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Myelodysplastic Syndromes

Revised **2022**

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Making the human connection

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

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- **Thousands of patients and caregivers sharing experiences and information, with support from knowledgeable staff**
- **Accurate and cutting-edge disease updates**
- **The opportunity to participate in surveys that will help improve care.**

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Acknowledgement

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Introduction

Myelodysplastic syndromes (MDS) are a group of blood cancers and bone marrow failure syndromes in which the bone marrow does not make enough healthy blood cells. This book provides information about MDS for patients and their families. It also includes brief descriptions of normal blood and bone marrow, as well as definitions of health terms related to MDS.

In the United States, an estimated 58,471 people are living with or in remission from MDS. An average of 15,099 new cases of MDS were diagnosed each year from 2013 to 2017.*

Doctors have learned a great deal about MDS in the last few decades. Today, patients who have MDS can anticipate improved outcomes and better quality of life than ever before. This is due to a greater understanding of the genetic features and biology of the disease, improved supportive care, the development of new drugs and progress in stem cell transplantation.

All LLS publications mentioned in this book are free and can be viewed, downloaded or ordered online at www.LLS.org/booklets.

Feedback. Visit www.LLS.org/PublicationFeedback to give suggestions about this booklet.

*Source: Facts 2020-2021. The Leukemia & Lymphoma Society. April 2021.

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Myelodysplastic Syndromes

Myelodysplastic syndromes (MDS) are a group of bold cancers in which the bone marrow does not make enough healthy blood cells. Bone marrow is the sponge-like tissue in the center of most bones, where blood cells form. There are three main types of blood cells: red blood cells, white blood cells and platelets. Red blood cells carry oxygen throughout the body. White blood cells help fight infections. Platelets help stop bleeding by clotting (clumping together) at the site of an injury.

Blood cells begin as blood stem cells in the bone marrow. A blood stem cell may become a myeloid stem cell or a lymphoid stem cell. In healthy bone marrow, myeloid stem cells eventually develop into red blood cells, platelets, and some types of white blood cells (basophils, eosinophils, monocytes and neutrophils).

MDS occurs when one of these myeloid blood stem cells undergoes a mutation or a series of mutations in the DNA (genetic material) that controls blood cell

development. A mutation can cause the abnormal growth of blood stem cells. Every cell that arises from an abnormal stem cell also has mutated DNA. In MDS, the abnormal stem cells, called “blast cells,” multiply and produce too many immature blood cells that do not develop into normal blood cells. These blast cells are often also abnormal in shape and size. This condition is called “dysplasia.” These abnormal blast cells do not mature into healthy blood cells, and they often die too early within the bone marrow or in the blood.

As the abnormal blast cells multiply and accumulate in the bone marrow, they slow down the production of normal, healthy red blood cells, white blood cells and platelets. As a result, there are too many immature blast cells and not enough mature red blood cells, white blood cells or platelets, or any combination of the three. When there are fewer healthy blood cells, anemia, infection or excessive bleeding may occur.

Medical Term	Definition
Anemia	Low red blood cell count
Thrombocytopenia	Low platelet count ("thrombocyte" is another word for platelet)
Neutropenia	Low neutrophil count (a neutrophil is a type of white blood cell)

There are several types of MDS. Some types progress slowly and may cause mild-to-moderate anemia (low red blood cell count) or decreases in other kinds of blood cells. Other types of MDS may cause severe low blood cell counts. In about 30 percent of cases, MDS may develop into acute myeloid leukemia (AML), a fast-growing cancer of the blood and bone marrow.

Please visit www.LLS.org/booklets to view the free LLS booklet *Acute Myeloid Leukemia in Adults* for more information about AML.

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 or feel. A person who has signs or symptoms that suggest the possibility of MDS is referred to a specialist called a hematologist-oncologist. This is a doctor who has special training in diagnosing and treating blood disorders and blood cancers. Large medical centers usually have hematologist-oncologists who specialize in treating MDS and acute leukemias.

Some patients initially have no symptoms of MDS, and abnormal results from routine blood tests may be the earliest signs of the disease. For patients with symptoms, it is common not to feel well because of the lack of normal, healthy blood cells.

- Symptoms of anemia (low red blood cell count) include:
  - Fatigue
  - Dizziness
  - Weakness
  - Shortness of breath during normal physical activity
  - Headache
  - Palpitations (noticeably rapid or irregular heartbeat)
  - Pale skin
- Symptoms of neutropenia (low white blood cell count) include:
  - Frequent infections, or infections that do not go away
  - Fever
- Symptoms of thrombocytopenia (low platelet count) include:
  - Bruising easily
  - Prolonged bleeding from minor cuts
  - Pinhead-sized red spots on the skin, called “petechiae”
  - Frequent and/or severe nosebleeds
  - Bleeding gums

The symptoms of MDS may be like those of other blood disorders or medical conditions. Speak with your doctor if you have any of these symptoms to ensure proper diagnosis and treatment.

Testing

While certain signs and symptoms may indicate that a person has MDS, a series of tests are needed to confirm the diagnosis. It is important to have an accurate diagnosis because it helps the doctor to:

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

MDS can sometimes be mistaken for other blood disorders, so repeated blood and bone marrow tests may be needed to establish a diagnosis of MDS. 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 the lymphatic system.

Talk to your doctor about:

- The diagnsotic tests that are being done
- What the results mean
- Getting copies of the results

Medical History. Your doctor will take a thorough medical history. This may include information about your past illnesses, injuries, medications and other treatments. It is also important to tell your doctor if you have had any blood transfusions in the past.

Some illnesses run in families, so the doctor may ask about the health of your blood relatives. Your doctor should find out if you have a family history of blood cancer. While MDS cannot be inherited, certain gene mutations present at birth may increase a person's risk of developing MDS or another cancer called acute myeloid leukemia (AML). Patients with a family history of leukemia and/or other cancers occurring in two or more closely related relatives or generations should be evaluated for an inherited predisposition syndrome to help better manage their treatment.

Physical Examination. Your doctor will want to know about your current symptoms, and will also conduct a physical examination. During the exam, the doctor may listen to your lungs and heart and carefully examine your body for signs of infection and disease. To check your internal organs, the doctor may feel different parts of your body. For example, the doctor may feel your abdomen to see if you have an enlarged spleen or liver. Your doctor may also check your lymph nodes to see if any of them are enlarged.

Complete Blood Count (CBC) With Differential. This test is used to measure the number of red blood cells, white blood cells and platelets in a sample of your blood. A complete blood count (CBC) also measures the amount of hemoglobin (a protein in red blood cells that carries oxygen) in the blood and the percentage of red blood cells in the sample. The CBC should include a "differential," which measures the numbers of the different types of white blood cells in the sample.

Most patients with MDS have low blood cell counts, called "cytopenias." Most often, they have too few red blood cells. They may also have low white blood cell and low platelet counts.

If there is a low red blood cell count, additional blood tests are done to look for the cause. Low red blood cell counts may be caused by thyroid disease, low vitamin levels (folate or B12) and iron deficiency.

Reticulocyte Count. Reticulocytes are newly produced, relatively immature red blood cells that are still developing. A reticulocyte count measures the level of reticulocytes in the blood. This test is done to determine if the bone marrow is

creating red blood cells at an appropriate rate. The body's normal response to anemia is for the bone marrow to produce and release more reticulocytes into the blood. In people with MDS, the reticulocyte count is often low, indicating that the bone marrow is not able to produce enough red blood cells to respond to the anemia.

Peripheral Blood Smear. In this test, a single drop of blood is spread on a glass slide, dried and then stained with a special dye. The sample is viewed under a microscope to examine the number, size, shape, appearance and maturity of various blood cells. In MDS, some blood cells exhibit "dysplasia" (an abnormal shape or size). A peripheral blood smear also checks for blast (immature) cells in the blood, which are are normally found in the bone marrow.

Serum Erythropoietin (EPO). This test measures the level of erythropoietin (EPO) in the blood. EPO is a hormone primarily made in the kidneys to stimulate the bone marrow to produce new red blood cells. The kidneys produce and release EPO into the blood in response to low blood oxygen levels. Your doctor may order this test to help diagnose the cause of anemia that does not appear to be the result of an iron deficiency, vitamin deficiency or internal bleeding. Most patients with MDS-related anemia have an EPO level that is higher than normal.

Lactate dehydrogenase (LDH). This test measures the level of lactate dehydrogenase (LDH) in the blood. LDH is a protein found in most cells. When a cell is damaged, LDH is released into the bloodstream. High levels of LDH in the blood may be caused by cancer and may also be a sign that the cancer is widespread. Two scoring systems for cancer, called the "IPSS Prognostic Scoring System" and the "IPSS-R Prognostic Scoring System" use LDH levels to determine the severity and probable outcome (prognosis) of cancer. See pages 15–18 for more information on these prognostic scoring systems.

Human Leukocyte Antigen (HLA) Typing. This blood test, called "HLA Typing," is done to identify certain proteins, called human leukocyte antigens (HLAs), found on the surface of most cells in the body. These proteins make up the body's tissue type, which varies from person to person. They also play an important role in the body's immune response to foreign substances by helping the body distinguish its own cells from foreign cells. An HLA test is done before allogeneic stem cell transplantation to find out if there is a tissue match between a potential donor and the patient receiving the transplant. While HLA typing is not used to diagnose MDS, it is an important test for newly diagnosed MDS patients if allogeneic stem cell transplantation is being considered as a treatment option. See pages 27–29 for more information on allogeneic stem cell transplantation.

Bone Marrow Tests: Aspiration and Biopsy. To confirm a diagnosis of MDS, these two tests are used to collect and examine bone marrow, the spongy tissue found inside most bones. They are frequently done at the same time, either at the doctor's office or in a hospital. These tests may also be repeated, both during and after therapy, to see if treatment is working.

In bone marrow aspiration and biopsy, the samples of bone marrow are usually taken from the patient's pelvis or "hip bone," after medicine has been given to numb the skin and surface of the bone. Bone marrow has both a solid and a liquid component. For a bone marrow aspiration, a special hollow needle is inserted through the hip bone and into the bone marrow to aspirate (remove) a liquid sample of cells. For a bone marrow biopsy, a wider needle is used to remove a sample of solid bone that contains bone marrow. Both samples are sent to the lab where they are examined under a microscope.

See **Figure 1** on page 8 for more information on blood and bone marrow tests.

Cell Assessment. At the laboratory, a doctor called a "hematopathologist" examines the blood and bone marrow samples. Hematopathologists are doctors who have special training in identifying blood diseases by studying cells under a microscope and performing other specialized tests on the blood and bone marrow cells.

The hematopathologist examines the blood and bone marrow cells under a microscope to determine their size, shape and type, and to identify other cell features. As part of this assessment, the hematopathologist will note any signs of MDS, such as:

- Dysplasia (cells that are abnormal in size or shape)
- An abnormal number of any type of blood cells (either too many or too few)
- The percentage of blasts (immature blood cells) in the bone marrow
- An abnormally low or high number of cells in the bone marrow
- Presence or absence of ring sideroblasts (red blood cells containing rings of iron deposits)
- Presence of blasts in the blood (blasts are not found in the blood)

The pathologist will perform additional tests to see if there are abnormalities in the chromosomes and genes of the cancer cells. These tests help in the diagnosis and treatment of MDS.

Cytogenetic Analysis. Cytogenetic analysis involves testing samples of tissue, blood or bone marrow to look for changes in chromosomes. In this test, a hematopathologist uses a microscope to examine the chromosomes inside of cells. Chromosomes are bundles of tightly coiled DNA that contain most of the genetic information in a cell. In patients with MDS, cytogenetic analysis is used to look for abnormal changes in the chromosomes of the cancer cells. Approximately 50 percent of people who have MDS have one or more chromosomal abnormalities, and 10 to 15 percent of patients have complex karyotypes (multiple chromosomal abnormalities).

Normal human cells contain 23 pairs of chromosomes, for a total of 46 chromosomes. Each pair of chromosomes is a certain size, shape and structure.

Figure 1. How Are the Blood and Bone Marrow Tests Done?

Blood Test. Blood is taken from the patient's arm with a needle. The blood is collected in tubes and sent to a lab for testing.

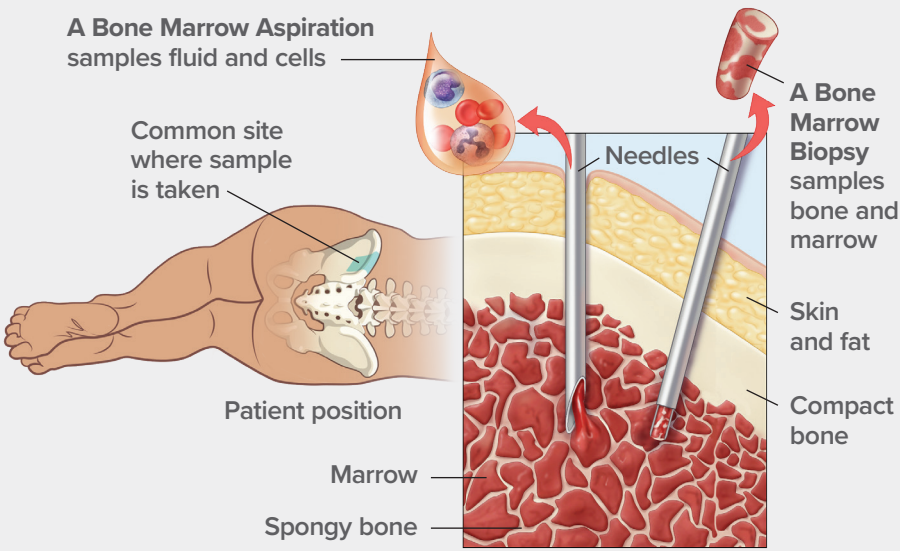
Bone Marrow Aspiration. A sample of fluid with cells is removed from the bone marrow and sent to a lab for testing.

Bone Marrow Biopsy. A very small amount of bone filled with bone marrow cells is taken from the body and sent to a lab for testing.

Both bone marrow tests are done with special needles. Adults and older teens may be given a local anesthetic and be awake for this procedure, but most children are under sedation or given general anesthesia, which makes them "sleep" briefly during the tests. The sample of cells is usually taken from the patient's hip bone.

Blood and bone marrow tests may be done in the doctor's office or in a hospital. A bone marrow aspiration and biopsy are almost always done at the same visit. Blood and bone marrow tests may be done both during and after treatment. The tests are repeated to see if treatment is working.

Bone Marrow Aspiration and Biopsy



Left: The place on the back of the patient's pelvic bone where a bone marrow aspiration or biopsy is done. **Right:** Where the needles go inside the bone to collect the liquid sample for aspiration (the needle on the left) and the bone sample for biopsy (the needle on the right). The needles are different sizes for each of these tests.

In some cases of MDS, the chromosomes of the cancer cells have abnormal changes that can be seen under a microscope. These changes include, for example: an extra chromosome, a deletion or an inversion. A deletion occurs when part of a chromosome is missing. An inversion occurs when a part of a chromosome breaks off, turns upside down and reattaches.

Cytogenetic testing is done using either a bone marrow or a blood sample. The cells in the sample are allowed to grow in the laboratory and then are stained prior to examination. The sample is then examined under a microscope and photographed to show the arrangement of the chromosomes. This is called a "karyotype" (see **Figure 2** on page 10). The karyotype shows if there are any abnormal changes in the size, shape, structure or number of the chromosomes.

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." In MDS, the most common abnormal chromosomal abnormalities are found in chromosomes 5, 7, 8 and 20.

Certain cytogenetic abnormalities are useful in predicting survival or progression to acute myeloid leukemia (AML) and are incorporated into the most common prognostic scoring systems for MDS. In some cases, cytogenetic analysis can also help guide treatment decisions.

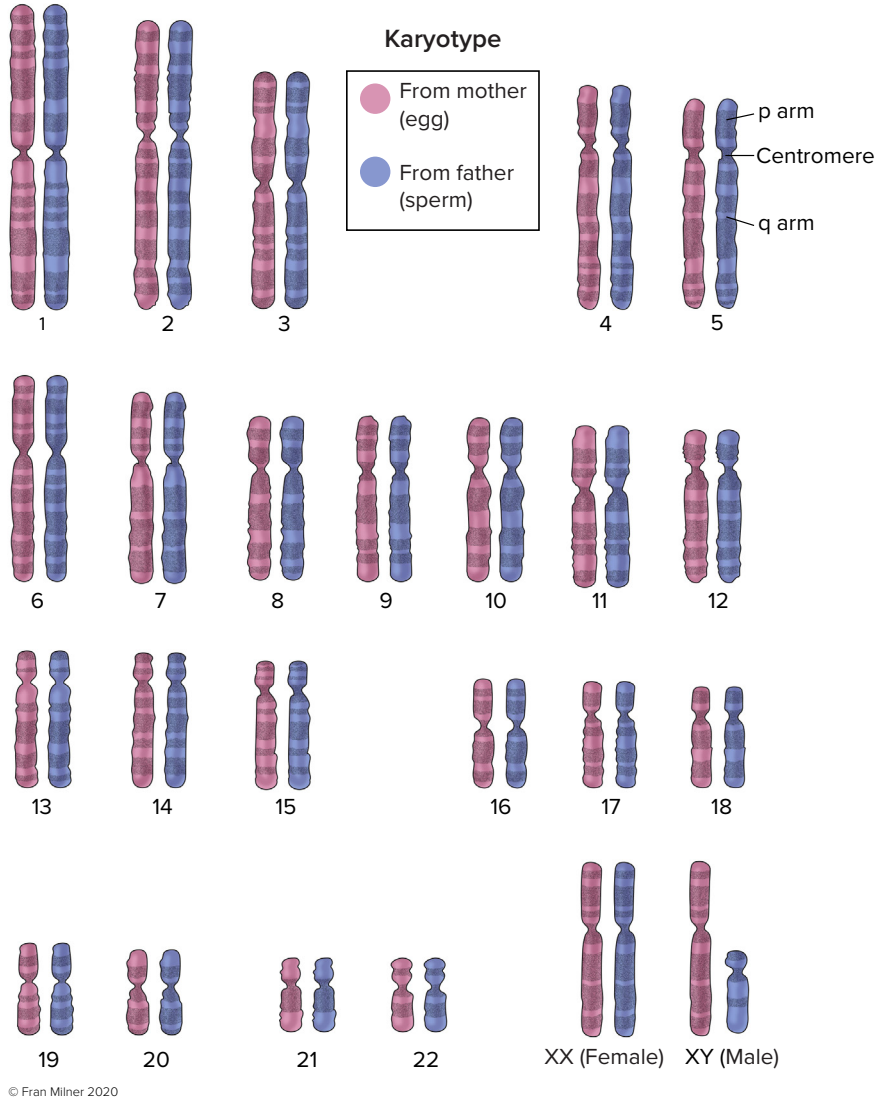
Fluorescence In Situ Hybridization (FISH). This very sensitive test is used to examine genes or chromosomes in cells and tissues. Doctors use FISH testing to detect certain abnormal changes in the chromosomes and genes of cancer cells. This test identifies specific gene or chromosome changes that are common in MDS patients.

Molecular Testing. Molecular testing is used to find mutations (changes) in the DNA of genes. DNA mutations may be found in 70-80 percent of patients with MDS. Certain mutations are associated with either a better or a worse prognosis (outcome). Doctors use the results of molecular testing to help plan treatment. Molecular testing can be done on either a sample of blood or a sample of bone marrow.

In recent years, researchers have found multiple inherited genetic conditions that can lead to blood diseases such as MDS. Patients with a family history of blood cancers should consider genetic testing to learn if their disease has an inherited component. This information may affect treatment plans.

DNA Sequencing. This refers to a number of different laboratory tests that examine the exact sequence (order) of a person's DNA. By comparing the sequence of DNA in cancer cells with the DNA in normal cells, doctors can find genetic changes that are unique to the cancer cells and may be driving the growth of the patient's cancer.

Figure 2. Normal Karyotype



There are targeted DNA sequencing tests (also called “multigene panels”) that look for specific mutations in a sample. A targeted DNA sequence test focuses on specific sets of genes or areas of DNA. There are also broad DNA sequencing tests (genomic screening tests) that analyze the sequence of large regions of DNA, rather than looking for mutations of specific genes. Doctors may also order sequencing of all the DNA in your entire genome. This test is known as “whole genome sequencing.”

The term “next-generation sequencing” is a catch-all term used to describe several different modern sequencing technologies. These technologies allow for sequencing of DNA much more quickly and cheaply than sequencing methods used in the past.

Since the introduction of DNA sequencing, the number of mutated genes that can be detected in MDS patients has increased considerably. The genes that are frequently mutated in MDS patients are: *TET2, SF3B1, ASXL1, DNMT3A, SRSF2, RUNX1, TP53, U2AF1, EZH2, ZRSR2, STAG2, CBL, NRAS, JAK2, SETBP1, IDH1, IDH2, ETV6, FLT3, NF1, CALR, MPL* and *GATA2*.

These mutations are important in guiding risk assessment and prognosis, and are also used to guide treatment decisions. For example:

- Some patients may be eligible to receive drugs called "inhibitors" that target specific gene mutations such as *FLT3*, *IDH1*, and *IDH2*.
- Although it is rare, some MDS patients have a mutation of the *NPM1* gene. These patients may be potentially cured with cytarabine and an allogeneic stem cell transplantation.

Certain mutations are associated with a better or worse prognosis or can help predict response to different treatments. For example:

- Patients with only an *SF3B1* mutation tend to have a more favorable prognosis.
- Mutations of the genes *TP53*, *EZH2*, *ETV6*, *RUNX1*, and *ASXL1* are associated with a decrease in overall survival, according to several studies.

Genetic testing should be done when the cancer is first diagnosed and again after a relapse. This is because it is possible for patients to acquire additional genetic abnormalities after the completion of their initial "first-line" treatment.

See the free LLS book *Understanding Genetics* for more information about genetics and genetic testing.

Diagnosis

Diagnostic Criteria. The diagnosis of MDS is based on:

- At least one cytopenia (low blood cell count) in one or more of red blood cell, white blood cell or platelet counts
- Dysplasia (cells that have an abnormal size or shape) in at least 10 percent or more of red blood cells, white blood cells or platelets on the blood smear or bone marrow examination
- Less than 20 percent blasts (immature blood cells) in the blood and bone marrow
- Specific MDS-associated cytogenetic (chromosome) abnormalities

In healthy people, there are usually no blast cells in the blood, and blast cells should make up less than 5 percent of all bone marrow cells. In MDS patients, blast cells may make up to 20 percent of cells in the bone marrow. A blast count of 20 percent or higher is considered acute myeloid leukemia (AML).

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

The classification of MDS has evolved a great deal 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 (immature cells) 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). This classification is rarely used anymore. However, definitions of the five subtypes that fall into this classification are included in the Health Terms section on pages 41–47.

In 2001, the World Health Organization (WHO) proposed an alternative classification that was a modified version of the original FAB classification. Since then, the WHO classification has been updated twice, once in 2008 and again in 2016 (see **Table 1** below). 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 characteristics of these subtypes, pages 13-14.

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

The WHO classifies MDS into subtypes based on how the cells within the bone marrow appear under a microscope as well as other factors. These include:

- Number of dysplastic lineages: the number of types of blood cells (red blood cells, white blood cells, or platelets) that exhibit dysplasia
- Cytopenias: how many low blood cell counts there are
- Ring sideroblasts: what portion of immature red blood cells contain rings of iron deposits around the center
- Blasts: the portion of immature forms of blood cells in the bone marrow and blood
- Chromosome abnormalities: certain chromosome changes that are specific to MDS

MDS with Single Lineage Dysplasia (MDS-SLD). In this subtype of MDS:

- Dysplasia in only 1 cell type (either red blood cells, white blood cells or platelets)
- Low numbers of 1 or 2 types of blood cells, but normal numbers of the other type(s)
- Less than 5 percent of blast cells in the bone marrow

MDS with Ring Sideroblasts (MDS-RS). In this type of MDS, many of the immature red blood cells are ring sideroblasts (red blood cells that have rings of iron deposits). For this diagnosis, at least 15 percent of the early red blood cells must be ring sideroblasts (or at least 5 percent if the cells also have the *SF3B1* mutation). This type of MDS is divided into 2 types, based on how many of the blood cell types in the bone marrow are affected by dysplasia.

1. **Single Lineage Dysplasia (MDS-RS-SLD).** This type of MDS has:
   - Dysplasia in only 1 type of cells (red blood cells, white blood cells or platelets)
   - Low numbers of 1 or 2 types of blood cells, but normal numbers of the other type(s)
   - Less than 5 percent of blast cells in the bone marrow.

2. **Multilineage Dysplasia (MDS-RS-MLD). This type of MDS has:**
   - Dysplasia in 2 or 3 cell types
   - Low numbers of 1 to 3 types of blood cells
   - Less than 5 percent blast cells in the bone marrow

MDS with Multilineage Dysplasia (MDS-MLD). This type of MDS has:

- Dysplasia in 2 or 3 cell types
- Low numbers of 1 to 3 types of blood cells
- Less than 5 percent blasts in the bone marrow

MDS with Excess Blasts (MDS-EB). In this type of MDS, there are higher than normal blasts in the bone marrow and blood, and there is at least one blood cell type with lower than normal numbers. There may or may not be dysplasia in the blood cells in the bone marrow. This subtype of MDS is further divided into 2 types based on the number of blasts.

1. **MDS with Excess Blasts-1 (MDS-EB1).** This type of MDS has:
   - Dysplasia in 0 to 3 types of blood cells
   - Low numbers of at least 1 type of blood cell
   - Blasts make up 5 to 9 percent of the cells in the bone marrow, or 2 to 4 percent of the cells in the blood

2. **MDS with Excess Blasts-2 (MDS-EB2).** This type of MDS has:
   - Dysplasia in 0 to 3 types of blood cells
   - Low numbers of at least 1 type of blood cell
   - Blasts make up 10 to 19 percent of the cells in the bone marrow, or 5 to 19 percent of the cells in the blood

MDS with isolated del(5q). In this type of MDS, the chromosomes of the MDS cells are missing part of chromosome number 5, called del(5q), and:

- Dysplasia in 1 to 3 types of blood cells
- Low numbers of 1 or 2 types of blood cells
- Blasts make up less than 5 percent of the cells in the bone marrow
- Cytogenetics showing del(5q) alone or with one additional abnormality as long as that abnormality is not a loss of part or all of chromosome 7

MDS, Unclassifiable (MDS-U). In this type of MDS, the blood and bone marrow test results do not fit any other type of MDS. Patients have decreased numbers of 1, 2, or 3 types of blood cells. They may not have dysplasia in the blood cells, or they may have dysplasia in 1, 2, or 3 types of blood cells.

Treatment Planning

Choosing a Hospital and Doctor. When you find out that you have cancer, you want to get the best possible medical care and treatment. MDS can be difficult to treat, and a diagnosis of MDS is associated with a wide range of outcomes. It is essential to seek treatment in a center that has hematologist-oncologists who have significant experience in the care of patients with MDS. A hematologist is a doctor who has special training in treating blood disorders, and an oncologist is a doctor who has special training in treating cancer. A hematologist-oncologist specializes in treating blood cancers.

If time allows, you may want to seek a second opinion from another doctor, as it may help you feel more confident about the recommended treatment plan.

The second opinion should come from another hematologist-oncologist, and preferably one who also treats MDS. A hematologist-oncologist will usually have the most knowledge and experience about the latest treatment options for MDS. If you are unsure about getting a second opinion or feel uncomfortable about how to tell your current doctor that you are seeking one, call our Information Specialists at (800) 955-4572 to discuss a way to do so that makes you feel comfortable. You may also want to check in advance with your insurance company to be sure that your plan covers the cost of getting a second opinion and to see if specific doctors or centers are recommended.

Prognostic Scoring Systems. A "prognosis" is a prediction of the likely outcome of a disease. It is your doctor's best estimate of how the cancer will affect you and how it will respond to treatment. In MDS, an important part of prognosis is predicting overall survival and whether the disease will transform to AML.

Certain factors may affect the prognosis of MDS, and they also help doctors determine when to start treatment and how intensive the treatment should be. These 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

Some factors are linked with better outcomes, and some factors are associated with poorer outcomes. Some factors help predict how a patient will respond to treatment. Doctors assign a risk score and risk group for each patient with MDS, based on the prognostic factors listed above.

Each prognostic factor is assigned a number based on its severity. The scores for all 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 it 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 two main prognostic scoring systems:

- The International Prognostic Scoring System (IPSS)
- The International Prognostic Scoring System-Revised (IPSS-R)

The International Prognostic Scoring System (IPSS). The IPSS was the first widely used prognostic scoring system for MDS, and it has been established as the backbone of prognostic systems since its development in 1997. It scores three main factors:

1. Percentage of blasts in the bone marrow
2. Cytogenetics (chromosomal changes)
3. Cytopenias (low blood cell counts)

Points are assigned to each of the three factors, and then the points are added together to determine one of four overall risk scores: Low, Intermediate-1, Intermediate-2, and High. See **Table 2** 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 points); no chromosome changes (0 points); and anemia but normal platelet and neutrophil (white blood cell) 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); and normal neutrophil (white blood cell) counts but with 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 2. IPSS Prognostic Scoring System and Risk Groups

Prognostic Factors Scored	Risk Groups Based on Total Risk Score
Percent of blast cells in bone marrow ○ Less than 5 = 0 points ○ 5 to 10 = 0.5 points ○ 11 to 20 = 1.5 points ○ 21 to 30 = 2 points	○ 0 points = Low ○ 0.5 to 1 point = Intermediate-1 ○ 1.5 to 2 points = Intermediate-2 ○ 2.5 or more points = High
Cytogenetics (chromosome changes) ○ None, del(5q), del(20q) = 0 points ○ 3 or more abnormalities, abnormal chromosome 7 = 1 point ○ Other abnormalities = 0.5 points	
Number of cytopenias (low blood cell counts) ○ None or 1 = 0 points ○ 2 or 3 = 0.5 points	

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 (chromosomal) abnormalities. It scores the types and severity of cytoepnias (low blood cell counts). It also gives a number value to a wider range of chromosomal changes. It classifies myelodysplastic syndromes into five risk groups: Very Low, Low, Intermediate, High, and Very High. See **Table 3** on page 17.

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 bone marrow 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.

Table 3. IPSS-R Prognostic Scoring System and Risk Group

Prognostic Factors Scored	Risk Groups Based on Total Risk Score
Percent of blast cells in bone marrow ○ Less than or equal to 2 = 0 points ○ Greater than 2 to less than 5 = 1 point ○ 5 to 10 = 2 points ○ Greater than 10 = 3 points	○ 1.5 or less points = Very Low ○ 2 to 3 points = Low ○ 3.5 to 4.5 points = Intermediate ○ 5 to 6 points = High ○ 6.5 or more points = Very High
Cytogenetics (chromosome changes) ○ –Y, del(11q) = 0 points ○ Normal, del(5q), del(12p), del(20q), double including del(5q)* = 1 point ○ del(7q), +8, +19, i(17q), any other single or double independent clone** = 2 points ○ –7, inv(3), +(3q), del(3q), double including –7/del(7q), complex: 3 abnormalities = 3 points ○ More than 3 abnormalities = 4 points	
Hemoglobin concentration (g/dL) ○ Equal to or greater than 10 = 0 points ○ 8 to less than 10 = 1 point ○ Less than 8 = 1.5 points	
Platelet count (x 10^9/L of blood) ○ Equal to or greater than 100 = 0 points ○ 50 to less than 100 = 0.5 points ○ Less than 50 = 1 point	
Absolute neutrophil count ([ANC] x 10^9/L of blood) ○ Equal to or greater than 0.8 = 0 points ○ Less than 0.8 = 0.5 points	

*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, grams/deciliter; inv, an inversion in a chromosome.

A link on the internet to the Revised International Prognostic Scoring System (IPSS-R) for Myelodysplastic Syndromes Risk Assessment Calculator is available for use by anyone at: https://www.mds-foundation.org/calculator/index.php

The IPSS and the IPSS-R 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 (other illnesses or diseases), previous cancers, or other health issues. Still, scoring system numbers are very important because they are indicators of the patient's prognosis. 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.

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 4** below). 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 patient's risk group and plan treatment accordingly.

Lower-risk MDS tends to grow and progress slowly. It 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 MDS is likely to progress more quickly. Without treatment, higher-risk MDS may also progress to AML in a shorter time. Higher-risk MDS may also cause more signs and/or symptoms and health complications within a shorter time. Therefore, more intensive treatment is often required.

Table 4. Risk Groups: Lower-Risk Versus Higher-Risk Myelodysplastic Syndromes

Lower-Risk Groups	Higher-Risk Groups
○ **IPSS** Low and Intermediate-1	○ **IPSS** Intermediate-2 and High
○ **IPSS-R** Very Low, Low, Intermediate	○ **IPSS-R** Intermediate, High, Very High

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

Key. IPSS, International Prognostic Scoring System; IPSS-R, International Prognostic Scoring System-Revised; MDS, myelodysplastic syndrome.

Treatment

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

Before you begin treatment, you and your doctor will discuss your treatment options. One option may be a clinical trial. Like all treatment options, clinical trials have risks and benefits. By considering all your treatment options, including clinical trials, you will be taking an active role in a very important decision that affects you.

Not everyone with MDS receives the same type of treatment. Your doctor will tailor your treatment based on your MDS subtype, your prognostic score, and other factors including your age and overall health, caregiver and social support, your goals and preferences.

Some people diagnosed with MDS who do not have very low blood cell counts or other symptoms may not need to start treatment immediately. Instead, your doctor may recommend regular exams and lab tests to monitor your condition.

If treatment is needed, certain patients may be cured with a stem cell transplant. Many MDS patients, however, are not good candidates for stem cell transplantation due to advanced age and other medical conditions. When a stem cell transplant is not a treatment option, MDS can still be treated to improve blood cell counts, relieve symptoms and slow disease progression. Your treatment may include chemotherapy, immunosuppressive therapy, immunomodulators and/or stem cell transplantation.

All patients should receive relevant supportive care if low blood cell counts are causing problems. Supportive care is important regardless of other treatments for MDS.

Supportive Care. Supportive care refers to specialized medical care focused on providing relief from symptoms and the stresses of a serious illness. 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 that helps relieve or prevent the symptoms of MDS, but it does not treat the disease itself. Supportive care may be given alone, or along with other treatments for MDS. Supportive care for MDS should be given whenever a person has symptoms that need to be controlled. Supportive care may include blood transfusions, growth factors and antibiotics.

Treating Anemia (Low Red Blood Cell Counts). Anemia is a condition in which the number of red blood cells is below normal. Treatment may include:

- **Red Blood Cell Transfusions.** A red blood cell transfusion is a procedure in which donated red blood cells are slowly injected into a patient's body through a vein. The doctor will determine whether a transfusion is appropriate based on the patient's hemoglobin concentration, the severity of 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. At the time of diagnosis, 60 to 80 percent of patients with MDS have anemia, and up to 90 percent of patients will require one or more transfusions during their illness.

  Please visit www.LLS.org/booklets to see the free LLS booklet *Blood Transfusion.*

- **Red Blood Cell Growth Factors**. Erythropoietin (EPO) is a hormone needed for normal production of red blood cells. It is made primarily by the kidneys and is released into the blood in response to decreased blood oxygen levels. Drugs with synthetic EPO, called erythropoietin-stimulating agents (ESAs), are available to help stimulate the bone marrow to make red blood cells. They are used for MDS patients who have anemia associated with low EPO levels. Treatment with ESAs may decrease the need for red blood cell transfusions and improve survival outcomes in some patients.

  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.

- **Erythroid Maturation Agent.** An erythroid maturation agent is used to treat anemia in adults who need to have regular blood cell transfusions. It is used when erythropoietin-stimulating agents (ESAs) are not effective in increasing red blood cell production.

  Luspatercept-aamt (Reblozyl®) is an erythroid maturation agent indicated for the treatment of anemia failing an erythropoietin-stimulating agent (ESA). Luspatercept-aamt requires 2 or more red blood cell units over 8 weeks for adult patients who have Very Low to Intermediate risk MDS with ring sideroblasts (MDS-RS).

Treating Thrombocytopenia (Low Platelet Count). MDS patients with a low platelet count can experience easy bruising or uncontrolled bleeding. Low platelet counts are also a common side effect of chemotherapy. Treatment may include:

- **Platelet Transfusion.** Platelet transfusions help increase the number of platelets in the blood. They are typically required if a patient's platelet count falls below 10,000/mcL, or for acute bleeding. A platelet transfusion is a slow injection of platelets into a vein.

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 to see the free LLS booklet *Blood Transfusion*.

- **Platelet Growth Factors.** Thrombopoietin (TPO) is a hormone made in the body that helps in the production of platelets.

  Romiplostim (Nplate®) and **eltrombopag (Promacta®)** are drugs that act like TPO. These drugs are being investigated for treatment of MDS patients who have low platelet counts. Although romiplostim and eltrombopag are not approved specifically for the treatment of MDS, they can sometimes 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.

Treating Leukopenia (Low White Blood Cell Count). MDS and its treatments often cause drops in white blood cell counts. 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, patients are treated with antibiotics. Antiviral drugs may be used to treat certain viral infections, and antifungal medications may be used to treat certain fungal infections.

White blood cell transfusions are generally not used for patients with MDS, so doctors sometimes use growth factors to help increase a patient's white blood cell count. Growth factors stimulate the bone marrow to make new white blood cells. Granulocyte colony-stimulating factors (G-CSF), such as **filgrastim (Neupogen®)** and **pegfilgrastim (Neulasta®),** stimulate the production and release of neutrophils into the bloodstream. Granulocyte-macrophage colony-stimulating factors (GMCSF), such as **sargramostim (Leukine®),** stimulate the production of three types of white blood cells: neutrophils, macrophages and dendritic cells.

During treatment for MDS, a low white blood cell count can lead to infections from bacteria and fungi that are normally present in the environment, on the skin, in the nose and mouth, on the gums or in the colon. Because of the increased risk of infection, medical staff and all family and friends need to practice frequent and vigorous handwashing and take other precautions to avoid exposing patients to bacteria, viruses and other infection-causing agents.

Patients at home should seek medical attention immediately if any signs of infection develop. A temperature of 100.4 °F or higher, or the onset of chills,

may be the only sign of infection in a patient who has a very low white blood cell count. Other signs of infection may include persistent coughing, sore throat, pain during urination, or diarrhea.

Patients with MDS are advised to receive certain vaccinations. For adult patients, these include vaccinations for influenza and pneumococcal pneumonia and the inactivated ("dead") vaccine for the herpes virus, called **Shingrix**. MDS patients should not receive live vaccines, such as Zostavax® (a live shingles vaccine). If a family member or friend of the patient receives a live vaccine, they should not go near the patient for a period of time.

COVID-19 vaccines are also recommended. Talk to your doctor for more information.

Iron Chelation Therapy. Red blood cells contain iron. When a person receives many red blood cell transfusions, too much iron can build up in the heart, liver and other organs, affecting how they work. This condition is called "iron overload."

Iron overload requires special treatment to remove the extra iron from the body. The treatment is called "iron chelation" therapy. Drugs called "chelating agents" bind with the iron so the body can get rid of it. 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 iron chelation therapy include:

- **Deferasirox (Exjade®, Jadenu®).** These iron chelators, taken by mouth, are indicated for the treatment of chronic iron overload due to blood transfusions in patients 2 years of age and older. The newer preparation, Jadenu®, can be easier on digestion in some patients, but it is the same medicine as Exjade®.
- **Deferoxamine mesylate (Desferal®).** This drug is usually given subcutaneously (a slow infusion under the skin) for the treatment of acute iron intoxication and of chronic iron overload due to transfusion-dependent anemias.

Treatment of Lower-Risk MDS. Lower-risk MDS is typically slow-growing, and the risk of progression to acute myeloid leukemia (AML) is low. The primary goals for patients with lower-risk MDS is to improve blood cell counts, reduce the need for blood transfusions, lower the risk of infection and improve quality of life. Patients with lower-risk disease are initially treated for specific complications of the disease such as low blood cell counts.

Lower-risk MDS includes the following prognostic risk groups:

- IPSS: Low and Intermediate-1
- IPSS-R: Very Low, Low, and Intermediate

Patients with low blood cells may need supportive care. Supportive care is treatment to relieve symptoms caused by cancer or cancer treatment and to improve quality of life. For more information on supportive care, see pages 19–22.

Lower-risk patients without symptoms may not need treatment immediately. People with lower-risk MDS may have decreased levels of red blood cells, white blood cells or platelets. If these levels are not low enough to cause symptoms, the doctor may recommend the "watch-and-wait" approach. This approach involves careful monitoring that includes regular exams and blood tests. Bone marrow biopsies may be necessary if the doctor suspects the syndrome is progressing. If there are signs and symptoms that the disease is progressing, the doctor will recommend starting treatment. Some of the most common drugs used in the treatment and supportive care of MDS are listed in **Table 5** on page 24.

Immunosuppressive Therapy. Drugs that suppress certain parts of the immune system can help some patients with lower-risk MDS. In some types of MDS, lymphocytes, a type of white blood cell, may attack the bone marrow, causing it to stop making enough healthy blood cells. Immunosuppressive therapy lowers the body's immune response to allow bone marrow stem cells to grow and make new blood cells.

Antithymocyte globulin (ATG, Atgam®, Thymoglobulin®), cyclosporine (Neoral®, Sandimmune®) and **tacrolimus (Prograf®)** are the main immunosuppressive therapy drugs used to treat MDS. However, these drugs do not work well for all types of MDS. They are most effective when the disease has features 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 taken orally.

Immunomodulators. These are drugs that modify different parts of the immune system and may help the body fight cancer. **Lenalidomide (Revlimid®)** is used to treat MDS with cells that are missing part of chromosome 5, referred to as del(5q). Lenalidomide is approved by the FDA for the treatment of transfusion-dependent anemia due to Low-risk or Intermediate-1 risk MDS associated with a del(5q) abnormality, either with or without additional cytogenetic abnormalities. Treatment with this drug may lessen the need for red blood cell transfusions in certain patients. Lenalidomide is an oral medication. If this treatment is not effective, treatment with hypomethylating agents is another option.

Table 5. Drugs Commonly Used for MDS in Standard Treatments and Clinical Trials

Hypomethylating Agents

- Azacitidine (Vidaza®)
- Decitabine (Dacogen®)
- Decitabine and cedazuridine (Inqovi®)

Immunosuppressive Therapy

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

Immunomodulator

- Lenalidomide (Revlimid®)

High-Intensity Chemotherapy

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

IDH Inhibitors

- Ivosidenib (Tibsovo®)
- Enasidenib (Idhifa®)

BCL2 Inhibitor

- Venetoclax (Venclexta®)

FLT3 Inhibitors

- Gilteritinib (Xospata®)
- Midostaurin (Rydapt®)
- Sorafenib (Nexavar®)

Iron Chelators

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

White Blood Cell Growth Factors

- G-CSF—granulocyte colony-stimulating factors: filgrastim (Neupogen®), pegfilgrastim (Neulasta®)
- GM-CSF—granulocyte-macrophage colony-stimulating factor: sargramostim (Leukine®)

Red Blood Cell Growth Factors

- Epoetin alfa (Procrit®)
- Darbepoetin alfa (Aranesp®)

Platelet Growth Factors

- Romiplostim (Nplate®)
- Eltrombopag (Promacta®)

Erythroid Maturation Agent

- Luspatercept-aamt (Reblozyl®)

Antifibrinolytic Agents

- Aminocaproic acid
- Tranexamic acid

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

Hypomethylating Agents. These drugs are a type of chemotherapy that work by blocking the DNA that helps cancer cells grow. They also help genes that are involved in cell growth work the way they should. Using one of these drugs may help improve blood cell counts, which may lead to fewer blood transfusions and

improve quality of life. They may also slow the progression of MDS. These drugs are, in general, less likely to produce severe side effects.

- **Azacitidine (Vidaza®).** Azacitidine is administered intravenously (IV, into a vein) or subcutaneously (under the skin). It is approved for treatment of both Low- and High-risk patients with MDS.
- **Decitabine (Dacogen®).** 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 MDS patients.
- **Decitabine and cedazuridine (Inqovi®).** This drug combines decitabine with cedazuridine, which helps stop the decitabine from being broken down in the digestive system. This allows the drug to be taken orally (by mouth) as a tablet at home, without having to receive intravenous (IV) therapy at a healthcare facility.

Some lower-risk patients, particularly younger patients, may benefit from allogeneic stem cell transplantation. See pages 27–29 for more information on allogeneic stem cell transplantation.

Higher-Risk MDS. Higher-risk MDS tends to grow quickly and is more likely to progress to acute myeloid leukemia (AML). Patients with higher-risk MDS are more likely to have multiple types of cytopenias (low blood cell counts) and are also more likely to require blood transfusions and treatment for infections.

Treatment goals for high-risk MDS patients include:

- Slowing disease progression and improving survival for patients who are not candidates for stem cell transplantation
- Potentially achieving a cure through stem cell transplantation

Higher-risk MDS includes the following risk groups:

IPSS: Intermediate-2, High

IPSS-R: Intermediate, High, and Very High

Treatment for higher-risk patients depends on whether they are candidates for an allogeneic stem cell transplantation. Regardless of therapy, supportive care should be given to all patients. See pages 19–22 for more information on supportive care.

Not a Candidate for Stem Cell Transplantation. Most higher-risk MDS patients are not eligible for stem cell transplantation. This may be due to many factors including advanced age, other major health problems or unavailability of a stem cell donor. Treatment for those not eligible for stem cell transplantation may include:

Hypomethylating Agents. The major alternative to stem cell transplantation is hypomethylating agents. These drugs are a type of chemotherapy drug that work by blocking the DNA that helps cancer cells grow. They also help genes

involved in cell growth work the way they should. Using one of these drugs may help improve blood cell counts which may lead to fewer blood transfusions and improved quality of life. They may also slow the progression of MDS.

- **Azacitidine (Vidaza®).** Azacitidine is administered intravenously (IV) or subcutaneously (under the skin). It is approved for treatment of both Low- and High-risk patients.
- **Decitabine (Dacogen®).** 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.
- **Decitabine and cedazuridine (Inqovi®).** This drug combines decitabine with cedazuridine, which helps stop the decitabine from being broken down in the digestive system. This allows the drug to be taken by mouth as a tablet at home without having to receive IV therapy at a healthcare facility.

Targeted Therapy. This type of treatment uses drugs or other substances to identify and attack specific types of cancer cells with less harm to normal cells. Not all cancers have the same targets. Each type of targeted therapy works a little bit differently, but they all interfere with the growth and survival of cancer cells. To find the most effective treatment, your doctor may run tests to identify genes, proteins and other factors in your cancer cells. This helps the doctor choose the most effective treatment for you based on the specific factors of your disease.

Some drugs that are not FDA-approved to treat MDS can be used as an "off-label" treatment for patients. "Off-label" prescribing is when a doctor gives a drug that is FDA approved to treat one condition for another condition.

Targeted therapy may be used alone or in combination with chemotherapy. Some types of targeted therapy for MDS include:

- **IDH Inhibitors.** In some people with MDS, the cancer cells have a mutation of the *IDH1* or *IDH2* gene. These mutations cause cells to remain immature and divide and multiply too quickly. For these patients, the following targeted therapy, used as off-label treatment, may be used:
  - **Ivosidenib (Tibsovo®),** taken by mouth, is an IDH1 inhibitor indicated for the treatment of MDS that has an *IDH1* mutation.
  - **Enasidenib (Idhifa®),** taken by mouth, is an IDH2 inhibitor indicated for the treatment of MDS that has an *IDH2* mutation.
- **BCL2 Inhibitors.** Overexpression of the BCL2 protein allows cancer cells to evade "programmed cell death," meaning it helps cancer cells live longer than they should. BCL2 inhibitors target the BCL2 protein. This helps restore what is called apoptosis, a process of natural cell death that is disrupted when you have cancer, restoring the body's natural ability to tell cancer cells to die. Once this process is restored, your body can begin to kill cancer cells. With

fewer cancer cells, there is more room for healthy blood cells to grow in the bone marrow.

- **Venetoclax (Venclexta®)** is an oral medicine taken by mouth each day. Research has shown that venetoclax in combination with hypomethylating agents or targeted IDH1/2 inhibitors may reduce the number of blood cells in the bone marrow for patients with high-risk MDS. This drug binds to the leukemia cells and triggers apoptosis, a process that causes the cancer cells to die. Venetoclax is not FDA-approved to treat MDS, but it is sometimes used as an off-label treatment for patients with MDS.

- **FLT3 Inhibitors.** Some MDS patients have a mutation in the *FLT3* gene that can increase the growth and division of cancer cells. FLT3 inhibitors are drugs that target these gene mutations. For MDS patients with *CBL* mutations, FLT3 inhibitors may also be helpful in treatment. For these patients, **midostaurin (Rydapt®), gilteritinib (Xospata®)** or **sorafenib (Nexavar®)** may be prescribed. These drugs are not FDA-approved to treatment MDS, but they are being studied in clinical trials and are also used as off-label treatments.

Intensive Chemotherapy. For patients eligible for intensive therapy but who do not have a stem cell donor, the same intensive chemotherapy regimens used for the treatment of acute myeloid leukemia (AML) may be used. Because these agents tend to cause more severe side effects, they are generally used for higher-risk MDS that is likely to progress to AML. 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).

Candidate for Allogeneic Stem Cell Transplantation. For patients eligible for stem cell transportation, allogeneic stem cell transplantation remains the only potential cure for MDS. Timing is an important factor influencing allogeneic stem cell transplantation outcomes. In most cases, it is very important to start a donor search as soon as possible after an MDS diagnosis. This is necessary to identify a suitably matched, related or unrelated donor, and to plan for the best time to perform a transplant safely and successfully.

The goal of stem cell transplantation is to cure the patient's cancer with very high doses of chemotherapy. Although administering such high doses of chemotherapy drugs can kill more cancer cells, such high doses of chemotherapy can also severely damage the stem cells in the bone marrow and cause dangerously low blood cell counts. This may result in anemia, serious infections and uncontrolled bleeding. Stem cell transplantation allows doctors to give higher doses of chemotherapy than can typically be given, either with or without radiation therapy.

This is because, after the intensive therapy, the patient receives an infusion of stem cells to replace those destroyed by the intensive therapy. The healthy blood stem cells grow and multiply, forming new bone marrow and blood cells.

Allogeneic stem cell transplantation is a complex treatment that can cause serious, life-threatening side effects. It is important to discuss the benefits and risks of this procedure with your doctor.

After diagnosis, patients receive treatment to reduce the number of blasts in their bone marrow. Treatment may include:

- Azacitidine
- Decitabine
- Decitabine-cedazuridine
- High-intensity chemotherapy

Once patients are ready for an allogeneic stem cell transplant, they receive a "conditioning therapy." This consists of very high doses of chemotherapy, either with or without radiation, to kill the cancer cells remaining in their bodies. It is also given to suppress their own immune systems, so their bodies do not reject the donor stem cells.

After the conditioning therapy, patients receive donor stem cells by IV infusion. A transfusion is a slow injection of blood products put into a patient's bloodstream through a vein. This procedure can take several hours to complete. Allogeneic transplantation uses healthy blood-forming cells from an HLA-matched donor. They can be from a family member or an unrelated person, or from a donated umbilical cord.

The transplanted blood stem cells travel to the bone marrow where they multiply and grow. The donated stem cells restore the bone marrow's ability to form new blood cells.

Ideally, an allogeneic stem cell transplant will generate a new immune system that helps the patient's body fight infections and other diseases. The new immune system also has the potential to recognize and attack any remaining cancer cells in the body. The transplanted immune cells (the graft) perceive the leukemia cells in the body as foreign and destroy them. This is called the "graft-versus-leukemia" effect.

One possible side effect of allogeneic stem cell transplantation is a serious condition called graft versus-host disease (GVHD). This occurs when the transplanted immune cells (the graft) from the donor identify the cells in the recipient's body (the host) as "foreign" and attack them. The parts of the body most commonly damaged by GVHD include the skin, liver, stomach, intestines and eyes. GVHD can develop within weeks after transplantation or much later. A doctor can order medications to help prevent or minimize the complications of GVHD. Most patients need to be closely monitored for GVHD for at least the first 100 days after the transplant.

Compared to other treatment options, allogeneic stem cell transplantation is associated with a higher rate of side effects and mortality. However, it may be considered for patients with higher-risk MDS, based on their cytogenetic and molecular test results and other prognostic factors. The decision to perform an allogeneic transplant also depends on other factors, including the patient's age, physical fitness, comorbidities (other co-existing medical conditions), and social supports (from family members, caregivers, friends), as well as the patient's understanding of the potential benefits and risks.

Reduced-Intensity Allogeneic Stem Cell Transplantation. This type of transplantation may be a treatment option for older patients who cannot tolerate the high doses of chemotherapy used 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. With a reduced-intensity conditioning regimen, the patient's blood counts may not fall as low as they would with high-dose chemotherapy. Additionally, the less toxic regimens put less strain on the patient's organs, making this regimen safer and more tolerable.

The success of reduced-intensity transplantation depends on the graft-versus-leukemia effect of the donor stem cells, rather than on high-dose treatments to kill the cancer cells. This therapy reduces the number of cancer cells, but it does not completely destroy the patient's bone marrow. The goal is to have the donor stem cells become established in the patient's bone marrow and produce white blood cells that will attack the patient's remaining cancer cells. As with standard allogeneic stem cell transplantation, the risk of graft-versus-host disease (GVHD is an important consideration and a potentially disabling side effect.

Please visit 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.

MDS in Children

While MDS typically develops in older adults, it can occur at any age. Pediatric (childhood) MDS is a rare disease, occurring in approximately 1 to 4 cases per million children (patients aged 18 years or younger) each year.

Many cases of pediatric MDS are due to inherited genetic mutations called "germline" mutations. Less common in adult MDS, germline mutations can be inherited from parents or can develop before birth and are found in every cell of the body (not just in the blood cells). Knowing if a genetic mutation is germline can make a difference in your child's prognosis and treatment. It may affect the types of medication your child receives, and may also affect which family members are eligible to be stem cell donors.

There are two types of pediatric MDS:

- Refractory cytopenia of childhood (RCC). This type of MDS is characterized by:
  - Dysplasia (abnormal growth or development) in one or more cell lines
  - Less than 2 percent of blasts in the blood
  - Less than 5 percent of blasts in the bone marrow
- MDS with Excess Blasts (MDS-EB). This type of MDS is characterized by:
  - Dysplasia found in one or more blood cell lines
  - More than 2 percent blasts in the blood
  - Elevated bone marrow blasts (between 5 and 9 percent)

Treatment for most types of pediatric MDS is allogeneic stem cell transplantation. This is a procedure in which a patient receives healthy bone marrow a related or unrelated donor. (See pages 27–29 for more information on allogeneic stem cell transplantation). An inherited genetic mutation can affect patients who need an allogeneic stem cell transplantation. Often a sibling or another family member serves as the patient's stem cell donor. If a patient has a hereditary genetic predisposition, all potential family member donors need to be tested for the genetic disorder before donating.

Most children with cancer receive treatment at hospitals that specialize in treating children with cancer. The doctors and other healthcare providers at these centers have special training and expertise in giving comprehensive care to children. These centers are often members of the Children's Oncology Group (COG). This is the world's largest organization devoted to clinical research to improve the care and treatment of children with cancer.

MDS is in children is rare. Going to a specialized children's cancer hospital helps ensure that your child will get the best available treatment. You can ask your child's pediatrician or your family doctor for a referral, or you can call an LLS Information Specialist at (800) 955-4572 to find hospitals that specialize in treating children with MDS.

Clinical Trials for Blood Cancers

Every new cancer drug goes through a series of carefully controlled research studies before it can become part of standard cancer care. These research studies are called clinical trials and they are used to find better ways to care for and treat people with cancer.

In the United States, the FDA (U.S. Food and Drug Administration) requires that all new drugs and other treatments be tested in clinical trials before they can be used. At any given time, there are thousands of cancer clinical trials taking place. Doctors and researchers are always looking for new and better ways to treat cancer.

Researchers use cancer clinical trials to study new ways to:

- Treat cancer using
  - A new drug
  - An approved drug to treat a different kind of cancer
  - A new combination of drugs
  - A new way of giving a drug—by mouth (pill), intravenously (IV)
- Manage cancer symptoms and ease treatment side effects
- Find and diagnose cancer
- Keep cancer from coming back after treatment
- Manage long-term side effects

By taking part in a clinical trial, patients can see doctors who are experts in their disease, gain access to new, cutting-edge therapies, and provide helpful information for future patients. The treatments and information we have today are due in large part to patients being willing to join clinical trials. Anyone interested in being part of a clinical trial should talk to their hematologist-oncologist about whether a clinical trial might be right for them. During this conversation it may help to:

- Have a list of questions to ask about the risks and benefits of each trial (visit www.LLS.org/WhatToAsk for lists of suggested questions).
- Ask a family member or friend to go with you to your doctor visit—both for support and to take notes.

Clinical trials can be difficult to navigate and figure out, but The Leukemia & Lymphoma Society is here to help. Patients and caregivers can work with **Clinical Trial Nurse Navigators** who will help find potential clinical trials, overcome barriers to enrollment and provide support throughout the entire clinical trial process. Our Clinical Trial Nurse Navigators are registered nurses who are experts in blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about your treatment goals
- Help you to understand the clinical-trial process, including your rights as a patient
- Ask you for details about your diagnosis (like past treatments, treatment responses, and your cancer genetic profile), your current health, and your medical history—because these may affect whether you can take part in certain clinical trials
- Help you understand how your finances, insurance coverage, support network, and ability and willingness to travel may affect your choice of clinical trials
- Guide you and help you in your efforts to find and enroll in a clinical trial, including connecting you with trial sites
- Help deal with any problems you might have as you enroll in a trial
- Support you throughout the clinical trial process

Please call an LLS Information Specialist at (800) 955-4572 or visit www.LLS.org/CTSC for more information about clinical trials and the Clinical Trial Support Center at LLS.

Also, visit www.LLS.org/booklets to view *Understanding Clinical Trials for Blood Cancers.*

Related Diseases

Myelodysplastic Syndromes/Myeloproliferative Neoplasms (MDS/MPN) Classification. These blood cancers have features of both myelodysplastic syndromes (MDS) and myeloproliferative neoplasms (MPNs). These disorders have bone marrow cells that are dysplastic (abnormal in shape and size) and proliferative (abnormally multiplying or increasing). See **Table 6** below for a list of subtypes of MDS/MPNs.

Table 6. 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**

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

Treatments vary based on the type of MDS/MPN. Options range from "watch-and-wait" to chemotherapy to stem cell transplantation. Since MDS/MPNs are rare, patients should seek treatment at a cancer center that has experience treating patients with these diseases.

Please visit www.LLS.org/booklets to view the free LLS publications *Chronic Myelomonocytic Leukemia (CMML) and Juvenile Myelomonocytic Leukemia (JMML) Facts* and *Myeloproliferative Neoplasms.*

Follow-up Care

Follow-up care for MDS varies from patient to patient. Patients with MDS require regular follow-up visits with their hematologist-oncologist that will include blood tests to detect worsening cytopenias (low blood cell counts). Bone marrow biopsies are done if there are worsening cytopenias or the appearance of blast cells in the blood. The frequency of these follow-up visits depends on the disease risk and choice of treatment.

Those who have been treated for MDS are encouraged to:

- Maintain regular follow-up appointments with their hematologist-oncologist. The doctor will monitor them for signs of relapse and detect any side effects from treatment. A follow-up visit may also discover the onset of any other medical problems.
- Keep a record of your cancer diagnosis, treatments, and follow-up care needs. This is often called a "survivorship care plan." Ask your doctor for a written survivorship care plan. Share this information with any new healthcare providers you see. The plan should include the following information:
  - List of all healthcare providers
  - Diagnosis summary with specifics such as subtype and/or genetic markers
  - Treatment summary with specifics such as the names, dates, and dosages of chemotherapy or other drugs, site of radiation treatment, surgery and/or transplantation information, response to treatment, and side effects
  - Maintenance treatment information, if applicable
  - List of possible late effects
  - Schedule for ongoing monitoring with recommended tests, frequency and coordinating provider
  - Health and wellness recommendations such as nutrition, exercise or other disease screenings
- Seek medical and psychosocial support for fatigue, depression and other long-term effects, if needed.
- Consider cancer risk-reduction strategies, such as smoking cessation, skin protection against prolonged sun exposure, healthy eating and exercising.

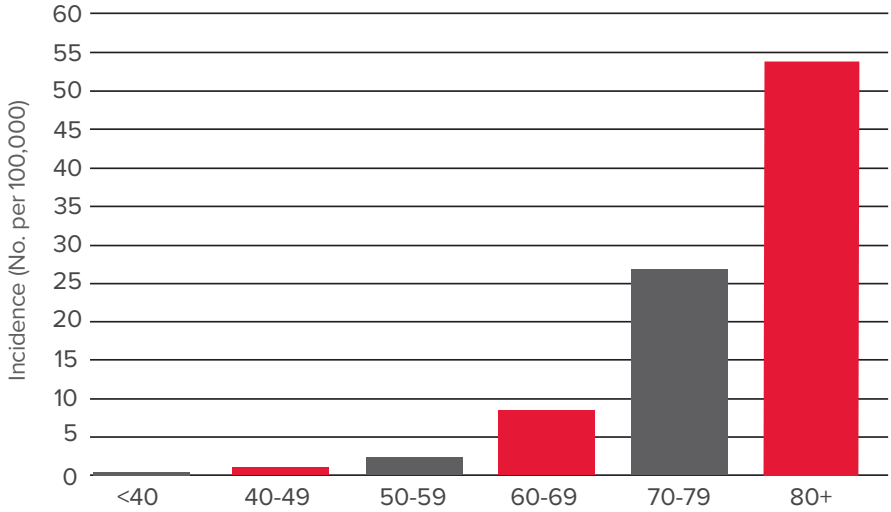
Please visit LLS.org/SurvivorshipWorkbook to view the free LLS survivorship publications *Navigating Life During and After a Blood Cancer Diagnosis* with versions for Adults, Young Adults and Children and Adolescents.

Incidence, Causes and Risk Factors

Incidence. An average of 15,099 new cases of MDS were diagnosed in the United States each year from 2013 to 2017. In the United States, the overall incidence rate of MDS is 4.3 cases per 100,000 population. This rate rises with age to approximately 26.3 cases per 100,000 individuals per year among patients age 70–79 years and to about 54.2 cases per 100,000 people in those who are age 80 years and older. See **Figure 3** on page 34. MDS is rare among children, adolescents and young adults. The disease affects more men than women.

Causes and Risk Factors. Although in most cases it is not clear what causes the genetic changes that lead to MDS, there are some known risk factors. A "risk factor" is anything that increases a person's chance of developing a disease.

Figure 3. Myelodysplastic Syndromes (MDS) Age-Adjusted Incidence Rates, 2013-2017



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 2013 to 2017, per 100,000 people.

Source: *SEER (Surveillance, Epidemiology and End Results) Cancer Statistics Review, 1975-2017.* National Cancer Institute; 2020.

However, having a risk factor does not mean that a person will develop the disease. Some people with several risk factors never develop the disease, while others with no known risk factors may develop the disease. There is no way to prevent MDS, and you cannot catch MDS from someone else.

The factors that are associated with an increased risk of developing MDS include:

- Age. The risk of developing MDS increases with age. While MDS can occur at any age, it typically affects older adults.
- Sex. Males are more likely than females to develop MDS.
- Genetic disorders. Certain genetic conditions present at birth seem to increase the risk of MDS, including:
  - Down syndrome
  - Neurofibromatosis type 1
  - Bloom syndrome
  - Trisomy 8
  - Fanconi anemia
  - Klinefelter syndrome
  - Wiskott-Aldrich syndrome
  - Kostmann syndrome
  - Shwachman-Diamond syndrome

- Familial risk/germline predisposition. Certain gene mutations present at birth may increase the risk of developing MDS.
- Previous cancer treatment. People who have received chemotherapy (especially with alkylating agents and purine analogues) or radiation therapy have an increased risk of developing MDS. This is referred to as "secondary MDS" or "treatment-related MDS."
- Smoking. MDS is linked to smoking and exposure to tobacco smoke, which contains benzene and other cancer-causing substances.
- Workplace exposure. Long-term workplace exposure to benzene can increase the risk of developing MDS. More cases of MDS are reported among agricultural and industrial workers.

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, the most common blood protein
  - Blood-clotting proteins (coagulation factors) made by the liver
  - Erythropoietin, a protein made by the kidneys that stimulates red blood cell production
  - Immunoglobulins, proteins that help the body fight infection
- Hormones, such as thyroid hormone 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. 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 4** on page 36. The blood cells are suspended in the plasma.

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

1. Red blood cells (the cells that carry oxygen)
   - These make up a little less than half of the body's total blood volume.

- They 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_2) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the CO_2 is removed from the lungs.

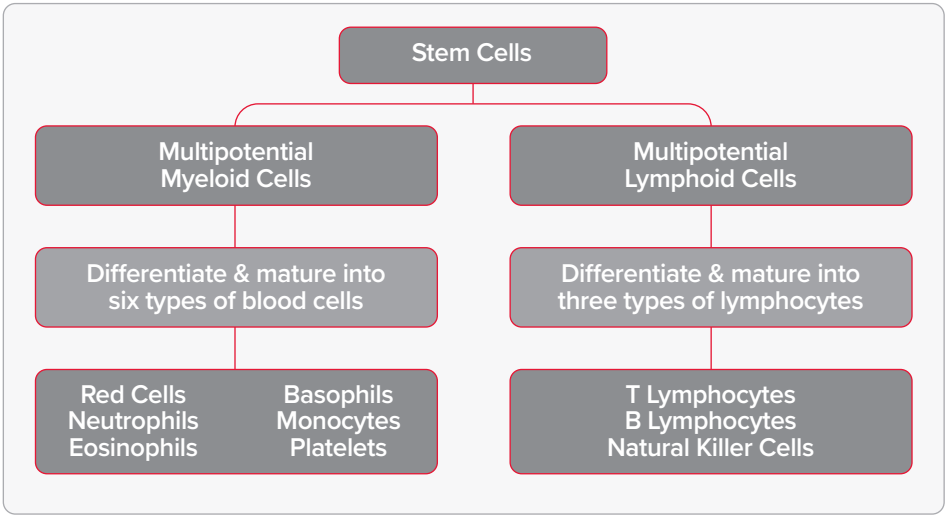
2. Platelets (cells that help blood clot)

- These are small cells (one-tenth the size of red blood cells).
- They help stop bleeding from an injury or cut.
- They 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 (or WBCs, the cells that fight infections), including:

- Neutrophils and monocytes. These are cells called "phagocytes" 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 the 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 cells (NK cells)

Figure 4. Blood Cell & Lymphocyte Development



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 used for transplants. Some stem cells enter the bloodstream and circulate. Doctors know how to stimulate the growth of these cells in the marrow and make 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 for 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 your healthcare team.

For Help and Information

Consult with an Information Specialist. Information Specialists are highly trained oncology social workers, nurses and health educators. They offer up-to-date information about disease, treatment and support. Language services are available. For more information, please:

- Call: (800) 955-4572 (Monday through Friday, 9 a.m. to 9 p.m. ET)
- Email and Live chat: www.LLS.org/InformationSpecialists

Clinical Trials (Research Studies). Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. 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 for more information.

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 for more information.

Free Information Booklets. LLS offers free education and support booklets that can either be read online or ordered. Please visit 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 for more information.

Financial Assistance. LLS offers financial support, including insurance premium and medication co-pay assistance, to eligible individuals with blood cancer. For more information, please:

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

LLS Health Manager™ App. This free mobile app helps you manage your health by tracking side effects, medication, food and hydration, questions for your doctor, and more. Export the information you've tracked in a calendar format and share it with your doctor. You can also set up reminders to take medications, hydrate, and eat. Please visit www.LLS.org/HealthManager to download for free.

LLS Coloring for Kids™. This free coloring app allows children (and adults) to express their creativity and offers activities to help them learn about blood cancer and its treatment. The app includes blank canvases, general coloring pages and pages from LLS coloring books. This app can be used anywhere and may help pass time in waiting rooms or during treatment. Visit www.LLS.org/ColoringApp to learn more and download.

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 healthcare professionals discuss diagnosis, treatment options, quality-of-life concerns, treatment side effects, doctor-patient communication and other important survivorship topics. Visit 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. Visit www.LLS.org/SuggestedReading to find out more.

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. Visit www.LLS.org/community to join.

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

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), local support groups and other great resources. For more information about these programs or to contact your chapter, please:

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

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

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). Please visit 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. For more information, please

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

World Trade Center Survivors. People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be able to get 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 and those who lived, worked or were in school in that 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: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov and enter “depression” in the search box

Health Terms

Absolute Neutrophil Count (ANC). The measure of the number of neutrophils in the blood. Neutrophils are a type of white blood cells that help the body fight infection. The lower a person's absolute neutrophil count is, the higher the risk of getting an infection.

Acute Myeloid Leukemia (AML). An aggressive, fast-growing type of blood cancer in which there are too many immature white blood cells in the blood and bone marrow. **See the free LLS book, *Acute Myeloid Leukemia in Adults.***

Allogeneic Stem Cell Transplantation. A treatment that uses stem cells from a healthy donor to restore a patient's bone marrow that is damaged or diseased after receiving high doses of chemotherapy and/or radiation therapy. **See the free LLS booklet, *Blood and Marrow Stem Cell Transplantation.***

Anemia. A condition in which the number of red blood cells is below normal. This results in reduced oxygen flow to the body's organs. Severe anemia can cause a pale complexion, weakness, fatigue, dizziness and shortness of breath.

Antigen. A substance that creates an immune response in the body, especially the production of antibodies. Examples of antigens include allergens, chemicals, bacteria, viruses and other substances that come from outside the body. Cells in the body, including cancer cells, also have antigens on their surfaces that can cause an immune response.

Basophil. A type of white blood cell that is involved in certain allergic reactions.

Blast Cell. An immature blood cell. In healthy people, blast cells make up no more than 5 percent of the cells in the bone marrow and are not typically found in the blood.

Blood Cells. There are three major types of blood cells: 1) red blood cells that carry oxygen; 2) white blood cells that fight infections; and 3) platelets that help stop bleeding.

Bone Marrow. A spongy tissue in the hollow central cavity of the bones where blood cells are made.

Bone Marrow Aspiration. A procedure in which a liquid sample of bone marrow is removed for examination by a pathologist. The sample is usually taken from the patient's hip bone using a special needle, after a medication is given to numb the area. Bone marrow aspiration and bone marrow biopsy can be done in a doctor's office or in a hospital and are usually done at the same visit.

Bone Marrow Biopsy. A procedure in which a sample of bone containing bone marrow is removed for examination by a pathologist. The sample is usually taken from the hip bone, using a special hollow needle, after medication is given to numb the skin and tissue in that area. Bone marrow aspiration and bone marrow biopsy can be done in a doctor's office or in a hospital and are usually done at the same visit.

CBC. See Complete Blood Cell Count.

Chemotherapy. Treatment that stops the growth of cancer cells, either by killing them or stopping them from dividing.

Chromosome. Threadlike structures within cells that carry genes in a linear order. Human cells have 23 pairs of chromosomes. **See the free LLS book *Understanding Genetics.***

Chronic Myelomonocytic Leukemia. A type of myelodysplastic/myeloproliferative blood cancer in which there are too many myelomonocytes (a type of white blood cell) in the bone marrow. **See the free LLS booklet *Chronic Myelomonocytic Leukemia (CMML) and Juvenile Myelomonocytic Leukemia (JMML) Facts.***

Colony-Stimulating Factor. See Growth Factor.

Comorbidity. Having two or more diseases at the same time.

Complete Blood Count. A laboratory test that measures the number of red blood cells, white blood cells and platelets in the blood. It also measures the amount of hemoglobin (the substance in the blood that carries oxygen) and the hematocrit (the amount of whole blood that is made up of red blood cells).

Cytogenetic Analysis. The process of analyzing the number and size of chromosomes in cells. It detects chromosome alterations and, in some cases, may identify the actual genes that have been affected. These findings help doctors diagnose specific types of blood cancer, determine which treatment approaches to use and monitor a patient's response to treatment.

Cytopenia. A condition in which the number of blood cells is lower than normal.

Deletion (del). In genetics, "deletion" refers to a type of mutation involving the loss of genetic material.

DNA. Abbreviation for deoxyribonucleic acid, the molecules inside cells that carry genetic information. 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 type of white blood cell that is released during infections and allergic reactions.

Erythrocyte. See Red Blood Cell.

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 in response to decreased blood oxygen levels. Drugs with synthetic EPO, called erythropoietin-stimulating agents (ESAs), are available to help the body produce red blood cells.

FDA. The abbreviation used to refer to the United States Food and Drug Administration. The FDA is responsible for assuring the safety, effectiveness and security of drugs, medical devices and the nation's food supply.

Fluorescence In Situ Hybridization (FISH). A test for finding abnormal chromosomes in cells and tissues. Pieces of DNA that contain fluorescent molecules are added to cells or tissues on a slide. When the pieces of DNA bind to certain genes or chromosomes, they light up when viewed under a specialized "fluorescence" microscope. This test can help diagnose some types of cancer, and results can help doctors plan treatment and monitor its effectiveness.

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

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

Graft-Versus-Host Disease (GVHD). A disease that occurs when stem cells transplanted from a donor (the graft) attack the healthy tissues of the transplant recipient (the host). Most often, GVHD affects a patient's skin, liver, stomach and gastrointestinal tract. **See the free LLS booklet *Graft-Versus-Host Disease.***

Graft-Versus-Leukemia (GVL) Effect. When transplanted blood stem cells from a donor (the graft) perceive leukemia cells in the patient's body as foreign and attack them.

Granulocyte. A type of white blood cell that has many particles (granules). Neutrophils, eosinophils and basophils are types of granulocytes.

Growth Factor. A substance that causes new blood cells to grow in the bone marrow.

Hematologist. A doctor who specializes in treating blood diseases.

Hematopathologist. A doctor who has special training in identifying blood diseases by examining blood, bone marrow, lymph and other tissue samples under a microscope and performing tests to determine if the blood cells are normal or not.

Hematopoietic Stem Cell. An immature cell that can develop into any type of blood cell, including red blood cells, white blood cells or platelets. Also called "blood stem cell."

Hemoglobin. A protein inside red blood cells that carries oxygen throughout the body.

HLA. A type of protein on cells that helps the body distinguish its own cells from foreign cells. HLA factors are inherited from a person's mother and father. HLAs make up a person's tissue type, which varies from person to person, and they are a critically important factor in allogeneic (donor) stem cell transplantation. Before transplantation takes place, tissue typing is performed to determine if the donor and recipient are compatible.

Inversion. A genetic abnormality that occurs when a section of a chromosome breaks off, turns upside down and then reattaches. As a result, the genetic material is inverted and is now in a different order. **See the free LLS book *Understanding Genetics.***

Iron Chelation Therapy. Treatment to remove excess iron from the body.

Karyotype. An organized profile of a person's chromosomes. It shows the size, shape and number of chromosomes in a sample of cells.

Leukocyte. See White Blood Cell.

Macrophage. A type of white blood cell that surrounds and kills micro-organisms, eats dead cells and helps lymphocytes with their immune system functions.

Monocyte/Macrophage. A type of white blood cell that forms in the bone marrow. Some monocytes travel through the blood to tissues in the body, where they become macrophages. Macrophages can combat infection in the body's tissues, ingest dead cells and assist lymphocytes in immune functions.

Mutation. A change in the DNA sequence of a cell. A mutation may be caused by an error in cell division or by contact with DNA-damaging substances in the environment.

Neutropenia. A condition in which the number of neutrophils, a type of white blood cell, is below normal. People with low neutrophil counts are susceptible to infections.

Neutrophil. A type of white blood cell, and the principal type of phagocyte (microbe-eating cell), in the blood. It is the main kind of cell that combats infection. People with some forms of blood cancer, or those who have received treatment such as chemotherapy for cancer, often have low neutrophil counts. People with low neutrophil counts are very susceptible to infection and may be advised to take antibiotics daily to prevent potentially life-threatening infections.

Next-Generation Sequencing. This refers to a number of different gene sequencing technologies that can rapidly examine stretches of DNA or RNA.

Off-Label. The legal use of a prescription drug to treat a disease for which the drug has not been approved by the FDA.

Oncologist. A doctor who has special training in diagnosing and treating cancer.

Peripheral Blood. The blood that circulates throughout the body.

Peripheral Blood Smear. A procedure in which a sample of blood cells is stained (dyed) and examined under a microscope to check for unusual changes in the size, shape and appearance of various types of blood cells and also for the presence of blast cells in the blood.

Petechiae. Pinhead-sized red or purple spots under the skin caused by bleeding. Petechiae may be a sign of a low platelet count.

Phagocyte. A type of white blood cell that protects the body from infection by eating and killing microorganisms, such as bacteria and fungi. Neutrophils and monocytes are the two main types of phagocytes. Once an infection occurs, phagocytes enter the infected tissue from the bloodstream.

Plasma. The liquid portion of the blood, in which blood cells, platelets, proteins and various other blood components are suspended. Also called "blood plasma."

Platelet. A small, colorless piece of a cell that helps control bleeding. Platelets are produced from large cells in the bone marrow, called "megakaryocytes." Platelets travel to and then collect at the site of a wound. The platelets' sticky surface helps them form clots at the site of a wound and stop bleeding. Also called "thrombocyte."

Prognosis. The probable outcome or expected course of a disease; the likelihood of recovery or recurrence of the disease.

Prognostic Scoring System. A method doctors use to rate the severity of MDS and to classify it into groups based on the likely outcome (prognosis).

Red Blood Cell. A type of blood cell that contains a protein called "hemoglobin," which carries oxygen from the lungs to the tissues of the body. Red blood cells make up about 40 to 45 percent of blood volume in healthy people. Also called "erythrocyte."

Reduced-Intensity (Nonmyeloablative) Allogeneic Stem Cell Transplantation. A type of allogeneic stem cell transplantation in which patients receive lower doses of chemotherapy drugs and/or radiation in preparation for the transplant. The chemotherapy and radiation do not completely kill all the leukemia cells, but the new immune cells that the patient receives in the transplant may attack the leukemia cells. This protocol may be safer than a traditional high-dose conditioning or "myeloablative" allogeneic stem cell transplant, especially for older patients. **See the free LLS book, *Blood and Marrow Stem Cell Transplantation.***

Refractory Anemia. In the French-American-British (FAB) classification, a myelodysplastic syndrome (MDS) with these characteristics: anemia (low red blood cell count); a high number of abnormal, immature red blood cells in the bone marrow; less than 5 percent of blasts in the bone marrow; and no blasts in the blood.

Refractory Anemia with Excess Blasts (RAEB). In the French-American-British (FAB) classification, a myelodysplastic syndrome (MDS) with these characteristics: one or more low blood cell counts; and excess blasts in the bone marrow and blood.

Refractory Anemia With Excess Blasts in Transformation (RAEB-T). In the French-American-British (FAB) classification, RAEB-T is a myelodysplastic syndrome (MDS) in which the bone marrow blast volume ranges from 20 to 30 percent.

Refractory Anemia With Ring Sideroblasts (RARS). In the French-American-British (FAB) classification, a myelodysplastic syndrome (MDS) 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.

Remission. When signs of a disease disappear, usually following treatment.

Risk Factor. A scientifically established factor that increases a person's chance of getting a disease. Risk factors can be classified as either genetic (inherited), lifestyle-related or environmental.

Stem Cell. A cell from which other types of cells develop. In the bone marrow, blood-forming stem cells mature into red blood cells, white blood cells and platelets. Stem cells can be collected, preserved and used for stem cell therapy.

Stem Cell Transplantation. See Allogeneic Stem Cell Transplantation; Reduced-Intensity (Nonmyeloablative) Allogeneic Stem Cell Transplantation.

Supportive Care. Care given to improve the quality of life of patients who have a serious disease. The goal of supportive care is to prevent or treat the symptoms of disease and side effects caused by treatment.

Thrombocytopenia. A condition in which the number of platelets in the blood is below normal.

Transfusion. A procedure in which whole blood or parts of blood are slowly injected into a patient's bloodstream through a vein.

White Blood Cell. A type of blood cell that is part of the body's immune system. The five major types of white blood cells are neutrophils, eosinophils, basophils, monocytes, and lymphocytes. Also called "leukocyte."

World Health Organization (WHO). An agency of the United Nations that deals with major health issues around the world. The WHO sets standards for healthcare and medicines and publishes scientific papers and reports.

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NOTES

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PS22 15M 4/22