LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

someday is today®

Myelodysplastic Syndromes

Pamela, MDS survivor

Support for this publication provided by

Celgene

Revised **2017**

A Message from Louis J. DeGennaro, PhD

President and CEO of The Leukemia & Lymphoma Society

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

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

Yet we are far from done.

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

This booklet has information that can help you understand myelodysplastic syndromes (MDS), prepare your questions, find answers and resources, and communicate better with members of your healthcare team.

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

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

Inside This Booklet

Acknowledgement

The Leukemia & Lymphoma Society gratefully acknowledges

David P. Steensma, MD, FACP
Senior Physician, Adult Leukemia Program,
Division of Hematological Malignancies,
Department of Medical Oncology, Dana-Farber Cancer Institute
Associate Professor of Medicine, Harvard Medical School
Boston, MA

for his critical review and important contributions to the material presented in this booklet.

Introduction

This booklet provides information about myelodysplastic syndromes (MDS) for patients and their families. MDS is a general term for a group of blood cancers that affect cells in the blood and bone marrow. Brief descriptions of normal blood and marrow and definitions of medical terms are included in this booklet.

For the 5-year period from 2009 to 2013, there were approximately 76,755 new cases of MDS throughout the US, averaging an estimated 15,351 cases per year. Advances in the treatment of MDS have resulted in improved remission rates. There are different types of MDS with varying degrees of severity, treatment approaches and life expectancy. New approaches to therapy are being studied in clinical trials for patients of all ages and for all disease stages.

Facts 2016-2017. The Leukemia & Lymphoma Society. 2017.

Resources and Information

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

For Help and Information

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

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

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

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

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

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

Sign Up for an E-Newsletter. Read the latest disease-specific news, learn about research studies and clinical trials, and find support for living with blood cancer. Please visit www.LLS.org/signup.

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

Community Resources and Networking

LLS Community. This is a one-stop virtual meeting place for chatting with other patients and staying up-to-date on the latest diagnosis and treatment news. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. To join, visit www.LLS.org/community.

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

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

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

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

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

Advocacy. The LLS Office of Public Policy (OPP) engages volunteers in advocating for policies and laws that encourage the development of new treatments and improve access to quality medical care. For more information, please

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

Additional Help for Specific Populations

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

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

Children. MDS is rare in children. Families face new and unfamiliar treatments and care protocols. The child, parents and siblings may all need support. For more information, please

- Call: (800) 955-4572
- Visit: www.LLS.org/booklets to read or order *Coping with Childhood Leukemia and Lymphoma*

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

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

For more information, please

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

People Suffering from Depression. Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time—for example, if you feel depressed every day for a 2-week period. For more information, please

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov. Enter "depression" in the search box

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

Myelodysplastic Syndromes

Myelodysplastic syndromes (MDS) is the general name for a group of diseases that affect the blood and marrow. For years, MDS was also known as "pre-leukemia," "refractory anemia," or "smoldering leukemia." These terms fell out of fashion because only a minority of patients with MDS develop acute leukemia, and patients often had other blood problems in addition to anemia. Today, MDS is classified as a type of blood cancer. There are many different subtypes of myelodysplastic syndromes.

MDS occurs when genetic changes (mutations) cause stem cells (immature bone marrow cells) to become abnormal, preventing the normal functioning of the bone marrow. When the bone marrow does not work properly, it cannot make enough healthy blood cells.

In every person, stem cells in the bone marrow are responsible for producing healthy blood cells throughout life. Healthy blood cells include:

- White blood cells (cells that fight infection)
- Red blood cells (cells that carry oxygen)
- Platelets (cells that help blood to clot)

When someone has MDS, the bone marrow fails to produce enough healthy red blood cells, white blood cells or platelets. Instead, it produces underdeveloped (immature) cells that are abnormal in size, shape or appearance. These cells are called "dysplastic" (abnormally formed) cells. There can also be an accumulation of the most immature bone marrow cells, called "blast cells," which cannot yet perform the specific function of a mature cell.

In healthy people, blast cells make up 5 percent or less (most of the time, less than 2 percent) of all bone marrow cells. In MDS patients, blast cells may comprise more than 5 percent of all the cells in their marrow. The higher the number of blast cells in the bone marrow is a main determinant of the severity of MDS. By definition, 20 percent blast cells in marrow indicates acute leukemia.

There are many types of MDS. A myelodysplastic syndrome can be mild or severe. It may first appear as anemia (a decrease in the level of hemoglobin in the

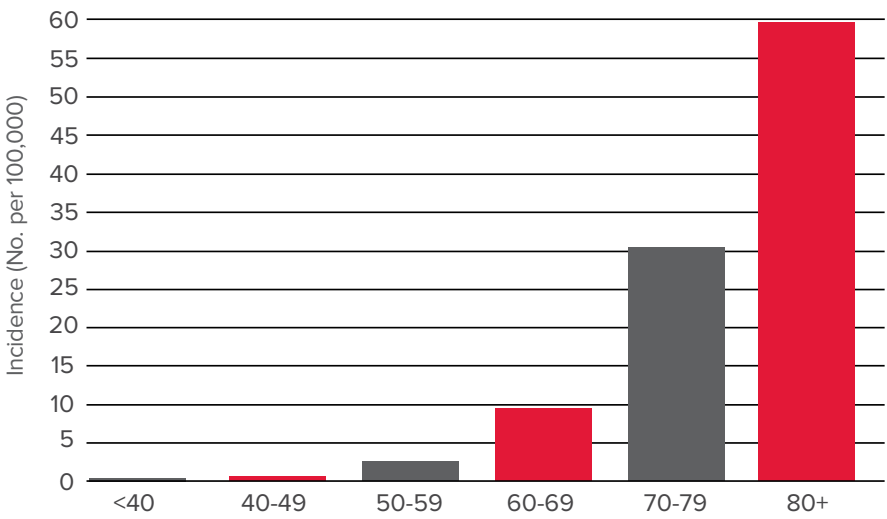
blood) and then progress very slowly, or it can be a fast-growing disease. More severe MDS cases carry a high risk of progressing to acute myeloid leukemia (AML). For more information about AML, see the free LLS publication, *Acute Myeloid Leukemia.*

Today, patients with MDS have improved outcomes and experience better quality of life than ever before. This is largely due to a better understanding of the genetic features and biology of the disease, improved supportive care, the development of new drugs, and progress in stem cell transplantation.

Incidence, Causes and Risk Factors

Incidence. For the 5-year period from 2009 to 2013, there were approximately 76,755 new cases of MDS throughout the US, averaging an estimated 15,351 cases per year. In the United States, the overall incidence rate of MDS is 4.9 cases per 100,000 population. This rate rises with age to approximately 30 cases per 100,000 individuals per year among patients 70 years and older and to about 60 cases per 100,000 people in those who are 80 years and older. MDS is rare among children, adolescents and young adults. The disease affects slightly more men than women, and white males have the highest incidence rates. See Figure 1.

Figure 1. Myelodysplastic Syndromes: Age-Specific Incidence Rates 2009-2013



The horizontal axis represents the age of patients from younger than age 40 years and then in 10-year age increments up to age(s) 80+ and older. The vertical axis shows the incidence of new cases of MDS from 2009 to 2013, per 100,000 people. Source: Howlader N, Noone AM, Krapcho M, et al, eds. *SEER Cancer Statistics Review*, 1975-2013. Bethesda, MD: National Cancer Institute; April 2016. http://seer.cancer.gov/csr/1975_2013/. Based on November 2015 SEER (Surveillance, Epidemiology, and End Results Program) data submission posted to the SEER Web site; April 2016.

Causes and Risk Factors. Doctors can't identify a specific cause in the majority of MDS cases. MDS can either be primary, also known as "de novo," when the cause is not known, or secondary, known as "treatment related."

- Primary or de novo MDS—Doctors can't identify a specific cause in the majority of MDS cases. These are called "de novo" MDS, which means the disease does not have a known cause. In most cases, random mutations (DNA changes) accumulate in the stem cells with aging, and if these mutations occur in specific genes and in particular locations, MDS results.
- Secondary (treatment-related) MDS—Some people who have received treatment for another cancer have a small risk of developing treatment-related MDS. This occurs only in a small number of patients exposed to chemotherapy and/or radiation therapy and is less common than cases of primary MDS. In general, the chance of developing MDS as a result of treatment for another cancer is very low. Some patients with rare inherited bone marrow disorders such as Fanconi anemia or dyskeratosis congenita can also develop secondary MDS, as can patients previously diagnosed with another bone marrow failure disorder called aplastic anemia.

Signs and Symptoms

A sign is a change in the body that the doctor sees in an exam or a test result. A symptom is a change in the body that a patient can see or feel. A person with signs or symptoms that suggest the possibility of MDS is usually referred to a specialist, typically a doctor called a hematologist-oncologist. The doctor will order additional tests to make a diagnosis (see *Diagnosis* on page 8). The signs and symptoms of MDS are also associated with a number of other, less serious diseases.

Some patients may have no symptoms of disease. MDS may be detected before symptoms appear, often when results of laboratory tests that were part of a routine medical examination show changes in the blood.

However, people with MDS often have low levels of one or more types of blood cells. A decrease below normal in the amount of blood cells is called cytopenia. Most MDS symptoms are caused by a lack of red blood cells, white blood cells or platelets in the blood. (See *Normal Blood and Marrow* on page 27.)

Anemia is a decrease in the number of healthy red blood cells. Red blood cells carry oxygen throughout the body. Anemia may cause symptoms such as

- Fatigue
- Dizziness
- Weakness

- Shortness of breath or chest discomfort, especially with exertion
- Pale skin

Neutropenia is a decrease in the number of healthy white blood cells. White blood cells help the body fight infection. Neutropenia can lead to patients having frequent or severe infections.

Thrombocytopenia is a decrease in the number of healthy platelets. Platelets help control bleeding and are involved in wound healing. Thrombocytopenia may cause symptoms such as

- Easy bruising
- Bleeding

Diagnosis

An accurate diagnosis is one of the most important aspects of a person's care. Obtaining a precise diagnosis will help the doctor

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

CBC with Differential. A doctor will order a complete blood count (CBC), which measures the number of red blood cells, white blood cells and platelets in the blood. These measurements indicate the degree to which the MDS cells in the marrow are affecting normal blood cell development. Patients with MDS often have low numbers of one or more types of blood cells. The CBC should include a differential. This measures the different types of white blood cells in the sample.

If anemia is detected, the red blood cells are further examined for

- A lack of iron, folate or vitamin B_{12}
- Some other type of cancer or bone marrow problem
- Another cause of anemia, such as kidney failure

Reticulocyte Count. Reticulocytes are precursor (immature) cells that develop into mature red blood cells. The reticulocyte count measures the number of reticulocytes in the circulating blood. It can show how quickly these cells are being made and released by the bone marrow and whether the bone marrow is functioning properly. When a person has anemia, the normal response is for the bone marrow to make more reticulocytes. A low reticulocyte count indicates that the bone marrow is not working well.

Serum Erythropoietin (EPO). Erythropoietin (EPO) is a substance made in the kidneys. EPO stimulates the bone marrow to produce more red blood cells.

Measuring the amount of EPO in the blood can help determine the cause of anemia. A low EPO level can cause anemia and may be a sign of a health problem other than MDS. A low EPO level can also worsen anemia in a person with MDS. Most patients with MDS-related anemia have relatively low serum levels of EPO.

Bone Marrow Tests: Aspiration and Biopsy. These tests are used to confirm MDS. A bone marrow aspiration removes a small amount of liquid bone marrow from inside a bone. A bone marrow biopsy removes a small piece of solid bone along with a small amount of bone marrow. After the samples are taken, a pathologist reviews the samples under the microscope to assess the type, size, appearance and maturity of the cells. During this assessment, the specialist will note any signs of MDS, such as

- Cells of abnormal size or shape (dysplasia)
- Abnormal number (too many or too few) of any type of blood cell
- An increased number of blast cells
- Abnormally low or high number of cells in the bone marrow
- Red blood cells that have too much or too little iron

Fluorescence in Situ Hybridization (FISH) or Karyotype. These are tests used to identify cells that contain chromosomal abnormalities. The tests can also help identify abnormal cells for diagnosis of disease, and can track and measure the effects of therapy. Chromosomal abnormalities are important factors in identifying specific subtypes of MDS, and they can sometimes help doctors determine the most effective treatment approach.

Molecular Testing. These tests look for mutations in genes that are associated with MDS. Sometimes, mutation testing results influence MDS treatment or its outcome. Molecular testing can be done on a sample of blood or bone marrow. It is performed in some patients with MDS to look for gene abnormalities. DNA sequencing is a type of molecular test that checks for specific gene mutations in cancer cells. Certain mutations are associated with a better or worse outcome. Doctors use the results of molecular testing to help plan treatment.

Cytogenetic Abnormalities. It is common for MDS cells to have abnormal chromosomes. Approximately 50 percent of patients have one or more chromosomal defects. There are different types of chromosome defects; for example, part of a chromosome or an entire chromosome may be missing. Or there may be an extra copy of a chromosome. Each chromosome is divided into two sections, or "arms." The short arm of the chromosome is labeled the "p arm." The long arm of the chromosome is labeled the "q arm."

The most common cytogenetic abnormalities seen in MDS involve

- **A deletion of the long arm (q) of one of the two chromosomes in a pair:**
  - Chromosomes 5, indicated as del(5q) or 5q–
  - Chromosomes 7, indicated as del(7q) or 7q–
  - Chromosomes 20, indicated as del(20q) or 20q–
- **A complete loss of one of the two chromosomes in a pair:**
  - Chromosomes 5, indicated as del(5) or –5
  - Chromosomes 7, indicated as del(7) or –7
- **Trisomy 8:** an extra copy of chromosome 8, so that there are three copies of chromosome 8 instead of two. This is indicated as T8M.

Genetic Mutations. In recent years, research has identified several gene mutations among MDS patients. Some of these mutations can have an impact in outcome of the disease. These are noteworthy because

- There are more than 40 genes that can be mutated in MDS.
- A large number of patients (over 80 percent) are likely to carry at least one mutation.
- Based on the functions of these mutated genes, researchers have learned about the molecular mechanisms responsible for the development of MDS.
- The specific pattern of mutations seen in MDS patients may partially explain the variability of their disease and will likely lead to newer classification systems based on these genetic abnormalities.
- A subset of mutations may have prognostic value. Mutations in specific genes have been associated with both better and worse prognoses than those predicted by the International Prognostic Scoring System (IPSS).
- The most frequently mutated genes are *TET2, SF3B1, ASXL1, DNMT3A, SRSF2, RUNX1, TP53, U2AF1, EZH2, ZRSR2, STAG2, GBL, NRAS, JAK2, SETBP1, IDH1, IDH2* and *ETV6.*

Several of these mutations have been associated with adverse clinical features such as complex karyotypes *(TP53)*, excess bone marrow blast percentage and severe thrombocytopenia *(RUNX1, NRAS* and *TP53)*.

Mutations of the *TP53, EZH2, ETV6, RUNX1* and *ASXL1* genes have been shown to predict a decrease in overall survival, according to several studies. *TET2* mutations have been shown to influence the response to treatment with medications called hypomethylating agents, such as azacitidine and decitabine.

SF3B1 mutations are associated with the presence of a type of bone marrow cell called a ring sideroblast (MDS-RS subtype). About 80 percent of patients with

MDS-RS subtype carry the *SF3B1* mutation, which tends to be a marker for a more favorable prognosis.

Testing for genetic mutations in MDS has progressed considerably in recent years and is becoming more widely available. This progress in the understanding of the genetic features of MDS, hopefully, will help doctors acquire a better understanding of a person's individual disease and develop targeted treatments.

Diagnostic Criteria. A diagnosis of MDS requires that at least one of the following characteristics be found in the marrow:

- Blasts making up between 5 and 19 percent of the marrow cells
- Obvious changes to the structure or form of the marrow cells (dysplasia)
- Cytogenetic abnormalities (chromosomal damage to the DNA in the cells)
  - "Simple" cytogenetics means fewer than three chromosomes are affected.
  - "Complex" cytogenetics means three or more chromosomes are affected.

Treatment Planning

MDS Classification. The classification of MDS has evolved considerably over the last several decades. In 1982, the French-American-British (FAB) Work Group devised a classification of MDS. The FAB classification divided MDS into five subtypes based on the percentage of blasts in the bone marrow and the peripheral blood, the number of ring sideroblasts (RS) and the degree of monocytosis (elevated number of white blood cells) as follows:

1. Refractory anemia (RA)
2. Refractory anemia with ring sideroblasts (RARS)
3. Refractory anemia with excess blasts (RAEB)
4. Refractory anemia with excess blasts in transformation (RAEB-T)
5. Chronic myelomonocytic leukemia (CMML)

In 2001, the World Health Organization (WHO) proposed an alternative classification that was modified from the original FAB and that incorporated molecular and cytogenetic factors. Since then, the WHO classification has been updated twice, once in 2008 and again in 2016.

The current WHO classification guidelines identify six subtypes of MDS based on the results of tests of the blood and bone marrow. See Table 1 on page 12.

Table 1. 2016 WHO Classification of MDS: Six Major Subtypes

Subtype
○ MDS with single lineage dysplasia (MDS-SLD) • Refractory anemia (RA) • Refractory neutropenia (RN) • Refractory thrombocytopenia (RT)
○ MDS with ring sideroblasts (MDS-RS) • Single lineage dysplasia (MDS-RS-SLD) • Multilineage dysplasia (MDS-RS-MLD)
○ MDS with multilineage dysplasia (MDS-MLD)
○ MDS with excess blasts (MDS-EB) • MDS with excess blasts-1 (MDS-EB-1) • MDS with excess blasts-2 (MDS-EB-2)
○ MDS with isolated del(5q)
○ MDS unclassifiable

Prognostic Scoring Systems. Specific factors may affect the prognosis (likely outcome) of MDS, and help doctors determine when to start treatment and how intensive the treatment should be. These factors include:

- MDS subtype
- Number and severity of cytopenias (low blood cell counts)
- Percent of blast cells in the bone marrow
- Type and number of chromosome changes

Doctors use prognostic scoring systems to rate the severity of the disease for each patient and help predict the outlook and the risk of progression to acute myeloid leukemia (AML). They assign a risk score and risk group for MDS based on the prognostic factors. Each factor is given a number based on its severity. A lower score generally indicates a better outlook. The scores for all the factors are then added together to create the overall risk score. The risk score describes how fast the disease is likely to progress, and is used to assign the patient to a particular risk group. Doctors use the information of a patient's risk group to choose a treatment approach.

There are three main prognostic scoring systems:

- IPSS (International Prognostic Scoring System)
- IPSS-R (Revised International Prognostic Scoring System)
- WPSS (WHO classification-based Prognostic Scoring System)

IPSS System. The IPSS (International Prognostic Scoring System) was the first prognostic scoring system for MDS to be widely used and has been established as the backbone of prognostic systems since its development in 1997. It scores three main factors (percentage of blasts, type of chromosomal changes and presence of cytopenias) to classify MDS into four risk groups. It is still the most commonly used system.

The following examples show how IPSS scores (see Table 2 on page 14) are used to determine the IPSS risk category for an MDS patient:

- A patient with less than 5 percent blasts (0 points), no chromosome changes (0), anemia but normal platelet and neutrophil counts (0) would have a total IPSS risk score of 0. This patient would be considered to be in the IPSS low-risk category.
- A patient with 5 to 10 percent blasts (0.5 points), an abnormal chromosome 7 (1.0), normal neutrophil counts, but low red blood cell and platelet counts that indicate anemia and thrombocytopenia (0.5), would have a total IPSS risk score of 2. This patient would be considered to be in the IPSS intermediate –2 risk category.

IPSS-R System. The recently revised version, IPSS-R, was developed in 2012 and aims to improve the ability to further define disease risk by increasing the prognostic significance of cytogenetic abnormalities. It scores the types and severity of low blood cell counts. It also gives a numeric value to a wider range of chromosomal changes. It classifies MDS into five risk groups.

A patient's IPSS-R risk category is determined by totaling the individual IPSS-R scores for the designated values within five disease factors. That number matches the patient to one of five IPSS-R risk categories. See Table 2 on page 15.

The following example shows how IPSS-R scores are used to determine the IPSS-R risk category for an MDS patient. A patient who has a blast percentage of 3 percent (1), normal cytogenetics (1), a hemoglobin concentration of greater than 10 grams (0), a platelet count of 101 (0) and an absolute neutrophil count (ANC) of 0.7 (0.5) would have a total IPSS-R risk score of 2.5 points. This patient would be considered to be in the IPSS-R low-risk category. See Table 2 on page 15.

WPSS System. The WHO Prognostic Scoring System (WPSS) is also a recently developed system but it is not used as often as the IPPS and IPSS-R. It differs from the other two systems in that it includes the MDS subtype as a prognostic

factor. It also assigns a score based on the presence or absence of severe anemia. (see Table 2 on page 16).

These three prognostic scoring systems are used to assess risk and determine the best treatment approach. The points for each of the factors are added together to make the overall risk score.

Table 2. Prognostic Scoring Systems and Risk Groups

System	Factors	Prognostic Factors Scored	Risk Groups Based on Total Risk Score
IPSS	Blast cells in bone marrow (percent)	• Less than 5 = 0 • 5 to 10 = 0.5 • 11 to 20 = 1.5 • 21 to 30 = 2.0	• Low Total IPSS Risk score = 0 • Intermediate –1 Total IPSS Risk Score = 0.5 to 1.0 • Intermediate –2 Total IPSS Risk Score = 1.5 to 2.0 • High Total IPSS Risk Score = 2.5 or higher
	Cytogenetics (chromosome changes)	• None, del(5q), del(20q) = 0 • 3 or more abnormalities, abnormal chromosome 7 = 1.0 • Other abnormalities = 0.5	
	Cytopenias	Number of cytopenias (anemia, neutropenia or thrombocytopenia) • None or 1 = 0 • 2 or 3 = 0.5	

Table 2. Prognostic Scoring Systems and Risk Groups *(cont)*

System	Factors	Prognostic Factors Scored	Risk Groups Based on Total Risk Score
IPSS-R	Blast cells in bone marrow (percent)	• Less than or equal to 2 = 0 • Greater than 2 to less than 5 = 1 • 5 to 10 = 2 • Greater than 10 = 3	• Very Low Total IPSS-R Score = 1.5 or lower • Low Total IPSS-R Score = 2 to 3 • Intermediate Total IPSS-R Score = 3.5 to 4.5 • High Total IPSS-R Score = 5 to 6 • Very High Total IPSS-R Score = 6.5 or higher
	Cytogenetics (chromosome changes)	• –Y, del(11q) = 0 • Normal, del(5q), del(12p), del(20q), double including del(5q) = 1 • del(7q), +8, +19, i(17q), any other single or double independent clone = 2 • -7, inv(3)/+(3q)/del(3q), double including -7/del(7q), complex: 3 abnormalities = 3 • Greater than 3 abnormalities = 4	
	Cytopenias	Hemoglobin level (g/dL) • Equal to or greater than 10 = 0 • 8 to less than 10 = 1 • Less than 8 = 1.5 Platelet count (x 10^9/L of blood) • Equal to or greater than 100 = 0 • 50 to less than 100 = 0.5 • Less than 50 = 1 Neutrophil count [(ANC) x 10^9/L of blood] • Equal to or greater than 0.8 = 0 • Less than 0.8 = 0.5	

Table 2. Prognostic Scoring Systems and Risk Groups *(cont)*

System	Factors	Prognostic Factors Scored	Risk Groups Based on Total Risk Score
WPSS	MDS subtype	• MDS-SLD, MDS-RS, MDS with isolated del(5q) = 0 • MDS-MLD = 1 • MDS-EB-1 = 2 • MDS-EB-2 = 3	• Very Low Total WPSS Risk Score = 0 • Low Total WPSS Risk Score = 1 • Intermediate Total WPSS Risk Score = 2 • High Total WPSS Risk Score = 3 to 4 • Very High Total WPSS Risk Score = 5 to 6
	Cytogenetics (chromosome changes)	• Good: normal, –Y alone, del(5q) alone, del(20q) alone = 0 • Intermediate: other abnormalities = 1 • Poor: 3 or more abnormalities, chromosome 7 abnormalities = 2	
	Anemia	Presence of severe anemia (hemoglobin less than 9 g/dL in men or less than 8 g/dL in women) • Absent = 0 • Present = 1	

Abbreviations: IPSS, International Prognostic Scoring System; IPSS-R, Revised International Scoring System; WPSS, WHO Prognostic Scoring System; MDS-SLD, MDS with single lineage dysplasia; MDS-RS, MDS with ring sideroblasts; MDS-MLD, MDS with multilineage dysplasia; MDS-EB, MDS with excess blasts; MDS-EB-1, MDS with excess blasts-1; MDS-EB-2, MDS with excess blasts-2.2

The IPSS, the IPSS-R and the WPSS scoring systems alone are not absolute predictors of risk. They do not take into account many treatment aspects of elderly patients, such as comorbidities, previous cancers, and other health issues. Still, scoring system numbers are very important as they have a major influence on the patient's ability to tolerate certain intensive treatments. Prognostic scores and risk categories are used in addition to the doctor's observation and assessment of the patient.

The IPSS-R has demonstrated improved ability over the IPSS to predict prognosis. The IPSS continues to be used to determine eligibility for some

clinical studies. The IPSS, IPSS-R, WPSS and other classifications are also useful in interpreting the results of cooperative clinical trials involving patients at different treatment centers.

Risk Groups. Before starting treatment, doctors group the patient's condition into one of two risk categories: "lower-risk" or "higher-risk" MDS. Each category includes certain risk groups from each of the scoring systems. Table 3 below shows how the risk groups are divided into these two main categories. It is important to note that prognostic systems and risk groups do not predict how MDS will respond to treatment but instead how MDS is likely to behave over time without treatment.

The Lower-Risk Prognostic Scoring System (LR-PSS) is a prognostic model used in the evaluation of MDS. It was designed to help identify patients with lower-risk disease (IPSS "Low or Intermediate –1") who may have a poor prognosis. The system includes the following factors as predictors of survival outcomes: unfavorable cytogenetics, older age (60 years and older), decreased hemoglobin (less than 10 g/dL), decreased platelet count (less than 200 x 109/L) and a higher percentage of bone marrow blasts (4 percent or more).

Lower-risk MDS tends to grow and progress slowly. It may not cause many or even severe symptoms for a long time. Hence, less intensive treatment is frequently used. In contrast, higher-risk MDS is likely to progress more quickly or become AML more quickly without treatment. It may cause more symptoms and health complications in a short amount of time. Thus, more intensive treatment is often required.

Table 3. Risk Category of MDS: Three Prognostic Scoring Systems

Lower-Risk MDS	Higher-Risk MDS
• **IPSS** Low and Intermediate –1	• **IPSS** Intermediate –2 and High
• **IPSS-R** Very Low, Low, Intermediate	• **IPSS-R** Intermediate, High, Very High
• **WPSS** Very Low, Low, Intermediate	• **WPSS** High, Very High

Abbreviations: MDS, myelodysplastic syndrome; IPSS, International Prognostic Scoring System; IPSS-R, Revised International Scoring System; WPSS, WHO Prognostic Scoring System.

Treatment

Every patient's situation should be evaluated individually by a hematologist-oncologist who specializes in treating MDS and who will discuss the disease subtype, prognostic factors and treatment options with the patient. It is also important to seek treatment at a center that has experience in treating the disease. Based on the results of blood and marrow testing, the doctor will assign each patient to either a low-risk or a high-risk category and create a specific treatment plan.

Because lower-risk MDS is more likely to progress slowly, low-intensity treatments are generally used first. The goals for low-risk MDS patients are to

- Improve blood counts
- Lessen the need for blood transfusions
- Lower the risk of infection
- Improve quality of life

High-risk MDS tends to grow quickly and progress to AML within a shorter time. For this reason, more intensive treatments are generally used. The goals for high-risk MDS patients are to

- Slow or stop MDS progression to AML
- Lengthen survival

Today, there are a number of treatments for people who have MDS. The treatments can be used alone or together. The most common treatments for MDS include

- "Watch and Wait" (observation of blood cell counts)
- Supportive care
  - Blood transfusions
  - Iron chelation therapy
  - Blood cell growth factors
  - Infection management
- Drug therapy
- Allogeneic stem cell transplantation
- Clinical trials

Watch and Wait. The watch-and-wait approach involves the careful monitoring of a patient's blood cell counts. This approach is generally recommended for patients who have

- An IPSS low or intermediate –1 risk or IPSS-R very low or low risk
- A hemoglobin concentration higher than 10 grams per deciliter (>10 g/dL) and platelet counts higher than 50,000 to 100,000 per microliter (>50,000/µL to >100,000/µL) without the need for transfusion

Patients in these risk categories and with these lab values may be fine without treatment. Regular observation by a hematologist-oncologist is recommended, because there is a risk of disease progression.

Supportive Care. Treatment given to relieve the symptoms of a disease and the treatment's side effects is known as supportive care. The goal of supportive care is to improve the patient's quality of life and to relieve discomfort as much as possible. Supportive care is an important part of MDS treatment.

Blood Transfusions. Transfusions of red blood cells can help some patients by improving their blood cell counts or by relieving anemia symptoms, such as shortness of breath, dizziness, extreme fatigue and chest pain. Transfusion can help relieve symptoms for a short time but more transfusions may be needed over time. In MDS, 60 to 80 percent of patients have anemia at the time of diagnosis and up to 90 percent of patients will require one or more transfusions during the course of their illness.

Thrombocytopenia (low platelet counts) can cause symptoms such as easy bruising or bleeding. Platelet transfusions may be used to treat bleeding problems; they are typically required once a patient's platelet count falls below 10,000/µL. Aminocaproic acid, an antifibrinolytic agent, is recommended for bleeding episodes that do not respond to platelet transfusion, and for cases of severe thrombocytopenia. This medication works by stopping blood clots from breaking down too quickly.

For more information on this topic, please see the free LLS booklet, *Blood Transfusion.*

Iron Chelation Therapy. Iron is found in red blood cells. When a person receives a large number of red blood cell transfusions, too much iron can build up in the body. This is called iron overload. Iron chelation therapy uses drugs called "chelators," which bind to excess iron and remove it from the body. This therapy may be appropriate for anemic patients who need frequent blood transfusions (more than 4 units of red blood cells over 8 weeks).

The most common drugs used in this therapy include

- Deferasirox (Exjade®, Jadenu®). This is an oral medication taken daily. The newer preparation, Jadenu, can be easier on the digestion of some patients, but it is the same medicine as Exjade.

- Deferoxamine mesylate (DFO; Desferal®). This drug is administered as a slow subcutaneous (SC, under the skin) or intramuscular (IM) infusion.

For patients who need frequent red blood cell transfusions, it is recommended that doctors monitor serum ferritin (iron) levels and check often for signs of organ damage.

Blood Cell Growth Factors. Agents called "growth factors" promote blood cell production in the bone marrow. There are red blood cell and white blood cell growth factors. These agents are used to treat some patients whose blood cell counts show decreased numbers of cells.

- **Red Blood Cell Growth Factors.** Erythropoietin (EPO) is a hormone created in the kidneys. It encourages red blood cell production in response to low oxygen levels in the body. A shortage of EPO can also cause anemia.

  Erythropoiesis-stimulating agents (ESAs) are red blood cell growth factors that are pharmaceutical analogues of natural EPO. They are used for MDS patients who have anemia associated with low EPO levels. Treatment with ESAs may decrease transfusion needs and possibly improve survival.

  Epoetin alfa (Procrit®) and darbepoetin alfa (Aranesp®) are synthetic forms of EPO. They are given by an injection under the skin (subcutaneously [SC]). Darbepoetin alfa is a longer-acting form of EPO than epoetin alfa.

  Most patients with MDS do not have low EPO levels, so administration of ESAs is not a useful treatment for their anemia. Nonetheless, all MDS patients should have their EPO levels checked.

- **White Blood Cell Growth Factors.** White blood cell growth factors are naturally produced by the body, and help increase the production of white blood cells. Synthetic versions of these substances may be used to treat patients with frequent infections due to neutropenia, but they are not known to help patients live longer. The two main types are

  - Granulocyte colony-stimulating factor (G-CSF) which helps the body increase white blood cell production. Filgrastim (Neupogen®) and Pegfilgrastim (Neulasta®) are examples of G-CSF medications. Some MDS patients with low EPO levels may not benefit from treatment with ESAs alone; however, an ESA given along with G-CSF may increase their hemoglobin concentration.
  - Granulocyte-macrophage colony-stimulating factor (GM-CSF) helps the body produce many different types of white blood cells. Sargramostim (Leukine®) is a GM-CSF medication.

- **Platelet Growth Factors.** Thrombopoietin (TPO) is a substance that helps the body produce platelets.
  - Romiplostim (Nplate®) and eltrombopag (Promacta®) are drugs that act like TPO. These agents are being investigated as treatment for MDS patients who have low platelet counts. Currently, these drugs are FDA-approved for the treatment of thrombocytopenia (low platelet counts) in patients who have chronic immune thrombocytopenic purpura (ITP), and who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
  - Although romiplostim and eltrombopag are not approved specifically for MDS, sometimes they can be helpful in patients with very low platelet counts.

Infection Management. A low number of white blood cells can increase the risk of infection. In some cases, infection may be frequent or severe. Your treatment team will pay close attention to any infection or unexplained fever. If a bacterial infection is identified or suspected, antibiotics may be needed. Antiviral drugs may be used to treat certain viral infections.

Drug Therapy. There are many different types of drugs used in the treatment of MDS.

Low-Intensity Therapy includes the use of low-intensity chemotherapy or immunotherapy. These drugs are, in general, less likely to produce severe side effects and are often given in an outpatient setting. There are two low-intensity chemotherapy drugs approved to treat MDS:

- Azacitidine (Vidaza®)
- Decitabine (Dacogen®)

Both of these drugs belong to a class of medications known as hypomethylating agents. They work by blocking the DNA that helps cancer cells grow. Azacitidine is given intravenously (IV) or under the skin (subcutaneously [SC]) and is approved for both low and high-risk patients. Decitabine is administered through a slow intravenous infusion and must be given in a hospital setting. It is also approved for both low- and high-risk patients. When treatment with these agents is successful, it may lead to improved blood cell counts, and patients may need fewer transfusions.

Immunosuppressive Therapy (IST) uses drugs that suppress certain parts of the immune system. For instance, in some types of MDS, lymphocytes may attack the bone marrow, causing it to stop making enough healthy blood cells. Anti-thymocyte globulin (ATG) (Thymoglobulin®) and cyclosporine (Neoral®) or tacrolimus (Prograf®) are the main IST drugs used to treat MDS. This type of therapy does not work well for all types of MDS; it is most effective when MDS has features that are associated with an immune-system attack, such as:

- Presence of HLA-DR15 protein
- A low number of cells in the bone marrow
- Younger patients with lower-risk MDS

ATG is given by IV infusion over a few hours in the hospital for 4 to 5 consecutive days, and cyclosporine and tacrolimus are administered orally.

Immunomodulators (IMIDs) are drugs that modify different parts of the immune system. Lenalidomide (Revlimid®) is approved to treat lower-risk MDS with 5q deletion [del(5q)]. A 5q deletion may occur in about 10 percent of all MDS cases. Treatment with this drug may lessen the need for red blood cell transfusions in certain patients. Lenalidomide is an oral medication.

Tyrosine Kinase Inhibitors are drugs that target the abnormal proteins that cause uncontrolled cell growth. Imatinib mesylate (Gleevec®), in specific situations, is FDA approved for adult patients with myelodysplastic syndromes/myeloproliferative neoplasms (MDS/MPN) associated with PDGFR (platelet-derived growth factor receptor) gene rearrangements. Gleevec is currently approved for treatment of Philadelphia chromosome-positive chronic myeloid leukemia, Philadelphia chromosome positive acute lymphoblastic leukemia as well as other rare diseases.

Some of the most common drugs used in the treatment and supportive care of MDS are listed in Table 4 on page 23.

Table 4. Common Drugs Used in MDS Treatment

Hypomethylating Agents

- Azacitidine (Vidaza®)
- Decitabine (Dacogen®)

Immunosuppressive Therapy

- ATG – anti-thymocyte globulin (Thymoglobulin®)
- Cyclosporine (Neoral®)
- Tacrolimus (Prograf®)

Immunomodulators

- Lenalidomide (Revlimid®)

High-Intensity Chemotherapy

- Cytarabine (cytosine arabinoside, Ara-C; Cytosar-U®)
- Idarubicin (Idamycin®)
- Daunorubicin (Cerubidine®)
- Mitoxantrone (Novantrone®)

Iron Chelators

- Deferoxamine mesylate (DFO, Desferal®)
- Deferasirox (Exjade®, Jadenu®)

Tyrosine Kinase Inhibitor

- Imatinib mesylate (Gleevec®)

Blood Cell Growth-Factors

- G-CSF – Granulocyte Colony-Stimulating Factor (Filgrastim, [Neupogen®, Granix® and others]; Pegfilgrastim, [Neulasta®])
- GM-CSF – Granulocyte-Macrophage Colony-Stimulating Factor (Sargramostim [Leukine®])
- Epoetin alfa (Procrit®)
- Darbepoetin alfa (Aranesp®)
- Romiplostim (Nplate®)
- Eltrombopag (Promacta®)

High-Intensity Therapy involves the use of intensive chemotherapy drugs or stem cell transplantation. High-intensity chemotherapy includes drugs and regimens typically used to treat AML. Because these agents tend to cause more severe side effects, they are generally only used for MDS that is likely to progress to AML (high-risk disease). Most of the high-intensity drugs are given through IV infusion.

MDS patients in the intermediate –2 and high-risk IPSS categories may require treatment with high-intensity chemotherapy. The drugs used may include

- Cytarabine (cytosine arabinoside, Ara-C; Cytosar-U®)
- Idarubicin (Idamycin®)
- Daunorubicin (Cerubidine®)
- Mitoxantrone (Novantrone®)

Chemotherapy may be given alone or in combinations of two or three different agents (combination chemotherapy). When treating with combination therapy

- Low-dose protocols may be used.
- A patient's blood cell count may worsen. If cell counts do get worse, a doctor will evaluate the patient's condition to decide whether intensive chemotherapy may be continued.

More information about these drugs can be found at www.LLS.org/drugs.

Allogeneic Stem Cell Transplantation. This type of treatment, which involves giving new stem cells from a donor to the patient, is the best-known curative option for MDS. Since allogeneic stem cell transplantation is a high-risk procedure, this treatment is mainly considered for

- Patients younger than age 60
- Patients up to age 75 who are in otherwise good health
- Patients who are in either the IPSS intermediate –2 or the IPSS high-risk category, or who have therapy-related (secondary) MDS
- Patients who have a human leukocyte-associated antigen (HLA)-matched stem cell donor (sibling or unrelated match).

Allogeneic stem cell transplants may also be considered for select lower-risk MDS patients with severe cytopenia. Autologous transplantation, using the patient's own stem cells, is used in some other diseases but is not used in MDS since the patient's own stem cells are abnormal because of the disease.

Reduced-Intensity (Nonmyeloablative) Stem Cell Transplantation. Patients being conditioned for a nonmyeloablative transplant receive lower doses of chemotherapy drugs and/or radiation. Immunosuppressive drugs are used to prevent rejection of the graft, and the engraftment of donor immune cells may allow these cells to attack the disease (graft-versus-cancer effect). Studies are researching the use of this type of transplant in older adults who have relapsed and/or who have refractory disease. Reduced-intensity stem cell transplantation is usually used for patients who are older than 55 to 60 years.

See the free LLS publications, *Blood and Marrow Stem Cell Transplantation* and *Cord Blood Stem Cell Transplantation Facts* for more information about stem cell transplantation.

Research and Clinical Trials

New approaches under study in clinical trials for MDS treatment, many of which are being supported by LLS research programs, hold promise of increasing the rate of remission and finding a cure for MDS.

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

LLS Information Specialists, at (800) 955-4572, can offer guidance on how patients can work with their doctors to determine if a specific clinical trial is an appropriate treatment option. Information Specialists will conduct individualized clinical-trial searches for patients, family members and healthcare professionals. When appropriate, personalized clinical-trial navigation by trained nurses is available.

Research Approaches. There are clinical trials for newly diagnosed patients and for patients with relapsed or refractory disease. A number of approaches are under study in clinical trials for the treatment of MDS patients.

Agents Under Study. The following drugs are examples of specific agents (drug treatments) under study:

- Several combinations of FDA-approved drugs, such as azacitidine and decitabine as well as AML-type chemotherapy agents are being studied in several clinical trials. Each drug works in different ways to kill cancer cells. When drugs are used together, they may kill more MDS cells or they may be as effective as standard MDS therapies, but have less toxic side effects.
- Rigosertib (Estybon™), a drug that promotes MDS cell death, is being researched in current trials for the treatment of intermediate –1, intermediate –2 or high-risk patients as a single agent. It is also being studied in patients whose MDS has stopped responding to azacitidine or decitabine.
- Luspatercept (ACE-536) is a type of TFG (transforming growth factor)-beta inhibitor. This drug is showing promising results in current trials for very low- to intermediate-risk MDS, in patients with the MDS-RS subtype and/or the SF3B1 mutation and who require frequent transfusions.

- Valproic acid (Depakene®), a histone deacetylase (HDAC) inhibitor, is being studied in combination with decitabine (Dacogen®) in the treatment of patients with high-risk MDS.
- Two current clinical trials are investigating the use of programmed death ligand 1 (PD-L1) inhibitors in MDS. Pembrolizumab (Keytruda®), a PD-L1 inhibitor approved for melanoma, is undergoing a trial as a single agent against MDS and certain types of lymphoma. Another PD-L1 inhibitor, atezolizumab (Tecentriq®), is being tested with and without azacitidine in an ongoing trial.
- The CTLA-4 inhibitor ipilimumab (Yervoy®), approved in melanoma, is being studied for treatment of relapsed and refractory MDS before or after stem cell transplantation.

Vaccine Therapy. Clinical trials are underway to see if an MDS vaccine is effective in treating patients who have higher-risk MDS. The vaccine is made from protein-building blocks called "peptides," which may help the body mount an effective immune response to MDS cells.

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

Follow-Up Care

Like the disease, MDS follow-up care varies from patient to patient. MDS patients

- Will need to see their doctors on a regular basis. The doctor will evaluate the patient's health, blood cell counts and, possibly, bone marrow status.
- May have some tests repeated to see if they are benefiting from treatment and whether or not to continue it.
- Are advised to receive certain vaccinations, including vaccinations for influenza and pneumococcal pneumonia. There are two types of pneumococcal vaccines available for adults: a pneumococcal polysaccharide vaccine (PPSV23) and a pneumococcal conjugate vaccine (PCV13). Immunizations using live organisms or with high viral loads, such as the herpes zoster or shingles vaccine, should not be administered. Your doctor can give you more information.
- Always need to keep good records and treatment notes. This information should include
  - Doctors' names and contact information
  - Diagnosis
  - Names of chemotherapy drugs taken

- Radiation treatment information
- Surgery information
- Transplant information
- Information about any other treatments
- Other medical history

Normal Blood and Marrow

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

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

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

Blood Cells. The blood cells are suspended in the plasma. Blood cells are formed in the bone marrow, a spongy tissue where blood cells grow and develop. Blood cells start as stem cells. The process of stem cells maturing into blood cells is called "hematopoiesis." See Figure 2 on page 29.

Once the cell is created, it will develop into one of the three types of blood cells. These include

1. Red blood cells (the cells that carry oxygen) that
- Make up a little less than half of the body's total blood volume
- Are filled with hemoglobin, which
  - Is a protein that picks up oxygen from the lungs and takes it around the body

- Binds with carbon dioxide (CO_2) and removes it from the cells, then brings it back to the lungs, from which the CO_2 is removed when we exhale

2. Platelets (cells that help blood to clot)

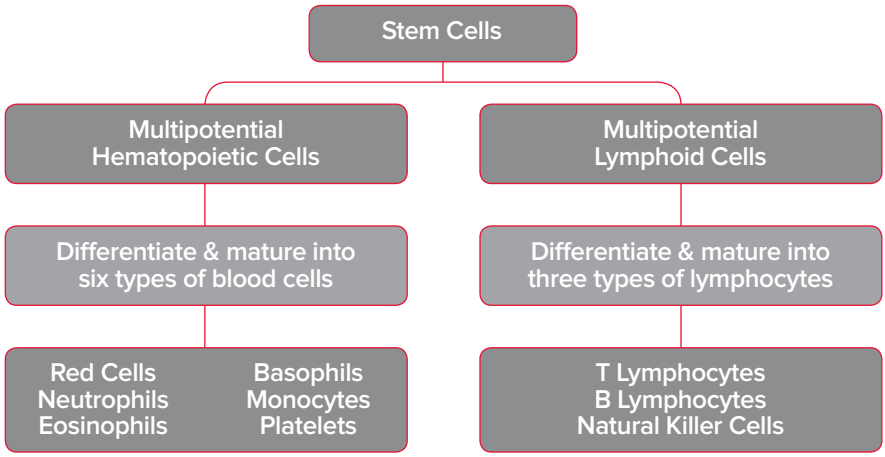
- Are small cells (one-tenth the size of red blood cells)
- Help stop bleeding from an injury or cut
- Stick to the torn surface of the vessel, clump together, and plug up the bleeding site
- Form a clot, with the help of proteins such as fibrin and electrolytes such as calcium

3. White blood cells (WBCs) fight infections. The several types of WBCs include

- Neutrophils and monocytes, also called "phagocytes" (eating cells), that ingest bacteria or fungi and kill them
  - Monocytes, unlike red cells and platelets, that can leave the bloodstream and enter tissues to attack invading organisms and fight off infection
- Eosinophils and basophils, types of WBCs that respond to allergens or parasites
- Lymphocytes, WBCs found in the lymph nodes, spleen and lymphatic channels that are a key part of the immune system. Some enter the bloodstream. Three major types of lymphocytes are
  - T lymphocytes (T cells)
  - B lymphocytes (B cells)
  - Natural killer (NK) cells

Hematopoiesis. In healthy people, stem cells in the bone marrow produce new blood cells continuously in a process called hematopoiesis. When blood cells are fully developed, they enter the bloodstream as it passes through the marrow and then circulate throughout the body.

Figure 2. Blood Cell & Lymphocyte Development (Hematopoiesis)



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

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

Hematopoietic stem cells are found in the marrow. These stem cells are important because they can be transplanted. Some stem cells enter the bloodstream and circulate, but there are not enough of them to be counted in standard blood tests. Doctors know how to stimulate the growth of these cells in the marrow and have them migrate into the bloodstream. Then a special technique called "apheresis" is used to separate them from the circulating blood so that they can be collected and stored. Stem cells from the placenta and the umbilical cord of a newborn infant can also be harvested and used for future transplantation.

Health Terms

Absolute Neutrophil Count (ANC). The number of neutrophils (a type of white blood cell that fights infection) that are identified in the blood count.

Acquired Sideroblastic Anemia. See Refractory Anemia with Ring Sideroblasts (RARS).

Acute Myeloid Leukemia (AML). A fast-moving cancer that starts with a cancerous change of a young cell in the bone marrow. The changed cancer cells that grow and live in the bone marrow are called "leukemic myeloblasts." See the free LLS booklet, *Acute Myeloid Leukemia*.

Allogeneic Stem Cell Transplantation. A treatment that uses healthy donor stem cells to restore a patient's marrow and blood cells. It uses high doses of chemotherapy and sometimes radiation to "turn off" a patient's immune system so that the donor cells are not rejected. See the free LLS booklet, *Blood and Marrow Stem Cell Transplantation.*

Anemia. A health condition that occurs when a person has a low number of red blood cells and therefore a low hemoglobin concentration. When this happens, it is hard for the blood to carry oxygen. People with severe anemia can be pale, weak, tired, and become short of breath easily. See Hematocrit; Hemoglobin.

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

Apheresis. A process using a machine to remove the needed parts of a donor's blood and return the unneeded parts back to the donor. This allows certain parts of blood, including red blood cells, white blood cells and platelets to be removed separately and in large volumes. See Platelet Transfusion.

Aplastic Anemia. A health condition that occurs when the body stops producing enough new blood cells. Any blood cells that the marrow does make are normal, but there are not enough of them. Aplastic anemia can be moderate, severe or very severe.

Autologous Stem Cell Transplantation. A treatment that uses a patient's own stem cells to slow the growth of certain blood cancers. See the free LLS booklet, *Blood and Marrow Stem Cell Transplantation*.

Autosome. See Karyotype.

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

Blast Cells. Young (or immature) cells in the bone marrow. In healthy people, blast cells make up 5 percent or less of normally developing marrow cells. In some cases of MDS, there are abnormal blast cells (abnormal myeloblasts) in the bone marrow. This can lead to the decreased numbers of red cells, neutrophils, and blood platelets that cause MDS and AML symptoms.

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

Blood Count. A lab test that measures the number and types of cells in the blood. Often called a "complete blood count" or CBC.

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

Bone Marrow Aspiration. A test to find abnormal marrow cells. The area around the hip bone is numbed and then a special needle is inserted and a marrow sample (fluid) is drawn out. Usually, this test is done at the same time as a bone marrow biopsy.

Bone Marrow Biopsy. A test to find abnormal marrow cells. The area around the hip bone is numbed and then a special needle is inserted and a piece of bone containing marrow is withdrawn. This test is usually done at the same time as a bone marrow aspiration.

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

Central Line (Indwelling Catheter). A special tube put into a large vein in the patient's upper chest. It is used to give medicines, fluids or blood products, or to take blood samples. See Port.

Chemotherapy. A treatment that uses medicine (chemical agents) to kill cancer cells.

Chromosome. Threadlike structures within cells that carry genes in a linear order. Human cells have 23 pairs of chromosomes: chromosome pairs 1 to 22 and one pair of sex chromosomes (XX for females and XY for males). See Translocation.

Clonal. An adjective that refers to a group of cells that originate from a single parent cell. Most cancers begin in one clonal cell (monoclonal) with a DNA injury. Clonal cancers include leukemia, lymphoma, myeloma and MDS.

Colony-Stimulating Factor. See Growth Factor.

Complete Remission. When a patient shows no sign of a disease after it has been treated, based on the results of standard tests specific to that disease.

Cytogeneticist. A health care expert who prepares and then examines, in a process called cytogenetic analysis, the chromosomes of cells.

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

Deletion. A chromosomal abnormality showing that either a part or all of a single chromosome is lost.

Differentiation. Occurs when stem cells develop, mature, and then take on a new function. Stem cells mature into either red blood cells, platelets or white blood cells. See Hematopoiesis.

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

Eosinophil. A white blood cell that helps fight some parasitic infections and participates in allergic responses.

Erythrocytes. See Red Blood Cells.

Erythrocytosis. See Hematocrit.

Erythropoietin (EPO). A hormone needed for normal production of red blood cells. It is made mainly by the kidneys and is released into the blood when blood oxygen levels are low. Synthetic EPO given in erythropoiesis stimulating agents (ESAs). Some drugs used to treat anemia include epoetin alfa (Procrit® or Epogen®) and darbepoetin alfa (Aranesp®).

5q– Syndrome (5q Minus Syndrome). A World Health Organization term for a subtype of MDS that causes refractory (treatment-resistant) anemia. It affects about 20 to 30 percent of patients with MDS. This subtype causes refractory (treatment-resistant) anemia associated with a deletion of the long arm (q) of chromosome 5, designated "del(5q)."

Fluorescence In Situ Hybridization (FISH). A technique used to study chromosomes in tissue. It uses probes with fluorescent molecules that emit light of different wavelengths and colors.

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

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

Germ Cell Mutation. A mutated cell in the egg or the sperm, which is passed from parent(s) to offspring.

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

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

Haploidentical. A potential stem cell donor that has a 50 percent HLA antigen-match with a patient. Parents are haploidentical with children. Siblings have a 50 percent chance of being haploidentical. See HLA; Allogeneic Stem Cell Transplantation.

Hemapheresis. See Apheresis.

Hematocrit. The portion of the blood occupied by red blood cells. Normal amounts are 40 to 54 percent in males and 35 to 47 percent in females. Anemia occurs when the hematocrit level is below normal; erythrocytosis occurs when the hematocrit is above normal.

Hematologist. A doctor who specializes in blood cell diseases.

Hematopathologist. A doctor or scientist who studies the blood cells and blood tissues to identify disease.

Hematopoiesis. The formation of all types of blood cells that starts in the marrow. For the blood cell development process, see *Normal Blood and Marrow* on page 27.

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

HLA. Human leukocyte-associated antigen. Proteins on the outer part of cells that help fight illness. HLAs are passed from parents to their children and one in four siblings has the same type of HLA.

Immunophenotyping. A process used to find specific types of cells within a blood sample. It looks at antigens or markers on the surface of the cell to identify antibodies.

Indwelling Catheter. See Central Line.

Karyotype. The order, number and appearance of chromosomes within a cell. There are 46 human chromosomes in each cell—22 pairs called "autosomes" and a 23rd pair which are the sex chromosomes (either XX or XY). See Fluorescence In Situ Hybridization.

Leukocytes. See White Blood Cells.

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

Macrophage. A monocyte in action (this is called a "scavenger cell"). When monocytes leave the blood and enter the tissue, they are known as "macrophages." Macrophages fight infection, eat dead cells and help lymphocytes with their immunity functions. See Monocyte.

Marrow. See Bone Marrow.

Maturation. See Hematopoiesis.

MDS-u. See Unclassifiable MDS.

Monoclonal. See Clonal.

Monoclonal Antibodies. Antibodies made by cells from a single clone. They are used in cancer treatment to target cancer cells. They can be made in a laboratory.

Monocyte. A type of white blood cell that represents about 5 to 10 percent of the cells in normal human blood.

Mutation. A change in the DNA that makes up a gene.

Myelodysplasia. See Refractory Anemia; Refractory Anemia with Ring Sideroblasts.

Neutropenia. An abnormal decrease in the number of neutrophils in the blood. See Neutrophil.

Neutrophil. A type of white blood cell and the main type that works to fight infection. People with some blood cancers, or those who have received treatment such as chemotherapy for cancer, often have low neutrophil counts. People with low neutrophil counts can easily get infections.

Nonmyeloablative Allogeneic Stem Cell Transplantation. See Reduced-Intensity Stem Cell Transplantation.

Oligoblastic Myelogenous Leukemia. Also known as "refractory anemia excess blasts" (RAEB), this type of MDS shows signs of leukemic blast cells when the blood or marrow is examined. There may only be a small number of these blast cells in the marrow, but their presence indicates that leukemic cells are developing.

Oncologist. A doctor who specializes in cancer.

Pancytopenia. A health condition in which there is a decrease in the numbers of all three major blood cell types: red blood cells, white blood cells and platelets.

Partial remission. When a disease is improved after treatment, but is still present.

Pathologist. A specialist doctor who finds disease by looking at body tissue and fluids.

Percutaneously Inserted Central Venous Catheter (PICC or PIC Line). A long, thin, flexible tube placed into the body under the skin. It can be used for weeks or months to help give a patient medicine, fluid or nutrition. It can also be used to get blood samples. Intravenous (IV) infusions can be administered via a PICC line.

Phagocytes. Cells that protect the body from infection by eating and killing microorganisms such as bacteria and fungi. The two main types are neutrophils and monocytes. Once an infection occurs, they migrate from the bloodstream and enter the infected tissue. Chemotherapy and radiation can decrease the numbers of these "good" cells, so patients are more likely to get an infection. PICC or PIC line. See Percutaneously Inserted Central Venous Catheter.

Platelet Transfusion. This procedure transfers blood platelets from a donor to a patient. About six single-unit blood donors are often needed to provide enough platelets to raise the patient's platelet level. Platelet transfusions may help some MDS patients. See HLA; Apheresis.

Platelets. Also known as "thrombocytes," platelets are small colorless blood cells. Their sticky surface helps them go to a wound, form clots and stop bleeding. Platelets make up about one tenth of the volume of red blood cells.

Port. A small device placed under the skin and attached to a central line or a PICC line. It permits access to the line. Medicines and nutrition can be administered and blood samples can be withdrawn through a port.

RA. See Refractory Anemia.

Radiation Oncologist. A cancer doctor who uses radiation to treat cancer.

RAEB. See Oligoblastic Myelogenous Leukemia.

RAEB-T. See Refractory Anemia with Excess Blasts in Transformation.

RARS. See Refractory Anemia with Ring Sideroblasts.

RCMD. See Refractory Cytopenia with Multilineage Dysplasia.

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

Red Blood Cells. Blood cells (also called erythrocytes) that contain hemoglobin, which carries oxygen to the body tissues. Red blood cells make up about 40 to 45 percent of blood volume in healthy people.

Reduced-Intensity or "Nonmyeloablative" Stem Cell Transplantation. A type of allogeneic transplantation. Patients receive lower doses of chemotherapy drugs and/or radiation to prepare for a reduced-intensity transplant. This protocol may be safer than a regular allogeneic stem cell transplant, especially for older patients. See the free LLS booklet, *Blood and Marrow Stem Cell Transplantation*.

Refractory Anemia (RA). Also known as "myelodysplasia," this clonal myeloid disorder mostly affects red blood cell production in the marrow. It can also be associated with mild to moderate decreases in the numbers of white blood cells and platelets. In some classification systems, it is an MDS subtype.

Refractory Anemia with Excess Blasts (RAEB). See Oligoblastic Myelogenous Leukemia.

Refractory Anemia with Excess Blasts in Transformation (RAEB-T). In the French-American-British (FAB) classification, an MDS subtype in which the bone marrow blast count ranges from 20 to 30 percent.

Refractory Anemia with Ring Sideroblasts (RARS). This is a form of anemia in which the bone marrow produces ringed sideroblasts rather than healthy red blood cells. In the case of abnormal sideroblasts, large amounts of iron are trapped in the developing red cells in abnormal sites. Refractory anemia and RARS are often associated with mild to moderate decreases in the numbers of white blood cells and platelets. This disorder is also called "myelodysplasia" or "acquired sideroblastic anemia." In some classifications, RARS is an MDS subclass. Also called "myelodysplasia" or "acquired sideroblastic anemia."

Refractory Cytopenia with Multilineage Dysplasia (RCMD). One of the more common World Health Organization MDS subtypes. In RCMD, there are too few of at least two types of blood cells (red blood cells, white blood cells, or platelets). In the bone marrow, those same types of cells look abnormal (dysplastic) under the microscope. Less than 5 percent of the cells in the bone marrow are blasts. In patients with more than 15 percent of ringed sideroblasts, this subtype is called "RCMD-RS."

Refractory Disease. A disease that does not go away or improve much after initial treatment.

Remission. When signs of a disease disappear, it is called "in remission," usually following treatment.

Risk Factor. Something that is scientifically linked to a person's chance of getting a disease. Risk factors can be genetic (inherited), lifestyle-related or environmental.

Smoldering Leukemia. See Oligoblastic Myelogenous Leukemia.

Somatic Cell Mutation. A change in the DNA that occurs in a specific tissue cell which may result in a tumor. Most cancers start after a somatic cell mutation.

Stem Cells. Early marrow cells that mature into red blood cells, white blood cells and blood platelets. Stem cells are mostly found in the marrow, but some leave marrow and circulate in the bloodstream. Stem cells can be collected, preserved and used for stem cell therapy. See Hematopoiesis.

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

Surgical oncologist. A cancer doctor who uses surgery to treat cancer.

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

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

Tissue typing. A test for the presence of HLA antigens.

Translocation. When a piece of a chromosome in a marrow or lymph node cell breaks off and attaches to the end of another chromosome.

Unclassifiable MDS (MDS-u). A World Health Organization MDS subtype classification that includes patients who do not have refractory anemia or other MDS subtypes, but have either neutropenia or thrombocytopenia with unusual features, such as marrow fibrosis. The number of blasts in the blood and bone marrow is not increased.

White Blood Cells. Also known as "leukocytes," these are infection-fighting cells in the blood. The five types include neutrophils, eosinophils, basophils, monocytes and lymphocytes.

More Information

Free LLS booklets include:

Acute Myeloid Leukemia
The AML Guide: Information for Patients and Caregivers
Blood and Marrow Stem Cell Transplantation
Blood Transfusion
Chronic Myelomonocytic Leukemia (CMML) and Juvenile Myelomonocytic Leukemia (JMML)
Each New Day: Ideas for Coping with Blood Cancers

Visit "Suggested Reading" at www.LLS.org/suggestedreading to see helpful books on a wide range of topics.

More Resources

Aplastic Anemia & MDS International Foundation (AA&MDSIF)

(800) 747-2820 or (301) 279-7202
www.aamds.org

AA&MDSIF is the world's leading nonprofit health organization dedicated to supporting patients and families living with aplastic anemia, myelodysplastic syndromes (MDS), paroxysmal nocturnal hemoglobinuria (PNH) and related bone marrow failure diseases. AA&MDSIF provides answers, support and hope to thousands of patients and their families around the world.

The Myelodysplastic Syndromes Foundation, Inc.

(800) 637-0839 or (609) 298-1035
www.mds-foundation.org

The MDS Foundation is a multidisciplinary, international organization devoted to MDS support, research, treatment and education for patients, caregivers, physicians, nurses and other healthcare providers. The organization is based on the premise that international cooperation will accelerate the process leading to the control and cure of these diseases.

References

Bennet J. Changes in the updated 2016: WHO Classification of the Myelodysplastic Syndromes and Related Myeloid Neoplasms. *Clinical Lymphoma, Myeloma & Leukemia.* 2016;16(11): 607-609.

Carreau N, Tremblay D, Savona M, Kremyanskava M, Mascarenhas J. Ironing out the details of iron overload in myelofibrosis: lessons from myelodysplastic syndromes. *Blood Reviews*. 2016;30:349-356.

Gangat N, Patnaik MM, Tefferi A. Myelodysplastic syndromes: contemporary review and how we treat. *American Journal of Hematology.* 2016;91(1):76-89.

Ganguly BB, Kadam NN. Mutations of myelodysplastic syndromes (MDS): an update. *Mutation Research.* 2016;769:47-62.

Howlader N, Noone AM, Krapcho M, et al, eds. *SEER Cancer Statistics Review, 1975-2013.* Bethesda, MD: National Cancer Institute; November 2016. http://seer.cancer.gov/csr/1975_2013/, based on November 2015 SEER (Surveillance, Epidemiology, and End Results Program) data submission, posted to the SEER Web site; April 2016.

Meers S. The myelodysplastic syndrome: the era of understanding. *European Journal of Haematology.* 2014;94(5):379-390.

Montalban-Bravo G, Garcia-Manero G. How do we treat…patients with myelodysplastic syndromes? *Oncology Times.* February 10, 2016.

National Comprehensive Cancer Network. Myelodysplastic syndromes. In: *Practice Guidelines in Oncology—v.2.2017.* www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed December 5, 2016.

National Comprehensive Cancer Network. Myelodysplastic syndromes. In: *NCCN Guidelines for Patients.* – Vol 1. 2016. www.nccn.org/patients/guidelines/mds/index.html. Accessed December 5, 2016.

Pellagatti A, Boultwood J. The molecular pathogenesis of the myelodysplastic syndromes. *European Journal of Haematology.* 2015;95(1):3-15.

Platzbecker U, Fenaux U. Recent frustration and innovation in myelodysplastic syndrome. *Haematologica.* 2016;101(8):891-893.

Prebet T, Zeidan A. Trends in clinical investigation for myelodysplastic syndromes. *Clinical Lymphoma, Myeloma & Leukemia.* 2016;16(suppl 1):S57-S63.

The Leukemia & Lymphoma Society. Facts 2015-2016. www.LLS.org/booklets. Accessed December 3, 2016.

Notes

LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

someday is today®

REACH OUT TO OUR **INFORMATION SPECIALISTS**

The Leukemia & Lymphoma Society's (LLS) Information Specialists provide patients, families and healthcare professionals with the latest information on leukemia, lymphoma and myeloma. Our team consists of master's level oncology social workers, nurses and health educators who are available by phone Monday through Friday, 9 am to 9 pm (ET).

Co-Pay Assistance
LLS's Co-Pay Assistance Program helps blood cancer patients cover the costs of private and public health insurance premiums, including Medicare and Medicaid, and co-pay obligations. Support for this program is based on the availability of funds by disease. **For more information, call 877.557.2672 or visit www.LLS.org/copay.**

For a complete directory of our patient services programs, contact us at

800.955.4572 or **www.LLS.org**

(Callers may request a language interpreter.)

LEUKEMIA & LYMPHOMA SOCIETY®

fighting blood cancers

For more information, please
contact our Information Specialists
800.955.4572 (Language interpreters
available upon request)
www.LLS.org

or:

National Office
3 International Drive, Suite 200
Rye Brook, NY 10573

Our Mission:

Cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families.

LLS is a nonprofit organization that relies on the generosity of individual, foundation and corporate contributions to advance its mission.

PS22 35M 5/17