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LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

# Myelodysplastic Syndromes

**Pamela**, MDS survivor

Revised **2014**

## A Message From Louis J. DeGennaro, Ph.D.

Interim President and CEO of The Leukemia & Lymphoma Society

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

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

Yet we are far from done.

Until there is a cure for cancer, we will continue to work hard—to fund new research, to create new patient programs and services, and to share information and resources about blood 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 great quality of life. Today, we hope our expertise, knowledge and resources will make a difference in your journey.

**Louis J. DeGennaro, Ph.D.**
*Interim President and CEO*
*Chief Mission Officer*

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## Acknowledgement

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# Introduction

Each year, an estimated 14,123 people are diagnosed with myelodysplastic syndromes (MDS), a group of diseases of the blood and marrow. About 70,615 cases of MDS were reported in the United States between 2006 and 2010.[1]

MDS occurs when the bone marrow does not make enough healthy blood cells and the cells in the marrow are damaged.

For years, MDS was known as "preleukemia" or "smoldering leukemia." Today, however, MDS is classified as cancer.

The outlook for people with MDS improves each day. Yet, because there are different subtypes and varying levels of severity, treatments, and life expectancy, MDS may be hard to understand.

At LLS, we know that the more you know about your disease, the better you can take care of yourself, your mind and body, and your health.

This MDS booklet provides information about MDS; defines often hard-to-understand terms; explains tests and treatments that you may encounter; and lists new research options and clinical trials.

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

We are here to help.

[1] Source: Howlader N, Noone AM, Krapcho M, et al. (eds). SEER Cancer Statistics Review, 1975-2010, National Cancer Institute. Bethesda, MD, based on November 2010 SEER data submission, posted to the SEER Web site, 2013.

# Resources and Information

LLS offers free information and services for patients and families touched 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 your health care team's 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 (M-F, 9 a.m. to 9 p.m. EST)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org
- Visit: www.LLS.org/informationspecialists.

**Free Materials.** LLS offers free education and support publications that can either be read online or downloaded. Free print versions can be ordered. For more information, please visit www.LLS.org/publications.

**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.

## Community Resources and Networking

**Online Blood Cancer Discussion Boards and Chats.** Online discussion boards and moderated online chats can provide support and help cancer patients to reach out and share information. For more information, please visit www.LLS.org/getinfo.

**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, locating summer camps and other needs. For more information, please visit www.LLS.org/resourcedirectory.

**Clinical Trials (Research Studies).** New treatments for patients with MDS are under way. Patients can learn about clinical trials and how to access them. For more information, please

- Call: (800) 955-4572 to speak with an LLS Information Specialists who can help conduct clinical-trial searches
- Visit: www.LLS.org/clinicaltrials and click on TrialCheck®.

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

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

## Additional Help for Specific Populations

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

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

**Children**. 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/publications
  - Click on Childhood Blood Cancer and choose *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 two-week period. For more information, please

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

**Feedback.** Like this booklet? Have suggestions? We'd love to know what you think. To tell us

- Visit: www.LLS.org/publicationfeedback
  - Click on "LLS Disease & Treatment Publications—Survey for Patients, Family and Friends."

# What is MDS?

Myelodysplastic syndrome (MDS) is a disease of the blood and marrow. It happens when the cells in the bone marrow are damaged. There are many different myelodysplastic syndromes.

**Normal Bone Marrow Production.** In every person, stem cells (immature blood cells) are formed in the bone marrow. Marrow is located within the bone. Each stem cell turns into either a

- White blood cell (a cell that fights infection)
- Red blood cell (a cell that carries oxygen)
- Blood platelet (a cell that helps blood to clot).

**MDS Bone Marrow Production.** When someone has MDS, there are changes to the stem cells in the bone marrow (See *Normal Blood and Marrow* on page 25).

Sometimes the stem cells never become mature cells. These young cells, called "blast cells" cannot yet perform the specific function of the mature cell. Instead, the immature cells linger in the bone marrow. In other cases the

- Marrow makes more blood cells than needed
- Marrow gets filled with too many cells
- Cells die before they are released into the bloodstream
- Person does not have enough blood cells.

In healthy people, the 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 comprise more than 5 percent of all the cells in their marrow. The number of blast cells in the bone marrow is a main determinant of the severity of MDS.

There are many types of MDS. A myelodysplastic syndrome can be mild or severe. It may first appear as anemia (a decrease in the levels of hemoglobin in the blood) and then progress very slowly: or, it can be a fast-growing disease and progress to acute myeloid leukemia (AML). For more information about AML, see the free LLS publication, *Acute Myeloid Leukemia*.

MDS has been known as

- Smoldering leukemia
- Preleukemia
- Oligoleukemia.

Some people may think that MDS only becomes a problem after it has progressed to AML. But MDS is a cancer. It should be treated by a hematologist/oncologist, a doctor who treats blood cancers.

The real impact of MDS is measured by how it affects a person's life. Today, patients with MDS have improved outcomes and experience better quality of life than ever before. This is largely due to

- Better supportive care
- Treatment and testing of newer drugs
- Progress in transplantation.

# Who MDS Affects and Why

The National Cancer Institute reports 70,165 cases or about 14,123 new cases of MDS between 2006 and 2010. See Figure 1.

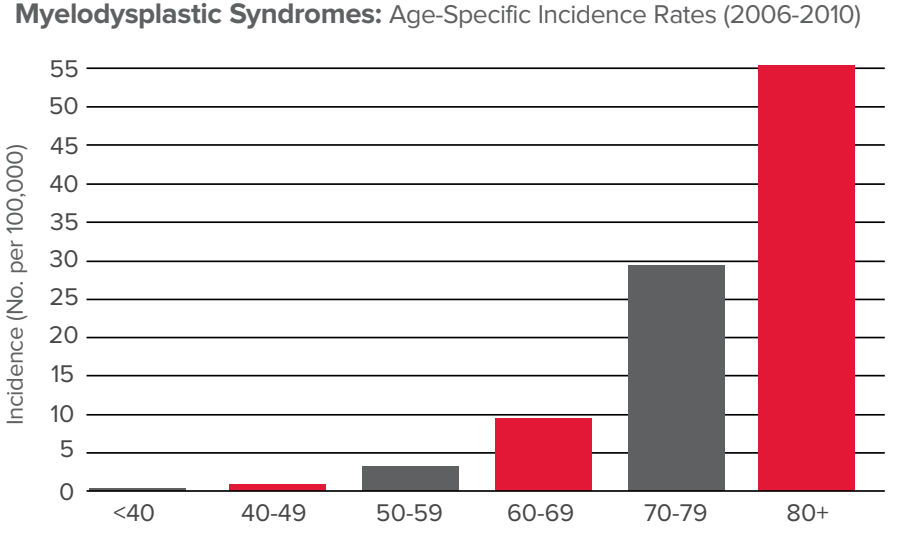


**Figure 1.** | The horizontal axis represents the age of patients from below age 40 years and then in 10-year age increments up to age 80+. The vertical axis shows the incidence of new cases of MDS from 2006 to 2010, per 100,000 people. Source: Howlader N, Noone AM, Krapcho M, et al. (eds). SEER Cancer Statistics Review, 1975-2010, National Cancer Institute. Bethesda, MD, based on November 2010 SEER data submission, posted to the SEER Web site, 2013.

Research reveals that the incidence of MDS

- Increases as people age, occurring more often in people over 65 years
- Is slightly more common in men than women
- Is less common in children (in whom the disease is often associated with abnormal cells that have an acquired loss of chromosome 7). See *Diagnosis* on page 9.

**Types of MDS.** MDS can either be primary, also known as "de novo" or secondary, known as "treatment related."

- Primary (de novo—"from the beginning")
  - Most common type
  - No obvious cause in most patients
  - One known risk factor is repeated exposure to benzene. This chemical is most commonly found in cigarette smoke. Benzene damages the DNA of normal stem cells.
- Secondary (treatment related)
  - Less common than cases of primary MDS
  - Only a small number of people exposed to chemotherapy and/or radiation therapy develop a treatment-related MDS.
  - Some people who have received treatment for another cancer have a small risk of developing a treatment-related MDS.

Causes of MDS are unclear, but one popular theory suggests that some people who develop MDS may have a gene that limits their ability to detoxify the causative agents.

# 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.

Some patients have no symptoms. These patients find out they have MDS during the course of a routine physical examination and/or a blood test, called a "complete blood count" (CBC). Fatigue and shortness of breath during physical activity can be symptoms of MDS.

# Diagnosis

To confirm an MDS diagnosis, a doctor will perform a complete blood count (CBC) to

- Evaluate a patient's blood cell count
- Examine the appearance of blood cells.

If anemia is detected, the red blood cells are further examined to see if there is

- A lack of iron, folate or vitamin $B_{12}$
- Some other type of cancer
- Another reason for the anemia.

Additional testing may be used to detect cases of MDS. Tests may include

- A bone marrow aspiration
- A bone marrow biopsy
- FISH (fluorescence in situ hybridization), a test used to identify cells whose nuclei contain chromosomal abnormalities. FISH can be used to identify abnormal cells for diagnosis and to follow the effects of therapy.

A diagnosis of MDS requires that at least one of the following characteristics is found in the marrow:

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

A chromosome is an organized package of DNA found in the nucleus of the cell. Chromosomes are arranged in pairs. Chromosome pairs are made up of one chromosome from each parent. Humans have 23 pairs of chromosomes—22 pairs of numbered chromosomes, called "autosomes," and one pair of sex chromosomes, X and Y.

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).

If a patient's doctor notes mild dysplasia (abnormal growth or development of cells), a diagnosis of MDS may be inconclusive. It is very important that a specialist, called a hematopathologist, examines the patient's marrow slides for cytogenetic abnormalities. The doctor will check to make sure other causes of anemia or low platelet or neutrophil counts are not present.

# MDS Classification and the International Prognostic Scoring Systems

**Classifying MDS.** Historically, MDS has been classified into different subtypes that were based on the appearance of the patient's marrow and the results of the blood cell counts. In 1982, the French-American-British (FAB) Work Group devised a classification of MDS. The FAB classification of MDS consists of the following five subtypes:

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 1999, the World Health Organization (WHO) modified the FAB classification of MDS. The WHO-modified classification differs from the FAB classification in a number of ways. The WHO classification

- Incorporates molecular and cytogenetic data

- Defines patients with more than 20 percent blasts in the marrow as having acute myeloid leukemia (AML)
- Has a new category of "myelodysplastic syndromes/myeloproliferative neoplasms" (MDS/MPN), which includes juvenile myelomonocytic leukemia (JMML) and chronic myelomonocytic leukemia (CMML)
- Adds the subtypes 5q- syndrome, refractory cytopenia with multilineage dysplasia (RCMD) and MDS unclassifiable (MDS-u)
- Considers RAEB-T to be leukemia rather than a subtype of MDS.

Note: MDS subtype definitions are provided in the *Health Terms* section on page 29.

**The International Prognostic Scoring System (IPSS) and the IPSS Risk Categories.** Many doctors who treat a patient who has MDS use the International Prognostic Scoring System (IPSS) (see Table 1 on page 12) to determine a patient's IPSS Risk Category (see Table 2 on page 13).

Introduced in 1997, the IPSS was created to translate the risk of progression of a patient's disease from broad descriptions into objective standards.

The IPSS identifies the following three specific patient disease factors:

- The percentage of marrow leukemic blast cells (blasts)
- The type of chromosomal changes, if any, in the marrow cells (cytogenetics)
- The presence of one or more cytopenias (decrease in the number of cells circulating in the blood), see Table 1 on page 12.

Each factor is assigned a numerical IPSS score.

The patient's IPSS risk category is determined by adding together all of the IPSS scores within the three disease factors. That number matches the patient to one of the following four IPSS risk categories:

- Low
- Intermediate-1
- Intermediate-2
- High.

Note: Low- and intermediate-1-risk categories are sometimes combined into a lower-risk group; intermediate-2-risk and high-risk categories are sometimes combined into a higher-risk group.

**Table 1.** International Prognostic Scoring System (IPSS)

| Factor | Notes | Value | IPSS Score |
|---|---|---|---|
| Blasts (percent) | | Less than 5 | 0 |
| | | 5 to 10 | 0.5 |
| | | 11 to 20 | 1.5 |
| | | 21 to 30 | 2.0 |
| Cytogenetics | • normal<br>• -Y only<br>• del(5q) only<br>• del(20q) only | Good | 0 |
| | abnormalities other than good or poor | Intermediate | 0.5 |
| | • complex<br>• 3 or more abnormalities<br>• abnormal chromosome 7 | Poor | 1.0 |
| Cytopenias | • hemoglobin less than 10g/dL<br>• absolute neutrophil count (ANC) less than 1,500 cells/µL | 0 or 1 | 0 |
| | • platelet count less than 100,000/µL<br>**Each cytopenia counts as a value of 1** | 2 or 3 | 0.5 |

**Table 1.** | The IPSS is used to assess risk and evaluate treatment for MDS patients. Patients with blast counts greater than 20 percent are diagnosed with acute myeloid leukemia (AML).

**Table 2. IPSS Risk Categories**

| IPSS Risk Score | Risk Category |
|---|---|
| 0 | Low |
| 0.5 to 1.0 | Intermediate-1 |
| 1.5 to 2.0 | Intermediate-2 |
| Greater than or equal to 2.5 | High |

**Table 2.** | The individual scores for marrow blast percentage, cytogenetics (chromosomal changes) and cytopenias (low red blood cell count, low neutrophil count and/or low platelet count) are combined to give the total IPSS score. See examples of total scores, below.

The following examples show how IPSS scores are used to determine the IPSS risk category for an MDS patient:

- A patient with less than 5 percent blasts (0), normal cytogenetics (0), a hemoglobin concentration of less than 10 grams per deciliter (<10 g/dL) (anemia) with normal platelet counts and normal neutrophil counts (value of 1; score of 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), an abnormal chromosome 7 (1), normal neutrophil counts and both a hemoglobin concentration of less than 10 grams per deciliter (<10 g/dL) (anemia) and a platelet count of less than 50,000 per microliter (<50,000/µL) (value of 2; score of 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.

Recently, doctors have revised the International Prognostic Scoring System to more accurately predict their patients' prognosis. The revised International Prognostic Scoring System (IPSS-R) is more detailed and thus improves upon the IPSS, but it is not yet universally used by doctors.

**The Revised International Prognostic Scoring System (IPSS-R) and the IPSS-R Risk Categories.** The revised IPSS, known as the "IPSS-R," covers the same disease factors as the IPSS, but the factors are identified in a more detailed way. The IPSS-R shows five disease factors (each accompanied by a description of its possible values). Each of these values is assigned a numerical score (shown in Table 3 on page 14).

**Table 3.** Revised International Prognostic Scoring System (IPSS-R)

| Factor | Notes | Value | IPSS-R Score |
|---|---|---|---|
| Blasts (percent) | | Less than or equal to 2 | 0 |
| | | Greater than 2 to Less than 5 | 1 |
| | | 5 to 10 | 2 |
| | | Greater than 10 | 3 |
| Cytogenetics | • -Y<br>• del(11q) | Very good | 0 |
| | • normal<br>• del(5q)<br>• del(12p)<br>• del(20q)<br>• double including del(5q) | Good | 1 |
| | • del(7q)<br>• +8<br>• +19<br>• i(17q)<br>• any other single or double independent clone | Intermediate | 2 |
| | • -7<br>• inv(3)/+(3q)/del(3q)<br>• double including -7/del(7q)<br>• complex: 3 abnormalities | Poor | 3 |
| | complex: Greater than 3 abnormalities | Very poor | 4 |
| Cytopenias | hemoglobin (grams per deciliter [g/dL]) | Greater than or equal to 10 | 0 |
| | | 8 to Less than 10 | 1 |
| | | Less than 8 | 1.5 |
| | absolute neutrophil count (ANC) (x$10^9$/L of blood) | Greater than or equal to 0.8 | 0 |
| | | Less than 0.8 | 0.5 |
| | platelet count (x$10^9$/L of blood [µL]) | Greater than or equal to 100 | 0 |
| | | 50 to Less than 100 | 0.5 |
| | | Less than 50 | 1 |

**Table 3.** | The IPSS-R is used to assess risk and evaluate treatment for MDS patients.

A patient's IPSS-R risk category is determined by totaling the individual IPSS-R scores for the designated values within the five disease factors. That number matches the patient to one of the following five IPSS-R risk categories:

- Very low
- Low
- Intermediate
- High
- Very high.

The following example shows how IPSS-R scores (Table 3) are used to determine the IPSS-R risk category for an MDS patient. A patient who has a blast percentage of 3 percent (1), good cytogenetics (1), a hemoglobin concentration of greater than 10 grams (0), an absolute neutrophil count (ANC) of 0.7 (0.5) and a platelet count of 101 (0) 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 4.

**Table 4. IPSS-R Risk Categories**

| IPSS-R Risk Score | Risk Category |
|---|---|
| Less than or equal to 1.5 | Very low |
| Greater than 1.5 to 3 | Low |
| Greater than 3 to 4.5 | Intermediate |
| Greater than 4.5 to 6 | High |
| Greater than 6 | Very high |

**Table 4.** | The individual scores for marrow blast percentage, cytogenetics (chromosomal changes) and cytopenias (low red blood cell count, low neutrophil count and/or low platelet count) are combined to give the total IPSS-R score.

The IPSS and the IPSS-R scoring systems alone are not precise predictors of risk. They do not take into account many aspects of treating elderly patients, such as comorbidities, previous cancers, and other health issues. These are very important considerations, so the IPSS and the IPSS-R scores and risk categories are used in addition to the doctor's observation and assessment of the patient.

The IPSS-R demonstrated improved ability over the IPSS to predict prognosis. The IPSS, IPSS-R and other classifications are also useful in interpreting the results of cooperative clinical trials involving patients at different treatment centers.

Research has identified gene mutations acquired by the abnormal cells (mutations that developed after the patient was born) as additional disease risk factors. These are noteworthy because

- There are more than 40 genes that can be mutated in MDS.

- Every MDS patient will be likely to carry one or more acquired mutations.
- 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 also have prognostic value.
- Mutations in specific genes have been associated with both better and worse prognoses than those predicted by the IPSS.

Testing for genetic mutations in MDS is just becoming available. Hopefully, the findings will help doctors acquire a better understanding of a person's individual disease. However, it is not yet clear how to best interpret this information in all cases.

Ask your doctor if genetic testing is an option for you.

# Treatment

Patients with MDS should work with a hematologist/oncologist, a doctor who treats blood cancers. Doctors create specific treatment plans for each patient and will assign each patient to either a low-risk category or a high-risk category.

The goals for low-risk MDS patients are to

- Manage the disease by reducing their transfusion needs
- Lower the risk of infection
- Increase the number of good-quality years of life.

The goal for high-risk MDS patients is to 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

- Observation of blood cell counts
- Transfusions and iron chelation therapy (medication that removes excess iron in the body; it is a possible treatment for patients who need repeated transfusions)
- Erythropoiesis-stimulating agents (ESAs) and other growth factors
- Antithymocyte globulin (ATG) therapy
- Drug therapy
- Chemotherapy

- Allogeneic stem cell transplantation
- Clinical trials.

**Observation of Blood Cell Counts (Watch and Wait).** Observation is generally recommended for patients who have

- An IPSS low- or intermediate-1–risk
- A hemoglobin concentration greater than 10 grams per deciliter (>10 g/dL) and platelet counts greater than 50,000 per microliter (>50,000/µL) to 100,000 per microliter (100,000/µL) without 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.

**Transfusions and Iron Chelation Therapy.** Transfusions of red blood cells can help some patients improve their blood cell counts or relieve symptoms, such as shortness of breath, dizziness, extreme fatigue and chest pain. Platelet transfusions are typically required once a patient's platelet count falls below 10,000/µL. However, the major indication for platelet transfusion is unusual bleeding or bruising.

Before a blood transfusion, doctors will

- Check a patient's hemoglobin concentration
- Look for symptoms, such as fatigue or shortness of breath as well as other health problems, such as heart disease. For more information, please see the free LLS booklet, *Blood Transfusion.*

**Iron Chelation Therapy.** Iron chelation therapy uses medicine to remove the excess iron in the body (iron-overload). These FDA-approved medicines are called "iron chelators." This therapy may be appropriate for anemic patients who need ongoing blood transfusions (ranging from 2 to 4 or more units per month). These patients may be at risk for iron-overload, a disorder that can damage the heart and liver. It is not known, however, if iron chelators prolong life.

These medications include

- Deferasirox (Exjade®) and deferiprone (Ferriprox®)—Both are oral medications that are taken daily.
- Deferoxamine mesylate (DFO; Desferal®)—This drug is administered as a slow subcutaneous (SC) infusion, intramuscularly, or intravenously.

**Erythropoiesis-stimulating agents (ESAs) and Other Growth Factors.** Agents called "growth factors" promote blood cell production. 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

- Erythropoiesis (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. They are used to treat the 10 to 20 percent of MDS patients who have anemia associated with low EPO levels. For this subgroup, usually IPSS low- or intermediate-1-risk patients, treatment with ESAs will 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]). Aranesp is a longer-acting form of EPO than Procrit.

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

Granulocyte-colony stimulating factor (G-CSF) is a hormone that increases white blood cell production. 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.

Used alone, neither a G-CSF, nor another white blood cell growth factor called a "granulocyte macrophage-colony stimulating factor" (GM-CSF), have a role in MDS treatment. Still, a G-CSF or a GM-CSF may be used to treat patients who have low neutrophil counts and develop infections. It is important to pay close attention to any infection or unexplained fever. If a bacterial or fungal infection is identified or suspected, antibiotics may be needed. Antiviral drugs may be used to treat certain viral infections.

### Platelet Growth Factors

Romiplostim (Nplate®) and eltrombopag (Promacta®) are agents being investigated as treatment for MDS patients who have low platelet counts. Currently, these drugs are FDA approved for the treatment of thrombocytopenia (too few platelets) in patients who have chronic immune (idiopathic) thrombocytopenic purpura (ITP)

and have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

**Antithymocyte Globulin (ATG; Thymoglobulin®, Atgam®) Therapy.** In some patients, lymphocytes (types of white blood cells) kill precursors of normal red blood cells, neutrophils and platelets. ATG, an immunoglobulin obtained from rabbits or horses, is given intravenously (IV). It destroys these lymphocytes and can improve some patients' blood cell counts. Fever and chills are common immediately after ATG administration.

**Table 5. Some Drugs Used to Treat Myelodysplastic Syndromes (MDS)**

| | |
|---|---|
| **Growth Factors** | epoetin alfa (Procrit®)<br>darbepoetin alfa (Aranesp®)<br>granulocyte-colony stimulating factor (G-CSF) |
| **Drug Therapy** | azacitidine (Vidaza®)<br>decitabine (Dacogen®)<br>lenalidomide (Revlimid®)<br>imatinib mesylate (Gleevec®) |
| **Chemotherapy** | cytarabine (cytosine arabinoside, ara-C; Cytosar-U®)<br>idarubicin (Idamycin®)<br>daunorubicin (Cerubidine®)<br>mitoxantrone (Novantrone®) |

Table 5. | Types of treatment for MDS patients.

**Drug Therapy.** The single-drug approaches that have been approved by the FDA for MDS patients include azacitidine (Vidaza®), decitabine (Dacogen®), lenalidomide (Revlimid®) and imatinib mesylate (Gleevec®).

### Azacitidine (Vidaza)

- A "hypomethylating" or "demethylating" agent
- Approved for low- and high-risk patients
- Helps bone marrow to function better
- Kills unhealthy cells
- Given intravenously (IV) or under the skin (subcutaneously [SC])
- Treatment runs for seven consecutive days and is repeated every four weeks. It is given for at least four cycles.

Generally, treatment with Vidaza leads to

- 40 percent of patients responding favorably
- Improved quality of life
- A fewer number of transfusions
- Side effects which can include
  - Nausea
  - Vomiting
  - Diarrhea
  - Lower numbers in blood cell counts
- In higher-risk MDS patients, treatment prolongs life (average increase of up to nine months).

Oral Vidaza is being studied in phase 3 clinical trials to determine its effectiveness.

**Decitabine (Dacogen)**

- A hypomethylating/demethylating agent
- Approved for low- and high-risk patients
- Administered intravenously two different ways
  - Over 3 hours repeated every 8 hours for 3 days. Repeat cycle every 6 weeks.
  - Over 1 hour repeated daily for 5 days. Repeat cycle every 4 weeks.

Treatment leads to

- Fewer number of transfusions
- Improved blood cell counts in 30 to 40 percent of patients

No known research shows an increase in survival for high-risk MDS patients.

**Lenalidomide (Revlimid)**

- Immunomodulating drug (IMiD)
- Same class as thalidomide
- Preferred therapy for patients with transfusion-dependent anemia due to low- or intermediate-1–risk MDS associated with a deletion of the long arm of chromosome 5 [del(5q)], either with or without additional cytogenetic abnormalities

- A 5q deletion may be involved in 20 to 30 percent of all MDS cases
- Non-neurotoxic (does not cause nerve damage)
- Nonsedating (does not cause sleepiness or grogginess)
- Allows most low-risk del(5q) patients to be independent of red blood cell transfusions for about 2 years
- Reduces red blood cell transfusion requirements in low-risk patients without del(5q), but not as well as in patients with del(5q)
- Unknown effect on life expectancy for patients who have IPSS intermediate-2– or high-risk MDS, either with or without del(5q).

In specific situations, **imatinib mesylate (Gleevec)** 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.

Further studies are needed to determine which of these drugs (Vidaza, Dacogen or Revlimid) are best for patients who have low-risk MDS without del(5q) but who have high EPO levels and therefore are unlikely to respond to treatment with ESAs. It is important to follow which ever treatment regimen your doctor recommends, as ordered, for four to six cycles before deciding whether or not the treatment is working.

**Chemotherapy.** Chemotherapy is the use of strong medicines to kill cancer. Treatment varies from patient to patient.

MDS patients in the intermediate-2– and high-risk IPSS categories may require treatment with the same type of chemotherapy that is used to treat acute myeloid leukemia (AML).

These drugs 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 would evaluate the patient's condition to decide whether intensive chemotherapy is needed. The doctor would consider
  - The severity of cell disturbances
  - A patient's potential for remission.

Chemotherapy has rarely cured patients with the common types of MDS (patients with abnormalities of chromosomes 5 and/or 7).

In clinical trials, newer drugs, such as clofarabine (Clolar®), are being explored as treatments for both MDS and AML patients. See *Research and Clinical Trials*, beginning on page 23.

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

**Allogeneic Stem Cell Transplantation.** The treatment with the best known potential to cure MDS is intensive radiation, either with or without chemotherapy, followed by allogeneic stem cell transplantation. This treatment is for

- Younger patients
- Patients in their 60s and 70s who are in otherwise good health
- Patients who are in either the IPSS intermediate-2– or the IPSS high-risk category
- Patients who have a human leukocyte-associated antigen (HLA)-matched stem cell donor (sibling or unrelated).

Allogeneic stem cell transplantation is a high-risk procedure. It is largely limited to patients with high-risk MDS because of its significant death rates (between 10 and 30 percent).

A reduced-intensity transplant (also called a "nonmyeloablative stem cell transplant") is a form of allogeneic transplant. In preparation for this type of transplant, patients receive a lower dose of chemotherapy, either with or without radiation. A reduced-intensity transplant is almost as effective in eliminating MDS as a standard (fully myeloablative) allogeneic transplant. Reduced-intensity transplants may also have lower death rates than standard allogeneic transplants. As a result, reduced-intensity transplantation may be an option for patients older than 70, the great majority of MDS patients.

### Outcomes

- About 40 to 50 percent of patients will be cured of their MDS.
- Stem cells from matched-unrelated donors compare well to outcomes of transplants with HLA-matched-related donors.
- Some patients relapse, usually within the first few years after the transplant.
- Some patients have long-term side effects following transplant.

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

MDS patients are encouraged to explore clinical trials. Clinical trials test new drugs and treatments, many of which are being supported by LLS research programs, before they are approved by the FDA as standard treatments.

Clinical trials are designed with great safety and accuracy. There are clinical trials for newly diagnosed patients and for patients who have already been treated. Sometimes, a clinical trial is the best option for a patient. Clinical trials hold great promise to increase remission rates and find a cure for MDS.

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. Information Specialists can search for clinical trials on behalf of patients, family members and healthcare professionals. This search service is also available at www.LLS.org/clinicaltrials.

At present, there are several types of clinical trials available for patients with MDS. Research includes studies directed at drug therapy, vaccine therapy, and reduced-intensity stem cell transplantation.

**Drug Therapy.** Treatment combinations of FDA-approved drugs, such as Vidaza® or Dacogen®, and AML-type chemotherapy 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.

Vidaza is also being studied as maintenance therapy for MDS patients who achieve a complete or partial remission after intensive chemotherapy. The purpose of the study is to see if Vidaza maintenance improves the duration of patient response.

The following list includes examples of drug combinations and single-agent drugs under study.

- Clofarabine (Clolar®) is a drug approved to treat childhood relapsed or refractory acute lymphoblastic leukemia (ALL). It is being studied when given in combination with AML-type chemotherapy.
- Rigosertib (Estybon™), a drug that increases MDS cell death, is being studied with intermediate-1–, intermediate-2– or high-risk patients as a single agent. It is also being studied in phase 3 trials with early data suggesting effectiveness in patients whose MDS has stopped responding to Vidaza or Dacogen.
- Ezatiostat (Telintra®), a glutathione S-transferase P1-1 inhibitor that activates the Jun-kinase pathway is being studied in lower-risk, transfusion-dependent patients as a single agent.
- Valproic acid (Depakene®), a histone deacetylase (HDAC) inhibitor, is being studied in combination with decitabine (Dacogen).
- Vorinostat (Zolinza®), a histone deacetylase (HDAC) inhibitor, is being studied in combination with azacitidine (Vidaza).
- Azacitidine (Vidaza), in combination with lenalidomide (Revlimid®), is being studied for higher-risk or transfusion-dependent patients.

**Vaccine Therapy.** Clinical trials are under way to see if an MDS vaccine is effective in treating patients who are aged 18 years and older and have lower-risk MDS. The vaccine is made from protein-building blocks, called "peptides," that may help the body mount an effective immune response to MDS cells.

Vaccine therapy and donor lymphocyte infusions are also being studied as treatments for MDS (and other blood cancer) patients who develop progressive or relapsed disease following allogeneic stem cell transplantation.

**Reduced-Intensity 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 refractory disease, as well as the use of unrelated umbilical cord blood and haploidentical ("half-matched") donors.

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

# Follow-Up Care

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

- Will need to see their doctor 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
  - All treatments
  - Names of chemotherapy drugs taken
  - Radiation treatment information
  - Surgery information
  - Transplant information
  - Information about any other treatments
  - Other medical history
  - Any other important information.

# 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 dissolved. These chemicals each have a special role. They include

- Proteins
  - Albumin, 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 $B_{12}$
- 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 27.

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); they

- Make up a little less than half of the body's total blood volume
- Are filled with hemoglobin, which
  - Is the 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 and then brings it back to the lungs. Then the $CO_2$ is removed when we exhale.

2. Platelets (cells that help blood to 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) (cells that fight infections). There are several types of WBCs, including

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

**Blood Cell & Lymphocyte Development (Hematopoiesis)**

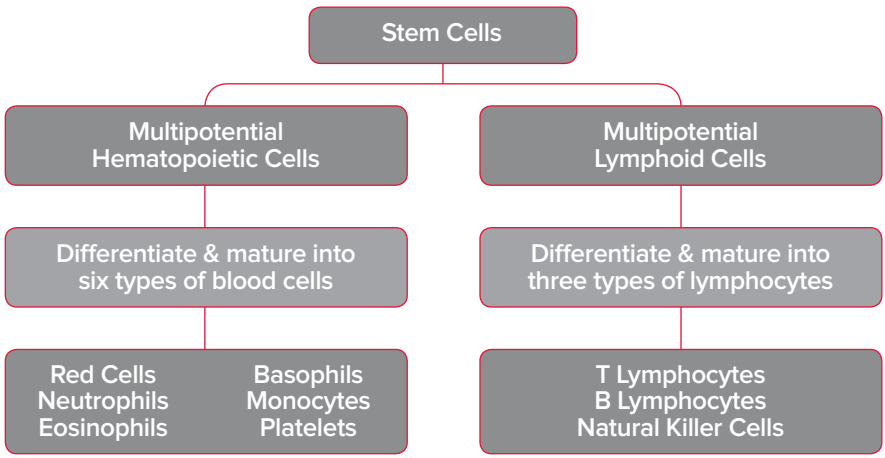


Figure 2. | **Stem cells** develop into blood cells (hematopoiesis) and lymphoid cells.

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, it 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 (not many) 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

For definitions of words you do not see in this section, visit **www.LLS.org/glossary**.

**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, mostly 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 take out needed parts of the donor's blood and return the unneeded parts to the donor. This process 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 your 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*.

**Autosomes.** See Karyotype.

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

**Blast Cells.** A young (or immature) type of cell 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 which cause symptoms for MDS and AML patients.

**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 in 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. Usually, this test is 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.** 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 there is no sign of the disease based on the results of standard tests specific to that disease.

**Cytogeneticist.** A health care expert who prepares and then examines the chromosomes of cells (cytogenetic analysis).

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

**Deletion.** A chromosomal problem when either a part or all of a single chromosome is lost.

**Differentiation.** When stem cells develop and mature and take on a new function. Stem cells will 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 to 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 due to decreased blood oxygen levels. Synthetic EPO is available as erythropoiesis-stimulating agents (ESAs). Epoetin alfa (Procrit® or Epogen®) and darbepoetin alfa (Aranesp®) are ESAs that are used to treat anemia.

**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 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 numbers of neutrophils after chemotherapy. Granulocyte-colony stimulating factor (G-CSF) and granulocyte-macrophage colony stimulating factor (GM-CSF) are growth factors that can be made in 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 25.

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

**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 the 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 of a single clone. They are used in cancer treatment to target cancer cells. They can be made in a lab.

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

**MPNs.** See Myeloproliferative Neoplasms.

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

**Myelodysplasia.** See Refractory Anemia; Refractory Anemia With Ring Sideroblasts.

**Myelodysplastic Syndromes/Myeloproliferative Neoplasms (MDS/MPN).** See Myeloproliferative Neoplasms.

**Myeloproliferative Neoplasms (MPNs).** A group of diseases that occur when certain types of blood cells are overproduced. Examples of MPNs are essential thrombocythemia, polycythemia vera and myelofibrosis. Some people with MPNs have abnormal-looking cells in their bone marrow that are similar to MDS cells.

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

**Neutrophil.** A type of white blood cell and 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 cancer doctor.

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

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

**Pathologist.** A 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 cells so patients are more likely to get an infection.

**PICC or PIC line.** See Percutaneously Inserted Central Venous Catheter.

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

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

**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 via a port.

**RA.** See Refractory Anemia.

**RAEB.** See Oligoblastic Myelogenous Leukemia.

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

**Radiation Oncologist.** A cancer doctor that uses radiation to treat cancer.

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

**Reduced-Intensity 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 an 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 where the bone marrow produces ringed sideroblasts rather than healthy red blood cells (erythrocytes). 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 WHO MDS subtypes. 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 (dysplasia) under the microscope. Less than 5 percent of the cells in the bone marrow are blasts. In patients with more than 15 percent ringed sideroblasts, the 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. This usually follows 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, white blood cells, and blood platelets. Stem cells are mostly found in the marrow, but some leave and circulate in the bloodstream. Stem cells can be collected, preserved, and used for stem cell therapy. See Hematopoiesis.

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

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

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

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

**Thrombocythemia.** A disorder characterized by too many 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 MDS (MDS-u).** A WHO 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," the five types of infection-fighting cells in the blood. These include neutrophils, eosinophils, basophils, monocytes and lymphocytes.

# More Information

For more information, see the following free LLS publications:

*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*
*Essential Thrombocythemia Facts*
*Myelofibrosis Facts*
*Polycythemia Vera Facts*

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

## Resources

**Aplastic Anemia & MDS International Foundation (AA&MDSIF)**
**(800) 747-2820 • 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 multi-disciplinary, international organization devoted to MDS support, research, treatment, and education for patients, caregivers, physicians, nurses and other health care providers. The organization is based upon the premise that international cooperation will accelerate the process leading to the control and cure of these diseases.

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# Notes

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# 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 professionals who are available by phone Monday through Friday, 9 am to 9 pm (ET).

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