles). It plays a role during allergic reactions and asthma.
  - Monocytes. A type of immune cell that is also a phagocyte. It can leave the bloodstream and enter tissues to attack invading organisms and fight off infection. It surrounds and kills microorganisms, ingests foreign material and removes dead cells.
  - Lymphocytes. This type of white blood cell is found mostly in the lymph nodes, spleen and lymphatic channels. It is a key part of the immune system. There are three major types of lymphocytes. They are
    - T lymphocytes (T cells)
    - B lymphocytes (B cells)
    - Natural killer (NK) cells.

New red blood cells, platelets and most white blood cells are formed in the bone marrow, a spongy tissue that is found in the central cavity of bones. The creation of new blood cells is controlled by the body's needs. The human body generates billions of new blood cells every day to replace old and worn out cells. Certain events also may prompt the body to produce additional blood cells. For example, the bone marrow will produce and release more white blood cells in response to an infection.

While red blood cells, white blood cells and platelets vary in appearance and function, they all originate from a single type of unspecialized cell called a "hematopoietic stem cell." Hematopoietic, or blood-forming, stem cells are found in the bone marrow of the femurs (thigh bones), hips, vertebrae (back bones) and the ribs. An unspecialized hematopoietic stem cell can give rise to specialized cells that have specific functions. For example, a hematopoietic stem cell can give rise to a red blood cell that carries oxygen throughout the body, or it can give rise to a neutrophil, a white blood cell, that helps fight infections. The process by which an immature cell becomes a mature cell with specific functions is called "differentiation."

The process of creating new blood cells through differentiation is called "hematopoiesis" (see Figure 4 below). When a stem cell divides, each "daughter" cell has the potential to either remain a stem cell or to become a specialized cell such as a red blood cell, a white blood cell or a platelet. For those cells "committed" to specialize, the stem cell generates an intermediate cell. The intermediate cell is called a "precursor" or "progenitor" cell. While the stem cell remains in an immature, unspecialized state, the progenitor cell divides and undergoes multiple stages of development, becoming more specialized at each stage, until it becomes a particular type of mature blood cell.

The hematopoietic stem cell can give rise to lymphoid stem cells and myeloid stem cells. The lymphoid stem cells create lymphoid progenitor cells. Different types of progenitor or precursor cells develop into different types of mature blood cells. Through the process of differentiation, lymphoid progenitor or precursor cells can mature into T cells, B cells and NK cells.

Myeloid stem cells create myeloid progenitor cells. These precursor or progenitor cells will develop into mature blood cells including red blood cells, platelets and certain types of white blood cells (eosinophils, basophils, neutrophils and monocytes.) For example, a myeloid progenitor cell will go through various stages of development to become a neutrophil: myeloid progenitor ➔ promyelocyte ➔ myelocyte ➔ metamyelocyte ➔ band ➔ neutrophil.

In healthy people, stem cells in the bone marrow produce new blood cells continuously. Once the blood cells have matured, they leave the bone marrow and enter the bloodstream.

Blood Cell & Lymphocyte Development

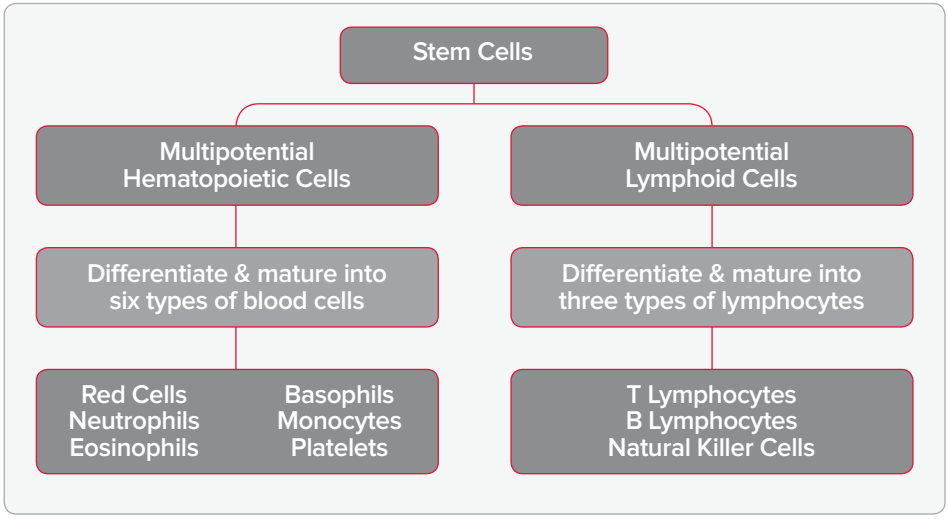

Figure 4. | Stem cells develop into blood cells (hematopoiesis) and lymphocytic cells.

Health Terms

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

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

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

Anthracycline (Antitumor Antibiotic). A type of antibiotic that is used to treat many types of cancer. Anthracyclines damage the DNA of cancer cells, causing them to die.

Antibody. A type of protein created by blood cells in response to an antigen (a substance that causes the body to mount a specific immune response). Antibodies help the body fight against invaders that make people get sick. Antibodies can also be made in the lab and are used to help identify certain types of cancer and to help treat cancer.

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

Autologous Stem Cell Transplantation. A treatment in which bone marrow is removed from a patient, stored and then returned to the patient after intensive treatment. See the free LLS booklet, *Blood and Marrow Stem Cell Transplantation.*

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

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

Blast Cell. A leukemia or cancer cell in the blood or bone marrow.

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

Bone Marrow. A spongy tissue in the hollow central cavity of the bones that is the site of blood cell formation. By puberty, the marrow in the spine, ribs, breastbone, hips, shoulders and skull is most active in blood cell formation. In adults, the bones of the hands, feet, legs and arms no longer contain blood-forming marrow—these bones are filled with fat cells. When marrow cells have matured into blood cells, they enter the blood that passes through the marrow and are carried in the bloodstream throughout the body.

Bone Marrow Aspiration. A test that examines bone marrow cells to find abnormal cells. A liquid bone marrow sample is usually taken from the patient's hip bone using a special needle. Usually this test is done at the same time as a bone marrow biopsy.

Bone Marrow Biopsy. A test to examine bone marrow cells to detect cell abnormalities. This test differs from a bone marrow aspiration in that a small amount of bone filled with marrow is removed, usually from the hip (pelvic) bone. After medication is given to numb the skin, a special hollow biopsy needle is used to remove a piece of bone containing marrow. Bone marrow aspiration and bone marrow biopsy may be done in the doctor's office or in a hospital. The two tests are almost always done together.

CBC. See Complete Blood Cell Count.

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

Central Nervous System (CNS) Prophylaxis. Treatment in which chemotherapy drugs are placed in the fluid that bathes the spinal cord and brain. In certain types of leukemia, particularly acute lymphocytic (lymphoblastic) leukemia and acute monocytic leukemia with high blood cell counts, the leukemic cells have a propensity to enter the covering of the spinal cord and brain.

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

Chloroma. See Myeloid Sarcoma.

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

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

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

Clone. The designation for a population of cells derived from a single transformed parent cell. Virtually all cancers are derived from a single cell with an injury (mutation) to its DNA and thus are monoclonal. Leukemia, lymphoma, myeloma and myelodysplastic syndromes are examples of clonal cancers; that is, cancers derived from a single abnormal cell.

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

Colony-Stimulating Factor. See Growth Factor.

Complete Blood Count. A lab test that measures the number of red blood cells, white blood cells and platelets in the blood. It also measures the amount of hemoglobin (the substance in the blood that carries oxygen) and the hematocrit (the amount of whole blood that is made up of red blood cells). Often called a "complete blood count" or "CBC."

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

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

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

Cycle of Treatment. A course of treatment followed by a period of rest to allow the body to recover. A cycle is the time between one round of treatment until the start of the next round of treatment. For example, chemotherapy given daily for one week followed by three weeks of rest is one cycle of treatment.

Cytogenetic Analysis. The process of analyzing the number and size of the chromosomes in cells. It detects chromosome alterations and, in some cases, may identify the actual genes that have been affected. These findings help healthcare professionals diagnose specific types of blood cancers, determine treatment

approaches and monitor a patient's response to treatment. The individual who prepares and examines the chromosomes and interprets the results is called a "cytogeneticist."

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

Cytotoxic Drugs. Anticancer drugs that act by killing cells or preventing them from dividing. See Chemotherapy.

Deletion. A portion of the chromosome is missing or deleted.

De Novo. The first occurrence of cancer in the body.

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

DNA. Deoxyribonucleic acid. The genetic matter found in all cells. DNA is passed to new cells during the process of cell division. A change or mutation in the DNA can lead to cell death, changes in the cell function, and in some cases, cancer.

Eosinophil. A type of white blood cell that promotes inflammation during allergic reactions and helps fight some parasitic infections.

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

Erythrocytes. See Red Blood Cell (Erythrocyte).

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. Synthetic EPO is available as erythropoiesis-stimulating agents (ESAs).

Extramedullary Myeloblastoma. See Myeloid Sarcoma.

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

FISH. See Fluorescence In Situ Hybridization.

Flow Cytometry. A test that measures certain characteristics of cells in a sample including the size, shape, and the presence of tumor markers on the cell's surface.

During this test, cells flow through an instrument called a "flow cytometer." When the cells pass through its laser beam, those with the antibody-specific features light up and can be counted. This test may be used to examine blood cells, bone marrow cells, or cells from a biopsy.

FLT3. An abbreviation for the fms-like tyrosine kinase 3 gene. The *FLT3* gene provides instructions for making a protein called fms-like tyrosine kinsase 3, which regulates blood cell development. *FLT3* mutations can be detected in about one-third of AML patients.

Fluorescence In Situ Hybridization (FISH). A technique for studying abnormal chromosomes in cells and tissues. Pieces of DNA that contain fluorescent molecules are added to cells or tissues on a slide. When the pieces of DNA bind to specific genes or chromosomes, they light up when viewed under a microscope. FISH can be helpful in assessing risk and treatment needs and for monitoring treatment effectiveness.

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

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

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

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

Graft-Versus-Tumor Effect (Graft-Versus-Leukemia Effect). Transplanted blood stem cells (the graft) perceive the leukemia cells in a transplant patient's body as foreign and attack the cancer cells.

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

Granulocytic Sarcoma. See Myeloid Sarcoma.

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

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

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

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

Hematopoiesis. The formation of all types of blood cells in the bone marrow. For the blood cell development process, see *Normal Blood and Bone Marrow* on page 41.

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

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

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

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

Immunity. The ability to resist infection.

Immunophenotyping. A process that uses antibodies to find specific types of cells based on the types of antigens or markers on the surface of the cells.

Indwelling Catheter. See Central Line (Indwelling Catheter).

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

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

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

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

Leukocyte. A type of blood cell that is part of the body's immune system. It defends the body against infections and other diseases. Types of leukocytes include granulocytes (neutrophils, eosinophils and basophils), monocytes and lymphocytes (T cells and B cells). Also known as "white blood cell." See White Blood Cell.

Leukocytosis. A high white blood cell count.

Leukopenia. A condition in which there is a lower than normal number of leukocytes in the blood.

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

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

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

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

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

Marrow. See Bone Marrow.

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

Minimal Residual Disease (MRD). The small amounts of cancer cells that may remain in the body after treatment. These cells are only identified by sensitive molecular tests.

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

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

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

Monocyte/Macrophage. A type of white blood cell that is made in the bone marrow and travels through the blood to tissues in the body. In the tissues it becomes a macrophage. Monocytes comprise about 5 to 10 percent of the cells in normal human blood. The macrophage is the monocyte-in-action: It can combat infection in the tissues, ingest dead cells (in this function it is called a "scavenger cell") and assist lymphocytes in their immune functions.

Multidrug Resistance (MDR). A cell characteristic that makes the cells resistant to certain types of drugs.

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

Myelocyte. An immature bone marrow cell that is a precursor to the mature granulocytes of the blood. Myelocytes are not present in the blood of healthy individuals.

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

Nucleus. The part of a cell that contains the chromosomes.

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

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

Oncogene. A gene that is a mutated form of a gene that is involved in normal cell growth. Oncogenes may cause the growth of cancer cells. See Mutation.

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

Pathologist. A doctor who finds disease by examining body tissue and fluids.

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

Peripheral Blood Smear. A sample of blood placed on a slide and dyed so that the cells can be examined under a microscope.

Petechiae. Pinhead-sized red spots under the skin caused by bleeding. It may occur due to 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 these phagocytes. Once an infection occurs, phagocytes migrate from the bloodstream and enter the infected tissue. Chemotherapy and radiation can decrease the numbers of these cells, so patients are more likely to get an infection.

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

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

Polymerase Chain Reaction (PCR). A technique used to expand trace amounts of DNA or RNA so that the specific type of DNA or RNA can be studied. This technique has become useful in detecting a very low concentration of residual blood cancer cells, too few to be seen using a microscope. PCR can detect the presence of one blood cancer cell among 500,000 to one million healthy blood cells.

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

Progenitor Cell. An early descendant of a stem cell that can differentiate to form one or more kinds of cells. It is often more limited than a stem cell in the kinds of cells it can become.

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

Promyelocyte. An immature blood cell that is in an intermediate stage of development between a myeloblast and a myelocyte.

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

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

Red Blood Cell (Erythrocyte). A type of blood cell that contains hemoglobin, which carries oxygen to the tissues of the body. Red blood cells make up about 40 to 45 percent of blood volume in healthy people.

Reduced-Intensity Stem Cell Transplantation. A type of allogeneic transplantation. In reduced-intensity stem cell transplantation (also called "nonmyeloablative stem cell transplantation"), patients receive lower doses of chemotherapy drugs and/or radiation to prepare for the transplant. The chemotherapy and radiation do not completely kill all of the leukemia cells. Instead, the new immune cells that the patient receives in the transplant may attack the leukemia cells. This protocol may be safer than an allogeneic stem cell transplant–especially for older patients. See the free LLS booklet, *Blood and Marrow Stem Cell Transplantation*.

Refractory Disease. A disease that does not respond to treatment.

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

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

Resistance to Treatment. When cancer cells do not respond to treatment. The cancer cells may be resistant to the drug at the beginning of treatment or may become resistant after being exposed to the drug over time.

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

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

Somatic Cell Mutation. A change in the DNA that occurs after conception. Somatic mutations can occur in any of the cells of the body except sperm and egg cells, and therefore cannot be passed on to the next generation.

Spinal Tap. See Lumbar Puncture.

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

Stem Cell. A primitive 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 are mostly found in the bone marrow, but some leave and circulate in the bloodstream. Stem cells can be collected, preserved and used for stem cell therapy. See Hematopoiesis.

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

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

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

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

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

Translocation. A chromosomal abnormality in which a piece of one chromosome breaks off and attaches to another chromosome. The location at which the break occurs may affect nearby genes, turning on oncogenes or turning off tumor suppressor genes. See Mutation.

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

Tumor Suppressor Gene. A gene that makes a protein that helps control cell growth.

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

More Information

Free LLS booklets include

Blood Transfusion

Cancer-Related Fatigue Facts

Choosing a Blood Cancer Specialist or Treatment Center Facts

Long-Term and Late Effects of Treatment in Adults Facts

Long-Term and Late Effects of Treatment in Childhood Leukemia and Lymphoma Facts

The AML Guide—Information for Patients and Caregivers

Understanding Clinical Trials for Blood Cancers

Understanding Lab and Imaging Tests

Understanding Side Effects of Drug Therapy

Visit www.LLS.org/booklets to reach these booklets and other information about blood cancer. Visit "Suggested Reading" at www.lls.org/support/suggested-reading to see a list of helpful books on a wide range of topics.

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