

# Myelodysplastic Syndromes



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## A six-word narrative about living with blood cancer from patients in our LLS Community

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Stay strong and keep moving forward. Find the positive in every day. Be your own best patient advocate. Changed my life for the better. Accept, learn and focus on present. Learning to live a different life. Sudden and life changing—be positive. Waiting, worrying, anxiousness/happy I'm alive! Embrace a new normal each day. 5 years, 41 infusions, constant fatigue. Patience, positive attitude, hope and faith. Test to test, I will survive! Treatment, fatigue, treatment, fatigue and survival. Love life, live better every day. I don't look back only forward. So far, so good, live life. Meditation, mindfulness, wellness, faith, nutrition and optimism. Finding the joy while living with uncertainty. Watch, wait, treat, regroup, rest, re-energize. Blessed to be doing so well! Eye opening needed learning and healing. Feel great: uncertain travel plans annoying. Renewed faith, meditation, diet, mindfulness, gratitude. Watchful waiting can be watchful worrying. Scary, expensive, grateful, blessings, hope, faith. Thank god for stem cell transplants! Do not know what to expect. Extraordinarily grateful, I love my life. Diagnosed; frightened; tested; treating; waiting; hoping. I'm more generous, impatient less often. Embrace your treatment day after day. Live today, accept tomorrow, forget yesterday. Strength you never realized you had. Challenging to our hearts and minds. Life is what we make it. Live life in a beautiful way.



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- Accurate and cutting-edge disease updates
- The opportunity to participate in surveys that will help improve care.

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The Leukemia & Lymphoma Society appreciates the review of this material by

#### **Amy Elizabeth DeZern, MD, MHS**

Associate Professor of Oncology and Medicine  
Sidney Kimmel Comprehensive Cancer Center  
Johns Hopkins Medicine  
Baltimore, MD

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# Introduction

The term “myelodysplastic syndromes” or “MDS” refers to a group of blood cancers and bone marrow failure syndromes in which the bone marrow does not produce enough healthy blood cells. Brief descriptions of normal blood and bone marrow and definitions of health terms are included in this booklet.

From 2011 to 2015, there were approximately 70,056 new cases of myelodysplastic syndromes throughout the United States, averaging an estimated 14,011 cases per year.<sup>1</sup> Advances in the treatment of myelodysplastic syndromes have resulted in improved outcomes for patients.

There are different subtypes of MDS. Identifying the subtype of MDS is important for two reasons.

- The severity of the disease and life expectancy of patients varies depending on the subtype.
- Treatment plans and drug regimens are determined according to the particular subtype of MDS.

New approaches to treatment are being studied in clinical trials for patients of all ages and for all disease stages.

<sup>1</sup>Facts 2018-2019. The Leukemia & Lymphoma Society. March 2019.

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## Myelodysplastic Syndromes (MDS)

Myelodysplastic syndromes are a group of diseases that affect the blood and bone marrow. For years, myelodysplastic syndromes were also known as “preleukemia,” “refractory anemia,” or “smoldering leukemia.” These terms stopped being used because only a minority of patients with MDS develop acute leukemia, and patients often have other blood problems in addition to anemia. Today, myelodysplastic syndromes are classified as blood cancers. There are many different subtypes of myelodysplastic syndromes, some mild and others severe.

In every person, blood stem cells (immature blood-forming cells) grow and divide in the bone marrow to make all types of mature blood cells. These include

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

Myelodysplastic syndromes (“myelo” means marrow and “dysplastic” means abnormal shape and appearance) occur when blood stem cells become abnormal because of genetic changes (mutations). The damaged blood stem cells and bone marrow do not work as well as they should. When the bone marrow is not working properly, it cannot make enough healthy blood cells. The most immature bone marrow cells (blast cells) cannot perform the specific function of mature cells and they accumulate in the marrow and blood.

In healthy people, blast cells make up less than 5 percent of all bone marrow cells. In MDS patients, blast cells may make up between 5 and 19 percent of the cells in the bone marrow. A high number of blast cells in the bone marrow is a determinant of MDS severity. By definition, 20 percent or more blast cells in the bone marrow indicates the disease has progressed to acute myeloid leukemia (AML).

There are many types of myelodysplastic syndromes. A myelodysplastic syndrome may first manifest as anemia (a decrease in the number of healthy red blood cells in the blood). Myelodysplastic syndromes can progress very slowly, or they can become fast-growing diseases. Severe MDS cases carry a high risk of progressing to AML. **Please visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view the free LLS booklet *Acute Myeloid Leukemia*.**

Today, patients who have an MDS can anticipate 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.

## Signs and Symptoms

A “sign” is a change in the body that the doctor sees in an examination or a test result. A “symptom” is a change in the body that a patient can see and/or feel. A person with signs and/or symptoms that suggest the possibility of a myelodysplastic syndrome (MDS) is referred to a specialist, a doctor called a “hematologist-oncologist,” who has special training in the diagnosis and treatment of blood cancers. If a patient has signs and/or symptoms of MDS, or if routinely ordered blood tests produce abnormal findings associated with MDS, the doctor will order additional tests to either diagnose or rule out MDS (see *Diagnosis* on page 4). The signs and symptoms of myelodysplastic syndromes are also associated with a number of other, less serious diseases.

Some patients initially have no signs or symptoms of the disease, so abnormal results from routine blood tests may be the earliest indicators of MDS.

People with myelodysplastic syndromes often have a “cytopenia,” which is a low level of one or more types of blood cells (red blood cells, white blood cells or platelets):

- Anemia—a decrease in the number of healthy red blood cells. Red blood cells carry oxygen throughout the body. Anemia may cause signs and/or symptoms such as
  - Fatigue
  - Dizziness
  - Weakness
  - Shortness of breath or chest discomfort, especially with exertion
  - Pale skin
- Neutropenia—a decrease in the number of healthy white blood cells. White blood cells help the body to fight infection. Neutropenia can lead to frequent or severe infections.
- Thrombocytopenia—a decrease in the number of healthy platelets. Platelets help control bleeding and are involved in wound healing. Thrombocytopenia may cause signs and/or symptoms such as
  - Easy bruising
  - Bleeding

(See *Normal Blood and Marrow* on page 27.)

## Diagnosis

Myelodysplastic syndromes (MDS) can be difficult to diagnose. An accurate diagnosis is one of the most important aspects of a person’s care. Obtaining a precise diagnosis will help the doctor to

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

Myelodysplastic syndromes can sometimes be mistaken for other blood disorders, so repeated blood and bone marrow tests may be needed to establish an MDS diagnosis. It is also important for an experienced hematopathologist to examine laboratory samples under a microscope. A “hematopathologist” is a doctor who has special training in diagnosing diseases of the blood, bone marrow and lymphatic system.

**Complete Blood Count (CBC) With Differential (Diff).** A doctor will order a CBC with differential to measure the number of red blood cells, white blood cells and

platelets in the blood. The differential test measures the different types of white blood cells in the sample. Patients with myelodysplastic syndromes often have low numbers of one or more types of blood cells. If anemia is detected, the red blood cells are further examined for

- A lack of iron, folate or vitamin B<sub>12</sub>
- Signs of another 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. A reticulocyte count measures the number of reticulocytes in the circulating blood. It shows how quickly these cells are being made and released by the bone marrow and whether the bone marrow is functioning properly. The body's response to anemia is for the bone marrow to make more reticulocytes. A low reticulocyte count indicates that the bone marrow is not working well.

**Peripheral Blood Smear.** A peripheral blood smear is a test in which a hematopathologist examines a drop of blood under a microscope to identify unusual changes in the number, size, shape, appearance and maturity of various blood cells. In myelodysplastic syndromes, blood cells have an abnormal shape or size (dysplasia). The hematopathologist will also check a peripheral blood smear for the presence of blast cells. Blast cells are normally found in the bone marrow, but they are not typically found in the blood of healthy individuals. In some cases of MDS, a small number of blast cells can be found in the blood.

**Serum Erythropoietin (EPO).** Erythropoietin is a substance made in the kidneys. It stimulates the bone marrow to produce more red blood cells. Measuring the amount of EPO in the blood can help determine if the EPO is low. A low EPO level can cause anemia and may be a sign of a health problem such as MDS. A low EPO level can also worsen anemia in a person who has an MDS. Most patients with MDS-related anemia have relatively low serum levels of EPO.

**Bone Marrow Tests: Aspiration and Biopsy.** To confirm a diagnosis of MDS, a sample of the patient's bone marrow must be removed for testing. Bone marrow aspiration and biopsy are two procedures done to obtain bone marrow samples that are examined for abnormalities. Both procedures are generally done at the same time. The samples are usually taken from the patient's hip bone (a local anesthetic is used to numb the insertion site). Bone marrow has both a liquid and a solid part. For bone marrow aspiration, a special hollow biopsy needle is inserted through the hip bone and into the marrow to remove (aspirate) a liquid sample of cells. In a bone marrow biopsy, a specialized wider needle is used to remove a core sample of solid bone that contains marrow.

After the samples are taken, a hematopathologist reviews the samples under a microscope to assess the type, size, appearance and maturity of the cells. As

part of this assessment, the specialist will note any signs of a myelodysplastic syndrome, such as

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

**Cytogenetic Testing (Karyotyping).** In this test, the hematopathologist uses a patient's blood or bone marrow sample to examine the chromosomes inside of cells. It is common for cancer cells to have abnormal chromosomes.

A normal human cell contains 23 pairs of chromosomes, for a total of 46 chromosomes. Each pair of chromosomes is a certain size, shape and structure. Approximately 50 percent of MDS patients have one or more chromosomal defects that can be seen in a blood sample viewed under a microscope.

There are different types of chromosomal defects. For example, either 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 myelodysplastic syndromes involve

- **A deletion (del) of the long arm (q) of one of the two chromosomes in a pair of chromosomes**
  - Chromosomes 5, indicated as del(5q) or 5q minus syndrome (5q-)
  - Chromosomes 7, indicated as del(7q) or 7q minus (7q-)
  - Chromosomes 20, indicated as del(20q) or 20q minus (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 (T8M)**, an extra copy of chromosome 8, so that there are three copies of chromosome 8 instead of two

**Fluorescence In Situ Hybridization (FISH).** This test uses special dyes that allow the hematopathologist to detect changes in a cell's genes and chromosomes. This test identifies specific gene or chromosome changes that are common in MDS patients.



**Molecular Testing.** These tests can be done on either a sample of blood or bone marrow to look for mutations in genes that are associated with myelodysplastic syndromes. Sometimes, molecular testing results influence treatment or its outcome. Certain mutations are associated with either a better or a worse outcome. Doctors use the results of molecular testing to help plan treatment.

In recent years, research has identified several gene mutations among MDS patients. These are noteworthy because

- There are more than 40 genes that can be mutated in MDS.
- Many patients (over 80 percent) are likely to have at least one mutation.
- Based on the functions of these mutated genes, researchers have learned about the molecular mechanisms responsible for the development of myelodysplastic syndromes.
- The specific pattern of mutations seen in MDS patients may partially explain the variability of the disease, and these specific patterns will likely lead to newer classification systems based on genetic abnormalities.
- A subset of mutations may have prognostic value. Mutations in certain genes have been associated with both better and worse prognoses than those predicted by the International Prognostic Scoring System (IPSS) (see *The International Prognostic Scoring System* on page 10).
- The genes that are most frequently mutated in MDS patients 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**.

About 80 percent of patients with a myelodysplastic syndrome with ring sideroblasts (MDS-RS) subtype have the *SF3B1* mutation, which tends to be a marker for a more favorable prognosis.

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

**Diagnostic Criteria.** The diagnosis of MDS is made based upon the results of blood and bone marrow tests. The main criteria that are used to diagnose an MDS are

- At least one cytopenia (low blood cell count) in one or more of red blood cell, white blood cell or platelet counts

And one or more of the following criteria

- Obvious changes to the structure or form of the bone marrow cells (dysplasia) in at least 10 percent of red blood cells, white blood cells or platelets
- Blasts making up between 5 and 19 percent of bone marrow cells
- Specific MDS-associated chromosome (cytogenetic) abnormality.

## Treatment Planning

**Myelodysplastic Syndrome (MDS) Classification.** There are several MDS subtypes. The subtype is determined from the results of the blood and bone marrow tests.

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

In 2001, the World Health Organization (WHO) proposed an alternative classification that was a modified version of the original FAB classification. The WHO classification incorporated molecular and cytogenetic factors. Since then, the WHO classification has been updated twice, once in 2008 and again in 2016 (see **Table 1** on *page 9*). The 2016 WHO classification is more commonly used today.

**Table 1. 2016 WHO Classification of Myelodysplastic Syndromes (MDS)\***

- **MDS with single lineage dysplasia (MDS-SLD)**
- **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-EB1)
  - MDS with excess blasts-2 (MDS-EB2)
- **MDS with isolated del(5q)**
- **MDS, unclassifiable (MDS-U)**

*Provisional entity: Refractory cytopenia of childhood*

\* For definitions of these subtypes, see *Health Terms* on page 34.

Source: Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*. 2016;127(2):2391-2405. doi:10.1182/blood-2016-03-643544

**Myelodysplastic Syndromes/Myeloproliferative Neoplasms (MDS/MPN) Classification.** The WHO also has a category called “myelodysplastic syndromes/myeloproliferative neoplasms (MDS/MPN).” See **Table 2** below. This category includes subtypes that have both dysplastic and proliferative features. “Dysplastic” refers to the abnormal growth or development of cells in the bone marrow, and “proliferative” means the bone marrow produces too many blood cells. **Please visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view the free LLS booklet *Myeloproliferative Neoplasms*.**

**Table 2. 2016 WHO Classification of Myelodysplastic Syndromes/Myeloproliferative Neoplasms (MDS/MPN)**

- **Chronic myelomonocytic leukemia (CMML)**
- **Atypical chronic myeloid leukemia (aCML), BCR-ABL1 negative**
- **Juvenile myelomonocytic leukemia (JMML)**
- **MDS/MPN with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T)**
- **MDS/MPN, unclassifiable (MDS/MPN-U)**

Source: Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood* 2016;127(2):2391-2405. doi:10.1182/blood-2016-03-643544

**Prognostic Scoring Systems.** A “prognosis” is a prediction of the likely outcome of a disease. Certain factors may affect the prognosis of myelodysplastic syndromes and they help doctors determine when to start treatment and how intensive the treatment should be. These prognostic factors include

- The MDS subtype
- The number and severity of cytopenias (low blood cell counts)

- The percentage of blast cells in the bone marrow
- The type and number of chromosome changes

Doctors use prognostic scoring systems to rate the severity of a myelodysplastic syndrome. The scores also help predict whether an MDS will progress to acute myeloid leukemia (AML).

Doctors assign a risk score and risk group for a myelodysplastic syndrome based on the prognostic factors. Some factors are associated with better outcomes and a lower chance that an MDS will progress to AML. Other factors are also associated with poorer outcomes and a higher chance that an MDS will progress to AML.

Each prognostic factor is assigned a number based on its severity. The scores for all of the factors are then added together to create the overall risk score. The risk score indicates 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 (see **Table 3, 4 and 5** on *pages 11, 12 and 13*). They are

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

**The International Prognostic Scoring System (IPSS).** The IPSS was the first widely used prognostic scoring system for myelodysplastic syndromes and it has been established as the backbone of prognostic systems since its development in 1997. It scores three main factors (the percentage of blasts, the type of chromosomal changes and the presence of cytopenias) to classify myelodysplastic syndromes into four risk groups. The points are assigned to each of the factors, and then the points for selected factors are added together to determine the overall risk score.

The following examples show how IPSS scores (see **Table 3** on *page 11*) 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 points), anemia but normal platelet and neutrophil counts (0 points) would have a total IPSS risk score of 0. This patient would be categorized in the IPSS low-risk group.
- A patient with 5 to 10 percent blasts (0.5 points), an abnormal chromosome 7 (1 point), normal neutrophil counts, but low red blood cell and platelet counts that indicate anemia and thrombocytopenia (0.5 points), would have

a total IPSS risk score of 2. This patient would be categorized in the IPSS intermediate-2 risk group.

**Table 3. IPSS Prognostic Scoring System and Risk Groups**

Prognostic Factors Scored	Risk Groups Based on Total Risk Score
<p><b>Percent of blast cells in bone marrow</b></p> <ul style="list-style-type: none"> <li>○ Less than 5 = 0 points</li> <li>○ 5 to 10 = 0.5 points</li> <li>○ 11 to 20 = 1.5 points</li> <li>○ 21 to 30 = 2 points</li> </ul>	<ul style="list-style-type: none"> <li>○ 0 points = Low</li> <li>○ 0.5 to 1 point = Intermediate-1</li> <li>○ 1.5 to 2 points = Intermediate-2</li> <li>○ 2.5 or more points = High</li> </ul>
<p><b>Cytogenetics (chromosome changes)</b></p> <ul style="list-style-type: none"> <li>○ None, del(5q), del(20q) = 0 points</li> <li>○ 3 or more abnormalities, abnormal chromosome 7 = 1 point</li> <li>○ Other abnormalities = 0.5 points</li> </ul>	
<p><b>Number of cytopenias (anemia, neutropenia or thrombocytopenia)</b></p> <ul style="list-style-type: none"> <li>○ None or 1 = 0 points</li> <li>○ 2 or 3 = 0.5 points</li> </ul>	

**Key.** IPSS, International Prognostic Scoring System; del, deletion.

**The International Prognostic Scoring System-Revised (IPSS-R).** The 2012 revised version of the IPSS 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 myelodysplastic syndromes into five risk groups. See **Table 4** on *page 12*.

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

For a link to the Revised International Prognostic Scoring System (IPSS-R) for Myelodysplastic Syndromes Risk Assessment Calculator, see *page 33*.

**Table 4. IPSS-R Prognostic Scoring System and Risk Group**

Prognostic Factors Scored	Risk Groups Based on Total Risk Score
<p><b>Percent of blast cells in bone marrow</b></p> <ul style="list-style-type: none"> <li>○ Less than or equal to 2 = 0 points</li> <li>○ Greater than 2 to less than 5 = 1 point</li> <li>○ 5 to 10 = 2 points</li> <li>○ Greater than 10 = 3 points</li> </ul>	<ul style="list-style-type: none"> <li>○ 1.5 or less points = Very Low</li> <li>○ 2 to 3 points = Low</li> <li>○ 3.5 to 4.5 points = Intermediate</li> <li>○ 5 to 6 points = High</li> <li>○ 6.5 or more points = Very High</li> </ul>
<p><b>Cytogenetics (chromosome changes)</b></p> <ul style="list-style-type: none"> <li>○ <math>-Y</math>, <math>del(11q)</math> = 0 points</li> <li>○ Normal, <math>del(5q)</math>, <math>del(12p)</math>, <math>del(20q)</math>, double including <math>del(5q)^*</math> = 1 point</li> <li>○ <math>del(7q)</math>, <math>+8</math>, <math>+19</math>, <math>i(17q)</math>, any other single or double independent clone** = 2 points</li> <li>○ <math>-7</math>, <math>inv(3)</math>, <math>+(3q)</math>, <math>del(3q)</math>, double including <math>-7/del(7q)</math>, complex: 3 abnormalities = 3 points</li> <li>○ More than 3 abnormalities = 4 points</li> </ul>	
<p><b>Hemoglobin concentration (g/dL)</b></p> <ul style="list-style-type: none"> <li>○ Equal to or greater than 10 = 0 points</li> <li>○ 8 to less than 10 = 1 point</li> <li>○ Less than 8 = 1.5 points</li> </ul>	
<p><b>Platelet count (<math>\times 10^9/L</math> of blood)</b></p> <ul style="list-style-type: none"> <li>○ Equal to or greater than 100 = 0 points</li> <li>○ 50 to less than 100 = 0.5 points</li> <li>○ Less than 50 = 1 point</li> </ul>	
<p><b>Absolute neutrophil count ([ANC] <math>\times 10^9/L</math> of blood)</b></p> <ul style="list-style-type: none"> <li>○ Equal to or greater than 0.8 = 0 points</li> <li>○ Less than 0.8 = 0.5 points</li> </ul>	

\*  $del(5q)$  plus another cytogenetic abnormality

\*\* A single clone can have many abnormalities, all of them occurring simultaneously in the same cell.

**Key.** IPSS-R, International Prognostic Scoring System-Revised; ANC, absolute neutrophil count; del, deletion; g/dL, gram/deciliter; inv, an inversion in a chromosome.

**WHO Classification-based Prognostic Scoring System (WPSS).** The WPSS, developed in 2016, is not used as commonly as the IPPS and IPSS-R scoring systems. 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 either the presence or absence of severe anemia. See **Table 5** on page 13. The points are assigned to each of the factors, and then the points for selected factors are added together to determine the overall risk score.

**Table 5. WPSS Prognostic Scoring System and Risk Group**

Prognostic Factors Scored	Risk Groups Based on Total Risk Score
<p><b>MDS subtype</b></p> <ul style="list-style-type: none"> <li>○ MDS-SLD, MDS-RS, MDS with isolated del(5q) = 0 points</li> <li>○ MDS-MLD = 1 point</li> <li>○ MDS-EB1 = 2 points</li> <li>○ MDS-EB2 = 3 points</li> </ul>	<ul style="list-style-type: none"> <li>○ 0 points = Very Low</li> <li>○ 1 point = Low</li> <li>○ 2 points = Intermediate</li> <li>○ 3 to 4 points = High</li> <li>○ 5 to 6 points = Very High</li> </ul>
<p><b>Cytogenetics (chromosome changes)</b></p> <ul style="list-style-type: none"> <li>○ Good: normal, -Y alone, del(5q) alone, del(20q) alone = 0 points</li> <li>○ Intermediate: other abnormalities = 1 point</li> <li>○ Poor: 3 or more abnormalities, chromosome 7 abnormalities = 2 points</li> </ul>	
<p><b>Presence of severe anemia (hemoglobin less than 9 g/dL in men or less than 8 g/dL in women)</b></p> <ul style="list-style-type: none"> <li>○ Absent = 0 points</li> <li>○ Present = 1 point</li> </ul>	

**Key.** WPSS, WHO Classification-based Prognostic Scoring System; ANC, absolute neutrophil count; del, deletion; g/dL, gram/deciliter; MDS, myelodysplastic syndrome; MDS-EB, MDS with excess blasts; MDS-MLD, MDS with multilineage dysplasia; MDS-RS, MDS with ring sideroblasts.

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 considerations associated with elderly patients, such as comorbidities, previous cancers, and other health issues. Still, scoring system numbers are very important as they are indicators of the patient's ability to tolerate certain intensive treatments.

The IPSS-R has demonstrated that it predicts prognosis better than the IPSS; however, the IPSS continues to be used to determine eligibility for some clinical studies. The IPSS, IPSS-R, WPSS and other classification systems are also useful in interpreting the results of cooperative clinical trials involving patients at different treatment centers.

**Risk Groups.** Each prognostic scoring system designates a lower-risk and a higher-risk MDS group. The risk groups are based on patient scores (see **Table 6** on page 14). Note that prognostic systems and risk groups do not predict how a patient who has an MDS will respond to treatment. They can, however, indicate how the disease is likely to progress over time without treatment. Doctors know which prognostic scoring system was used to evaluate their patients, so they can determine their patients' risk group and plan treatment accordingly.

Lower-risk myelodysplastic syndromes tend to grow and progress slowly. They may not cause many or severe signs and/or symptoms for a long time. Therefore, less intensive treatment is frequently used. In contrast, higher-risk myelodysplastic syndromes are likely to progress more quickly. Without treatment, higher-risk myelodysplastic syndromes may also progress to AML in a shorter time. They may cause more signs and/or symptoms and health complications within a short time. Therefore, more intensive treatment is often required.

**Table 6. Risk Groups: Lower-Risk Versus Higher-Risk Myelodysplastic Syndromes**

Lower-risk groups	Higher-risk groups
○ <b>IPSS</b> Low and Intermediate-1	○ <b>IPSS</b> Intermediate-2 and High
○ <b>IPSS-R</b> Very Low, Low, Intermediate	○ <b>IPSS-R</b> Intermediate, High, Very High
○ <b>WPSS</b> Very Low, Low, Intermediate	○ <b>WPSS</b> High, Very High

This table includes lower-risk and higher-risk MDS categories from each of the three main prognostic scoring systems.

**Key.** IPSS, International Prognostic Scoring System; IPSS-R, International Prognostic Scoring System-Revised; MDS, myelodysplastic syndrome; WPSS, WHO Classification-based Prognostic Scoring System.

## Treatment

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

Every patient should be evaluated individually by a hematologist-oncologist who specializes in treating myelodysplastic syndromes (MDS). The doctor should discuss the disease subtype, prognostic factors and treatment options with the patient. It is also important for the patient to seek treatment at a center with specialists who have experience in treating the disease.

Based on the results of blood and bone marrow testing, the doctor will categorize each patient in either a low-risk or a high-risk group and create a specific treatment plan.

Low-risk myelodysplastic syndromes are more likely to progress slowly, so low-intensity treatments are generally used first. Treatment goals for low-risk MDS patients include

- Improving blood counts



- Lessening the need for blood transfusions
- Lowering the risk of infection
- Improving quality of life

High-risk myelodysplastic syndromes tend to grow quickly and progress to acute myeloid leukemia (AML) within a shorter time, so more intensive treatments are generally used. Treatment goals for high-risk MDS patients include

- Slowing or stopping MDS progression to AML
- Lengthening survival

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

- The watch-and-wait approach (observation of blood cell counts)
- Clinical trials (see *Research and Clinical Trials* on page 22)
- Supportive care
  - Blood transfusions
  - Iron chelation therapy
  - Blood cell growth factors
  - Infection management
- Drug therapy
- Allogeneic stem cell transplantation

**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

- Either a low or intermediate-1 risk classification per the International Prognostic Scoring System (IPSS), or a very low or low-risk classification per the revised IPSS (IPSS-R).
- A hemoglobin concentration higher than 10 grams per deciliter (10 g/dL) and platelet counts higher than 50,000 (50,000/ $\mu$ L to 100,000/ $\mu$ L) without the need for transfusion

Patients in these risk groups and with these laboratory values may be fine without treatment. Regular observation by a hematologist-oncologist is needed because there is a risk of disease progression.

**Supportive Care.** Treatment given to relieve the signs and/or 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.** Blood transfusions can be done to replace red blood cells or platelets in people with myelodysplastic syndromes. A blood transfusion is a slow infusion of blood cells into a vein.

Transfusions of red blood cells may be done to treat anemia that is causing symptoms. Symptoms may include shortness of breath, dizziness, extreme fatigue and chest pain. The doctor will determine whether a transfusion is appropriate based on the patient's hemoglobin concentration, the severity of the patient's symptoms, the patient's other treatments and the availability of blood products.

A transfusion can help relieve symptoms for a short time, but more transfusions may be needed over time. Sixty to 80 percent of patients with myelodysplastic syndromes 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 (a low platelet count) can cause signs and/or 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 per microliter (10,000/ $\mu$ L), or for acute bleeding. **Aminocaproic acid** and **tranexamic acid** are antifibrinolytic agents recommended for bleeding episodes that do not respond to platelet transfusion and for cases of severe thrombocytopenia. These medications work by stopping blood clots from breaking down too quickly and can reduce blood loss in patients who have recurrent mucosal bleeding.

**Please visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to see the free LLS booklet *Blood Transfusion*.**

**Iron Chelation Therapy.** Red blood cells contain iron. When a person receives a large number of red blood cell transfusions, too much iron can build up in the body. This condition is called "iron overload." Iron chelation therapy uses drugs to treat patients who will be receiving frequent red blood cell transfusions. It is recommended that doctors monitor serum ferritin (iron) levels in these patients. The members of the treatment team should also check often for signs of organ damage due to iron overload. It can be challenging for patients to tolerate these medications, so it is important for patients to discuss the risks and benefits of this therapy with their doctors.

The most common drugs used in this therapy include

- **Deferasirox (Exjade<sup>®</sup>, Jadenu<sup>®</sup>).** This is an oral medication taken daily. The newer preparation, Jadenu, can be easier on digestion in some patients, but it is the same medicine as Exjade.
- **Deferoxamine mesylate (DFO; Desferal<sup>®</sup>).** This drug is administered as a slow subcutaneous (SC, meaning under the skin) or intramuscular (IM) infusion.

**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 who have low blood cell counts.

- **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 man-made versions 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 outcomes.

**Epoetin alfa (Procrit®) and darbepoetin alfa (Aranesp®)** are synthetic forms of EPO. They are given by subcutaneous injection (under the skin). Darbepoetin alfa is a longer-acting form of EPO than epoetin alfa. Most patients with myelodysplastic syndromes 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 produced naturally by the body and help to 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 a 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 to produce platelets.
  - **Romiplostim (Nplate®) and eltrombopag (Promacta®)** are drugs that act like TPO. These agents are being investigated for treatment of MDS patients who have low platelet counts. These drugs are approved by the Food and Drug Administration for the treatment of thrombocytopenia (a low platelet count) 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 the

treatment of myelodysplastic syndromes, sometimes they can be helpful for MDS patients who have very low platelet counts. It is important for the patient and doctor to discuss the potential risks and benefits of these treatments.

**Infection Management.** Having a low number of white blood cells can increase the risk of infection. In some cases, infections may be frequent and/or severe. Members of the 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, and antifungal medications may be used to treat certain fungal infections.

**Drug Therapy.** Many different types of drugs are used in the treatment of myelodysplastic syndromes.

**Low-Intensity Therapy.** This term refers to the use of low-intensity chemotherapy or immunotherapy drugs. These drugs are, in general, less likely to produce severe side effects. Two low-intensity chemotherapy drugs are approved by the FDA to treat myelodysplastic syndromes:

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

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

**Immunosuppressive Therapy.** This type of therapy 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. **Antithymocyte globulin (ATG) (Thymoglobulin®), cyclosporine (Neoral®) and tacrolimus (Prograf®)** are the main immunosuppressive therapy drugs used to treat myelodysplastic syndromes. However, these drugs do not work well for all types of MDS; they are most effective when the disease has features that are associated with an immune-system attack, such as

- The presence of human leukocyte antigen-DR15 (HLA-DR15) protein
- A low number of cells in the bone marrow

Antithymocyte globulin is given by IV infusion over a few hours for 4 consecutive days in the hospital. Cyclosporine and tacrolimus are administered orally.

**Immunomodulators (IMiDs).** These are drugs that modify different parts of the immune system. **Lenalidomide (Revlimid®)** is approved by the FDA for the treatment of transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with a del(5q) abnormality, either with or without additional cytogenetic abnormalities. 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.** These are drugs that target the abnormal proteins that cause uncontrolled cell growth. **Imatinib mesylate (Gleevec®)** is FDA approved for the treatment of adult patients who have myelodysplastic syndromes/myeloproliferative neoplasms (MDS/MPN) associated with platelet-derived growth factor receptor (*PDGFR*) gene rearrangements, as determined by an FDA-approved test.

Some of the most common drugs used in the treatment and supportive care of myelodysplastic syndromes are listed in **Table 7** on *page 20*.

**High-Intensity Therapy.** This type of therapy involves the use of intensive chemotherapy drugs and stem cell transplantation. This 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 high-risk MDS that are likely to progress to AML. Most of the high-intensity drugs are given through IV infusion.

Patients who have a myelodysplastic syndrome that is in either the intermediate-2 or high-risk IPSS category 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 regimens may consist of a single drug or combinations of two or three different drugs (combination chemotherapy). When treating with combination therapy

- Low-dose regimens 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 and decide whether or not intensive chemotherapy can be continued.

More information about these drugs can be found at [www.LLS.org/drugs](http://www.LLS.org/drugs).

**Table 7. Drugs Commonly Used in Standard Treatments and Clinical Trials for Myelodysplastic Syndromes (MDS)**

**Hypomethylating Agents**

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

**Immunosuppressive Therapy**

- Antithymocyte globulin (ATG, Thymoglobulin®)
- Cyclosporine (Neoral®)
- Tacrolimus (Prograf®)

**Immunomodulator**

- 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®)

**Tyrosine Kinase Inhibitor**

- Imatinib mesylate (Gleevec®)

**Blood Cell Growth Factors**

- G-CSF—granulocyte colony-stimulating factors: filgrastim (Neupogen®), pegfilgrastim (Neulasta®)
- GM-CSF—granulocyte-macrophage colony-stimulating factor: sargramostim (Leukine®)
- Epoetin alfa (Procrit®)
- Darbepoetin alfa (Aranesp®)
- Romiplostim (Nplate®)
- Eltrombopag (Promacta®)

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

**Allogeneic Stem Cell Transplantation.** This type of treatment, in which stem cells obtained from a donor are given to the patient by IV infusion, is the best-known and only potentially curative option for patients with myelodysplastic syndromes.

In an allogeneic transplant, the stem cells are obtained from a donor whose cells are compatible with those of the patient, usually either a brother or sister, or an unrelated donor. The cells are then infused into the patient after he or she is given very strong doses of chemotherapy, either with or without radiation therapy. This is called the “conditioning regimen.” The conditioning regimen not only destroys the abnormal cells in the bone marrow, it also destroys normal, healthy cells. Additionally, it weakens the immune system so that the body does not kill the transplanted blood stem cells.

High-dose chemotherapy can cause very bad side effects, and not all patients can tolerate it. Since allogeneic stem cell transplantation is a high-risk procedure, this treatment is mainly considered for

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

Allogeneic stem cell transplantation may also be considered for select lower-risk MDS patients with severe cytopenias. Autologous transplantation is used in some other diseases, but not in patients with MDS. The reason is that autologous transplantation uses the patient's own cells, and patients with MDS have abnormal cells due to the disease.

**Reduced-Intensity Allogeneic Stem Cell Transplantation.** This is a treatment option for older patients who cannot tolerate the high doses of chemotherapy drugs used for the conditioning regimen in preparation for a standard allogeneic stem cell transplant. The conditioning therapy in a reduced-intensity transplant uses lower doses of chemotherapy and/or radiation to prepare the patient for the infusion of the donor stem cells. Clinical trial researchers are evaluating the use of this type of transplant in older adults with relapsed and/or refractory MDS. Reduced-intensity stem cell transplantation is usually used for patients who are 55 years of age and older.

**Please visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view the free LLS booklets *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 to myelodysplastic syndromes (MDS) treatment are being studied in clinical trials. They hold the promise of increasing the rate of remission and eventually finding a cure for myelodysplastic syndromes. Many of these clinical trials are being supported by LLS research programs.

**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, researchers and patient advocates to ensure safety and scientific accuracy. Participation in a carefully conducted clinical trial may be the best available treatment option and should be considered each time the doctor and patient discuss treatment options. The outcomes of patient participation in past clinical trials have resulted in the therapies we have today.

LLS Information Specialists, available at (800) 955-4572, offer guidance on how patients can work with their doctors to determine if a specific clinical trial is an appropriate treatment option. The Leukemia & Lymphoma Society offers help for patients and caregivers in understanding, identifying and accessing clinical trials. When appropriate, patients and caregivers can work with Clinical Trial Nurse Navigators who will help patients find appropriate clinical trials and then personally assist them throughout the entire clinical-trial process. Please visit [www.LLS.org/CTSC](http://www.LLS.org/CTSC) for more information.

**Research Approaches.** A number of approaches are under study in clinical trials for the treatment of patients with myelodysplastic syndromes.

**Drug Therapy.** Several combinations of FDA-approved drugs, such as **azacitidine (Vidaza®)** and **decitabine (Dacogen®)**, as well as chemotherapy agents used for acute myeloid leukemia (AML) treatment, are being studied in clinical trials. Each drug works in a different way to kill cancer cells. When these drugs are used in combination, they may kill more MDS cells. Or, the drug combination may be just as effective as standard MDS therapies, but the combination drug therapy has less toxic side effects.

- **Targeted therapy.** This type of treatment uses drugs or other substances to block the action of certain enzymes, proteins or other molecules involved in the growth and survival of cancer cells, but causes less harm to healthy cells
  - **B-cell lymphoma 2 (BCL-2) inhibitors.** A mutation in the *BCL-2* gene allows cancer cells to evade “programmed cell death.” This mutation has been linked to chemotherapy resistance and poor outcomes. One drug under study is **venetoclax (Venclexta®)**, a BCL-2 inhibitor that binds to the cancer cell and leads to apoptosis (cell death).
  - **IDH1 and IDH2 inhibitors.** Mutations in *IDH1* and *IDH2* genes cause cells



to remain immature and multiply too quickly. **Ivosidenib (AG-120)**, an IDH1 inhibitor, and **enasidenib (AG-221)**, an IDH2 inhibitor, are being studied.

- **Histone deacetylase (HDAC) inhibitor.** Histone deacetylase (HDAC) inhibitors are agents that cause a chemical change that stops cancer cells from dividing. **Valproic acid (Depakene®)** is an HDAC inhibitor that is being studied.
- **Erythroid maturation agents (EMAs).** “Erythropoiesis” is the formation of red blood cells in blood-forming tissue. In some blood disorders, such as myelodysplastic syndromes, there are defects in the later stages of red blood cell maturation. These defects lead to a decrease in the formation of healthy red blood cells and to the development of chronic anemia. **Luspatercept (ACE-536)** is a fusion protein that targets defects in the process of red blood cell (erythrocyte) maturation by blocking transforming growth factor beta (TGFβ). This drug is known as an “erythroid maturation agent” and is being studied in clinical trials.
- **Cell signaling pathway inhibitor. Rigosertib (Estybon™),** a small molecule agent that promotes MDS cell death by blocking important cellular pathways, is being studied in trials.
- **Novel hypomethylating agents (HMAs).** New formulations of HMAs are under study in clinical trials for treatment of myelodysplastic syndromes. **Guadecitabine (SGI-110)**, a drug administered subcutaneously, is being studied. The **oral formulation of azacitidine (CC-486)** and the **oral formulation of decitabine (ASTX/27)** allow long-term, lower-dose regimens that may enhance therapeutic activity by increasing exposure to the cancer cells.
- **Immunotherapy.** This is a type of biological therapy that is designed to either boost or suppress the immune system to help the body fight cancer. It uses substances made either by the body or in a laboratory to improve, target or restore immune system function.
- **Immune checkpoint inhibitors.** A vital part of the immune system is its ability to distinguish between healthy cells in the body and those that are foreign or harmful. The immune system depends on multiple checkpoints. “Checkpoints” are molecules on certain immune cells that need to be activated in order to start an immune response. Cancer cells sometimes take advantage of these checkpoints to escape the detection of active immune cells. **Nivolumab (Opdivo®)** (anti-PD1), **ipilimumab (Yervoy®)** (anti-CTLA-4) and **atezolizumab (TecentriQ®)** (anti-PDL-1) are all checkpoint inhibitors being studied in clinical trials.
- **Vaccine therapy.** Researchers are developing vaccines made from protein-building blocks called “peptides,” that can be customized for individual patients to stimulate a strong immune response against their cancer. The Wilms tumor 1 (WT1) antigen has been shown to be expressed on leukemic cells and to be associated with a poor prognosis both in AML and

myelodysplastic syndromes. Researchers continue to evaluate the efficacy of an MDS vaccine in treating patients who have high-risk MDS.

### **Studies to Improve Assessment of Quality of Life for MDS Patients.**

Due to the chronic nature of myelodysplastic syndromes and the lack of curative options, quality of life is a major focus of treatment decisions. It is important for doctors to be able to measure how a myelodysplastic syndrome and its treatments are affecting a patient's daily life. Scientists at the Dana-Farber Cancer Institute used input from patients, caregivers, and healthcare providers to create the Quality of Life in Myelodysplasia Scale (QUALMS). Researchers are using QUALMS to determine how different treatments affect patients' quality of life. Please visit <https://qualms.dana-farber.org/> for more information.

**Study to Improve Prognosis in Myelodysplastic Syndromes.** A team of researchers at the Cleveland Clinic is developing a personalized, machine learning-based prediction model to help doctors to classify patients with MDS into risk categories. Currently, doctors use the International Prognostic Scoring System-Revised (IPSS-R) to assess risk. However, according to recent data, this system may either underestimate or overestimate risk in up to one-third of patients. The Cleveland Clinic prediction model is designed to incorporate individual patient genomic and clinical data using an algorithm to better predict survival probabilities and outcomes. The patients' data are entered into a Web application that runs the personalized prediction model and provides overall survival and AML transformation probabilities at different time points that are specific to each patient. To further improve the model, researchers are gathering feedback from clinicians and working to incorporate more outcomes, such as quality of life, into the model.

**The National Myelodysplastic Syndromes Study.** The purpose of the National Myelodysplastic Syndromes Study is to build a resource that scientists can use to learn more about MDS. This resource will enable scientists to conduct research on how to improve the ways in which myelodysplastic syndromes are diagnosed and treated. The study is enrolling patients who have either suspected or newly diagnosed myelodysplastic syndrome, myelodysplastic syndromes/ myeloproliferative neoplasms (MDS/MPN) overlap disorder, or idiopathic cytopenia of undetermined significance (ICUS). Study participants will donate biological samples (such as bone marrow and blood) and provide medical information, including details of their signs and/or symptoms, how they perceive their quality of life and the treatments they receive. Study participants may be monitored for life.

Please visit <https://thenationalmyelodysplasticsyndromestudy.net/>

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

## Follow-up Care

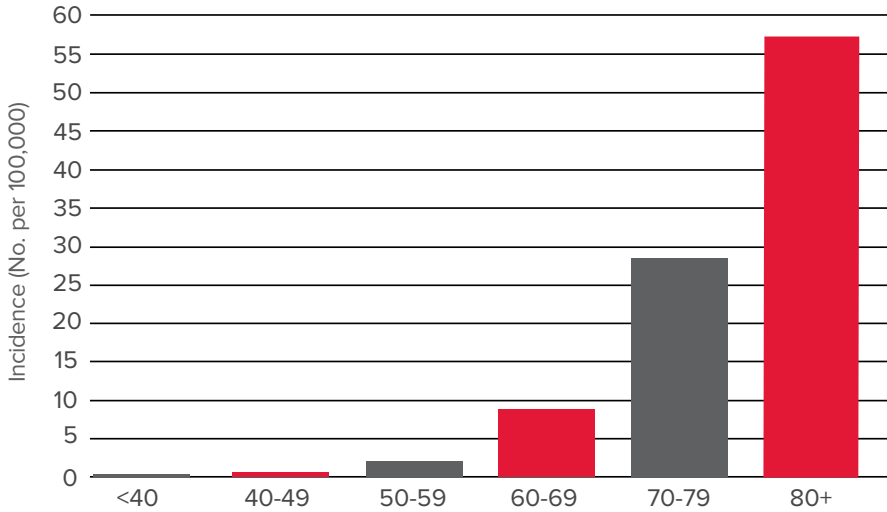
Follow-up care for myelodysplastic syndromes (MDS) varies from patient to patient. Patients who have myelodysplastic syndromes

- 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 need to 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. Patients who have MDS can receive the shingles vaccine **Shingrix**<sup>®</sup> because it is an “inactivated” rather than a “live” vaccine. Speak to your doctor for more information.
- Need to keep good records and treatment notes. This information should include
  - Doctors' names and contact information
  - Diagnosis
  - Names of treatment received
  - Radiation treatment information
  - Surgery information
  - Transplant information
  - Information about any other treatments
  - Other medical history

## Incidence, Causes and Risk Factors

**Incidence.** For the 5-year period from 2011 to 2015, there were 70,056 new cases of myelodysplastic syndromes (MDS) throughout the United States, averaging 14,011 cases per year. In the United States, the overall incidence rate of MDS is 4.6 cases per 100,000 population. This rate rises with age to approximately 28 cases per 100,000 individuals per year among patients age 70 years and older and to about 57 cases per 100,000 people in those who are age 80 years and older. See **Figure 1** on page 26. Myelodysplastic syndromes are rare among children, adolescents and young adults. The disease affects slightly more men than women, and white males have the highest incidence rates.

**Figure 1. Myelodysplastic Syndromes (MDS)  
Age-Adjusted Incidence Rates, 2011-2015**



The horizontal axis represents the age of patients, starting from younger than age 40 years and then in 10-year age increments up to age 80 and older. The vertical axis shows the incidence of new cases of MDS from 2011 to 2015, per 100,000 people.

**Source:** SEER (Surveillance, Epidemiology and End Results) Cancer Statistics Review, 1975-2015. National Cancer Institute; 2018.

**Causes and Risk Factors.** Myelodysplastic syndromes can be classified as either a primary (de novo) MDS or a secondary (treatment-related) MDS.

- Primary or de novo myelodysplastic syndromes—Doctors cannot identify a specific cause in most MDS cases. Random mutations of DNA (deoxyribonucleic acid) accumulate in the stem cells with aging. If these mutations occur in specific genes and in particular locations, they generally lead to MDS. The incidence of primary MDS is much greater than that of secondary MDS.
- Secondary (treatment-related) myelodysplastic syndromes—A small number of patients who have received chemotherapy and/or radiation therapy in the past for another cancer have a small risk of developing treatment-related MDS. Generally, the chance of developing a myelodysplastic syndrome 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 a secondary MDS, as can patients who have been previously diagnosed with aplastic anemia, another bone marrow failure disorder.

**Feedback.** Please visit [www.LLS.org/PublicationFeedback](http://www.LLS.org/PublicationFeedback) to give suggestions about this booklet.

# Normal Blood and Bone Marrow

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

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

- Proteins
  - Albumin. This is the most common blood protein.
  - Blood-clotting proteins (coagulation factors). They are made by the liver.
  - Erythropoietin. It is made by the kidneys and stimulates red blood cell production.
  - Immunoglobulins. These are cells that fight infection.
- Hormones, such as thyroid and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin B<sub>12</sub>
- Electrolytes, such as calcium, potassium and sodium.

**Blood cells.** Blood cells are formed in the bone marrow, a spongy tissue where blood cells grow and develop. Blood cells start as stem cells. The process of stem cells maturing into blood cells is called "hematopoiesis." The blood cells are suspended in the plasma. See **Figure 2** on page 28.

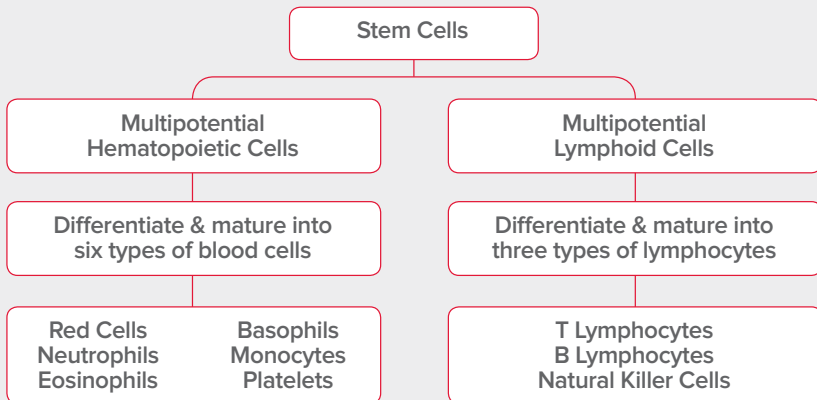
Once the blood cell is created, it will develop into one of the three types of blood cells.

These are

1. Red blood cells (the cells that carry oxygen); they
  - Make up a little less than half of the body's total blood volume
  - Are filled with hemoglobin, the protein that picks up oxygen from the lungs and takes it around the body. It binds with carbon dioxide (CO<sub>2</sub>) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the CO<sub>2</sub> is removed from the lungs.
2. Platelets (cells that help blood clot); they
  - 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. They form a clot, with the help of proteins, such as fibrin, and electrolytes, such as calcium.
3. White blood cells (WBCs) are cells that fight infections, including:
- Neutrophils and monocytes: These are “phagocytes” (eating cells) that ingest and destroy bacteria and fungi. Unlike red blood cells and platelets, monocytes can leave the bloodstream and enter tissues to attack invading organisms and fight off infection.
  - Eosinophils and basophils: These are WBCs that respond to allergens or parasites.
  - Lymphocytes: These are the WBCs found mostly in the lymph nodes, spleen and lymphatic channels that are a key part of the immune system. Some enter the bloodstream. There are three major types of lymphocytes:
    - T lymphocytes (T cells)
    - B lymphocytes (B cells)
    - Natural killer (NK cells)

**Figure 2. Blood Cell & Lymphocyte Development**



**Figure 2.** Stem cells develop into blood cells (hematopoiesis) and lymphocytic cells.

**Bone Marrow.** In healthy people, stem cells in the bone marrow produce new blood cells continuously. When blood cells are fully developed, they enter the bloodstream as it passes through the marrow and then circulates throughout the body.

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

Hematopoietic stem cells are found in the marrow. These stem cells are important because they can be transplanted. Some stem cells enter the bloodstream and circulate; 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 they can be collected and stored. Stem cells from the placenta and the umbilical cord of a newborn infant can also be harvested and used for future transplantation.

# Resources and Information

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

## For Help and Information

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

- Call: (800) 955-4572 (Monday through Friday, 9 am to 9 pm EST)
- Email: [infocenter@LLS.org](mailto:infocenter@LLS.org)
- Live chat: [www.LLS.org/InformationSpecialists](http://www.LLS.org/InformationSpecialists)
- Visit: [www.LLS.org/InformationSpecialists](http://www.LLS.org/InformationSpecialists)

**Clinical Trials Support Center (CTSC).** Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. When appropriate, patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist them throughout the entire clinical trial process. Visit [www.LLS.org/CTSC](http://www.LLS.org/CTSC) for more information.

**Free Information Booklets.** LLS offers free education and support booklets that can be either read online or ordered. Please visit [www.LLS.org/booklets](http://www.LLS.org/booklets) for more information.

**Telephone/Web Education Programs.** LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit [www.LLS.org/programs](http://www.LLS.org/programs) for more information.

**Financial Assistance.** LLS offers financial assistance to individuals with blood cancer. Please visit [www.LLS.org/finances](http://www.LLS.org/finances) for more information.

**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](http://www.LLS.org/copay)



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

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

**Suggested Reading.** LLS provides a list of selected books recommended for patients, caregivers, children and teens. Please visit [www.LLS.org/SuggestedReading](http://www.LLS.org/SuggestedReading) to find out more.

**Continuing Education.** LLS offers free continuing education programs for health care professionals. Please visit [www.LLS.org/ProfessionalEd](http://www.LLS.org/ProfessionalEd) for more information.

## Community Resources and Networking

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

**Weekly Online Chats.** Moderated online chats can provide support and help cancer patients to reach out and share information. Please visit [www.LLS.org/chat](http://www.LLS.org/chat) to join.

**LLS Chapters.** LLS offers community support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection Program* (a peer-to-peer support program), 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](http://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](http://www.LLS.org/ResourceDirectory) to obtain our directory.

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

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

### **Additional Help for Specific Populations**

**Información en español (LLS information in Spanish).** Please visit [www.LLS.org/espanol](http://www.LLS.org/espanol) for more information.

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

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

- Call: the VA (800) 749-8387
- Visit: [www.publichealth.va.gov/exposures/AgentOrange](http://www.publichealth.va.gov/exposures/AgentOrange)

**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](http://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](http://www.nimh.nih.gov). Enter “depression” in the search box.

## More Resources

### **The Aplastic Anemia & MDS International Foundation (AA&MDSIF)**

(800) 747-2820 or (301) 279-7202

[www.aamds.org](http://www.aamds.org)

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

### **Revised International Prognostic Scoring System (IPSS-R) for Myelodysplastic Syndromes Risk Assessment Calculator**

is available at

<https://www.mds-foundation.org/calculator/index.php>

### **The Myelodysplastic Syndromes Foundation, Inc.**

(800) 637-0839 (within the United States)

(609) 298-1035 (outside the United States)

[www.mds-foundation.org](http://www.mds-foundation.org)

The Myelodysplastic Syndromes 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.

## 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.

**Acute Myeloid Leukemia (AML).** A fast-growing cancer that starts with a cancerous change of an immature 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 bone 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 are likely to be pale, weak, tired, and become short of breath easily. See 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.

**Aplastic Anemia.** A health condition that occurs when the body stops producing enough new blood cells. The 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*.**

**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 bone marrow cells. In some cases of myelodysplastic syndrome (MDS), there are abnormal blast cells (myeloblasts) in the bone marrow. This can lead to the decreased numbers of red blood cells, neutrophils, and platelets that cause the signs and/or symptoms of MDS and acute myeloid leukemia (AML).

**Blood Cells.** There are three major 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 laboratory test that measures the number and types of cells in the blood. Often called a “complete blood count (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 in the bloodstream throughout the body.

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

**Bone Marrow Biopsy.** A test to find abnormal marrow cells. A local anesthetic is used to numb the area around the hip bone and then a special wide-bore 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.

**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.

**Colony-Stimulating Factor.** See Growth Factor.

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

**Deletion (del).** 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, white blood cells or platelets. See Hematopoiesis.

**DNA.** Deoxyribonucleic acid. The genetic matter found in all cells. It 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.

**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. Erythropoiesis-stimulating agents (ESAs) deliver synthetic EPO. Some drugs used to treat anemia include **epoetin alfa (Procrit<sup>®</sup>, Epogen<sup>®</sup>)** and **darbepoetin alfa (Aranesp<sup>®</sup>).**

**5q-Syndrome (5q Minus Syndrome).** A World Health Organization term for a subtype of myelodysplastic syndrome (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.

**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 laboratory.

**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 information about 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. Human leukocyte-associated antigens are passed from parents to their children; one in four siblings has the same type of HLA.

**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.

**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, Unclassifiable (MDS-U).** See Unclassifiable Myelodysplastic Syndrome (MDS-u).

**MDS with Excess Blasts (MDS-EB).** See Refractory Anemia With Excess Blasts.

**MDS with Isolated del(5q).** See 5q-Syndrome (5q Minus Syndrome).

**MDS with Multilineage Dysplasia (MDS-MLD).** See Refractory Cytopenia With Multilineage Dysplasia.

**MDS with Ring Sideroblasts (MDS-RS).** See Refractory Anemia With Ring Sideroblasts.

**MDS with Single Lineage Dysplasia (MDS-SLD).** This type of MDS is not common. In MDS-SLD, the marrow shows dysplastic changes in only one of the three types of blood cells; there are one or two cytopenias in the blood; and there is less than 5 percent of blasts cells in the bone marrow.

**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 (deoxyribonucleic acid) that makes up a gene.

**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 (Nonmyeloablative) 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.

**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 patients who have a myelodysplastic syndrome (MDS).

**Platelets.** Also known as “thrombocytes,” platelets are small colorless blood cells. They migrate to a wound and then their sticky surface helps them form clots and stop bleeding. Platelets make up about one tenth of the volume of red blood cells.



**RARS.** See Refractory Anemia With Ring Sideroblasts.

**RCMD.** See Refractory Cytopenia With Multilineage Dysplasia.

**Red Blood Cells.** Blood cells (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 (Nonmyeloablative) Allogeneic 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 With Excess Blasts (RAEB).** See Oligoblastic Myelogenous Leukemia.

**Refractory Anemia With Excess Blasts in Transformation (RAEB-T).**

In the French-American-British (FAB) classification, a myelodysplastic syndrome (MDS) in which the bone marrow blast volume 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. When abnormal sideroblasts are present, large amounts of iron are trapped in the developing red blood 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. In some classifications, RARS is an myelodysplastic syndrome subclass. Also called “myelodysplasia” or “acquired sideroblastic anemia.”

**Refractory Cytopenia With Multilineage Dysplasia (RCMD).** One of the more common World Health Organization myelodysplastic syndrome (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.

**Stem Cells.** Early marrow cells that mature into red blood cells, white blood cells and platelets. Stem cells are mostly found in the marrow, but some leave the 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.

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

**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 Myelodysplastic Syndrome (MDS-u).** A World Health Organization MDS subtype classification that includes patients who do not have refractory anemia or any other myelodysplastic syndrome subtypes, but do 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.

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# Get support. Reach out to our **INFORMATION SPECIALISTS**

The Leukemia & Lymphoma Society team consists of master's level oncology social workers, nurses and health educators who are available by phone Monday through Friday, 9 a.m. to 9 p.m. (ET).

- Get one-on-one personalized support and information about blood cancers
- Know the questions to ask your doctor
- Discuss financial resources
- Receive individual clinical-trial searches



Contact us at  
**800-955-4572** or  
**www.LLS.org/  
informationspecialists**

(Language interpreters can be requested)



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LYMPHOMA  
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For more information, please  
contact our Information Specialists  
**800.955.4572** (Language interpreters  
available upon request).

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OUR BLOOD.**

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The mission of The Leukemia & Lymphoma Society (LLS) is to cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families. Find out more at [www.LLS.org](http://www.LLS.org).