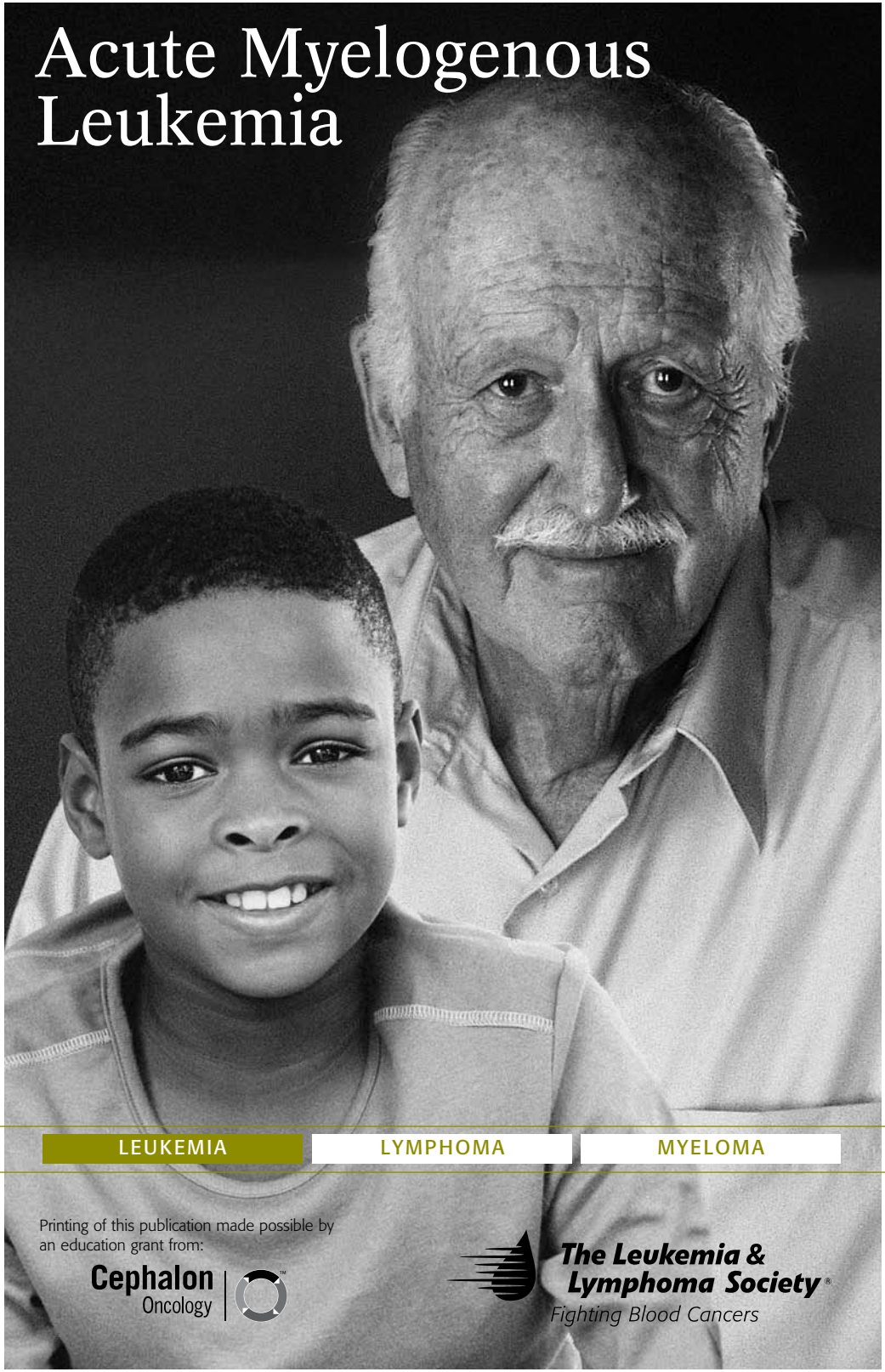
Acute Myelogenous Leukemia



LEUKEMIA | LYMPHOMA | MYELOMA

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Introduction

Advances in the treatment of acute myelogenous leukemia (AML) have resulted in improved remission and cure rates.

About 13,410 new cases of AML will be diagnosed in the United States in 2007 (source: *Surveillance, Epidemiology and End Results [SEER] Program; Cancer Statistics Review, 2000-2004; National Cancer Institute, 2007)*. Although AML can occur at any age, adults aged 65 years and older are more likely to develop the disease than younger people are. In 2004, AML accounted for almost 15 percent of childhood acute leukemia cases (source: Surveillance, Epidemiology, and End Results [SEER] Program; 1969-2004 Counties, National Cancer Institute, 2007).

This booklet provides information about AML for patients and their families. A brief description of normal blood and marrow is provided for background, followed by a detailed description of AML and its treatment. The booklet includes a glossary to help readers understand medical terms.

Some of the medical terms used throughout this booklet may be synonyms for other words or phrases used by healthcare professionals. For example, acute myelogenous leukemia may be called AML or other names, including acute myelocytic leukemia, acute myeloblastic leukemia, acute granulocytic leukemia or acute nonlymphocytic leukemia. Another example is "neutrophil," a type of white blood cell that may also be called a "polymorphonuclear neutrophil," a "PMN" or a "poly" for short. Check with your physician if you have questions about how the terms used in this booklet apply to you. We hope this information is of assistance, and we welcome comments about the booklet.

Normal Blood and Marrow

A brief description of normal blood and marrow is provided to help readers understand the AML-specific information that follows.

Blood is composed of plasma and cells suspended in plasma. The plasma is largely made up of water in which many chemicals are dissolved. These chemicals include

- Proteins, such as albumin; antibodies, including those developed by the body after vaccination (such as poliovirus antibodies); and clotting factors
- Hormones, such as thyroid hormones
- Minerals, such as iron, calcium, magnesium, sodium and potassium
- Vitamins, such as folate and B_{12}.

The cells suspended in plasma include red cells, platelets and white cells (neutrophils, eosinophils, basophils, monocytes and lymphocytes).

- The red cells make up about 40 to 45 percent of the blood. They are filled with hemoglobin, the protein that picks up oxygen in the lungs and delivers oxygen to the cells all around the body.
- The platelets are small cell fragments, one-tenth the size of red cells, which help stop bleeding at the site of an injury in the body. For example, when a person gets a cut, the vessels that carry blood are torn open. Platelets stick to the torn surface of the vessel, clump together and plug up the bleeding site. Later, a firm clot forms. The vessel wall then heals at the site of the clot and returns to its normal state.
- The neutrophils (also called "polymorphonuclear leukocytes," "PMNs" or "polys") and monocytes are white cells. They are called "phagocytes" (eating cells) because they can ingest bacteria or fungi and kill them. Unlike the red cells and platelets, the white cells leave the blood and enter the tissues, where they can ingest invading organisms and help combat infection. Eosinophils and basophils are two additional types of white cells that respond to allergens.
- Most lymphocytes, another type of white cell, are in the lymph nodes, the spleen and the lymphatic channels, but some enter the blood. There are three major types of lymphocytes: T cells, B cells and natural killer cells. These cells are a key part of the immune system.

Marrow is a spongy tissue where blood cell development takes place. It occupies the central cavity of bones. In newborns, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms and legs no longer have functioning marrow. The back bones (vertebrae), hip and shoulder bones, ribs, breastbone and skull contain marrow that makes blood cells in adults. Blood passes through the marrow and picks up formed red and white cells and platelets for circulation.

The process of blood cell formation is called "hematopoiesis." A small group of cells, the hematopoietic stem cells, develop into all the blood cells in the marrow by the process of differentiation (see Figure 1).

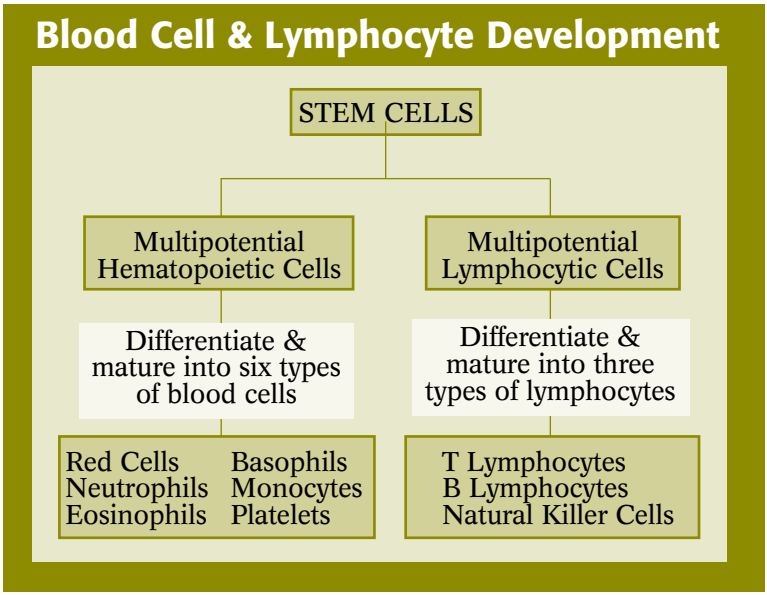


Figure 1. This simplified diagram depicts the process in which stem cells develop into functional blood cells (hematopoiesis) and lymphatic cells.

When the fully developed and functional cells are formed, they leave the marrow and enter the blood. In healthy individuals, there are enough stem cells to keep producing new blood cells continuously. Some stem cells enter the blood and circulate. They are present in such small numbers that they cannot be counted or identified in the usual type of blood cell counts. Their presence in the blood is important because they can be collected by a special technique and transplanted into a recipient if enough stem cells are harvested from a compatible donor. Stem cell circulation, from marrow to blood and back, also occurs in the fetus. After birth,

placental and umbilical cord blood can be collected, stored and used as a source of stem cells for transplantation. (To learn more about stem cell transplantation, see The Leukemia & Lymphoma Society's free booklet *Blood and Marrow Stem Cell Transplantation* and the fact sheet *Cord Blood Stem Cell Transplantation*.)

Leukemia

Leukemia is a cancer of the marrow and blood. The earliest observations of patients who had marked elevation of their white cells were made by European physicians in the 19th century and led to coinage of the term *Weisses Blut*, or "white blood," as a designation for the disorder. Later, the term "leukemia," derived from the Greek words *leukos*, meaning "white," and *haima*, meaning "blood," was used to designate the disease.

The major forms of leukemia are divided into four categories. The terms "myelogenous" and "lymphocytic" denote the cell type involved. Myelogenous and lymphocytic leukemia each have an acute or chronic form. Thus, the four major types of leukemia are acute or chronic myelogenous leukemia and acute or chronic lymphocytic leukemia. The term "acute lymphocytic leukemia" is synonymous with "acute lymphoblastic leukemia." The latter term is more frequently used to denote cases in children.

Acute leukemia is a rapidly progressing disease that affects mostly cells that are immature (not yet fully developed or differentiated). These immature cells cannot carry out their normal functions. Chronic leukemia progresses slowly and permits the growth of greater numbers of more developed cells. In general, these more mature cells can carry out some of their normal functions.

The ability to observe additional specific features of cells has led to further subclassification of the major categories of leukemia. The categories and subtypes allow the physician to decide what treatment works best for a given cell type and assess how quickly the disease may progress.

Acute Myelogenous Leukemia

AML results from acquired changes (mutations) in the DNA (genetic material) of a developing cell in the marrow. Once the marrow cell undergoes the leukemic change, it multiplies into many cells. These cells grow and survive better than normal cells and crowd out healthy cells. The uncontrolled growth leads to an accumulation of cells called "leukemic blasts," which 1) fail to function as normal blood cells and 2) block production of normal marrow cells, leading to a deficiency of red cells (anemia), of platelets (thrombocytopenia), and of normal white cells, especially neutrophils (neutropenia), in the blood.

Leukemia cells look somewhat like normal immature white cells. However, their developmental process is incomplete. When leukemia is diagnosed, the quantity of normal, healthy blood cells is insufficient (see Figure 2).

AML Blast Cells

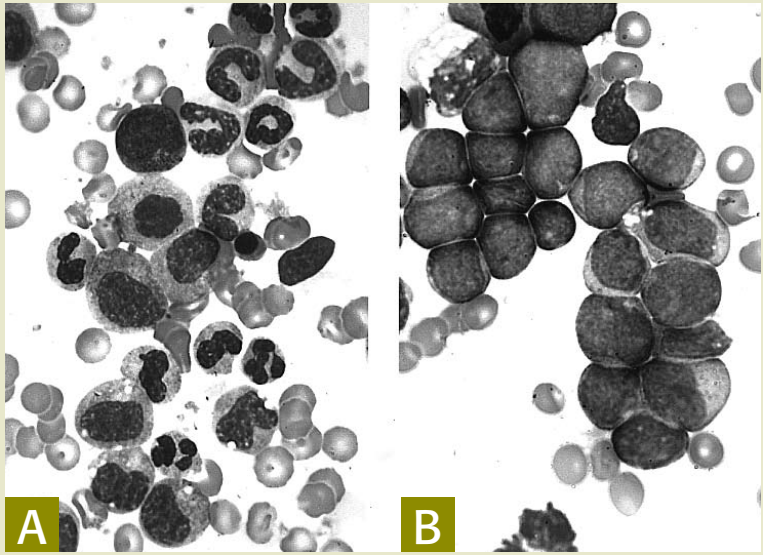


Figure 2. Panel A shows normal marrow cells as seen through a microscope. The darker silhouettes are the nuclei of the cells. Note the differences in their shapes. Some are circular and some are horseshoe shaped. The distinct nuclear configurations reflect the different developmental stages of the cells as well as different types of cells. Panel B shows the blast cells of acute myelogenous leukemia as seen through a microscope. The consistent appearance of these cells, which are "arrested" in an earlier stage of development, is in contrast to the appearance of the normal cells shown in panel A.

Incidence, Causes and Risk Factors

Older people are more likely to develop AML than younger adults or children. However, almost 15 percent of acute childhood leukemias are cases of AML. The risk for developing AML increases about 10-fold from age 30 to 34 years (about 1 case per 100,000 people) to age 65 to 69 years (about 11 cases per 100,000 people; see Figure 3).

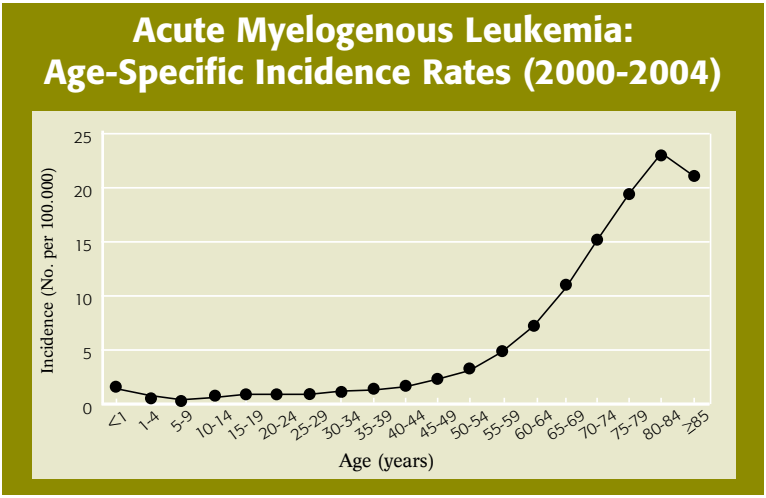


Figure 3. The horizontal axis shows five-year age intervals. The vertical axis shows the frequency of new cases of AML per 100,000 in a given age-group (source: Surveillance, Epidemiology, and End Results [SEER] Program; National Cancer Institute; 2007).

In most cases the cause of AML is not known. Several factors have been associated with an increased risk of the disease. These include exposure to

- Very high doses of radiation, as carefully studied in the survivors of atomic bomb detonations in Japan during World War II
- The chemical benzene, above threshold levels for prolonged periods of time, usually in an industrial setting; the stringent regulation of benzene use in the workplace has diminished the frequency of benzene as a risk factor for AML
- Chemotherapy used to treat cancers such as breast cancer, ovarian cancer or the lymphomas; the chemotherapy drug classes known as alkylating agents and topoisomerase II inhibitors are most frequently associated with an increased risk of AML
- Therapeutic radiation, depending on the dose and duration of treatment
- Tobacco smoke.

AML is not contagious. Uncommon genetic disorders such as Fanconi anemia, Shwachman-Diamond syndrome and Down syndrome are associated with an increased risk of AML. Very rarely, an unexpectedly high number of cases of AML may be diagnosed within the same family. It is thought that offspring in these families inherit a gene that makes them more susceptible to developing AML.

Signs and Symptoms

Most patients with AML feel a loss of well-being. They tire more easily and may feel short of breath in the course of normal physical activities. They may have a pale complexion from anemia. Several signs of bleeding caused by a very low platelet count may be noticed. These include black-and-blue marks or bruises occurring for no reason or because of a minor injury, the appearance of pinhead-sized spots under the skin, called "petechiae," or prolonged bleeding from minor cuts. Mild fever, swollen gums, frequent minor infections such as pustules or perianal sores, slow healing of cuts, or discomfort in bones or joints may occur. Rarely, a chloroma, also called a "granulocytic sarcoma" or an "extramedullary myeloid tumor," which is a collection of leukemic cells outside the marrow, occurs in patients with AML.

Diagnosis

Blood and marrow cells are examined to diagnose AML. An accurate diagnosis is important to aid the physician in determining the most appropriate treatment. Discuss the diagnostic tests that are being done and the results, including cytogenetic and genetic testing, with your physician. Your oncologist will work with a hematopathologist, a physican who studies diseases of blood cells by looking at peripheral blood smears, bone marrow aspirates and biopsies, and other tissues, and uses his or her expertise to identify diseases such as AML and its subtypes.

In addition to findings such as lower-than-expected red cell and platelet counts, a peripheral blood smear, an examination of the stained (dyed) blood cells with a microscope, usually shows the presence of leukemic blast cells. The diagnosis is confirmed by bone marrow aspiration and biopsy, an examination of the marrow that also shows leukemic blast cells. The blood and/or marrow cells are also used for

- Studies of the number and size of chromosomes (cytogenetic analysis)
- Genetic testing (which may include polymerase chain reaction [PCR])
- Immunophenotyping, a process for identifying cells based on the types of markers (antigens) on the cell surface.

These tests are important in determining the patient's AML subtype. Some of the tests may be repeated during and after therapy to measure the effects of treatment.

Subtypes of Acute Myelogenous Leukemia

The subclassification of AML provides important information about the expected course of the disease. Cytogenetic analysis, a microscopic examination of a sample of blood or marrow cells to look for changes in the chromosomes, provides information that helps in predicting the expected outcome of both induction and postremission therapy. The cell immunophenotype and the age and general health of the patient are also important in predicting expected outcomes of treatment.

Physicians are aided in identifying subtypes based on seeing different types and patterns of cells in a patient's blood or marrow. Most people who are diagnosed with AML clearly have one of eight different patterns (see Table 1). Treatment is similar for most subtypes, with the exception of acute promyelocytic leukemia (APL). Treatment for APL (subtype M3; see Table 1) is described on page 18.

Table 1. Acute Myelogenous Leukemia Cell Subtypes

Designation	Cell Subtype
M0	Myeloblastic, on special analysis
M1	Myeloblastic, without maturation
M2	Myeloblastic, with maturation
M3	Promyelocytic
M4	Myelomonocytic
M5	Monocytic
M6	Erythroleukemia
M7	Megakaryocytic

Myeloblasts. A myeloblast is a type of undeveloped white cell.

- If myeloblasts are the dominant leukemic cells in the marrow at the time of diagnosis, the leukemia is referred to as a "myeloblastic" type (M0, M1 subtypes; see Table 1).
- If there are many myeloblasts but some cells are developing toward fully formed blood cells, the added designation "with maturation" is used (M2 subtype; see Table 1).
- If there are cells developing features of monocytes ("monocytic" type), red cells ("erythroleukemia" type) or platelets ("megakaryocytic" type), these designations are used (M5, M6, M7 subtypes; see Table 1).

Chromosomal Changes. Certain chromosomal changes can give important information for patient management. For example, three chromosomal changes—which account for between 20 and 25 percent of all cases of AML—indicate a relatively favorable prognosis, especially in younger patients. They are

- AML associated with a translocation between chromosomes 8 and 21 (t8;21), (M2 subtype; see Table 1)
- AML associated with an inversion or translocation of chromosome 16 (t16;16) (M4 subtype; see Table 1)
- AML associated with a translocation between chromosomes 15 and 17 (t15;17) (M3 subtype; see Table 1). AML characterized by this translocation requires different treatment than other types of AML (see Acute Promyelocytic Leukemia Treatment on page 18).

AML in both younger and older patients with certain leukemic cell characteristics, including the *FLT3* gene mutation, may be more difficult to treat.

More information about acute monocytic leukemia is on page 16 and page 19.

Treatment

Nearly all patients with AML need treatment as soon after diagnosis as possible. The principal goal of treatment is to bring about a remission, in which

- There is no evidence of leukemic blast cells in the blood or marrow, and
- Normal blood cell production is restored and blood cell counts return to normal levels.

Certain factors may help in assessing the patient's treatment options and chances for recovery. These include

- The patient's age and general health
- The subtype of AML (see Table 1, page 9)
- The involvement of the central nervous system
- The presence of systemic infection at diagnosis
- A history of myelodysplastic syndrome or another type of cancer
- A history of AML (relapsed AML).

In most patients, intensive chemotherapy is required to achieve complete remission. At least two drugs are combined to treat patients initially (see Chemotherapy on page 12). Variations on standard approaches to treatment are undergoing intensive study throughout the world. Thus, a patient may receive a different number of drugs, a different sequence of drugs, or drugs different from those described here and still be receiving appropriate and effective treatment. However, it is essential to seek treatment in a center where physicians are experienced in the care of patients with acute leukemia.

In order to prepare the patient for chemotherapy, an indwelling catheter or port is placed surgically in a vein in the upper chest. The catheter, sometimes called a central line or a port, is tunneled under the skin of the chest so that it stays firmly in place. The external end of the port can be used to administer medications, fluids, or blood products or to withdraw blood samples. This is to give ready access for the infusion of drugs or blood cells and the removal of blood samples for cell counts and chemical tests. (Please see the Society's free booklet *Understanding Drug Therapy and Managing Side Effects* for additional information about drug administration.)

Some AML patients may build up uric acid in their blood as a result of a very high white cell count. The use of chemotherapy may also increase uric acid, which is a chemical in the cell. Uric acid enters the blood and is excreted in the urine. If many cells are killed simultaneously by therapy, the amount of uric acid in the urine can be so high that kidney stones can form. This may seriously interfere with the flow of urine. Drugs such as allopurinol or rasburicase can be given to minimize the buildup of uric acid in the blood.

Chemotherapy. The initial phase of chemotherapy treatment is called "induction therapy." AML patients must be hospitalized for induction therapy, often for four to six weeks or sometimes longer.

In most cases, an anthracycline drug, such as daunorubicin, doxorubicin, or idarubicin, is combined with cytarabine (also called "cytosine arabinoside," or "ara-C"; see Table 2). The anthracycline and the cytarabine act in different ways to prevent DNA synthesis in leukemia cells, stopping their growth and leading to their death. The anthracycline is usually given in the first three days of treatment. Cytarabine is started at the same time but is given for seven to 10 days of treatment. Both drugs are dissolved in fluids and given to the patient via an indwelling catheter.

The goal of induction therapy is to rid the blood and marrow of visible leukemic blast cells. If blast cells are still evident, a second course of chemotherapy may be required to rid the marrow of blasts. Usually, the same drugs described above and shown in Table 2 are used for each course of treatment.

When chemotherapy is effective, normal blood cells are eliminated from the marrow along with leukemia cells. This results in a severe deficiency in the patient's blood of

- Red cells (anemia)
- Phagocytes (neutropenia and monocytopenia)
- Platelets (thrombocytopenia).

Table 2. Some Drugs Used in the Treatment of and/or in Clinical Trials for Acute Myelogenous Leukemia

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

Antitumor Antibiotics

These drugs interact directly with the DNA in the nucleus of cells, thus interfering with cell survival

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

Antimetabolites

These chemicals are generally similar to natural building blocks of DNA, RNA or some vitamins. However, they are changed from the natural chemical. When they substitute for the DNA or RNA building blocks within a leukemic cell, the cell is unable to form normal DNA or RNA. This prevents the cell from growing.

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

DNA Repair Enzyme Inhibitors

These drugs act on certain proteins (enzymes) that help to repair injury to the DNA. The drugs prevent the enzymes from working and make the DNA more susceptible to injury.

- etoposide (VP-16, VePesid®, Etopophos®)
- teniposide (VM-26; Vumon®)
- topotecan (Hycamtin®)

DNA Synthesis Inhibitor

This drug reacts with DNA to alter it chemically and keep it from permitting cell growth.

- carboplatin (Paraplatin®)

Cell-Maturing Agents

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

Monoclonal Antibody

- gemtuzumab ozogamicin (Mylotarg®)

Hypomethylating Agents

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

Transfusion of red cells, and often platelets, may be required. During this time, the deficiency of phagocytes (microbe-eating cells) permits bacteria and fungi normally present on the skin or in the nose, mouth or large bowel (colon), or present in the environment, to cause infection. As a result, antibiotic therapy is frequently needed to treat infection. Growth factors are sometimes given to increase white cells. G-CSF (Granulocyte-Colony Stimulating Factor or filgrastim; Neupogen®) and GM-CSF (Granulocyte-Macrophage Colony Stimulating Factor or sargramostim; Leukine®) are drugs that may be used in certain circumstances to increase a patient's white cell counts.

Normal blood cell production will return in most patients several weeks after treatment is completed; transfusion of cells and antibiotics will no longer be needed. Blood cell counts gradually approach normal, well-being returns and leukemia cells cannot be identified in blood or marrow. This is called a remission. In this state, residual leukemic cells cannot be detected. They do not interfere with normal blood cell development but have the potential to regrow and cause a relapse of the leukemia.

Radiation Therapy. Occasionally, radiation therapy may be used to treat a large, localized accumulation of leukemia cells, called a "chloroma." A chloroma is an uncommon occurrence in AML.

Consolidation Therapy. Consolidation therapy, also called "postremission therapy," is needed to rid the patient of remaining leukemia cells in order to prevent relapse. Postremission treatment of AML consists of additional intensive chemotherapy after remission has been achieved, with or without autologous stem cell infusion or allogeneic stem cell transplantation. There is no consensus on the best approach. Some of the main factors that influence the approach used are

- The age of the patient
- The patient's ability to tolerate intensive treatment
- Cytogenetic findings
- The availability of a stem cell donor.

Patients are hospitalized for consolidation, or postremission, therapy. The length of stay will vary depending on the treatment and other factors. If chemotherapy is to be used, the best results occur if intensive treatment is applied. Intensive chemotherapy can be given with high dosages of cytarabine or other drugs.

Some patients may not benefit from intensive chemotherapy alone but may benefit from an allogeneic stem cell transplant or an autologous stem cell infusion. These treatment options are described below. Cytogenetic test results, the availability of an HLA-related or -unrelated matched donor and the patient's age are some of the factors that aid the physician in determining the appropriate postremission therapy for a given patient.

Intensive Chemotherapy and Autologous Stem Cell Infusion. Therapy can be further intensified for AML patients who do not have an HLA-matched stem cell donor by giving very intensive chemotherapy and reinfusing the patient's own marrow or blood stem cells. An autologous stem cell infusion involves harvesting the patient's own stem cells from blood or marrow after remission is achieved, freezing the cells for later use, then thawing them and infusing them into the patient after intensive chemotherapy. Reinfusion will restore blood cell production that would otherwise be profoundly impaired by this amount of chemotherapy. Special techniques are required to keep marrow cells from being damaged during the freezing and thawing process. (For more information about autologous stem cell infusion, see the Society's free booklet *Blood and Marrow Stem Cell Transplantation*.)

Allogeneic Stem Cell Transplantation. Patients between the ages of approximately one and 55 years who are in remission and have an HLA-matched stem cell donor may be candidates for allogeneic stem cell transplantation. Allogeneic stem cell transplantation is a high-risk procedure and the decision to perform a transplant depends on the features of the patient's leukemia, the age of the patient and the patient's (or his or her family's) understanding of the potential benefits and risks. For example, a younger patient with cytogenetic findings that are associated with a higher probability of relapse would be a candidate for allogeneic stem cell transplantation early in treatment. (See the Society's free materials *Blood and Marrow Stem Cell Transplantation* and *Cord Blood Stem Cell Transplantation* for comprehensive information about allogeneic stem cell transplantation.)

See *Nonmyeloablative Allogeneic Stem Cell Transplantation* on page 26 for information about reduced-intensity or "mini" transplantation.

AML Treatment in Children. Acute myelogenous leukemia accounts for about 15 percent of cases of acute childhood leukemias. Most cases of acute leukemia in children are acute lymphocytic (lymphoblastic) leukemia.

Children are treated with a similar remission-induction regimen as adults with AML: cytarabine and an anthracycline antibiotic, such as doxorubicin or daunomycin, and often a third drug, such as mitoxantrone. This regimen is followed by a complex multidrug program that results in about an 80 percent remission rate and a nearly 50 percent five-year, relapse-free remission rate. Slightly more than half of those children in relapse-free remission are considered cured. Infants and older children are usually treated with the same regimens.

Central nervous system (CNS) therapy may be given during the induction phase of therapy because AML cells may collect in the lining of the spinal cord and brain, called the "meninges." If not treated, the meninges can harbor leukemia cells, and relapse can occur in this site (meningeal leukemia). The treatment involves injecting drugs, such as methotrexate, into the spinal column (intrathecal therapy), or irradiating the covering of the CNS using x-rays. Sometimes both forms of treatment are used. These areas of the body that are less accessible to chemotherapy when given by mouth or injected into the vein are sometimes referred to as "sanctuary sites."

Very young children with AML (less than two years of age) also have a decreased rate of remission and cure. In addition, acute monocytic leukemia, a subtype of AML, and a very high blast count leukemia referred to as "hyperleukocytic leukemia" are variants of AML that are much more difficult to treat, with resultant lower remission and cure rates than the average results noted above.

Certain gene abnormalities (for example, *FLT3* mutations) and various chromosomal abnormalities (such as those involving chromosome 5 or chromosome 7) are markers that suggest a poor outcome. Allogeneic stem cell transplantation may be used in children who have a poor prognosis, who relapse after intensive multidrug therapy or who have primary induction failure. Multi-institution clinical trials are needed to determine the best treatments for high-risk patients. When chromosomal abnormalities occur in children with AML, their prognoses may be different from those of adults who have the same chromosomal abnormalities. Many of the chromosomal abnormalities that occur in childhood AML are under study. Other factors also influence prognosis in children.

See the Society's free 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.

AML Treatment in Older Adults. Acute myelogenous leukemia occurs more frequently with advancing age. At least half of patients are more than 65 years of age when the disease is diagnosed. Today there are curative options available for older patients, including those who may have other significant health issues.

Patient age alone is a limited predictor of tolerance to chemotherapy. Standardized measures of strength, reaction time, balance, and other indicating factors, developed by experts in geriatrics, are being applied to determine the patient's physiological age. The latter measurement rather than chronological age is a better indicator of tolerance to therapy. Such determinations may permit some older patients to receive more intensive therapy, when appropriate and desired by the patient. However, older patients are more difficult to treat and may have a poorer response to therapy for several reasons:

- The principal reason is that the leukemic cells of older patients with AML are more resistant to treatment with chemotherapy. Older patients' leukemia cells have a much higher occurrence of unfavorable cytogenetics (chromosome abnormalities). Mutated genes may also be more common. For example, the *FLT3* gene is more likely to be mutated in older AML patients than in younger ones. The leukemic cells of older patients more frequently overexpress drug resistance genes as compared to cells of younger patients. Thus, the response to therapy is usually inadequate to produce a remission or to lead to sustained remission.
- Older patients may have other medical problems, including heart, lung or kidney disease or diabetes mellitus. The treating physician often has to select less toxic but less effective drugs or decrease the dosage and frequency of treatment to avoid further compromising the patient's general health.
- Patients of advanced age, even in the absence of other medical disorders, tend to be more intolerant than younger patients to optimal dosages of chemotherapy. The drugs, dosages, and frequency of treatment are often individualized to take into account the features of the leukemia, the health of the patient and the patient's anticipated tolerance of therapy.

See *Research and Clinical Trials* on page 24 for treatment studies of interest to older patients. Patients should discuss these treatment options with their physicians.

Acute Promyelocytic Leukemia Treatment

The treatment of the acute promyelocytic leukemia (APL) subtype of AML (M3 subtype; see Table 1 on page 9) differs from the treatment for other AML subtypes described in the previous section. With APL, the cells that accumulate in the marrow can be identified as promyelocytes, the step in blood cell formation that follows the development of myeloblasts. These cells also have a specific chromosome abnormality involving chromosome 15, usually in conjunction with chromosome 17.

A derivative of vitamin A called all-trans retinoic acid, often abbreviated as ATRA, is administered with chemotherapy. ATRA is also known as tretinoin (Vesanoid®). Retinoic acid is capable of inducing the leukemic promyelocytes to develop into mature cells (neutrophils). It causes a marked decrease in the concentration of leukemic blast cells in the marrow, and a remission frequently follows.

Treatment with ATRA must be followed by or given with chemotherapy in order for the remission to be long-lasting. ATRA often minimizes the side effects of chemotherapy because blood cell counts may be improved and the number of leukemic cells may be decreased at the time that chemotherapy is started.

Arsenic trioxide (Trisenox®) has been approved by the Food and Drug Administration (FDA) to treat patients who have relapsed or are resistant to treatment with chemotherapy and ATRA.

The remission rate of patients with APL treated with ATRA and an anthracycline, such as idarubicin, is about 70 to 80 percent. Patients with this subtype of AML are among the most frequently cured. Nevertheless, problems with hemorrhage during the initial phases of treatment, resistance to treatment and relapse occur in a proportion of patients, as they do in some patients with other types of AML. Therefore, long-term follow-up of patients in remission is required to identify those who are cured and those who may require further therapy.

A small number of APL patients have persistent minimal residual disease (MRD) at the end of consolidation therapy. These patients may benefit from treatment with arsenic trioxide with or without gemtuzumab ozogamicin (Mylotarg®), followed by allogeneic stem cell transplantation, if an HLA-matched donor is available. Patients who do not have a donor or cannot have an allogeneic stem cell transplant for other reasons may be candidates for an autologous stem cell infusion.

See page 28 for information about study treatments for APL.

Acute Monocytic Leukemia Treatment

In some types of leukemia, including the AML subtype of monocytic leukemia (M5; see Table 1, page 9), the leukemic blast cells may invade the lining of the spinal cord or brain. This does not usually occur with other types of AML. When the lining of the spinal cord or brain is involved, chemotherapy is injected into the spinal fluid. A spinal tap (lumbar puncture) is a commonly used medical procedure, performed under local anesthesia or with heavy sedation. During a spinal tap, a needle is placed into the spinal canal and the spinal fluid is removed and examined for leukemia cells. The extracted fluid volume is then replaced with fluid containing appropriate drugs, usually cytarabine or methotrexate.

Treatment Side Effects and Their Management

Most side effects of treatment for AML, although severe, are temporary and subside once the body adjusts to therapy or when therapy is completed. Severe side effects are treated on an in-patient basis. During and following the completion of therapy, healthy new cells begin to grow and develop each day. Less commonly, a drug or drug combination used to treat blood cancer has side effects that continue for a period of time after treatment ends. Some effects may be permanent. (See *Long-Term and Late Effects of Treatment* on page 21.) Physicians and patients should discuss the possible side effects of treatment so that proper planning, evaluation and follow-up can take place.

AML decreases the production of normal blood cells, and the blood cell counts are further decreased by the added effects of chemotherapy. The intensity of chemotherapy required to destroy sufficient numbers of leukemia cells to permit a remission leads to even more severe decreases in the numbers of red cells, phagocytes and platelets. Severe anemia, risk of bleeding due to a low platelet count and a high likelihood of infection result. Red cell and platelet transfusions are usually effective replacements until the beneficial effects of treatment occur several weeks later and blood cell counts return toward normal. Practical methods for transfusion of phagocytes are not currently available, except occasionally in infants and very small children. Therefore, when the white count is low and infection risk is increased, antibiotic prophylaxis is used.

A severe or prolonged low white cell count may occur, especially after intensive drug therapy, and may increase the patient's risk of developing an infection. Medical staff and visitors need to take precautions—such as frequent and vigorous hand washing—to avoid exposing patients to bacteria, viruses and other infection-causing agents. They may also wear masks, gowns and gloves in some circumstances. Caregivers for patients with ports need to be meticulous in the cleaning of the catheter to reduce the risk of bacteria infecting the body through this device.

A rise in temperature or the onset of chills may be the only sign of infection in a patient with a very low white cell concentration. In such patients, 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.

Blood cell growth factors may be used to stimulate the production of phagocytes and can shorten the time during which the white cell count is low. The growth factors used most frequently are granulocyte-colony stimulating factor (G-CSF) and granulocyte-macrophage colony stimulating factor (GM-CSF). These agents are used in children only in special circumstances. The identification of pediatric AML patients most likely to benefit from treatment to prevent infection with growth factors is under study.

Chemotherapy affects tissues that normally have a high rate of cell turnover (also called "cell division" or "mitosis"). Thus, the lining of the mouth, the lining of the intestines, the skin and the hair follicles may be affected. As a result, mouth ulcers, diarrhea, and hair loss are common after chemotherapy. Hair loss from chemotherapy is temporary, and hair growth resumes when treatment is completed. Rashes may also occur. Treatment for these side effects can make patients more comfortable and may prevent serious problems from developing. Nausea and vomiting may also be side effects of chemotherapy. These side effects result from actions both on the intestines and on centers of the brain that, when triggered, lead to vomiting. Fortunately, in most cases drugs can be given to prevent nausea and vomiting. Diarrhea can be managed with treatment. Cancer-treatment-related fatigue affects many individuals. It is an important issue that can have a major impact on quality of life. (For more information see the Society's free materials *Fatigue* [fact sheet] and *Understanding Drug Therapy and Managing Side Effects.*)

Refractory Leukemia and Relapsed Leukemia

Some patients have residual leukemic cells in their marrow even after intensive treatment. This is referred to as "refractory leukemia." There are other patients who have a return of leukemia cells in the marrow and a decrease in normal blood cells after achieving a remission of leukemia following therapy. This situation is referred to as "relapse."

With refractory leukemia, approaches such as drugs not used in the first course of treatment or stem cell transplantation may be used in an effort to induce remission. In patients who relapse, the duration of the remission, the patient's age and the cytogenetic findings in the leukemia cells influence the approach to therapy. Drugs similar to those administered initially, different drugs or stem cell transplantation may be used to treat the leukemia. Gemtuzumab ozogamicin (Mylotarg®), a monoclonal antibody that is coupled with a potent cell-killing agent that targets myelogenous leukemia blast cells, has been approved for treatment of older patients who have relapsed AML (see Table 2 on page 13). This agent is also being studied in clinical trials in combination with other drugs to treat relapsed AML. For more information on clinical trials for relapsed and refractory leukemia see page 28.

Several drugs and drug combinations that can be used to treat AML are being studied in clinical trials. Among these are clofarabine (Clolar®), either alone and with other drugs; azacitidine (Vidaza®); several *FLT3* inhibitors; farnesyl transferase inhibitors such as tipifarnib; and the alkylating agent VNP40101M (Cloretazine®).

Long-Term and Late Effects of Treatment

Treatment for individuals with AML may cause complications that persist long after treatment ends (long-term effects) or develop much later in life (late effects). Not everyone who is treated for AML will develop long-term or late effects. Various factors can influence the risk of developing long-term or late effects, including the type and duration of treatment, age at the time of treatment, gender and the patient's overall health.

With induction therapy for AML, most 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 may not become apparent until many years after therapy ends.

Stem cell transplantation may be used to treat patients with AML. Stem cell transplantation has been associated with a variety of long-term or late effects, including infertility, thyroid dysfunction, chronic fatigue, and risk for developing a second cancer (lymphoma, melanoma of the skin, or cancer of the tongue and salivary glands, brain, CNS, bone, soft tissue, and thyroid gland). The number of patients who develop secondary cancers is small.

Various options exist to manage long-term and late effects. It is important that patients be aware of the potential for long-term and late effects of treatment, and that some of these effects may not appear until years after treatment ends.

For more information on long-term and late effects, see the Society's free fact sheets *Long-Term and Late Effects of Treatment for Childhood Leukemia or Lymphoma* and *Lymphoma and Long-Term and Late Effects of Treatment in Adults.*

Follow-up Care

Patients who are in remission continue to be examined regularly by their physicians. After the induction of remission and the completion of postremission therapy, careful periodic assessment of the patient's state of health, blood cell counts and, if necessary, marrow is required. As time progresses, the interval between assessments may be lengthened, but assessments should continue indefinitely.

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 physician for general health examinations at least once a year. They should also be examined regularly by an oncologist.

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 approach can be used if the leukemia cells have a detectable molecular abnormality. This feature 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, a finding that 1 to 5 percent of the white 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.

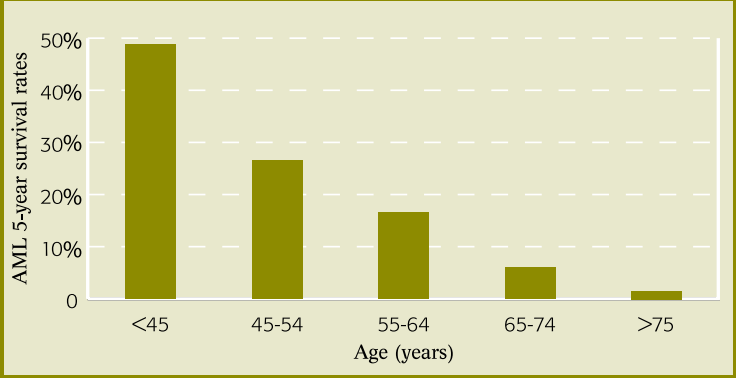
Outcomes

Patients with AML have 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.

Age is the most important determinant of cure rate. Children with the disease have a cure rate just below 50 percent. Younger patients with certain cytogenetic patterns and with certain subtypes, such as APL, have a greater possibility of cure. The application of allogeneic stem cell transplantation can also cure some patients.

Relative survival compares the survival rate of a person diagnosed with a disease to that of a person without the disease. The relative survival rates for AML differ by age of the patient at diagnosis, as well as by gender, race and subtype of AML. Patients diagnosed with AML before age 65 have an overall five-year relative survival rate of 34.9 percent. Children under 15 years of age have an overall five-year survival rate of 54.1 percent. Patients diagnosed at age 65 and older have an overall five-year survival rate of 4.1 percent. Table 3 shows additional five-year relative survival by age data. Note that these numbers do not take into account significant individual factors, such as the patient's cytogenetics.

Table 3. Acute Myelogenous Leukemia: Five-Year Survival Rates (1996-2003)



Source: Surveillance, Epidemiology, and End Results [SEER] Program, 1996-2003; National Cancer Institute, 2007.

Research and Clinical Trials

The proportion of patients with AML who enter remission, stay in remission for years or are cured has increased during the last 30 years. Research in several areas has contributed to this progress. In children from birth to 14 years, the expectation of a cure is now just below 50 percent; with each decade of life, the probability of cure decreases. However, AML is still one of the most difficult cancers of the blood and marrow to treat. The challenge remains to develop treatment programs that cure all younger and older patients.

Society Research Program. The Leukemia & Lymphoma Society invests research funds in both basic and applied research programs to improve the cure rate for AML patients. Society-supported research under way includes studies to

- Identify new drug targets
- Find methods to overcome drug resistance
- Explore ways to attack leukemic stem cells thought to give rise to and sustain the disease
- Develop new immune therapies, such as vaccines
- Improve techniques of stem cell transplantation.

The following strategies, along with other new approaches, hold the promise of increasing the rate of remission and cure of patients with AML.

Clinical Trials. New approaches to therapy are under study in clinical trials. These trials, conducted under rigorous guidelines, help physicians to determine the beneficial effects of new treatments and what, if any, adverse effects they have. New drugs, new combinations of drugs, new types of immunotherapy, and new approaches to stem cell transplantation are being explored to bring new and better treatments to patients. Clinical trials are conducted at many hospitals throughout the United States and also at hospitals worldwide.

The Society's Information Resource Center, at (800) 955-4572, offers guidance to help patients work with their physicians to find out 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. This service is also available on the Society's Web site, at www.LLS.org. Information about clinical trials that is maintained by the U.S. National Institutes of Health can be accessed at www.clinicaltrials.gov.

Research Approaches. To find better treatments, researchers are studying the

- Causes of AML
- Cell changes that make AML cells resistant to treatment
- Criteria for identifying disease subtypes, such as chromosome abnormalities
- Approaches that will permit patients to get the least toxic therapies without compromising treatment goals
- Better ways to manage side effects of therapy.

Oncogenes and Mutations. Understanding the ways that certain DNA changes cause a normal cell to become an AML cell may lead to the development of new therapies. These therapies would work by blocking instructions from cancer-causing genes (called "oncogenes"). A new therapy might target the oncogene. For example, a new drug might block the making of a protein that carries cancer-causing instructions, or it might block the cancer-causing instructions from being executed. Most likely, in order for AML to arise, several interacting gene mutations are necessary. This means that any of the interacting gene mutations may also be therapeutic targets. *FLT3* inhibitors are an example of a new class of drugs under study to target mutations of the gene *FLT3*, which is found in the AML cells of about 30 percent of patients. Several *FLT3*-inhibitor drugs are being studied in AML treatment.

Overcoming Drug Resistance. Among patients with AML, a subset has leukemia cells that are resistant to drug therapy; current treatment options may not cure these patients' disease or bring them into remission. Research is uncovering mechanisms in the leukemia cell that protect it from the effects of chemotherapy, and ways to reverse drug resistance are being studied.

Immunotherapy and Cytokines. Extensive testing is being conducted to synthesize new drugs or find them from natural (botanical) sources. Researchers are also investigating new combinations of existing drugs for their usefulness in AML treatment (see examples of specific agents under study in Table 4 on page 27). Research is being conducted to develop approaches that may enhance the body's natural defenses.

- An antibody that targets specific AML cells and carries a potent cell toxin, gemtuzumab ozogamicin (Mylotarg®), has been approved for use by the Food and Drug Administration (FDA) in patients in first relapse who are 60 years of age or older and who are not considered candidates for cytotoxic chemotherapy. Mylotarg® specifically targets leukemic cells that have the CD33 receptor. The safety and efficacy of Mylotarg® are now being studied in other patient populations, including children.
- Antibodies that target leukemic cells and carry a radioactive element, such as isotopes of iodine or yttrium (radioimmunotherapy), have been developed and are being tested.
- Another approach uses vaccines made of immune cells that have been primed to attack leukemia cells.
- Cytokines are naturally occurring chemicals that can be made commercially using the techniques of biotechnology. Some cytokines are used to help restore normal blood cells during treatment. Others are being studied for their effectiveness in enhancing the immune system to better attack leukemic cells.

Nonmyeloablative Allogeneic Stem Cell Transplantation. This type of stem cell transplantation therapy may be useful for older patients with AML. The conditioning therapy used for a nonmyeloablative transplant (also called a "mini" transplant or "reduced-intensity" transplant) is of much lower intensity than a standard stem cell transplant; it does not completely inactivate the patient's immune system or treat the AML as intensively. A nonmyeloablative transplant is based on two considerations: 1) Much-improved immunosuppressive therapy prevents the patient from rejecting the donor's stem cells, even though the patient's immune system has not been fully suppressed by the lower intensity conditioning therapy, and 2) the anticipated attack of the donor's immune cells successfully suppresses the leukemia cells of the patient. This attack is referred to as "graft versus leukemia" or "GVL." Over time, if successful, the donor's stem cells result in the replacement of the patient's immune system. The donor's immune cells, which are now engrafted into the patient, recognize minor tissue antigens on the patient's leukemia cells and continue to suppress their growth.

Nonmyeloablative transplantation is relatively new, and its risks and benefits have not yet been clearly established. It has benefited some patients. Thus, in patients with a matched-related donor, it may be an appropriate option for carefully selected older individuals. As is the case with allogeneic stem cell transplantation in middle-aged individuals, the risk of graft versus host disease (GVHD) is an

important consideration and a potentially disabling side effect of nonmyeloablative stem cell transplantation. A patient who is interested in exploring the option of nonmyeloablative transplantation should talk with his or her physician. If appropriate, the physician can help the patient locate a transplant center that is investigating the procedure through a clinical trial.

Cord Blood Stem Cell Transplantation. Umbilical cord blood, like bone marrow and peripheral blood, is a rich source of stem cells for transplantation. A cord blood stem cell transplant may be a consideration for a patient who could benefit from allogeneic stem cell transplantation but does not have a related or unrelated HLA-matched donor. Research studies of cord blood transplantation outcomes, including transplants with two or more cord blood units, show promising results. This topic is presented in detail in the Society's free fact sheet *Cord Blood Stem Cell Transplantation.*

Table 4 describes some of the drugs under study for AML treatment.

Table 4. Some Drugs Under Study for AML Treatment

- Farnesyl transferase inhibitors (tipifarnib [Zarnestra®], lonafarnib [Sarasar®])
- *FLT3* inhibitors (CEP-701, lestaurtinib for children; sorafenib [Nexavar®] in people 60 years of age and older)
- Proteasome inhibitor (bortezomib [Velcade®]))
- Multidrug resistance modulators (cyclosporine A, PSC-833 [valspodar])
- Antisense molecules (G3139, oblimersen sodium, [Genasense®], GTI-2040)
- Hypomethylating agents (azacitidine [Vidaza®], decitabine [Dacogen®])
- Histone deacetylase inhibitors (depsipeptide)
- Histamine dichloride (Ceplene®) and IL-2*
- Alkylating agents (VNP40101M [Cloretazine®])
- Monoclonal antibodies (gemtuzumab ozogamicin [Mylotarg®])
- Immunosuppressive agents_mTOR inhibitors (sirolimus, rapamycin [Rapamune®], tacrolimus [Prograf®])

*These drugs are not used as first-line treatment for AML. They are being studied for maintenance of remission after induction therapy.

Examples of specific agents under study in clinical trials for adults with AML include:

- **Gemtuzumab ozogamicin (Mylotarg®)**, an anti-CD33 antibody, in combination with other drugs such as daunorubicin and cytarabine, is being studied to find out if it is better than standard treatment for adult patients with newly diagnosed AML.
- ***FLT3* inhibitors**, such as **CEP-701**, **sorafenib**, and others are being studied in older, newly diagnosed AML patients, along with standard primary therapy to see if *FLT3* inhibitors produce better outcomes than chemotherapy alone. *FLT3* inhibitors are also being studied in patients with relapsed or refractory AML.
- **Farnesyl transferase inhibitors**, such as **tipifarnib (Zarnestra®)**, are being studied in older patients in second or subsequent remission to determine how well the drug can keep the AML in remission and to see what side effects the drug may cause. Tipifarnib is also being studied for older adults in combination with **bortezomib (Velcade®).**
- **Clofarabine (Clolar®)** is being studied as a single agent in newly diagnosed older adults with AML for whom standard induction chemotherapy is unlikely to be of benefit. The drug is also being studied in older adults with relapsed or refractory AML in combination with intermediate-dose cytarabine.

Examples of specific therapies under study in clinical trials for adults with APL include:

- **ATRA** and **arsenic trioxide** used together are being studied in APL patients who have a good prognosis. This approach does not include chemotherapy.
- **ATRA** and **arsenic trioxide**, combined with **gemtuzumab ozogamicin (Mylotarg®)** is being studied in APL patients who have a poorer prognosis in comparison with ATRA and an anthracycline drug.

Clinical Trials for Childhood AML. AML is one of the most challenging childhood cancers to treat. Chemotherapy has been used in different combinations and dosages over the past several decades, leading to improved childhood AML cure rates, but more research is needed to further improve cure rates and decrease the side effects and long-term and late effects of chemotherapy.

Researchers have identified cell targets that appear to be the key to treatment with the new generation of chemotherapy agents. These new targeted agents are being studied in conjunction with chemotherapy to examine their impact upon cure rates and their effect on toxic complications associated with traditional chemotherapy.

Gemtuzumab ozogamicin (Mylotarg®) is currently being tested in children with newly diagnosed AML.

Researchers are also studying how to group patients by their risk for relapsed AML. Patients with higher risks may benefit from more intensive treatments, including stem cell transplantation, while patients at a lower risk may benefit from less intensive treatment.

Researchers are studying risk factors and treatments for AML chemotherapy complications, especially infections, to make AML therapy safer for children.

Social and Emotional Effects

A diagnosis of AML often brings a strong emotional response in patients, family members and friends. Denial, depression, hopelessness and fear are some of the reactions or emotions people may experience. No one response is either universal or unexpected. Most people with AML are able to cope with what at first may seem too hard to accept. This adjustment usually takes a while. However, with information and time, many people shift their focus to the therapy process ahead and the prospect of recovery.

Patients may initially want to focus on learning about their disease and its treatment. Knowing more about the disease and its treatment helps many individuals to cope. Patients and caregivers are advised to discuss the disease and its treatment, to ask questions and convey fears or concerns to the patient's physicians, nurses, social workers and other members of the oncology team. They are available to spend time with the patient, answer questions, lend emotional support and provide referrals to other useful resources.

During and after treatment, patients may want to have friends, family members or caregivers help them obtain and process information from the physician and other members of the oncology team. The presence of another individual may help ease the patient's stress. This person can also help the patient ask questions and record and retain information. While it is not always possible to have this type of support, patients can reach out in other ways—for example, local or Internet support groups can provide a forum for discussion. Often, patients with cancer become acquainted with one another, and these friendships provide support. Over time, some patients form supportive relationships with members of their healthcare team.

Treatment for AML will mean changes in daily life, at least for a time. Hospitalizations, disease and treatment side effects, and concerns about survival, finances, work or family life may cause a person to question his or her self-worth or identity. These issues may affect relationships, including intimate relationships. Recognition that these feelings are normal and knowing that many side effects are temporary may be reassuring. Open, honest communication regarding fears and concerns can be very helpful.

Finances. Cancer treatment can be financially difficult for many families due to loss of income and the high cost of many medications and procedures. The Society's Patient Financial Aid Program offers financial reimbursement for some medications, transportation and procedures for those in need. The Society's Co-Pay Assistance Program offers patients assistance with private health insurance premiums, private insurance co-pay obligations, Medicare Part B, Medicare Plan D, Medicare Supplementary Health Insurance and Medicare Advantage premium or co-pay obligations. Prescription drugs covered under this program include those supplied to the patient by a pharmacy or administered in an office or hospital by a healthcare provider. Public or private prescription drug coverage is required to qualify for this program.

Depression. It is important to seek medical advice if a patient's mood does not improve over time—for example, if a patient is feeling depressed every day for a two-week period. Depression is an illness that should be treated even when a person is undergoing treatment for AML. Treatment for depression has proven benefits for people living with cancer. There are many sources of help available to patients and caregivers. Aspects of care such as making treatment choices, finding the time and money for medical care and communicating with family members and friends can be stressful. Contact the Society or ask the healthcare team for guidance and referrals to other sources of help such as support groups, counseling services or community programs. The National Institute of Mental Health (NIMH) has several publications about depression that may be helpful. For more information go to www.nimh.nih.gov and enter "depression" in the search box at the top of the Web page or call NIMH at (866) 615-6464.

Children's Concerns. Children with AML may face long periods of treatment, including hospitalizations. However, many can expect to enter or return to school, attend college, enter the workforce, marry and become parents. Still, each family living with a childhood AML diagnosis is thrown into an unfamiliar world. The child, parents and siblings need support. Remember that help is available. Don't hesitate

to ask for assistance for your child, yourself or other family members, even if you are already working with a psychologist, social worker or child life specialist. Many families will benefit from extra support.

A child with AML is usually admitted to the hospital as soon as the diagnosis is known. For some children this is the first time they have stayed away from home for an extended period of time. Providing age-appropriate information to your child about the illness and treatment will help him or her build trust in both you and the treatment team and feel comfortable talking about fears and concerns. For practical guidance on how to support your child and other family members, deal with your own concerns, share the news with extended family and friends and make the transition to life after treatment ends, see the Society's free booklet *Coping With Childhood Leukemia and Lymphoma*.

We Can Help. The Leukemia & Lymphoma Society also offers financial assistance and support programs through its national office and local chapters to help ease the economic and emotional pressure and that comes with a cancer diagnosis. Visit the Society's Web site at www.LLS.org or contact the Society's Information Resource Center at (800) 955-4572 to locate a chapter in your area, order free publications or speak directly to an Information Specialist.

For more information, see the Society's free booklets.

Acute Myelogenous Leukemia: A Guide for Patients and Caregivers; 2007 (in press).

Coping: Support for People Living with Leukemia, *Lymphoma or Myeloma;* 2007 (in press).

Coping With Childhood Leukemia and Lymphoma; 2007.

Each New Day: Ideas for Coping with Leukemia, *Lymphoma or Myeloma;* 2006.

Learning & Living with Cancer: Advocating for your child's educational needs; 2006.

Touching Lives: A Directory of Patient Services Programs; 2007 (in press).

For children:

Pictures of My Journey: Activities for kids with cancer; 2007.

The Stem Cell Transplant Coloring Book; 2007.

Glossary

Absolute Neutrophil Count (ANC)

The number of neutrophils (a type of white cell) that a person has to fight infection. It is calculated by multiplying the total number of white blood cells by the percentage of neutrophils.

Allogeneic Stem Cell Transplantation

A treatment that uses donor stem cells to restore a patient's marrow and blood cells. First, the patient is given "conditioning therapy" (high-dose chemotherapy or high-dose chemotherapy with total body radiation) to treat the leukemia and to "turn off" the patient's immune system so that the donor stem cells will not be rejected. A type of transplant called a "nonmyeloablative" transplant (or "mini" transplant) is under study. It uses lower doses of conditioning therapy and may be safer, especially for older patients. (For more information, see the Society's free booklet *Blood and Marrow Stem Cell Transplantation*.)

Anemia

A decrease in the number of red cells and, therefore, the hemoglobin concentration of the blood. This results in a decreased ability of the blood to carry oxygen. If severe, anemia can cause a pale complexion, weakness, fatigue and shortness of breath on exertion.

Antibodies

Proteins released by plasma cells (derived from B lymphocytes) that recognize and bind to the specific foreign substances called antigens. Antibodies coat, mark for destruction or inactivate foreign particles like bacteria and viruses or harmful toxins. Antibodies can also be made in the laboratory in two ways. If one injects material from one species into another, the latter will recognize the material as foreign and make antibodies to it. These antibodies are usually polyclonal antibodies, that is, they react to multiple targets (antigens). A laboratory technique is used to produce a specific antibody known as a monoclonal antibody. Monoclonal antibodies react to only one target (antigen) and can be used in several important ways. They can be used to identify and classify human leukemias and lymphomas or can be altered to make them useful in antibody-mediated immunotherapy.

Antigen
A foreign substance, usually a protein, that stimulates an immune response when it is ingested, inhaled or comes into contact with the skin or mucous membranes. Examples of antigens are bacteria, viruses, or allergens. Antigens stimulate plasma cells to produce antibodies.

Antioncogene See Tumor Suppressor Gene.

Apheresis
The process of removing components of a donor's blood and returning the unneeded parts to the donor. The process, also called hemapheresis, uses continuous circulation of blood from a donor through an apparatus and then back to the donor. This process makes it possible to remove desired elements from large volumes of blood. Platelets, red cells, white cells and plasma can be removed separately. For example, this technique permits the harvest of enough platelets for transfusion from one donor (rather than six to eight separate donors). In so doing, the recipient of the platelets is exposed to fewer donors or can be given HLA-matched platelets from a single related donor. This technique is also used to remove circulating blood stem cells, which can be frozen, stored and later used, instead of marrow stem cells, for transplantation.

Autologous Stem Cell Infusion
A technique, often referred to as "autologous stem cell transplantation," involving 1) harvesting the patient's stem cells from blood or marrow, 2) freezing them for later use and 3) thawing and infusing them via an indwelling catheter after the patient has been given intensive chemotherapy or radiation therapy. The blood or marrow may be obtained from a patient with a disease of the marrow, such as acute myelogenous leukemia, when in remission or when the marrow and blood are not overtly abnormal (for example, in lymphoma). Technically, this procedure is not transplantation, which implies taking tissue from one person (donor) and giving it to another person (recipient). The purpose of this procedure is to restore blood cell production from the preserved and reinfused stem cells after intensive therapy has severely damaged the patient's remaining marrow. This procedure can be performed using marrow or blood stem cells. The latter can be harvested by hemapheresis. (For more information, see the Society's free booklet *Blood and Marrow Stem Cell Transplantation*.)

Banding of Chromosomes
The staining of chromosomes with dyes that highlight transverse bands or regions on the chromosome. The bands give the chromosomes more specific features, allowing individual distinctions to be made among them. This technique permits more precise identification of chromosomes. (See Fluorescent In Situ Hybridization.)

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

Blast Cells
The earliest marrow cells identified by the light microscope. Blasts represent about 1 percent of normally developing marrow cells. They are largely myeloblasts, which are cells that will develop into neutrophils. In normal lymph nodes, blasts are lymphoblasts; that is, cells that are part of lymphocyte development. In the acute leukemias, blast cells similar in appearance to normal blast cells accumulate in large numbers, perhaps constituting up to 80 percent of all marrow cells. In acute myelogenous leukemia, myeloblasts accumulate, and in acute lymphocytic leukemia, lymphoblasts accumulate. Normal myeloblasts give rise to granulocytes (neutrophils, eosinophils, and basophils). With acute myelogenous leukemia, abnormal myeloblasts displace or otherwise interfere with the production of normal red cells, white cells and platelets in the marrow. Sometimes the distinction between myeloblasts and lymphoblasts can be made by examination of stained marrow cells through the microscope. Often, immunophenotyping or use of special staining of marrow cells is required to be sure of the distinction.

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, hip, shoulders and skull is most active in blood cell formation. In adults, the bones of the hands, feet, legs and arms do not contain marrow in which blood cells are made. In these sites the marrow is filled with fat cells. When marrow cells have matured into blood cells, they enter the blood that passes through the marrow and are carried throughout the body.

Bone Marrow Aspiration
A test to examine marrow cells to detect cell abnormalities. A marrow sample is usually taken from the patient's hip bone. After medication is given to numb the skin, the sample is removed using a special needle inserted through the bone into the marrow. The sample is looked at under a microscope for abnormal cells such as

leukemic blast cells. The cells obtained can also be used for cytogenetic analysis, flow cytometry and other tests.

Bone Marrow Biopsy
A test to examine 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 bone. After medication is given to numb the area, a special biopsy needle is used to remove a core of bone containing marrow. The marrow is examined under a microscope to determine if abnormal cells are present. Bone marrow aspiration and biopsy may be done in the doctor's office or in a hospital. The two tests are almost always done together. Both tests are also done after treatment to determine the proportion of blood cancer cells that have been killed by therapy.

Bone Marrow Transplantation See Allogeneic Stem Cell Transplantation; Autologous Stem Cell Infusion.

Central Nervous System (CNS) Prophylaxis
In certain types of leukemia, particularly acute lymphoblastic leukemia and the AML subtype, acute monocytic leukemia with high blood cell counts, there is a propensity for the leukemic cells to enter the covering of the spinal cord and brain (the meninges). This process is often not apparent until months or years after remission when the leukemia returns, first in the coverings of the CNS, then in the marrow and blood. To prevent this type of relapse (meningeal leukemia), virtually all children and adults with acute lymphocytic leukemia who enter remission, and at-risk patients with AML, are treated by placing appropriate chemotherapy in the space that bathes the spinal cord and brain to prevent the leukemia from returning in these sites. In some cases, x-ray therapy is administered to the head as well. These approaches are very effective in eliminating leukemia cells in the coverings of the brain and spinal cord.

Chemotherapy
The use of chemicals (drugs or medications) to kill malignant cells. Numerous chemicals have been developed for this purpose, and most act to injure the DNA of the cells. When the DNA is injured, the cells cannot grow or survive. Successful chemotherapy depends on the fact that malignant cells are somewhat more sensitive to the chemicals than normal cells. Because the cells of the marrow, the gastrointestinal tract, the skin and the hair follicles are most sensitive to these chemicals, injury to these organs causes the common side effects of chemotherapy for example, mouth sores and hair loss.

Chloroma
A solid tumor composed of immature granulocytes, including blast cells. Chloromas tend to occur in the brain or spinal cord, bones, skin, or soft tissue of the head and neck, although they can develop anywhere in the body. They are usually treated with radiation or chemotherapy. Chloromas are an uncommon complication of AML. Other terms for chloroma are "granulocytic sarcoma" and "extramedullary myeloblastoma."

Chromosome
One of the 46 structures in all human cells made up principally of genes, which are specific stretches of DNA. "Genome" is the term for an organism's complete set of DNA. It is estimated that the human genome has about 30,000 genes. The genes on the X and Y chromosomes, the sex chromosomes, are the determinants of our gender: two X chromosomes in females and an X and a Y chromosome in males. The number or size of chromosomes may be altered in lymphoma or leukemia cells as a result of chromosome breakage and rearrangement (translocation).

Clonal
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 to its DNA (mutation) and thus are monoclonal. Leukemia, lymphoma, and myeloma are examples of clonal cancers; that is, cancers derived from a single abnormal cell.

Colony Stimulating Factor See Cytokines.

Computed Tomography (CT) Scan
A technique for imaging body tissues and organs. X-ray transmissions are converted to detailed images using a computer to synthesize x-ray data. The images are displayed as a cross-section of the body at any level from the head to the feet. A CT scan of the chest or abdomen permits detection of an enlarged lymph node, liver or spleen. A CT scan can be used to measure the size of these and other structures during and after treatment.

Cord Blood Stem Cells
Stem cells that are present in blood drained from the placenta and umbilical cord. These stem cells have the capability to repopulate the marrow of a compatible recipient and produce blood cells. Frozen cord blood is a source of donor stem cells for transplantation to HLA-matched recipients. Most cord blood transplants are given by matched or nearly matched unrelated donors.

CT Scan See Computed Tomography Scan.

Cycle of Treatment

The designation for an intensive, clustered period of chemotherapy (and/or radiation therapy). The therapy may be given for several days or weeks, and this time period represents one cycle of treatment. The treatment plan may call for two, three or more cycles of treatment.

Cytogenetic Analysis

The process of analyzing the number and size of the chromosomes of cells. In addition to detecting chromosome alterations, in some cases it is possible to identify the actual genes that have been affected. These findings are very helpful in diagnosing specific types of leukemia and lymphoma, in determining treatment approaches and in following the response to treatment. The individual who prepares and examines the chromosomes and interprets the results is called a "cytogeneticist."

Cytokines

Cell- (cyto-) derived chemicals that are secreted by various types of cells and act on other cells to stimulate or inhibit their function. Chemicals derived from lymphocytes are called "lymphokines." Chemicals derived from lymphocytes that act on other white cells are called "interleukins"; that is, they interact between two types of leukocytes. Some cytokines can be made commercially and used in treatment. Granulocyte-colony stimulating factor (G-CSF) and granulocyte macrophage-colony stimulating factor (GM-CSF) are two such cytokines. They stimulate the production of neutrophils and shorten the period of low neutrophil counts in the blood after chemotherapy. Cytokines that stimulate cell growth are sometimes referred to as "growth factors."

Differentiation

The process by which stem cells give rise to functional cells of a single blood cell line. The differentiation of stem cells forms the red cells, platelets, neutrophils, monocytes, eosinophils, basophils and lymphocytes.

DNA

The genetic material in the cell. It is made up of a sugar-phosphate backbone, with ladder-like "steps" composed of purines and pyrimidines. It contains all the genes that are passed on from generation to generation. It can become highly abnormal in cancer cells. DNA is an abbreviation for deoxyribonucleic acid.

Eosinophil
A type of white cell that participates in allergic reactions and helps fight certain parasitic infections.

Erythrocytes See Red Cells.

FISH See Fluorescent In Situ Hybridization.

FLT3
An abbreviation for the FMS-like tyrosine kinase 3 gene. *FLT3* is expressed on blood-forming stem cells and plays a role in cell development. *FLT3* mutations can be detected in about one-third of AML patients. These mutations have been identified as part of the AML disease process and may become the basis for new targeted therapies.

Fluorescent In Situ Hybridization (FISH)
A technique in which DNA probes tagged with fluorescent molecules that emit light of different wavelengths (and different colors) are used on tissue. The probes match to the chromosomes within the cells, and the chromosomes fluoresce in color. FISH is a means of studying chromosomes in tissue.

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

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

Graft Versus Host Disease (GVHD)
The immune attack by lymphocytes in the donor's marrow or blood cell suspension (the graft) against the tissues of the recipient (the host). The immune cells most engaged in this reaction are donor T lymphocytes, which are present in the donor's blood or marrow, the source of stem cells. The principal sites of injury are the skin, the liver and the gastrointestinal tract. The reaction does not occur in identical twin transplants. The reaction may be minimal in closely matched individuals or severe in less well-matched individuals. These reactions are mediated in part by antigens that are not in the major HLA system and cannot be matched prior to transplant. For example, in the case of a female stem cell donor and a male recipient, factors that are produced by genes on the Y chromosome may be seen as foreign by the female donor's cells, which do not share the genes on the Y chromosome. This fact does not prohibit female donors and male recipients, but it makes the risk of immune reaction higher.

Granulocyte
A type of white cell that has a large number of granules in the cell body. Neutrophils, eosinophils and basophils are types of granulocytes.

Granulocytic Sarcoma See Chloroma.

Growth Factors See Cytokines.

Hemapheresis See Apheresis.

Hematologist
A physician who specializes in the treatment of blood cell diseases. This person is either an internist who treats adults or a pediatrician who treats children.

Hematopathologist See Pathologist.

Hematopoiesis
The process of blood cell development in the marrow. The most undeveloped cells in the marrow are stem cells. They start the process of blood cell development. The stem cells begin to develop into young or immature blood cells such as red cells or white cells of various types. This process is called "differentiation." The young or immature blood cells then further develop into fully functional blood cells. This process is called "maturation." The cells then leave the marrow and enter the blood and circulate throughout the body (see Figure 1 on page 4.) Hematopoiesis is a continuous process that is active normally throughout life. The reason for this activity is that most blood cells live for short periods and must be continually replaced. Red cells die in four months, platelets in 10 days and most neutrophils in two or three days. About 500 billion blood cells are made each day. This requirement for very rapid replacement explains the severe deficiency in blood cell counts when the marrow is injured by replacement with leukemia, lymphoma or myeloma cells.

HLA
The abbreviation for human leukocyte-associated antigens. These proteins are on the surface of most tissue cells and give an individual his or her unique tissue type. 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. The testing for HLA antigens is referred to as "tissue typing." There are six major groups of HLA antigens: A, B, C, D, Dr, and Dq. These proteins on the surface of cells act as antigens when donated (transplanted) to

another individual, the recipient. If the antigens on the donor cells are identical (for example, in identical twins) or very similar (for example, in HLA-matched siblings), the transplant (donated stem cells) is more likely to survive (engraft) in the recipient. In addition, the recipient's body cells are less likely to be attacked by the donated immune cells (a result called "graft versus host disease").

Immunophenotyping

A method that uses the reaction of antibodies with cell antigens to determine a specific type of cell in a sample of blood cells, marrow cells or lymph node cells. The antibodies react with specific antigens on the cell. A tag is attached to an antibody so that it can be detected. The tag can be identified by the laboratory detector used for the test. As cells carrying their array of antigens are tagged with specific antibodies, they can be identified; for example, myelogenous leukemic cells can be distinguished from lymphocytic leukemic cells. Normal lymphocytes may be distinguished from leukemic lymphocytes. This method also helps subclassify cell types, information which may, in turn, help in deciding on the best treatment to apply in that type of leukemia or lymphoma. The antigen on a cell is referred to as a "cluster of differentiation" or "CD," with an associated number. For example, CD10, also referred to as "CALLA" (common acute lymphoblastic leukemia antigen) may be present on leukemic lymphoblasts, and CD33, the target of the drug Mylotarg®, may be present on leukemic myeloblasts.

Indwelling Catheter

Several types of catheters (for example, Groshong®, Hickman®, and Broviac®) can be used for patients receiving intensive chemotherapy or nutritional support. An indwelling catheter, sometimes called a central line or a port, is a special tubing inserted into a large vein in the upper chest. The catheter is tunneled under the skin of the chest to keep it firmly in place. The external end of the catheter can be used to administer medications, fluids, or blood products or to withdraw blood samples. With meticulous care, catheters can remain in place for long periods of time (many months) if necessary. They can be capped and remain in place in patients after they leave the hospital, and be used for outpatient chemotherapy or blood product administration. An implanted port is another type of long-term catheter to a central vein. The port is surgically inserted under the skin's surface on the upper chest wall. After the site heals, no dressings are needed and no special home care is required. When medicines are needed, a physician, physician assistant or nurse inserts a needle through the skin to access the port. The patient can choose to have a local numbing cream applied to the injection site before the port is used. Blood can be drawn, and blood products can be received through this device.

Intrathecal
The space between the covering or lining of the central nervous system (CNS) and the brain or spinal cord. The lining is called the meninges. In some situations drugs have to be administered directly into the spinal canal when leukemia cells are in the meninges. This is called "intrathecal therapy."

Karyotype
The systematic arrangement, using images, of the 46 human chromosomes of a cell in 22 matched pairs (maternal and paternal member of each pair) by length from longest to shortest and other features. These 22 pairs are referred to as "autosomes." The sex chromosomes are shown as a separate pair (either XX or XY). (See Fluorescent In Situ Hybridization.)

Leukocytes See White Cells.

Leukopenia
A decrease below normal in the concentration of blood leukocytes (white cells).

Lymphatic System
The system comprising the lymph nodes, the thymus gland (in the first several decades of life), the lymphatic channels, the lymphatic tissue of the marrow, the gastrointestinal tract, the skin and the spleen, and including the T, B and NK lymphocytes contained in those sites.

Lymph Nodes
Small structures, the size of beans, that contain large numbers of lymphocytes and are connected with each other by small channels called "lymphatics." These nodes are distributed throughout the body. In patients with lymphoma and some types of lymphocytic leukemia, the malignant lymphocytes grow and expand the lymph nodes so that they may become enlarged. This enlargement of lymph nodes can be seen, felt or measured by computed tomography (CT) scan or magnetic resonance imaging (MRI), depending on the degree of enlargement and location.

Lymphocyte
A type of white cell that is the essential cell type in the body's immune system. There are three major types of lymphocytes: B lymphocytes that produce antibodies to help combat infectious agents like bacteria, viruses and fungi; T lymphocytes that have several functions, including assisting B lymphocytes to make antibodies; and natural killer cells, which can attack virus-infected cells or tumor cells.

Lymphokines See Cytokines.

Macrophage See Monocyte.

Marrow See Bone Marrow.

Monoclonal See Clonal.

Monocyte
A type of white cell that represents about 5 to 10 percent of the cells in normal human blood. The monocyte and the neutrophil are the two major microbe-eating and killing cells in the blood. When monocytes leave the blood and enter the tissue, they are converted to macrophages. The macrophage is the monocyte in action, and 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.

MRI (Magnetic Resonance Imaging)
A technique that provides detailed images of body structures. It differs from the CT scan in that the patient is not exposed to x-rays. The signals generated in the tissues in response to a magnetic field produced by the instrument are converted by computer into images of body structures. Thus, the size, or a change in size, of organs such as the lymph nodes, liver and spleen or of tumor masses can be measured. This technique provides detailed images of body structures.

Multidrug Resistance (MDR)
A characteristic of cells that makes them resistant to the effects of several different classes of drugs. There are several forms of drug resistance. They are each determined by genes that govern how the cell will respond to the chemical agents. One type of multidrug resistance (MDR) involves the ability to eject several drugs out of cells. The outer wall, or membrane, of the cell contains a pump that ejects chemicals, preventing them from reaching a toxic concentration. The resistance to drugs can be traced to the expression of genes that direct the formation of high amounts of the protein that prevents the drugs from having their effects on the malignant cells. If the gene or genes involved are not expressed or are weakly expressed, the cells are more sensitive to the drug's effect. If the genes are highly expressed, the cells are less sensitive to the drug's effect.

Mutation
An alteration in a gene that results from a change to a part of the stretch of DNA that represents a gene. A "germ cell mutation" is present in the egg or the sperm and can be transmitted from parent(s) to offspring. A "somatic cell mutation" occurs in a specific tissue cell and can result in the growth of that specific tissue cell into a tumor. Most cancers start after a somatic mutation. In leukemia, lymphoma or myeloma, a primitive marrow or lymph node cell undergoes a somatic mutation (or mutations) that leads to the formation of a tumor. Cases of leukemia, lymphoma or myeloma are caused by a somatic mutation in a primitive marrow (blood-forming) or lymphatic system cell. If the mutation results from a major abnormality of chromosomes such as a translocation, it can be detected by cytogenetic examination. Sometimes the alteration in the gene is more subtle and requires more sensitive tests to identify the oncogene.

Myeloblasts See Blast Cells.

Neutropenia
A decrease below normal in the concentration of neutrophils, a type of white cell.

Neutrophil
The principal phagocyte (microbe-eating) cell in the blood. This blood cell is the main cell that combats infections. Often, it is not present in sufficient quantities in patients with acute leukemia or after chemotherapy. A severe deficiency of neutrophils increases the patient's susceptibility to infection. A neutrophil may be called a "poly" (polymorphonuclear neutrophil) or "seg" (segmented neutrophil) because its nucleus has several lobes.

Oncogene
A mutated gene that is the cause of a cancer. Several subtypes of acute myelogenous leukemia, acute lymphocytic leukemia and lymphoma, and nearly all cases of chronic myelogenous leukemia, are each associated with a mutated gene (oncogene).

Oncologist
A physician who diagnoses and treats patients with cancer. Oncologists are usually internists who treat adults or pediatricians who treat children. Radiation oncologists specialize in the use of radiation to treat cancer, and surgical oncologists specialize in the use of surgical procedures to diagnose and treat cancer. These physicians cooperate and collaborate to provide the best treatment plan (surgery, radiation therapy, chemotherapy or immunotherapy) for the patient.

Pancytopenia
A decrease below normal in the concentration of the three major blood cell types: red cells, white cells and platelets.

Pathologist
A physician who identifies disease by studying tissues under a microscope. A hematopathologist is a type of pathologist who studies diseases of blood cells by looking at peripheral blood smears, bone marrow aspirates and biopsies, and lymph nodes and other tissues and uses his or her expertise to identify diseases such as acute myelogenous leukemia. In addition to using a microscope, a hematopathologist also uses laboratory values, flow cytometry and molecular diagnostic tests to make the most accurate diagnosis. The hematopathologist works closely with the hematologist/oncologist who sees the patient and decides on the best treatment based upon the diagnosis.

Petechiae
Pinhead-sized sites of bleeding in the skin. This type of bleeding results from a very low platelet count. The small punctate hemorrhages are frequently seen on the legs, feet, trunk and arms. They evolve from red to brown and eventually disappear. They stop developing when the platelet count increases.

Phagocytes
Cells that readily eat (ingest) microorganisms such as bacteria and fungi and can kill them as a means of protecting the body against infection. The two principal phagocytes are neutrophils and monocytes. They leave the blood and enter tissues in which an infection has developed. A severe decrease in the blood level of these cells is the principal cause of susceptibility to infection in patients treated with intensive radiotherapy and/or chemotherapy. The latter treatments suppress blood cell production in the marrow, resulting in deficiencies of these phagocytic cells.

PICC (Peripherally Inserted Central Catheter or PIC line)
A long, thin flexible tube that is used to administer medications, antibiotics, fluids and nutrition for an extended period of time; it can also be used to obtain blood samples. Prior to insertion of the PICC, the patient is given a local anesthetic to numb the arm in the area above the elbow and below the shoulder. The PICC is inserted through the skin into a vein in the arm and advanced until it reaches the superior vena cava just above the heart. The superior vena cava is one of the veins in the central venous system. The PICC can be maintained for several weeks to months, eliminating the need for standard intravenous (IV) administration.

Platelets
Small cell fragments (about one-tenth the volume of red cells) that stick to the site of blood vessel injury, aggregate and seal off the injured blood vessel to stop bleeding. "Thrombocyte" is a synonym for platelet and is often used as the prefix in terms describing disorders of platelets, such as thrombocytopenia or thrombocythemia.

Platelet Transfusion
The transfusion of donor platelets that is frequently needed to support patients treated for acute leukemia. The platelets can be pooled from several unrelated donors and given as pooled, random-donor platelets. The platelets from about six one-unit blood donors are required to significantly raise the platelet count in a recipient. Sufficient platelets can be obtained from one donor by a procedure known as apheresis. This technique skims the platelets of large volumes of blood passing through the apheresis machine. The red cells and plasma are returned to the donor. The advantage of single-donor platelets is that the patient is not exposed to the different antigens on platelets from many different people and is less likely to develop antibodies against donor platelets. HLA-matched platelet transfusion can be given from a related donor with an identical or very similar HLA tissue type.

Polymerase Chain Reaction (PCR)
A technique to expand trace amounts of DNA or RNA so that the specific type of the DNA or RNA can be studied or determined. This technique has become useful in detecting a very low concentration of residual leukemia or lymphoma cells, too few to be seen using a microscope. PCR can detect the presence of one leukemic cell among 500,000 to one million nonleukemic cells. PCR requires a specific DNA (or RNA) abnormality or marker, like an oncogene, in the leukemic or lymphomatous cells in order to be used for identifying residual abnormal cells.

Recurrence See Relapse.

Red Cells
Blood cells (erythrocytes) that carry hemoglobin, which binds oxygen and carries it to the tissues of the body. The red cells make up about 40 to 45 percent of the volume of the blood in healthy individuals.

Refractory Disease
Disease that does not go into remission or improve substantially after initial treatment with standard therapy for the disease.

Relapse (Recurrence)
A return of the disease after it has been in remission following treatment.

Remission
A disappearance of evidence of a disease, usually as a result of treatment. The terms "complete" and "partial" are used to modify 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. Long-term benefit usually requires a complete remission, especially in acute leukemia or progressive lymphomas.

Resistance to Treatment
The ability of cells to live and divide despite their exposure to a chemical that ordinarily kills cells or inhibits their growth. Refractory leukemia is the condition in which a proportion of malignant cells resist the damaging effects of a drug or drugs. Cells have several ways to develop drug resistance. (See Multidrug Resistance.)

Sanctuary Sites
Areas of the body in which it is difficult to get a sufficient concentration of chemotherapy to destroy leukemia cells. In acute myelogenous leukemia, the coverings (meninges) of the brain and spinal cord and the testes are notable sanctuary sites.

Somatic Mutation See Mutation.

Spleen
An organ located in the left upper portion of the abdomen just under the left side of the diaphragm. It contains clusters of lymphocytes and also filters the blood of old or worn-out cells. It is often affected in lymphocytic leukemias and lymphomas. Enlargement of the spleen is called splenomegaly. Removal of the spleen by surgery is known as splenectomy. Removal of the spleen is used to treat certain diseases. Most of the functions of the spleen can be performed by other organs, such as the lymph nodes and liver, but a person whose spleen has been removed is at higher risk for infection. He or she is given antibiotic therapy immediately at the first sign of infection, such as a fever.

Stem Cells
Primitive cells in marrow that are required to make red cells, white cells and platelets. Stem cells are largely found in the marrow, but some leave the marrow and circulate in the blood. Using special techniques, the stem cells in blood can be collected, preserved by freezing and later thawed and used for stem cell therapy. (See Hematopoiesis.)

Stem Cell Transplantation See Allogeneic Stem Cell Transplantation; Autologous Stem Cell Infusion.

Thrombocytopenia
A decrease below normal in the concentration of the blood platelets.

Translocation
An abnormality of chromosomes in marrow or lymph node cells that occurs when a piece of one chromosome breaks off and sticks to the end of another chromosome. In a balanced translocation, genetic material is exchanged between two different chromosomes with no gain or loss of genetic information. When a translocation occurs, the gene at which the break occurs is altered. This is one form of somatic mutation that may transform the gene into an oncogene (cancer-causing gene). (See Chromosome.)

Tumor Suppressor Gene
A gene that acts to prevent cell growth. If a mutation occurs in this gene that "turns off" the gene and causes loss of function, it may make the individual more susceptible to the development of cancer in the tissue in which the mutation occurred. Another term for tumor suppressor gene is "antioncogene."

White Cells
Leukocytes. There are five major types of white cells in the blood: neutrophils, eosinophils, basophils, monocytes and lymphocytes.

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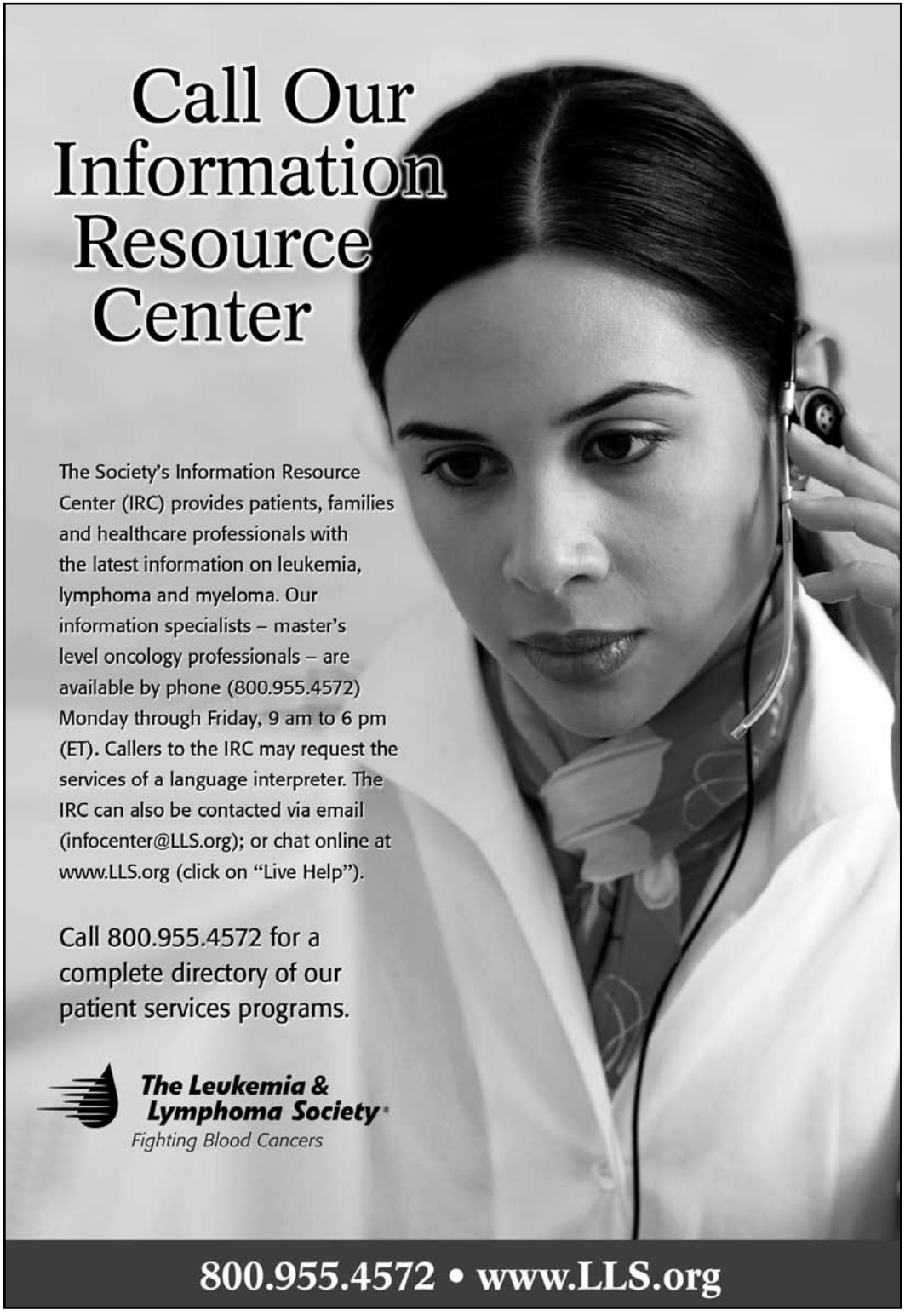
Notes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