



Myelodysplastic Syndrome



**The Leukemia &
Lymphoma Society®**

Fighting Blood-Related Cancers



Making cancer more treatable



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Table of Contents

Introduction	2
Normal Blood and Marrow	3
Myelodysplastic Syndromes	5
Incidence	6
Disease Subgroups	7
Signs and Symptoms	9
Causes and Risk Factors	10
Diagnosis	10
Emotional Aspects	13
The Future	14
Glossary	15
Further Readings	28
Other Resources	29

Words in the glossary are italicized the first time that they appear in the text.

Neoplasms or cancers of the blood-forming cells have a wide expression. This means that *blood counts* may be low or high. Counts of *red cells*, *white cells*, and *platelets* may be affected to different degrees and abnormalities of cell structure and function may vary widely among the several blood cell types. The blood cell–related cancers referred to as myelodysplastic diseases may be non-progressive and have little consequence to ones health and life-expectancy or, more often, are slower progressing types of myelogenous *leukemia* that may have a profound effect on health and life-expectancy.

In the 1970's the full spectrum of myelogenous cancers was not well catalogued. In the late 1970's, the term myelodysplastic syndrome, abbreviated as MDS, was coined to encompass a subset of these neoplasms. Use of the suffix -dysplasia is both misleading and imprecise for medical usage because these are not dysplastic diseases; they are neoplastic diseases. Moreover, the subset of disorders included in this category that result in *anemia* and sometimes slight or moderate changes in white cell or platelet counts may be stable for decades without dramatic health consequences. Those cases that have severe *cytopenias* and leukemic *blast cells* usually result in serious problems related to severe anemia and sometimes exaggerated bleeding and recurrent infections. Each group may progress to more full-blown myelogenous leukemia but this occurs more frequently and sooner in the more severe type of myelodysplastic syndrome.

Features that are often common among these disorders include: 1) the propensity to changes in the structure of cells that are visible using the light microscope. These size and shape changes in red cells and alterations in the appearance of white cells and platelets, which can be

appreciated through the microscope, are helpful in diagnosis and account for the application of the term “myelodysplasia”; 2) a propensity to low red cell, white cell, and often platelet counts is a frequent feature; 3) in close parallel to acute and chronic myelogenous leukemia, the incidence of the nonprogressive and progressive types of myelodysplastic syndrome increase exponentially with age and most cases occur after age 60 years.

Normal Blood and Marrow

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 (e.g., albumin), hormones (e.g., thyroid hormone), minerals (e.g., iron), vitamins (e.g., folic acid), and antibodies, including those we develop from our immunizations (e.g., polio virus antibodies). The cells include red *blood cells*, platelets, neutrophils, monocytes, eosinophils, basophils, and lymphocytes.

The red cells make up half the volume of the blood. They are filled with *hemoglobin*, the protein that picks up oxygen in the lungs and delivers oxygen to the tissues. The platelets are small cells (one-tenth the size of red cells) that help stop bleeding if one is injured. For example, when one has a cut, the blood vessels that carry blood are torn open. Platelets stick to the torn surface of the vessel, clump together, and plug up the bleeding site. The vessel wall then heals at the site of the clot and returns to its normal state.

The neutrophils and monocytes are white blood cells. They are phagocytes (or 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 move into the tissues where they can ingest invading bacteria or

fungi and help cure an infection. Eosinophils and basophils are two additional types of white cells that participate in allergic responses.

Most lymphocytes, another type of white blood cell, are in the lymph nodes, spleen, and lymphatic channels, but some enter the blood.

There are three major types of lymphocytes: T cells, B cells, and natural killer (NK) cells.

Bone marrow is the spongy tissue where blood cell development takes place. It occupies the central cavity of bone. All bones have active marrow at birth. 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, breast bone, and skull contain marrow that is actively making blood cells.

The process of blood cell formation is called hematopoiesis. A small group of cells, the *stem cells*, are responsible for making all the blood cells in the marrow. The stem cells eventually develop into the specific blood cells by a process of differentiation (see Figure 1). In healthy individuals, there are sufficient 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 counts. Their presence in the blood is important, because they can be collected by special techniques and transplanted into a recipient if enough stem cells are harvested from a compatible donor. This stem cell circulation from marrow to blood and back occurs in the fetus as well. That is why, after birth, the placental and umbilical cord blood can be used as a source of stem cells for transplantation.

In summary, blood cells are made in the marrow and when the cells are fully formed and able to function, they leave the marrow and

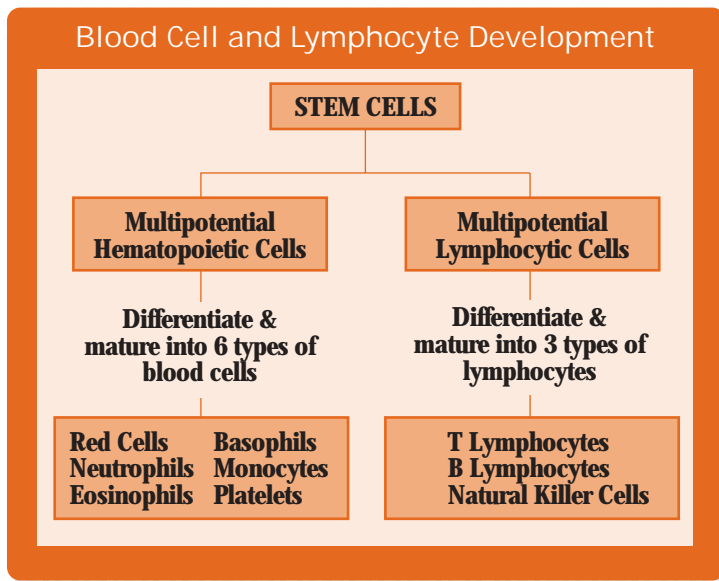


Figure 1. This figure depicts an abbreviated diagram of the process of hematopoiesis. This process involves the development of functional blood and lymphatic cells from stem cells.

enter the blood. The red cells and the platelets perform their respective functions of delivering oxygen and plugging up injured blood vessels in the circulation. The neutrophils, eosinophils, basophils, monocytes and lymphocytes, which are collectively the white blood cells, move into the tissues of the lungs, for example, and can combat infection, such as pneumonia, and perform their other functions.

Myelodysplastic Syndromes (MDS)

Myelodysplastic Syndromes are a group of diseases that originate in an early blood-forming cell in the marrow. In patients with this disorder, the marrow produces too few red blood cells, white blood cells and often platelets. In the myelodysplastic syndromes, the maturing blood cells often die in the marrow before they reach full maturity and enter the blood, accounting for the low blood cell concentrations.

There may also be an accumulation of very immature marrow cells, called leukemic blast cells. (See Appendix for description of normal blood and marrow.)

The severity of the marrow cell disturbance is varied and can range from mild to very severe.

Thus, the disease may be indolent or chronic and be manifest primarily as mild anemia; it may have severe decreases in red and white blood cells and platelets and be more troublesome; or, it may have severe decreases in blood cells and have leukemic blast cells in the marrow and be even more threatening to the health of the patient. In addition, the disease can progress such that the leukemic blast cells take over the marrow and the disease evolves into *acute* myelogenous leukemia. The marked decrease in blood cell formation makes it difficult for patients to prevent or fight infection and it predisposes them to exaggerated bleeding. (See the Society booklet on *Acute Myelogenous Leukemia*).

Incidence

The annual incidence of new cases of MDS in the United States is not known. There are about 10,000 cases of acute myelogenous leukemia each year and about 5000 cases of unclassified leukemia. The annual incidence may be in the range of 4000 to 6000 cases per year. The age of onset closely follows that of acute myelogenous leukemia increasing dramatically after age 50 years. The disorder uncommonly can occur in children and may be associated with certain abnormalities of chromosome 5 or 7. The disorder affects both genders but, like other leukemias, is more common in men than women.

Disease Subgroups

Although myelodysplastic syndrome covers a spectrum of neoplastic myeloid diseases, most cases can be placed into several subgroups based on the blood cell counts and the appearance of blood cells under the microscope. The two principal subgroups are:

Chronic and nonprogressive anemia

Blood cell count deficiencies without evidence of leukemic blast cells make up about one third of the myelodysplastic disorders. The disorder may cause principally a deficiency 1) of red cells, 2) of red cells and white cells, or 3) of red cells, white cells, and platelets. These situations are often referred to as *refractory anemia* (even though white cell and platelet counts may be low as well as red cell counts). These situations may be nonprogressive for years or decades. If the blood cell count deficiencies are mild, the circumstance may have little effect on the patient's ability to conduct his or her usual activities. About ten to fifteen percent of patients in this subgroup may later develop acute myelogenous leukemia.

A special feature, abnormal sideroblasts, may be present in the developing red cells in the marrow. In such cases, the disease is often referred to as "refractory sideroblastic anemia." Sidero- is a prefix meaning iron, from the Greek word for iron "sideros." All normal developing red cells contain fine particles of iron that are incorporated into hemoglobin, the oxygen-carrying protein that give red cells their color and functional capability. In the case of abnormal sideroblasts, large quantities of iron are trapped in the developing red cells in abnormal sites. Staining marrow cells for iron and examining them under the microscope can identify these cells or abnormal sideroblasts.

The terms “acquired sideroblastic anemia” or “refractory sideroblastic anemia” are often used to designate a myelodysplastic syndrome in which anemia is a prominent feature and the iron stain of marrow cells uncovers abnormal iron deposits in the developing red cells. In situations in which the iron stain of the marrow does not uncover abnormal sideroblasts, the disorder is sometimes referred to as “acquired or refractory nonsideroblastic anemia.” (Table 1.) The term “refractory” is obsolescent but deeply entrenched. This term was applied in the early decades of the twentieth century to indicate that these anemias did not respond to iron or vitamin therapy. Thus anemias were divided into those that responded to iron or vitamins and those that were refractory or nonresponsive to those treatments. Today, we recognize that these anemias are secondary manifestations of a malignant change in an early blood-forming marrow cell. Like other malignancies, some are less progressive (benign) and others more rapidly progressive (malignant).

Table 1. Terms associated with various manifestations of the myelodysplastic syndrome

Acquired refractory anemia (syn. *clonal anemia*)

**Acquired refractory sideroblastic anemia
(syn. *clonal sideroblastic anemia*)**

**Pancytopenia with hyperplastic marrow
(syn. *clonal pancytopenia*)**

**Refractory anemia with excess blasts
(syn. *oligoblastic myelogenous leukemia*)**

**Refractory anemia with excess blasts in transformation
(syn. *acute myelogenous leukemia*)**

See text and Glossary for further descriptions of table entries

Progressive and symptomatic blood cell deficiencies

The second principal subgroup of myelodysplastic disease shows evidence of leukemic blast cells in the marrow. This finding is associated often with low red cell, white cell, and platelet counts, and other changes of blood cell shape and structure under the microscope that is characteristic of these leukemic syndromes. This category of disease has been variously designated as low blast count myelogenous leukemia, *refractory anemia with excess blasts*, smoldering leukemia and other designations. Like the other category of myelodysplastic syndrome, it may have a wide range of severity and a difference in the rate of worsening. If the leukemic blast count was high the designation “refractory anemia with excess blasts in transition” (to acute myelogenous leukemia) was used but the designation is not useful and it has been recommended that it be dropped. (Table 1). Such patients are considered to have acute myelogenous leukemia. In fact, these disorders are each gradations of severity of myelogenous leukemia. The proportion of leukemic blasts cells in the marrow and the degree of the abnormalities in blood cell counts correlates with the rate of progression of the disease.

Signs and Symptoms

In the chronic or nonprogressive form of the disorder, the diagnosis may first be suspected from a finding of anemia during a medical evaluation. If the anemia is moderate or severe, exaggerated fatigue, shortness of breath on exertion (such as during climbing stairs), pale skin, or weakness may be present. In this form of the disease abnormalities in white cells or platelets, which may be present, are usually insufficient to contribute to signs or symptoms. In the more advanced and progressive form of the disease, which is a low blast cell count myelogenous leukemia, the patient often comes to medical attention

because of loss of sense of well being, fatigue, weakness, or loss of appetite. Occasionally skin bleeding, also called *purpura*, and prolonged bleeding from cuts is the result of very low platelet counts. Skin, sinus or urinary tract infections or infections in other sites may occur because of low white cell counts. In general, recurrent infections of consequence are not usually prominent at the time of onset.

Causes and Risk Factors

The causes of MDS are similar to those of acute myelogenous leukemia. In most cases the disease has no external antecedent cause. The use of certain drugs that are designed to damage DNA and are used to treat lymphoma, myeloma, or other cancers such as breast or ovarian cancer increase the risk of developing acute myelogenous leukemia or a myelodysplastic disorder. The same sequence of events can follow the use of therapeutic radiation for lymphoma. Benzene exposure above threshold levels for protracted periods of time usually in an industrial setting may increase the incidence of acute myelogenous leukemia and may precede the onset of myelodysplasia. The increasingly stringent regulation of benzene use in the workplace has diminished this sequence of events.

Diagnosis

A diagnosis can only be made by measuring the blood cell counts and examining the appearance of blood cells through the microscope, usually supplemented by a microscopic examination of marrow cells. Evaluation of chromosome structure using techniques applicable to blood and marrow cells can be performed on the samples obtained. This cytogenetic evaluation can be helpful in reaching a conclusion about the diagnosis.

Determining the Need for Treatment and Treatment Approaches

When a serious disease is diagnosed and the physician recommends watchful waiting, patients are sometimes dismayed. In this group of diseases, those at the chronic and stable or indolent end of the spectrum are often not treated. Patients can tolerate mild or moderate decreases in blood cell counts without impairment of their usual activities.

In patients with more troublesome decreases in blood cell counts, drugs that can stimulate blood cell production may be useful. Erythropoietin, granulocyte-colony stimulating factor (G-CSF), and interleukin-11(IL-11) are examples of drugs that can increase red cell, white cell, or platelet counts. These approaches work in some but not all patients and if necessary periodic red cell or *platelet transfusion* therapy may be required.

Prompt attention to overt infection or unexplained fever is also important. Where bacterial or fungal infections are identified or strongly suspected appropriate antibiotics may be required. In certain viral infections responsive to special antiviral drugs, these may be used.

In more severe and progressive cases, the disease may require treatment with cytotoxic drugs. This form of treatment, *chemotherapy*, is planned depending on the age and coexisting medical conditions of the patient, the severity of the manifestations of the disease, and the rate of progression of the disease. Cytosine arabinoside (ara-c), idarubicin, daunorubicin, 6-thioguanine, or mitoxantrone are drugs that may be used. The drugs may be given alone or in a combination (combination chemotherapy) of two or three different agents. In some cases, low-dose programs are used. The application of chemotherapy

will make the cell counts worse, initially. Thus, the physician has to make a judgment that intensive chemotherapy is warranted because of the severity of the cell disturbances and that the patient has a reasonable chance of responding to the initial cytotoxic phase of therapy with a *remission*. In the very small proportion of patients who are under 50 years of age with a severe form of myelodysplastic syndrome, intensive radiation and/or chemotherapy followed by *allogeneic stem cell transplantation* can be considered.

Disease Management and Health Problems (Complications)

Living with a serious disease can be a difficult challenge. Patients may need to make changes in their lifestyle, which can be distressing. MDS also places a strain on family members and friends. Talking to the physicians and nurses who provide care may help ease concerns about the disease and the future. The professional staff is also prepared to offer referrals to other resources. Many patients feel emotional relief once they can reestablish a sense of control in their lives. The following information may assist in the management of common health problems for patients with the disease.

The Course of the Disease

In patients who have the least consequential type of myelodysplastic syndrome, such as mild refractory anemia with mild to moderate decreases in white cell and platelet counts, the abnormalities may not require treatment and activity levels are little affected. It is prudent to have a physician familiar with the problem evaluate the patient and monitor the blood cells periodically. It is not uncommon for years or decades to pass with little change in status. Since there is a risk of evolution to a more severe disturbance in blood cell formation, which

in the extreme is acute myelogenous leukemia, periodic surveillance is important. In patients who have more severe problems, treatment to improve blood cell counts may lead to alleviation of symptoms. Curative therapy is not available for most patients at this time. Younger individuals who are candidates for allogeneic stem cell transplantation may have restoration of normal blood cell formation after a successful transplant.

Emotional Aspects

The diagnosis of myelodysplastic syndrome may provoke a profound emotional response in patients, family members and friends. Denial, depression, a feeling of hopelessness, and fear are normal and usual reactions. No one response is either expected or unexpected.

A lack of understanding of what's in store, the unknown, and what's next should be met by thoughtful, straightforward, and frequent discussions between physician, nurse, patient, and family. An inability to work, tend to business affairs, or interact with family and friends in the usual manner may contribute to emotional distress. Thorough explanations, including the plans for treatment, may bring some emotional relief as the patient focuses on the treatment ahead and the prospect of improvement.

Family members or loved ones may have questions about chemotherapy and alternative methods of treatment. It is best to speak directly with physicians regarding specific medical questions. Family members or loved ones should discuss any problems or reactions they may have. Nurses and other health professionals understand the complexity of emotions and the special ongoing needs of those living with the disease. They also will spend time with patients, becoming their

confidants, and can be very helpful in their emotional support. For more information about the social and emotional aspects of the disease, you may request a copy of the following Society publication: *Coping With Survival*, a booklet dealing with the psychosocial aspects of the disease for patients.

The Future

New Drugs or the New Application of Current Drugs

It is anticipated that new drugs and the combination of drugs will prove useful in treatment. As an example, thalidomide (Thalomid), which can be useful in the treatment of myeloma, is being studied as a means of improving red cell counts and decreasing transfusion requirements in patients with myelodysplasia. Early results have been promising. Arsenic trioxide (Trisenox), which is used principally to treat acute promyelocytic leukemia, may be useful in treating myelodysplasia. Clinical studies of its usefulness are underway.

New Approaches to Stem Cell Transplantation

The use of allogeneic transplantation using approaches that are less toxic to the patient (marrow or blood stem cell recipient) may become available to those patients with a donor. These “nonablative” transplants or “mini” transplants are being studied in order to make transplantation available in an older age group for whom transplantation has heretofore not been a reasonable treatment option.

Acute Leukemia

A rapidly progressive malignant disease of the bone marrow and blood that results in the accumulation of immature, functionless cells called blast cells in the marrow and blood. The accumulation of blast cells in the marrow blocks normal blood cell development. As a result, red cells, white cells and platelets are not produced in sufficient numbers. When the disease originates in a marrow lymphocyte progenitor cell, it results in acute lymphoblastic leukemia and when the disease originates in a myeloid progenitor, it results in acute myelogenous leukemia. AML has the greatest incidence of leukemia in adults, with an estimated 10,000 new cases per year in all age groups. ALL is the most common type of childhood leukemia, with 3,000 new cases per year in all age groups.

Allogeneic Stem Cell Transplantation

The transfer of stem cells from one person, the donor, to another, the recipient who is not an identical twin. In practice one makes an effort to find a donor who is very similar in tissue type to the recipient by matching their HLA types. The closer the similarity the higher the probability that the transplant will be a success and that harmful immune reactions will be minimized. Siblings are the most likely to be closely matched, but other family members and unrelated matched donors can be similar enough to achieve a successful transplant if the optimal match is not available and the severity of the illness justifies the risk. In the treatment of leukemia, lymphoma, and myeloma, the cells to be transplanted are pluripotential stem cells, but they are

admixed with other marrow or blood cells when infused. (See Society booklet *Blood and Marrow Stem Cell Transplantation*.)

Anemia

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

Autologous Stem Cell Infusion

This technique, often referred to as transplantation, involves 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 (for example, acute myelogenous leukemia) when in remission or when the marrow and blood are not overtly abnormal (for example, lymphoma). Technically, this procedure is not transplantation, which implies taking tissue from one individual (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. (See Society booklet *Blood and Marrow Stem Cell Transplantation*.)

Blast Cells

This term refers to 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 up to 80 percent of all marrow cells. In acute myelogenous leukemia, myeloblasts accumulate and in acute lymphoblastic leukemia, lymphoblasts accumulate. 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.

Blood Cells

There are three main types of cell in the blood: red cells that carry oxygen, white cells that principally prevent or combat infections, and platelets that help prevent bleeding. There are several types of white cell in the blood. Each cell type is represented in blood in the numbers that meet the functions they serve. One fluid ounce of blood contains about 150 billion red cells, 8 billion platelets, and 20 million white cells. Red cells live for months, platelets for a week or two, and white cells for a few days. The marrow must replace over 200 million cells removed from the blood each day.

Blood Count

A laboratory test requiring a small blood sample with which to measure the number and types of cells circulating in the blood. The term complete blood count or CBC is often used to refer to this test. (See Society Fact Sheet on Blood Counts)

Bone Marrow

The bones are hollow and their central cavity is occupied by marrow, a spongy tissue 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 the adult, 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 Aspirate and Biopsy

In this procedure, a small volume of bone marrow is removed under local anesthesia from either the hipbone (pelvis) or breastbone (sternum). The cells in the sample are placed on a glass slide, stained, and examined under the microscope to identify any abnormality in the developing blood cells. Marrow cells may also be used to immunophenotype cells and to study their chromosomes. A trephine biopsy may be taken at the same time. In this procedure a core of bone with enclosed marrow is removed with a special needle. The specimen is treated to soften the bone, fixed in preservative, sectioned into thin slices, stained and examined under the microscope.

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 normal cells of the marrow, the intestinal tract, the skin and hair follicles are most sensitive to these chemicals, injury to these organs cause the most common tissue effects of chemotherapy i.e., low blood cell counts, mouth sores, diarrhea, and hair loss.

Clinical Trial

A carefully planned study of a new drug or treatment approach or a new application of an existing drug or approach. In a Phase I trial, a new agent that has been tested on cells and then animals in the laboratory is examined in a relatively small number of volunteers, often with advanced disease and poorly responsive or unresponsive to existing treatment, to assess dosages, patient tolerance, and acute toxic effects. If efficacy is evident, the new approach may be tested in a Phase II trial in which more patients are studied and more information gathered on dosage, effects, and toxicity. In a phase III trial, the drug or drugs or new approaches are compared in patients who are randomized to receive the current existing best treatment or the new treatment. Larger numbers of patients are studied. An effort is made to minimize observer bias. Careful analysis of results is performed. Such trials are required to gain the information required by the Food and Drug Administration to determine efficacy and safety before approving a drug for marketing. Federal guidelines for informed consent of participants must be followed.

Clonal (monoclonal)

A population of cells derived from a single transformed (neoplastic) parent cell. Virtually all neoplasms (cancers), benign and malignant, are derived from a single cell with an injury to DNA (mutated) and, thus, are monoclonal. The mutated cell has an alteration in its DNA, which forms an oncogene and leads to its transformation into a cancer-causing cell. The clone (cancer) is the total accumulation of cells that grow from the single mutated cell. Leukemia, lymphoma, and myeloma are examples of cancers that are monoclonal, that is, derived from a single malignant cell.

Clonal anemia or pancytopenia

Terms that may be applied to manifestations of the myelodysplastic syndrome to replace the obsolescent designations “acquired” and “refractory.” The latter two terms do not connote the neoplastic nature of these disorders and their presence in the spectrum of leukemic or clonal myeloid disorders.

Cytogenetics

The process of analyzing the number and shape of the chromosomes of cells. The individual who prepares, examines and interprets the number and shape of chromosomes in cells is called a cytogeneticist. In addition to identifying chromosome alterations, the specific genes affected can be identified in some cases. These findings are very helpful in diagnosing specific types of leukemia and lymphoma, in determining treatment approaches, and in following the response to treatment.

Cytokines

These are cell-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 blood 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) is one such cytokine. It stimulates the production of neutrophils and shortens the period of low neutrophil counts in the blood after chemotherapy. Cytokines that stimulate cell growth are sometimes referred to as “growth factors.”

Cytopenia

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

Cytotoxic Drugs

Anti-cancer drugs that act by killing or preventing the division of cells. (See chemotherapy.)

Hemoglobin

The iron containing pigment in red blood cells that carries oxygen to the tissue cells. A reduction in red blood cells decreases the blood hemoglobin. A decreased blood hemoglobin concentration is called anemia. The decrease in hemoglobin concentration decreases the oxygen carrying capacity of blood. If severe, this decreased capacity may limit a person's capacity to exert him or herself. Normal values of blood hemoglobin are 12 to 18 grams per 100 ml of blood. Healthy women have on average about 10 percent less hemoglobin in their blood than men do.

Hematocrit

The proportion of the blood occupied by the red blood cells. Normal values are 40-54 percent in males, 35-47 percent in females. If the hematocrit is below normal, one has anemia. If the hematocrit is above normal, one has erythrocytosis.

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. Hematopathologists are pathologists who specialize in the diagnosis of blood cell diseases and who perform the specialized laboratory tests often required to make a conclusive diagnosis.

Hematology

The study of blood diseases, including leukemia, lymphoma, and myeloma.

Leukemia

From the Greek meaning “white blood.” Leukemia is a cancer of a marrow cell. The disease appears in one of four major forms. Acute lymphocytic or acute myelogenous leukemia characterized by the uncontrolled proliferation and accumulation of abnormal immature cells, referred to as leukemic blasts. These cells fill the marrow spaces and enter the blood. Chronic myelogenous leukemia and chronic lymphocytic leukemia are less rapidly progressive. The former, however, requires treatment in nearly all cases at the time of diagnosis, whereas the later may, in some cases, be nonprogressive for long periods.

Oligoblastic myelogenous leukemia

A term that more accurately describes the nature of the disorder referred to as refractory anemia with excess blasts. The latter name is commonly used to designate a type of myelodysplastic syndrome that displays overt evidence of leukemic blast cells on examination of the blood or marrow. The proportion of blast cells in the marrow may be small but sufficient to indicate that leukemic hematopoiesis is present. The term “smoldering leukemia” has also been used for this manifestation but the implication of very slow progression is not always the case.

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.

Opportunistic Infection

The term applied to infections with bacteria, viruses, fungi, or protozoa to which individuals with a normal immune system are not usually susceptible. These organisms take advantage of the opportunity provided by immunodeficiency. Immune deficiency can be acquired as a result of cancers of the lymphatic system such as chronic lymphocytic leukemia or myeloma, can be induced or made more severe in patients who require intensive, prolonged chemotherapy or radiotherapy, can result as a consequence of infection with the human immunodeficiency virus (HIV), and can occur as a sequel to allogeneic stem cell transplantation and severe graft-versus-host disease.

Pancytopenia

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

Petechiae

Pin-head-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.

Platelets

Small blood cells (about one-tenth the volume of red cells) that stick to the site of blood vessel injury, aggregate with each other 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 thrombocytopenia.

Platelet Transfusion

The transfusion of donor platelets may be required to treat or prevent

bleeding in patients treated with high-dose chemotherapy or radiotherapy who develop severe platelet deficiency. The platelets can be pooled from several unrelated donors and given as “pooled random-donor platelets.” It requires the platelets from at least six one-unit blood donors to significantly raise the platelet count in a recipient. Sufficient platelets can be obtained from one donor by hemapheresis. The latter technique skims off the platelets of large volumes of blood passing through the hemapheresis 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 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. The platelets are collected by hemapheresis.

Purpura

The presence of skin bleeding. This may be in the form of black and blue patches of varying sizes (ecchymoses) or pin-head-sized spots called petechiae or both.

Red Cells

Blood cells that contain hemoglobin. Hemoglobin binds oxygen when red cells pass through the lung and releases it to the tissues of the body. The red cells make up a little less than half the volume of blood in healthy individuals.

Refractory Anemia

A clonal myeloid disorder that primarily affects red cell production in the marrow. In some cases the developing red cells have an abnormal accumulation of iron granules around the nucleus. These cells are called ringed sideroblasts. Refractory anemia (RA) and refractory anemia with ringed sideroblasts (RARS) are often associated with mild to

moderate decreases in white cells and platelets. These disorders are also referred to as myelodysplasia.

Refractory Anemia With Excess Blasts

A clonal myeloid disorder characterized by the marrow and blood features of refractory anemia but with overt leukemic myeloblasts evident in the marrow and sometimes the blood. Usually the marrow blast cell proportion is between two and twenty percent. The disorder is also referred to as oligoblastic (low blast count) leukemia. The disease is less rapidly progressive than florid acute myelogenous leukemia but often evolves into a more acute leukemia.

Relapse or 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” or “partial” are used to modify the term “remission.” Complete remission means all evidence of the disease is gone. Partial remission means 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.

Somatic Mutation

The alteration of a gene in the cell of a specific tissue. If the mutation occurs in a gene that normally controls cell growth or cell life-span, referred to as proto-oncogene, the mutated gene may become a cancer-causing gene or oncogene. This change is called “somatic” to distinguish it from a germ cell mutation, which can be passed from parent to offspring. 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.

Stem Cell

These are primitive cells in marrow that are required to make red cells, white cells and platelets (see “hematopoiesis”). Generally, the 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.

Stem Cell Transplantation

This is a technique that was developed to restore the marrow of patients who had lethal injury to that site. Such injury can occur because of primary marrow failure, destruction of marrow by disease, or intensive chemical or radiation exposure. As first designed, the source of the transplant was the marrow cells of a healthy donor who had the same tissue (HLA) type as the patient. Usually, the source was a brother or sister. Donor programs have been established to identify unrelated donors who have a matching tissue type. This approach requires screening tens of thousands of unrelated individuals of similar ethnicity.

The transplant product is a very small fraction of the marrow cells called “stem cells.” These stem cells not only reside in the marrow but also circulate in the blood. They can be harvested from the blood of a donor by treating the donor with an agent or agents that cause a release of larger numbers of stem cells into the blood and collecting them by hemapheresis. The stem cells circulate in large numbers in

fetal blood also, and can be recovered from the placental and umbilical cord blood after childbirth. The harvesting, freezing and storing of “cord blood” has provided another source of stem cells for transplantation. Since blood as well as marrow is a very good source of cells for transplantation, the term “stem cell transplantation” has replaced “bone marrow transplantation” as the general term for these procedures.

If the donor is an identical twin, the transplant is called “syngeneic,” the medical term for genetically identical. If the donor is a nonidentical sibling, the transplant is called “allogeneic,” indicating it is from the same species and in practice nearly always matching in tissue type. The term “matched-unrelated” is applied to the donor recruited from large volume screening programs searching for the rare individual who is very similar in tissue type to the patient.

The important technique of harvesting a patient’s marrow, freezing it and returning it to them after they have received intensive chemotherapy and/or radiotherapy for their underlying disease has been referred to as autologous (self) or auto-transplantation. This term is a well-entrenched misnomer since transplantation implies transferring tissue from one individual to another. This technique would better be referred to as autologous marrow infusion (see Autologous Stem Cell Infusion).

Thrombocytopenia

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

White Cells

A synonym for leukocytes. There are five major types of white cells in the blood: neutrophils, eosinophils, basophils, monocytes and lymphocytes.

Marshall A. Lichtman, M.D. Executive Vice President for Research and Medical Programs of The Leukemia & Lymphoma Society contributed the material presented in this booklet.

Further Readings

Nontechnical Sources

Acute Myelogenous Leukemia, The Leukemia & Lymphoma Society, 2001.

Chronic Myelogenous Leukemia, The Leukemia & Lymphoma Society, 2001.

Blood and Marrow Stem Cell Transplantation, The Leukemia & Lymphoma Society, 2001.

Blood Transfusion, The Leukemia & Lymphoma Society, 2000.

Understanding Chemotherapy, The Leukemia & Lymphoma Society, 2001.

Coping with Survival, The Leukemia & Lymphoma Society, 2000.

Technical Sources

Myelodysplastic Disorders (Indolent clonal myeloid diseases and oligoblastic leukemia) in *Williams Hematology*, edited by E. Beutler, M.A. Lichtman, B. Collier, T.J. Kipps, U. Seligsohn, 6th Edition, McGraw-Hill Book Company, 2001.

Myelodysplasia or myeloneoplasia: Thoughts on the nosology of the clonal myeloid disorders, *Blood Cells, Molecules, and Diseases* 26:572-581, 2000

Other Resources

The Leukemia & Lymphoma Society, Inc. Contact the Information Resource Center at (800) 955-4572 or contact your local Society chapter listed in the telephone directory. Internet address: www.leukemia-lymphoma.org

NIH/National Cancer Institute
Office of Cancer Communications, Building 31 Room 10A16,
9000 Rockville Pike, Bethesda, MD 20892, (301) 496-5583,
(800) 422-6237 Internet address: www.nci.nih.gov

Chapters and Free Information

Information about leukemia, lymphoma and myeloma is available from The Leukemia & Lymphoma Society's offices located in the states and cities listed below. Please refer to your telephone directory for local address and telephone number, or call 800-955-4572.

Alabama Birmingham	Georgia Atlanta	Mississippi Ridgeland	Pennsylvania Harrisburg Philadelphia Pittsburgh
Arizona Phoenix	Hawaii Honolulu	Missouri St. Louis	Rhode Island Cranston
Arkansas Little Rock	Idaho Boise	Nebraska Omaha	South Carolina Irmo
California Culver City Fresno Orange Sacramento San Diego San Francisco San Jose Santa Ana	Illinois Chicago	Nevada Reno	Tennessee Nashville
Colorado Denver	Indiana Indianapolis Ft. Wayne	New Jersey Springfield Westmont	Texas Austin Dallas Houston San Antonio
Connecticut Meriden Stamford	Iowa Des Moines	New Mexico Albuquerque	Utah Salt Lake City
Delaware Wilmington	Kansas Shawnee Mission Wichita	New York Albany Melville New York City Syracuse White Plains Williamsville	Virginia Hampton Richmond
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Florida Hollywood Jacksonville Orlando Tampa Palm Beach	Maryland Baltimore	Ohio Cincinnati Cleveland Columbus	West Virginia Huntington
	Massachusetts Framingham	Oklahoma Oklahoma City	Wisconsin Madison Milwaukee
	Michigan Grand Rapids Madison Heights	Oregon Portland	
	Minnesota St. Louis Park		

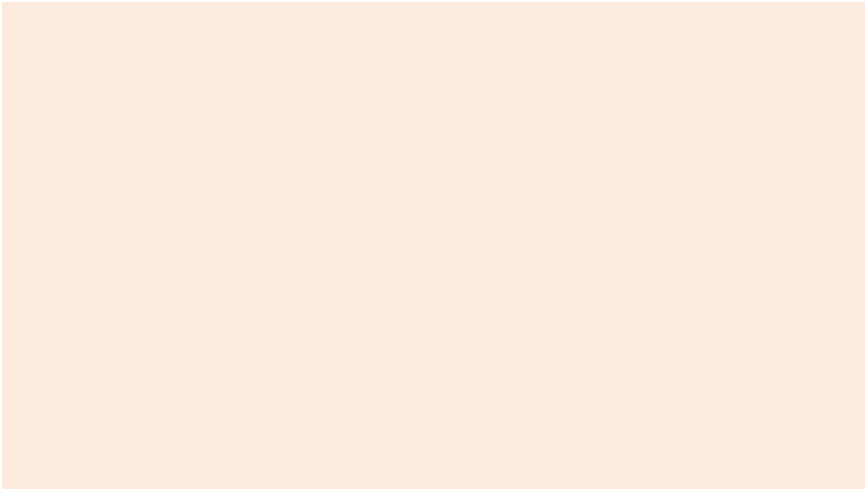
Home Office *The Leukemia & Lymphoma Society*
1311 Mamaroneck Avenue – Suite 310
White Plains, NY 10605

Free Literature: (800) 955-4572
www.leukemia-lymphoma.org

Mission

The mission of The Leukemia & Lymphoma Society is to cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families.

Contact for more information:



or the Home Office numbers listed above



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***Fighting Leukemia, Lymphoma,
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