

Building Blocks of Hope[®]

Strategies for Patients & Caregivers **LIVING** with MDS

by Sandra Kurtin

A global MDS Foundation print and online patient advocacy initiative, providing a personalized educational program for the patient and caregiver to prepare, participate, and *LIVE* with MDS.



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You or someone you know has been diagnosed with MDS. Hearing the words Myelodysplastic Syndrome or MDS can be frightening. The diagnosis of MDS is often unexpected and filled with both immediate and long-term challenges. You probably have many questions. We are pleased that you have requested a copy of the Building Blocks of Hope booklet. It is designed to help you get you the information that you are looking for and take an active part in your MDS journey.

We would like to offer some tips for assembling and personalizing your Building Blocks of Hope binder.

- A 1½-inch three-ring binder with front and back sleeves is suggested.
- Slip the cover page into the front sleeve of the binder.
- Slip the page which describes the meaning of the Building Blocks of Hope in the back sleeve.
- This will create a colorful cover for your personalized copy of the booklet.

The remaining content can now be placed inside the binder. There are six tabs, or chapters, each with an index and pages that follow the tab:

- **Tab 1—Understanding MDS:** A complete description of the disease process of MDS and answers to common questions.
- **Tab 2—Seeking Treatment:** The treatment of MDS can vary based on the type of MDS you have and how severe it is. This section will provide details about the various approaches to treatment.
- **Tab 3—Quick Tips:** The quick tips offered in this section include guidelines for monitoring and managing your symptoms.
- **Tab 4—Iron Overload:** Iron overload is a possible outcome of receiving repeated red blood cell transfusions. This section answers common questions, including how iron overload can be treated.
- **Tab 5—My MDS Plan:** Understanding the diagnosis of MDS will help you and your caregiver take an active part in your individual treatment plan. My MDS plan provides several tools to allow you to track and manage your journey. You may want to make extra copies of some of these tools before writing on them so that you can continue to track your progress.
- **Tab 6—The MDS Foundation:** The MDS Foundation is an international publicly supported organization dedicated to serving the MDS patient, their caregivers, and the professionals that are working to improve the lives of patients living with MDS. The MDS Foundation provides a number of resources which support the Building Blocks of Hope program.

There are several components to the Building Blocks of Hope program. You have received the printed version. These printed materials, along with digital materials, videos, brief educational slide sets, links to online resources, and a number of very practical tools, can be accessed online on the MDS Foundation website www.mds-foundation.org. You can also view the complete handbook in a beautiful page-turning format at <http://buildingblocksofhope.com>. This includes a search feature and thumbnail views that will help you quickly find the information that you are looking for, and is a great way to share information with others. This is a continuously updated document. You can visit the MDS Foundation website or contact the MDS Foundation directly to learn more and check for any new information. (contact information below)

Allow yourself time to adjust to the diagnosis of MDS. Take time to explore the Building Blocks of Hope. We wish you the best in your journey, and hope that the Building Blocks of Hope program will provide you and your caregivers with tools and strategies for LIVING with MDS.

The MDS Foundation

800-MDS-0839 (*within US only*)

609-298-1035 (*outside US*)

609-298-0590 fax

website: www.mds-foundation.org

email: patientliaison@mds-foundation.org

UNDERSTANDING MDS


The Myelodysplastic Syndromes (MDS) are a group of bone marrow failure disorders. There are several types of MDS. Each type of MDS has a variable onset, prognosis, treatment options, and risk of developing leukemia. Understanding MDS, the first chapter in the Building Blocks of Hope, provides a description of what happens to the normal bone marrow when MDS develops and what symptoms you may have as a result. Details about how MDS is diagnosed, and how the type is determined are included. Understanding your MDS diagnosis will help you and your caregiver take an active part in your individual treatment plan.

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What Is MDS? Is MDS Cancer?

What is MDS?

Definition: The Myelodysplastic Syndromes (MDS) are a group of bone marrow failure disorders. Various subtypes of the disease exist with variable onsets, prognoses, treatment options, and risks of developing leukemia.

What happens?

The bone marrow is the factory for the production of blood cells including red blood cells, white blood cells, and platelets. Bone marrow is a very complicated organ with many working parts and processes (see: *What does bone marrow do?*).

Bone marrow changes in MDS

In MDS, the bone marrow does not make blood cells normally due to a number of potential problems including:

Dysplasia: abnormal shape and appearance (morphology) of a cell

Chromosome changes: Also known as cytogenetic abnormalities

Changes in the bone marrow support system also known as the **microenvironment**

Molecular changes in the cells or the microenvironment

The result is too few cells or low blood counts (cytopenias) and cells that do not function properly.

The most common cytopenias include:

Anemia: low red blood cells (oxygen carrying cells)

Thrombocytopenia: low platelets (cells that help to clot the blood)

Leukopenia: low white blood cells (WBC) (help to fight infection)

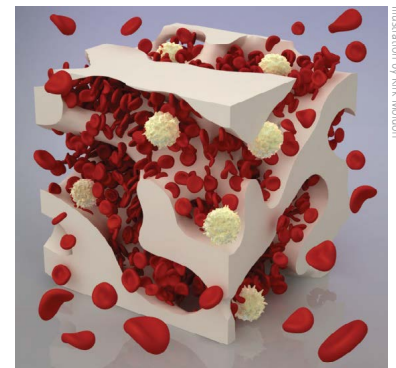
Neutropenia: low neutrophils (most important type of WBC for fighting infection)

Is MDS cancer?

The diagnosis of MDS requires a bone marrow biopsy and aspirate (see: *Bone Marrow Biopsy and Aspirate*). The specimen is analyzed by pathologists specializing in blood disorders (hematopathologist).

The diagnosis of MDS requires specific malignant features such as dysplasia or cytogenetic abnormalities. More recent research has identified molecular abnormalities thought to play a role in the development of MDS. Given the underlying malignant features required for the diagnosis of MDS, it is considered a form of blood cancer.

Failure of the bone marrow to produce mature healthy cells is a gradual process, and therefore MDS is not necessarily a terminal disease. Some patients do succumb to the direct effects of the disease due to bone marrow failure and cytopenias. In addition, for roughly 30% of the patients diagnosed with MDS, this type of bone marrow failure syndrome will progress to acute myeloid leukemia (AML).



normal bone marrow



Abnormal bone marrow with dysplastic blood cells and abnormal chromosomes

What is MDS?



References:

- Bejar, R., Levine, R., & Ebert, B.L. (2011) *Unraveling the molecular pathophysiology of Myelodysplastic Syndromes*. *Journal of Clinical Oncology*, 29, 504–515
- Kurtin, S.E., Demakos, E., Hayden, J., & Boglione, C. (2012) *Initial treatment of Myelodysplastic Syndromes: Practical tools and effective management*. *Clinical Journal of Oncology Nursing*, 16 (3, Suppl.1), 23–35

The cause of MDS is unknown in more than 80% of diagnosed patients. What do we know about trends in patients diagnosed with MDS?

- 1. It is more common in men (male to female ratio is 4.5:2 per 100,000).**
 - a. As with many types of cancer, older age is a predisposing factor. The average age of patients with MDS is 73, and 86% of patients with MDS are older than age 60.
- 2. Exposure to chemicals and other toxins are known to increase the risk of developing MDS**
 - a. Chronic and high exposure to benzene, other solvents, insecticides or herbicides. Whereas in the past, over 25 years ago, reports of benzene induced MDS/AML in the petrochemical industry were reported no such series have been published in the recent literature.
 - b. There are no known foods that cause MDS.
 - c. While alcohol consumed on a daily basis may lower red blood cell and platelet counts, alcohol is not known to cause MDS.
 - d. Tobacco smoke/use has been linked to the development of MDS. One of the primary components of tobacco is benzene. Benzene is highly regulated by federal agencies. There are published guidelines for exposure limits.
- 3. Patients who receive certain types of chemotherapy or radiation treatment for other cancers may be at increased risk of developing treatment-related MDS.**
 - a. Patients who take chemotherapy drugs or who receive radiation therapy for potentially curable cancers, such as breast or testicular cancers, Hodgkin's disease and non-Hodgkin's lymphoma, are at risk of developing MDS for up to 10 years following treatment. MDS that develops after use of cancer chemotherapy or radiation is called "secondary MDS" and is usually associated with multiple chromosome abnormalities in cells in the bone marrow. This type of MDS often is more difficult to treat and more often develops into AML.

Is MDS hereditary? Can I give MDS to my loved ones?

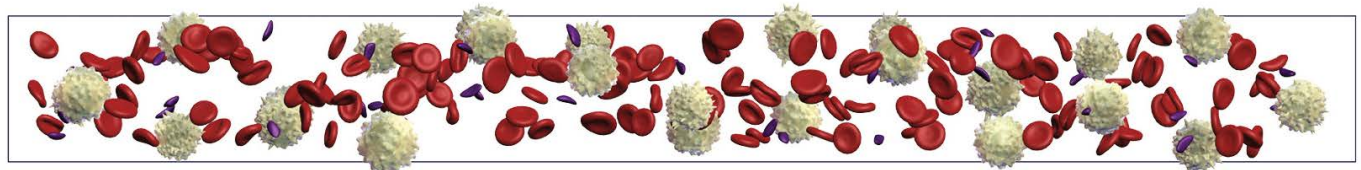
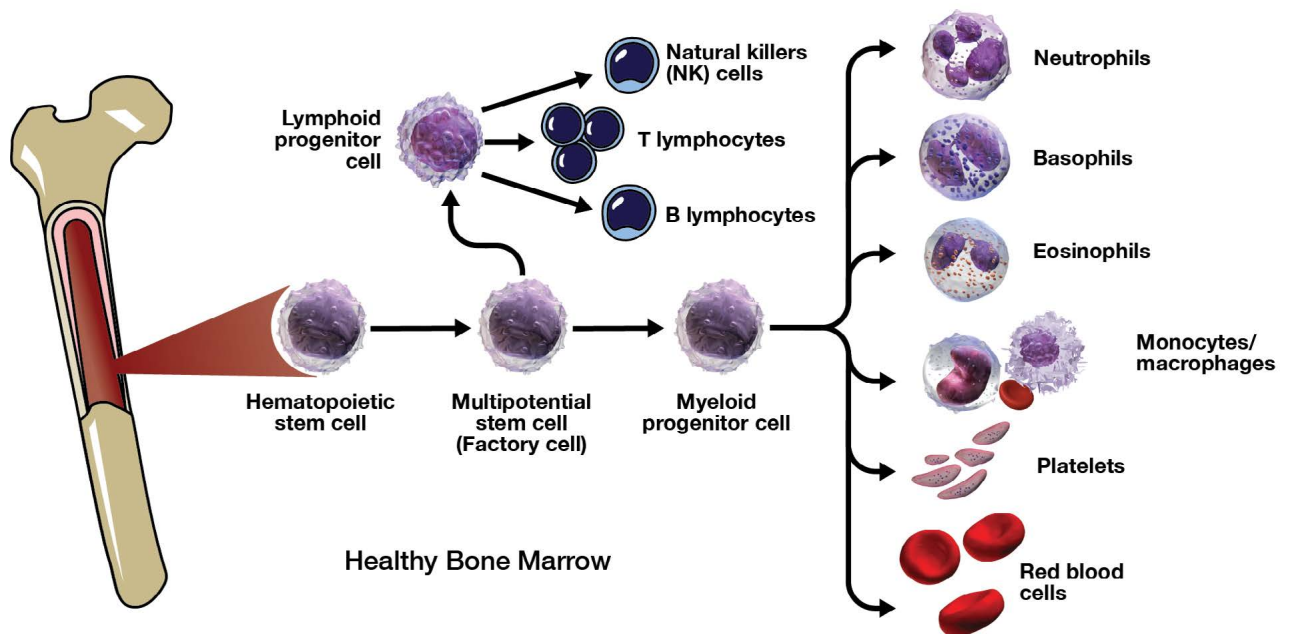
1. Inherited genetic predisposition for developing MDS and congenital abnormalities are rare. Therefore, the chance of passing MDS to children or grandchildren is extremely rare.
2. MDS is not contagious. Patients and their families often worry that MDS might be contagious. No evidence exists to suggest that a virus causes MDS; thus, MDS cannot be transmitted to loved ones.

References:

- Sekeres, M. (2011) *Epidemiology, Natural History, and Practice Patterns of Patients with Myelodysplastic Syndromes in 2010*, JNCCN, 9, 57-63
- Kurtin, S. 2011- JAdPro.

What does bone marrow do?

- All blood cells begin as hematopoietic (*hee-muh-toh-poi-et-ik*) stem cells. These cells are often referred to as factory cells. In healthy persons, hematopoietic stem cells (the factory cells) develop and mature (differentiate) in the bone marrow to form the different blood cells.
- In the initial stage, the hematopoietic stem cell differentiates to form a multipotent stem cell. These cells have the ability to form new blood cells.
- The multipotent stem cell further differentiates to form a lymphoid progenitor cell or a myeloid progenitor cell (progenitor cells).
- The myeloid progenitor cell gives rise to white blood cells, platelets, and red blood cells
 - White blood cells (WBCs)**—(neutrophils, basophils, eosinophils, monocytes, macrophages)—help to fight infection
 - Platelets (Plts)**—help to clot blood, stop bleeding
 - Red blood cells (RBCs)**—carry oxygen to all the cells in the body
- The lymphoid progenitor cell gives rise to T lymphocytes, B lymphocytes, and natural killer cells. These cells provide important immune functions that help to fight common bacterial or viral infections.



References:

Bejar, R., Levine, R., & Ebert, B.L. (2011) *Unraveling the molecular pathophysiology of Myelodysplastic Syndromes.* Journal of Clinical Oncology, 29, 5-4-515

What Are the Symptoms of MDS?

What are the symptoms of MDS?

Many patients do not have symptoms when they are diagnosed with MDS. They may have blood work performed by their physician as a part of a routine health checkup.

Other patients will seek medical care due to symptoms that are most often a result of low blood counts. The most common initial symptoms in patients not yet diagnosed with MDS are related to the type of cytopenia(s):

- **Low red blood cells (anemia):** fatigue, shortness of breath, heart skipping a beat (palpitations)
- **Low white blood cells (neutropenia):** fever, recurrent or prolonged infections
- **Low platelets (thrombocytopenia):** bruising, petechiae, or bleeding



Illustration by Kirk Molodt

Cytopenias resulting from abnormal bone marrow production of blood cells due to MDS

What tests are used to diagnose MDS?

Abnormal blood counts are the most common finding in the early stages of MDS. The physician will then order additional testing to determine the possible causes of the abnormal blood counts. If there are no clear explanations, a bone marrow biopsy and aspirate will be necessary to evaluate the factory cells that can only be sampled in the bone marrow and are necessary to confirm the diagnosis of MDS.

Common laboratory testing used to evaluate abnormal blood counts, including cytopenias

Laboratory Testing	What are we looking for?
CBC, differential, and platelet count, reticulocyte count	The presence of cytopenias, peripheral blasts, morphological abnormalities, and bone marrow response to anemia.
Serum iron, ferritin, TIBC, folic acid, B12	Iron deficiency, B12 deficiency, Folic acid deficiency; may also cause anemia and in some cases thrombocytopenia.
LDH, haptoglobin, reticulocyte count, coombs	Red blood cells can be destroyed by an overactive immune system. These blood tests are used to look for hemolysis (immune destruction of red blood cells).
Serum erythropoietin (EPO)	Erythropoietin (EPO) is a hormone produced in the kidneys that is necessary to make normal red blood cells. Some patients with MDS do not have enough EPO.

Bone marrow examination

When blood tests indicate the presence of low blood counts (cytopenias), your physician may recommend a bone marrow examination. A bone marrow examination can reveal abnormalities in the cells of the marrow (e.g., dysplastic cells) and will allow evaluation of the chromosomes (cytogenetics). These tests provide additional information that can help in establishing the diagnosis. There are two parts to a bone marrow examination: the aspirate and the core biopsy. Both the aspiration and biopsy are usually performed at the same time.

The bone marrow aspirate

The bone marrow aspirate is a sample of the liquid portion of the bone marrow. It is used to obtain spicules—a small collection of blood forming cells. This provides information about the shape of the cells (morphology), how the cells are maturing (differentiation) and the number of blasts (immature cells) in the bone marrow. The aspirate may also be used for additional testing that may help to determine the cause of the cytopenias, such as cytogenetics.

The bone marrow biopsy

The bone marrow biopsy is a small core (the shape and size of a medium pencil lead) of the spongy center of the bone marrow. The bone marrow core is usually 1.5–2.0 cm in length. It provides information about the cellularity of the bone marrow (crowded = hypercellular, empty = hypocellular). It will also provide useful information about iron storage, scarring (fibrosis), and the presence of any other abnormal cells.

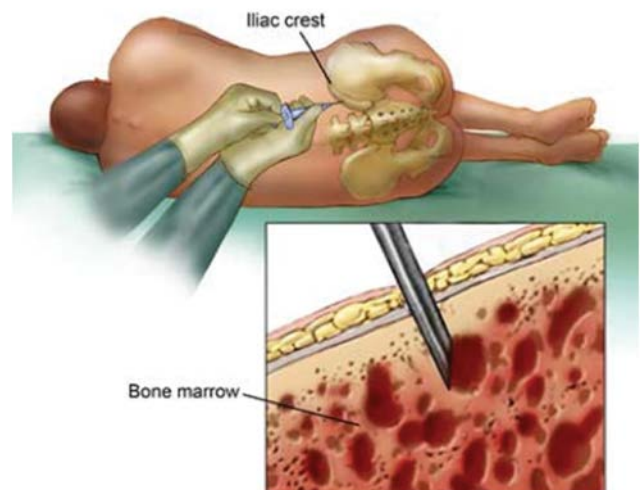
Processing the sample

The bone marrow biopsy and aspirate samples are placed on glass slides and in various laboratory tubes. These are sent to a hematopathologist—a physician trained to evaluate blood and bone marrow samples to diagnosis diseases. The physician uses a microscope to examine the cells in the bone marrow aspirate and biopsy samples. The results of a bone marrow biopsy and aspirate generally take 2–4 days. Cytogenetic studies and other special studies may require up to 2 weeks.

The bone marrow and biopsy procedure

A bone marrow examination can be performed in the physician's office usually in about twenty minutes. It can be performed with local anesthesia or, in some cases, mild sedation or analgesia.

1. The patient is placed either on their side or on their abdomen. It is always useful to empty your bladder prior to the procedure. It is important to continue to breathe slowly throughout the procedure to help relax the muscles.
2. The health care provider performing the procedure will prepare a sterile field, including cleaning the skin over the posterior iliac crest, a bony protrusion on the right or left back side of the hip (near where your back pocket might be on a pair of jeans).
3. The skin above the site will be anesthetized (numbing the skin) using a form of lidocaine (numbing medicine). You may feel a pin prick from the needle and a very brief sting from the lidocaine.



4. A second needle is then inserted to numb the surface of the bone (periosteum)—this is where all of the nerve endings are. You may feel a brief stinging sensation with the first injection, similar to having the gums numbed for a dental procedure.
5. Once the skin and bone has been anesthetized, a small incision may be made on the surface of the skin to allow insertion of the bone marrow needle. There are a variety of needles being used today. Most allow for both the aspirate and the biopsy to be obtained during the same procedure.
6. The larger bone marrow needle allows for penetration through the hard outer layer of the bone (cortical bone). It is roughly the size of a meat thermometer with a hollow core. You will feel pressure. Some patients have very hard bones requiring more pressure to be used to penetrate the bone. Be sure to let your provider know if you are experiencing sharp pain at the site or pain that is traveling down your leg.
7. Once the needle reaches the spongy bone marrow (red marrow), the inner portion of the needle is removed and the aspirate is obtained. You may experience a brief (few seconds) quick pressure sensation, almost like a cramp, with the first draw of the bone marrow. It will help to take a deep breath when the aspirate is being drawn. The number of samples drawn will be determined by the tests being ordered by your physician.
8. The same needle is then used to obtain the core biopsy. The inner sheath is removed once the cortical bone has been penetrated. The hollow needle is then inserted into the bone marrow. Your provider will twist and shake the needle gently to loosen the bone core to help remove it in one piece. You will feel pressure and some shaking very briefly. There is sometimes a quick sting when the bone is removed.
9. After the procedure, the provider will apply pressure to the site to prevent any bleeding. A pressure dressing is generally applied.
10. You should not shower for 24 hours. No soaking in water (bath, swimming, hot tubs) for 48-72 hours. Ask your provider for instructions on how to care for the biopsy site.
11. Some patients may develop a bruise or swelling under the skin, particularly patients with a low platelet count or patients taking medication to thin the blood. Be sure to let your health care provider know if you are taking aspirin or other medications that thin the blood.
12. Mild pain or discomfort may be experienced at the procedure site for two to three days after the bone marrow exam.
13. For safety reasons, the patient should have a friend, family member, or caretaker travel home with them. The patient should not drive.

What happens to bone marrow in MDS?

In patients with MDS, the development and maturation (differentiation) of the factory cells in the bone marrow (hematopoietic stem cells) is impaired.

This leads to an accumulation of immature cells (blasts) in the bone marrow and the inability of the bone marrow to make normal blood cells that come from the myeloid factory cell causing low blood counts (cytopenias).

Most patients with MDS have a crowded bone marrow, known as a hypercellular bone marrow. There are a small number of patients with MDS that have a low number of cells in the bone marrow, known as hypocellular MDS.

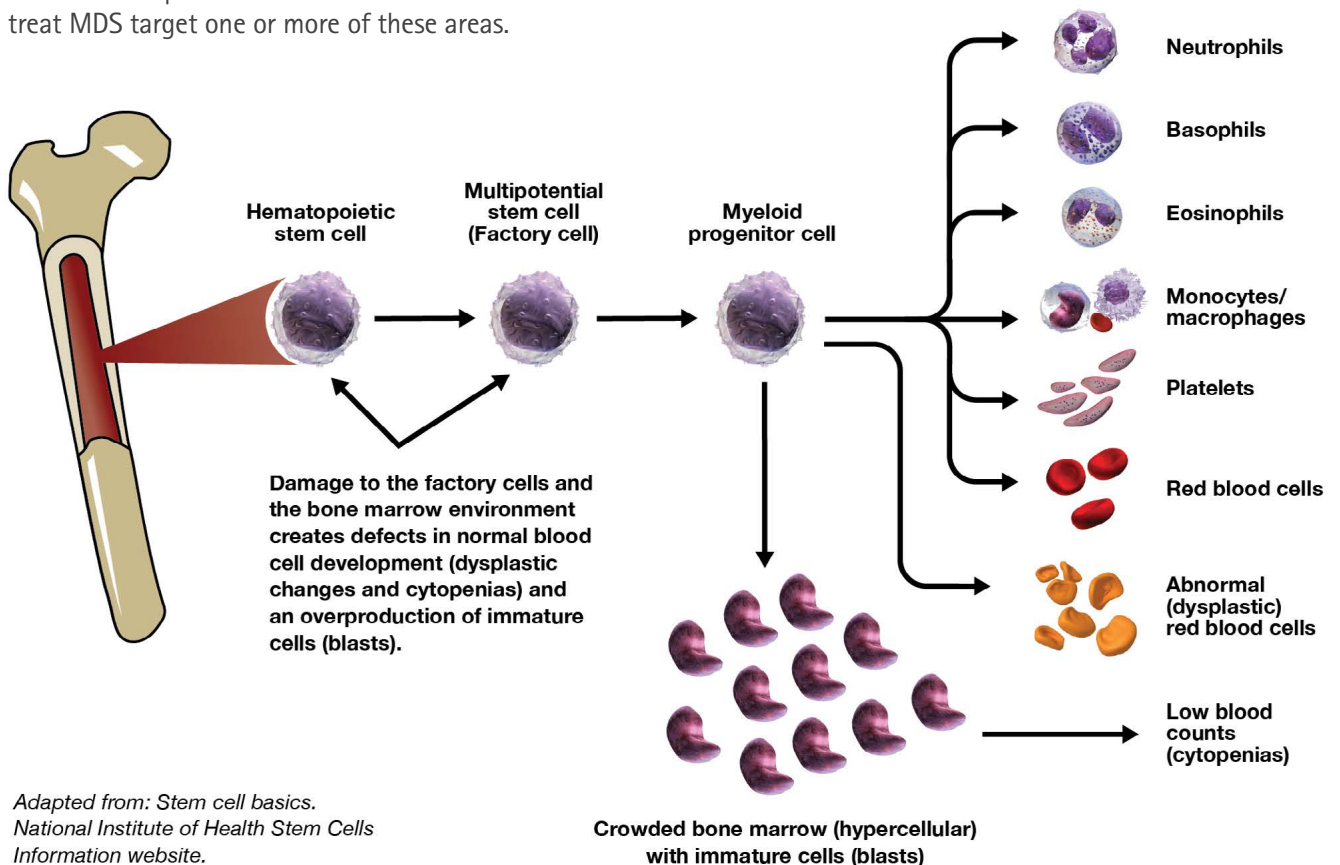
Red blood cells, white blood cells, and platelets all come from the same myeloid factory cell (progenitor cell). These are the cells that we can measure in the peripheral blood. In MDS, these cells are often low in number (cytopenias) and do not function normally.

The causes of the damage to the myeloid factory cells are thought to result from changes within the cell and changes in the bone marrow environment, known as the microenvironment.

The most common changes within the myeloid factory cells that are thought to cause MDS include chromosome changes and epigenetic changes.

Changes in the bone marrow microenvironment that promote MDS

There are several changes in the bone marrow microenvironment that are thought to promote the development of MDS. Some of the changes in the bone marrow microenvironment also help to explain the abnormal or ineffective development of the components of blood. Several of the current medications used to treat MDS target one or more of these areas.



Adapted from: *Stem cell basics.*
National Institute of Health Stem Cells
Information website.

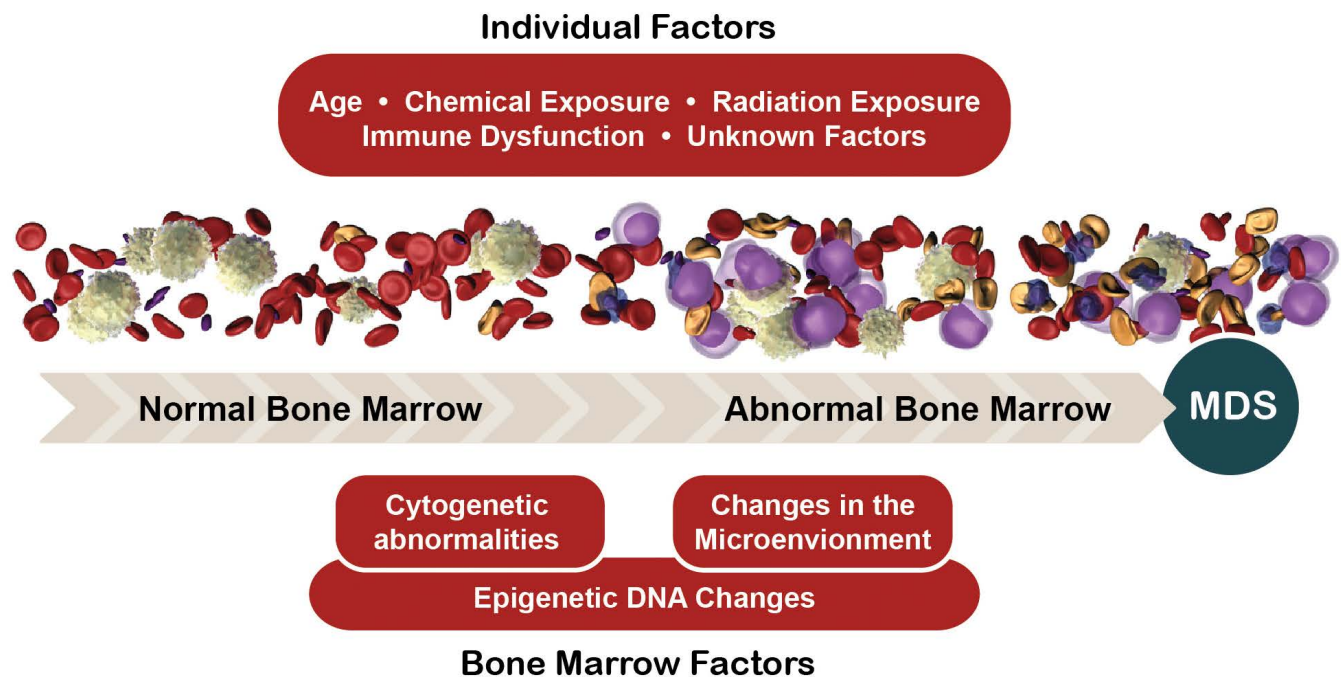
Epigenetic changes

Genes serve as blueprints for proteins. Proteins are the primary component of all living cells. They contain information that is required for the structure, function, and regulation of the body's tissues and organs. When a cell needs a protein, it activates the corresponding gene. The information contained in the DNA is translated into a code that is then used as a template for constructing the protein.

The DNA in our cells is wrapped around complexes of proteins called histones, like thread around a spool; the combination of DNA and histone protein is known as chromatin.

Epigenetic marks are chemical groups of various sorts that decorate the histones and DNA—they can be added or subtracted to turn a gene on or off. In this way, they can either help to transmit the code or block it.

In MDS, methyl compounds (chemical complexes) may attach to the genes needed for normal hematopoiesis (the development of the components of blood). When too many of these compounds attach to the gene it is known as hypermethylation. Hypermethylation turns off the genes that are needed for normal blood cell development. Hypermethylation is common in MDS. It is a constant process and is associated with the development of acute myeloid leukemia. Some treatments for MDS, known as hypomethylating agents, block the methyl groups to allow the transfer of information needed for normal blood cell development.



What happens to the bone marrow in MDS

What is cytogenetics?

Cytogenetics is a branch of genetics that is concerned with the study of the structure and function of the cell, especially the chromosomes. A bone marrow aspirate sample is necessary to perform cytogenetic analysis for MDS.

Cells are the fundamental working units of every living system. All of the instructions needed to direct their activities are contained within the DNA. The DNA, a combination of proteins, provides a blueprint for making all of the cells in the human body.

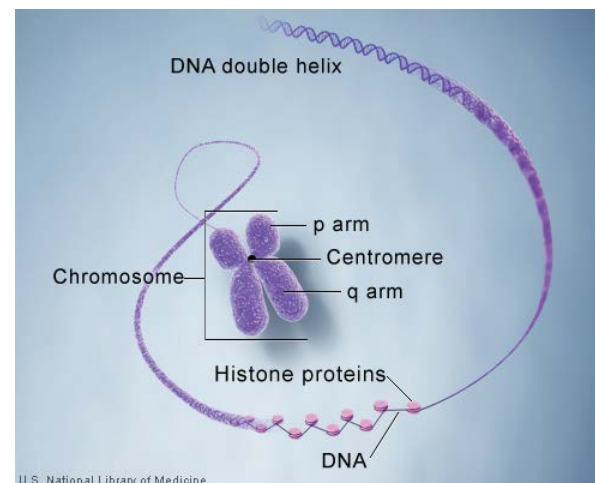
DNA is found in the nucleus of every cell in the body (except red blood cells, which have no nucleus). Inside the nucleus of a cell, long strings of DNA are coiled up onto chromosomes.

Most of what researchers know about chromosomes has been learned by observing chromosomes during cell division (metaphase). A standard chromosome analysis will study 20 metaphases.

Certain treatments for MDS, such as the hypomethylating agents Azacitidine (Vidaza®) and Decitabine (Dacogen®), are known to work best when the cells are dividing.

The number of chromosomes in human cells is 46 with 22 autosomal pairs (one of each type contributed by the mother and one of each type from the father) and 2 sex chromosomes - 2X chromosomes for females (one from mother and one from father) or an X and a Y chromosome for males (the X from the mother and the Y from the father).

Each chromosome has a narrow central point called the centromere, which divides the chromosome 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."



Genes and MDS

Chromosomes contain several thousand genes. Genes are shorter sections of DNA. Each gene acts as a code or set of instructions for making a particular protein. These proteins control the cell's activity—telling the cell what to do, giving the organism particular characteristics (such as male or female), and determining the way the body functions. Many diseases, including MDS, have abnormal proteins as a result of chromosome abnormalities. Some of these genes are thought to play a part in the development of MDS and, in some cases, the response to treatments for MDS. Abnormal changes in the gene are referred to as mutation.

How are cytogenetic and molecular study results used in MDS?

Your cytogenetic results are used to identify the type of MDS you have and to calculate the International Prognostic Scoring System (IPSS) and the revised IPSS (IPSS-R) risk category.

Cytogenetic abnormalities are present in approximately 40% of all cases of primary MDS, and in the majority of cases of secondary MDS. The most common chromosome abnormalities in MDS include changes in chromosomes 5, 7, 8, and 20. The changes are described based on the actual structural changes seen when evaluating the chromosomes. These include deletions (missing a portion of the chromosome); additions (parts added to a chromosome), and translocations (switching parts of chromosomes).

References:

Genetics Home Reference, National Library of Medicine (Bethesda, MD) (online).
Available from: <http://ghr.nlm.nih.gov/handbook/basics?show=all#chromosome> (Accessed November 2012)

You can ask about your cytogenetics. The report will describe the number of cell divisions (usually 20), the number of normal chromosomes, and any chromosomes that are abnormal. The number of cell divisions (metaphases) is represented in brackets [].

Normal male chromosome profile (karyotype) = 46XY [20]

Normal female chromosome profile (karyotype) = 46XX [20]

Example of abnormal cytogenetics in MDS: 46XX, del(5)(q13q33) [19], 46XX[1]:

This patient has 19 metaphases with the deletion of 5q – noted as del(5)(q13q33), and one normal female metaphase 46XX.

Cytogenetics are used to calculate the IPSS and IPSS-R score. Certain cytogenetic changes are considered favorable, while others are considered less favorable. Some cytogenetic abnormalities are associated with a more favorable response to certain treatments, such as del(5q). MDS patients with del(5q) have been shown to respond more favorably to Lenalidomide (Revlimid®).

The TET2 mutation (Ten-eleven translocation-2) is the most common gene mutation in MDS. It is involved in epigenetic regulation of gene expression and is associated with improved response to Azacitidine (Vidaza®).

Myelodysplastic Syndromes are a group of myeloid malignancies that vary widely in disease course and prognosis based on the type of MDS and the risk category (estimate of severity).

The type of MDS is based on the bone marrow biopsy and aspirate, cytogenetics, and results of the CBC, differential and aspirate drawn from the peripheral blood.

There are two primary classification systems used to determine the subtype of MDS: the World Health Organization (WHO) classification system and the French–American–British (FAB) classification system. You may see both classification systems mentioned in your bone marrow biopsy and aspirate report.

The system most widely used to estimate the severity of MDS is the International Prognostic Scoring System (IPSS). This system has recently been revised and is now known as the IPSS-R.

French-American-British (FAB) classification system

The FAB Classification was developed in the early 1980s by a group of physicians with expertise in diagnosing MDS. These experts were from France (F), America (A), and Great Britain (B); the central criterion for classification in the FAB system was the percentage of blast cells in the bone marrow. The FAB classification recognized five MDS subtypes:

- Refractory anemia (RA)
- Refractory anemia with ringed sideroblasts (RARS)
- Refractory anemia with excess blasts (RAEB)
- Refractory anemia with excess blasts in transformation (RAEB-t)
- Chronic myelomonocytic leukemia (CMML)

The World Health Organization (WHO) classification system

The World Health Organization (WHO) Classification System, recognizes distinct MDS subtypes based on large, world-wide patient data sets and increased understanding of the disease processes involved in MDS. The WHO classification system has incorporated the key parts of the FAB classification system. The major features of the MDS subtypes recognized by the WHO classification system are described below.

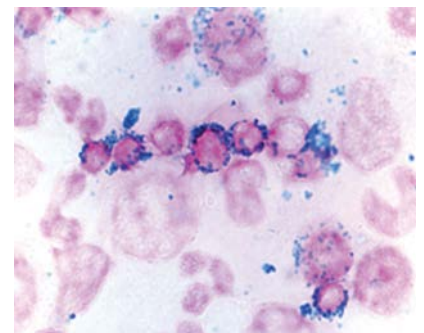
Refractory anemia (RA) and refractory anemia ringed sideroblasts (RARS)

- Anemia that is refractory (not responding) to iron or vitamin therapy. The anemia may be accompanied by mild to moderate thrombocytopenia and neutropenia.
- Sideroblasts are red blood cells containing granules of iron; ring sideroblasts are abnormal and contain iron deposits in a "necklace" pattern.
- Refractory anemia (RA) and RA with ring sideroblasts (RARS) are considered more favorable subtypes in the WHO classification system.

Refractory cytopenia with multilineage dysplasia (RCMD) or Refractory cytopenias with unilineage dysplasia (RCUD)

- Patients with refractory cytopenias are included in this category. They have persistently low counts of any of the blood cells types; e.g., refractory neutropenia (low white cells) or refractory thrombocytopenia (low platelet count) and minimal dysplasia in more than one blood cell type and less than 5% blasts or less than 15% ringed sideroblasts.
- When a patient with RCMD has greater than 15% ringed sideroblasts, the diagnosis is RCMD-RS.

ringed sideroblasts



Refractory anemia with excess blasts (RAEB)

- This category is divided into two subtypes, distinguished by the number of blasts in the bone marrow. Patients with RAEB-1 are those with 5 to 9% blasts and patients with RAEB-2 have 10 to 19% blasts.

5q- (5q minus) syndrome

Is defined by a cluster of findings including:

- 5q deletion as sole cytogenetic abnormality
- More common in women (female to male ratio =7:3)
- Median age at diagnosis–68 years
- Macrocytic anemia, mild leukopenia (low white blood cell count), normal or increased platelet count (thrombocytosis)
- Indolent course, favorable prognosis (median survival >5 years), with only 12–16% risk of AML transformation

What stage
is my MDS?



Unclassified MDS

This unclassified MDS category will likely comprise no more than 1–2% of all MDS cases. The category was created to accommodate the few patients with single blood cell type cytopenias (e.g., thrombocytopenia or neutropenia) and unusual features (e.g., fibrosis in the bone marrow).

Myelodysplastic Syndromes are a group of myeloid malignancies that vary widely in disease course and prognosis based on the type of MDS and the risk category (estimate of severity). The system most widely used to estimate the severity of MDS is the International Prognostic Scoring System (IPSS). This system has recently been revised and is now known as the IPSS-R.

International Prognostic Scoring System (IPSS)

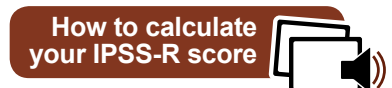
A system for grading the severity of MDS is the International Prognostic Scoring System (IPSS). Following a patient's evaluation (findings from physical examination and blood tests), the disease is "scored" in terms of the risk to the patient, that is, life expectancy and the chances of progression or transformation of the disease to AML. This is termed "prognosis." The IPSS Score is a score assigned to certain values. First, the percentage of blasts in the bone marrow; second, the cytogenetic findings (identification of chromosomal abnormalities) in bone marrow blood cells; and third, the blood cell counts and other blood test findings.

Determining the IPSS Score	
IPSS Score: Total of individual score values for blasts, cytogenetic finding, and blood test findings	
Blasts In Bone Marrow	Score Value
5% or less	0.0
5–10%	0.5
11–20%	1.5
21–30%*	2.0
Cytogenetic Finding [†]	
Good	0.0
Intermediate	0.5
Poor	1.0
Blood Test Findings [‡]	
0 or 1 of the findings	0.0
2 or 3 of the findings	0.5
<p>* Patients whose marrow contains more than 20% blasts have acute myeloid leukemia (AML).</p> <p>† "Good" cytogenetics include: normal set of 23 pairs of chromosomes, or a set having only partial loss of the long arm of chromosomes #5 or #20, or loss of the Y chromosome. "Intermediate" cytogenetics include: Other than "Good" or "Poor." "Poor" cytogenetics include: anomalies of the number 7 chromosome, or 3 or more total abnormalities.</p> <p>‡ Blood Test Findings defined as: Neutrophils <1,800 per microliter; Hematocrit <36% of red blood cells in total blood volume; Platelets <100,000 per microliter</p>	

Determining the IPSS score

The IPSS Score is determined by adding the individual scores for the percentage of blasts and for the cytogenetic and blood test findings, and is used to assess the clinical outcome for the MDS patient. The IPSS Score indicates which of the following risk groups a patient falls into:

- **Low-risk Group:** IPSS Score of 0
- **Intermediate-1 risk Group:** IPSS Score of 0.5 to 1.0
- **Intermediate-2 risk Group:** IPSS Score of 1.5 to 2.0
- **High-risk Group:** IPSS Score over 2.0



The Revised International Prognostic Scoring System (IPSS-R)

The IPSS-R has been developed by a group of International MDS experts representing 11 countries and 7012 patients. These data has been used to estimate life expectancy (survival) for a patient newly diagnosed with MDS without treatment and the risk of developing acute myelogenous leukemia (AML). The risk category (measure of severity) is estimated using results from the bone marrow biopsy and aspirate, the cytogenetics and the peripheral blood draw (CBC, differential and platelet count).

IPSS-R for MDS: Prognostic Score Values/Risk

Score/Attribute	0	0.5	1	1.5	2	3	4
Cytogenetics	Very Good		Good		Intermediate	Poor	Very Poor
Blasts (%)	<2%		>2%–<5%		5–10%	>10%	
Hemoglobin (g/dL)	≥10		8–<10	<8			
Platelets	≥100,000	50–<100,000	<50,000				
ANC	≥0.8	<0.8					

Cytogenetics play a very important role in estimating prognosis for a patient with MDS. The IPSS-R is based on a revised grouping of cytogenetic abnormalities (see: *IPSS-R calculator at www.mds-foundation.org/ipss-r-calculator*)

Cytogenetic Risk Grouping	Cytogenetic Types	Estimated Survival
Very Good	del(11q), -Y	5.4 years
Good	Normal, del(5q), del(12p), del(20q), double including del(5q)	4.8 years
Intermediate	del(7q), +8, +19, i(17q), any other single or double independent clones	2.7 years
Poor	-7, inv(3)/t(3q)/del(3q), double including -7/del(7q) Complex: 3 abnormalities	1.5 years
Very Poor	Complex: >3 abnormalities	0.7 years

There are five risk categories defined by the IPSS-R with estimated survival and median risk of AML:

Score	≤1.5 Very Low	>1.5-3 Low	>3-4.5 Intermediate	>4.5-6 High	>6 Very High
Overall Survival (mean)	8.8 years	5.3 years	3.0 years	1.6 years	0.8 years
Risk of AML in 25% of patients (median)	Not reached	10.8 years	3.2 years	1.4 years	0.73 years

It is important to know that these criteria are used to guide treatment selection and to guide patient and caregiver counseling. They do not represent patients who are receiving treatment where survival may be extended.

SEEKING TREATMENT


The goals of treatment for MDS are based on the specific type of MDS you have, how the disease is affecting you, and what treatments are available to you. There can be great variability in the way MDS is managed. Treatment for MDS can be grouped into three primary types: Observation, Supportive Care, and Disease Modifying Treatment. Bone Marrow Transplantation and Clinical Trials Participation may be options for you. It is important to understand the treatment recommendations suggested by your oncology provider, how they may affect you on a day-to-day basis, and what the goals of treatment are so that you can ask questions and make an informed choice.

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What will happen after the diagnosis of MDS is made?

Once the diagnosis of MDS has been established, you will meet with your oncology provider to discuss the diagnosis, prognosis, available treatment options, and the treatment recommended for you, if any. The diagnosis of MDS, as with any type of cancer, can create a variety of emotions including fear, uncertainty, anxiety, and sorrow. The amount and complexity of information that you receive during the diagnostic process and following the diagnosis of MDS can be overwhelming. There are a number of strategies to help you organize your thoughts, your questions, and your concerns so that you can discuss them with your health care providers. Understanding the goals of treatment, how treatment is selected, and what the effects of the treatment might be for you will help you to make decisions about your treatment plan, prepare for the treatment, and plan your daily activities. Being prepared will allow you to ask for help when needed.

Preparing for the initial visit

1. It is helpful to organize any information you have received from the diagnostic procedures you have had so far and bring these with you to your initial visit. Make an extra copy so you do not give your only copy to your provider.
2. Make a list of other health problems, any surgeries and dates, and any family history of cancer or blood disorders.
3. Create a current list of medications including any over-the-counter medications (see: *My MDS Plan*).
4. Make a list of current providers you might be seeing for other health needs, include the phone and fax numbers to assist with communication between providers (see: *My MDS Plan*).
5. Prepare your questions for your initial visit. Some of the questions you may want to ask your oncology provider include:
 - What type of MDS do I have and what is my prognosis?
 - What treatment do you recommend for my type of MDS and what are the goals of treatment?
 - When do I need to start treatment?
 - How is the treatment given? How often is it given? How long does each treatment take?
 - What would happen if I do not receive treatment?
 - Am I a candidate for a clinical trial?
 - Am I a candidate for a bone marrow transplant?

Preparing for your doctor's visit



It is helpful to write your questions down and have a caregiver take notes during the visit so that you can concentrate on what the provider is telling you. Understanding some of the principles of treatment for MDS will help you to prepare for your visit. Ask for copies of your blood counts, bone marrow report, and any other diagnostic information so that you can organize the information to create your own MDS Profile (see: *My MDS Plan*).

If you have questions about your diagnosis or treatment options, you may wish to contact the MDS Foundation or one of the MDS Foundations Centers of Excellence for more information. (see: *About the MDS Foundation*).

To be recognized as a Center of Excellence, an institution must have:

- An established university (or equivalent) program
- Recognized morphologic expertise in MDS
- Available cytogenetics and/or molecular genetics
- Ongoing research, including Institutional Review Board-approved clinical trials
- Documentation of peer-reviewed publications in the field

References:

Kurtin, S., et. al. (2012) *Clin J Oncol Nurs*, 16(3,suppl), 58-64

What type of MDS do I have and what is my prognosis?

The Myelodysplastic Syndromes (MDS) are a group of bone marrow failure disorders with variable onsets; prognoses, treatment options, and risk of developing leukemia (see: *What is MDS? How is MDS classified? How Severe is My MDS?*).

How is treatment selected?

The type of treatment selected and the goals of treatment for MDS are based on a number of factors including:

- Your individual health profile
- Other illnesses, how well they are controlled
- Current medications
- General health and ability to be independent in the activities of daily living
- Your individual social and emotional profile
- Your personal choice for proceeding with the recommended treatment options
- The availability of a caregiver
- Proximity to the health care setting
- How the individual treatment may affect your quality of life and lifestyle
- Insurance coverage and finances
- The characteristics of your MDS
- The IPSS-R risk category (see: *What is my IPSS score?*) Low-risk vs. High-risk
- The presence of certain genetic markers: for example the deletion of 5q or the TET2 mutation (see: *Cytogenetics and Molecular Testing in MDS*)
- Currently available treatment options including clinical trials (these may be based on geographical location)
- Eligibility for a bone marrow transplant

How is MDS treated?



What are the goals of treatment?

The goals of treatment for MDS are based on the specific type of MDS you have, how the disease is affecting you, and what treatments are available for you. It is important to understand the treatment recommendations suggested by your oncology provider, how they may affect you on a day to day basis, and what the goals of treatment are so you can make an informed choice.

The general goals of treatment vary for the type of disease (low risk vs. high risk) and the type of treatment. There can be variation in the way MDS is managed based on the unique needs of each patient. Treatment for MDS can be grouped into three primary types: Observation, Supportive Care, and Disease Modifying Treatment.

Observation

Observation includes continued monitoring of your blood counts and your symptoms. The frequency of visits for a patient under observation will vary based on the individual trends and any changes in the blood counts or symptoms. Observation is generally reserved for patients with low-risk MDS who have not required blood transfusions or who require them very infrequently.

Supportive care

Supportive care includes blood transfusions, growth factors, and other treatments aimed at improving symptoms, such as antibiotics for an infection, nutritional support, treatment of transfusion related iron overload, spiritual and emotional support. Supportive care is appropriate for any patient with the diagnosis of MDS. Certain types of supportive care are administered based on specific criteria. The benefits of supportive care are generally temporary as these strategies do not affect the underlying disease.

Common forms of supportive care aimed at improving blood counts include:	
Blood transfusion	Packed red blood cells, platelets Regulations for the administration of blood products vary by region.
Red blood cell growth factors	Approved for patients with lower-risk MDS in Europe. Approved for use in the United Kingdom, Nordic countries, and Canada. Administered in the United States as part of the APPRISE REMS program.
White blood cell growth factors	Approved for use in Nordic countries. Administered in the United States off-label or under special conditions.
Common forms of supportive care for transfusion-related iron overload include: (see: <i>What Is Iron Overload?</i> and <i>Is Iron Overload Treatable?</i>)	
Deferasirox (Exjade®)	Approved for patients with iron overload in the United States and Nordic countries. Approved in Europe for patients who are deferoxamine intolerant or unresponsive. Approved in Canada for patients with retinopathy or deferoxamine allergy.
Deferoxamine (Desferal®)	Approved for iron overload in Canada, Europe, Japan, Nordic countries, the United Kingdom, and the United States.

Disease modifying treatment

The decision to start disease modifying treatment is generally made based on changes in blood counts, changes in symptoms, or the presence of higher-risk disease. These “treatment triggers” include: blood counts getting worse (progressive cytopenias: anemia, thrombocytopenia, or neutropenia), increasing blasts, or increased frequency of blood transfusions. All of these findings suggest the MDS is changing and limiting the normal function of the bone marrow (see: *What Happens to the Bone Marrow in MDS*). Disease modifying treatments have the ability to change one or more of the abnormal components of the MDS.

Common disease modifying treatments for MDS

Antithymocyte globulin, cyclosporine	Off-label use for low-risk and hypocellular MDS in Canada, Europe, Japan, Nordic countries, and the United States.
Azacitidine (Vidaza®)	Approved for treatment of higher-risk MDS in Europe, Nordic countries, and the United States.
Decitabine (Dacogen®)	Approved for treatment of IPSS higher-risk or low-risk MDS with thrombocytopenia or neutropenia in the United States.
Lenalidomide (Revlimid®)	Approved for treatment of low-risk MDS with del(5q) in the United States. Available in Canada for use through a special access program only.

Low-risk MDS

Low-risk MDS is classified as having a lower IPSS score and favorable genetic features.

IPSS	Low Risk	Score of 0
	Intermediate-1 Risk	Score of 0.5-1.0
IPSS-R	Very Low	Score of <1.5
	Low	Score of >1.5-3.0
	Intermediate	Score of >3.0-4.5

Treatment of low-risk MDS



Goals of treatment for low-risk MDS:

1. Improve hematopoiesis (production of the components of blood).
2. Reduce the number of blood transfusions and optimally eliminate the need for transfusions completely (transfusion-independence).
3. Improve quality of life.
4. Extend survival.

High-risk MDS

High-risk MDS is classified as having a higher IPSS or IPSS-R score or selected high-risk features. (see: *What is my IPSS score?* and *How Severe is My MDS?*).

IPSS	Intermediate-2 Risk	Score of 1.5-2.0
	High Risk	Score >2.0
IPSS-R	High	Score of 4.5-6.0
	Very high	Score of >6.0

Treatment of high-risk MDS



Goals of Treatment for high-risk MDS:

1. Delay time to leukemic transformation.
2. Improve quality of life by improving symptoms and treatment burden.
3. Improve survival.

References:

- Kurtin, S., et. al. (2012) *Clin J Oncol Nurs*, 16(3, suppl. 1), 23-35
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 Komrokji, R., Skeres, M. & List, A.F. (2011) *Curr Hematol Malig Rep*, doi: 10.1007/s11899-011-0086-x
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Red blood cell transfusions are defined as the intravenous (IV, through a vein) infusion of red blood cells. Whole blood is collected from donors and then separated into various blood components. Red blood cells (RBCs) or packed red blood cells (PRBCs) are one component of whole blood.

Why are red blood cells given?

Red blood cell transfusions are a common way to provide temporary relief of the symptoms of anemia associated with MDS. Nearly 90% of patients with MDS are treated with red blood cell transfusions at some point during their diagnosis with MDS.

How are red blood cells administered?

Red blood cells are administered through an intravenous (IV) catheter in the arm, a peripherally inserted central catheter in the upper arm (PICC line) or an implanted central catheter in the chest (port-a-cath or Hickman catheter).

How do I know if I need a blood transfusion?

Most patients with MDS will have regular blood tests to monitor their disease. Your provider will notify you if your hemoglobin is at a level that may require a PRBC transfusion. The decision to transfuse PRBCs will be based on your symptoms as well as your blood counts. You may also notice symptoms of anemia such as increasing fatigue, a pale complexion, shortness of breath with exertion, or a faster heart rate. These symptoms should be reported to your health care team (see: *Quick Tips: Anemia*).

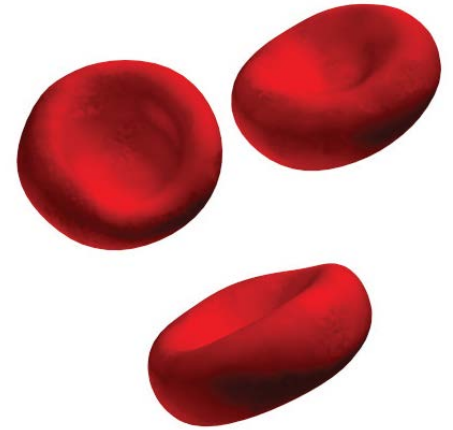


Illustration by Kirk Moldoff

What is the process for receiving a red blood cell transfusion?

Once the decision is made to transfuse, you will need a laboratory test (blood sample) to “crossmatch” your blood to available units of blood in your nearest blood bank. This test is necessary to ensure the transfused donor cells are compatible with your blood cells. This is also how your blood type and whether you have any antibodies in your blood are determined. The blood sample will be sent to the blood bank in your area for testing. The blood bank will then search the available donor units for blood that matches your blood type and any antibodies you may have. This can take a few hours to several days depending on blood availability and your individual blood profile.

You will have a wrist band (usually red) placed on your wrist when the sample is taken. This should not be removed until after you have received the transfusion. The blood identification band will be used to verify the blood match prior to you receiving the transfusion.

What can I expect on the day that I receive the transfusion?

The process for obtaining matched red blood cells and infusing them may require more than one day. Each facility has its own policy for the rate of red blood cell transfusion. Most often, 2 units of PRBCs are administered based on the patient’s symptoms and hemoglobin level. Each unit of red blood cells is administered over 2-4 hours and should never take longer than 4 hours because of the risk of bacterial growth in the blood product. You will need to have an IV catheter placed for the transfusion unless you have an existing intravenous access device. The transfusion of 2 units of PRBCs may take anywhere from 4-5 hours once the blood is obtained.

How often will I receive red blood cell transfusion?

How frequently transfusions need to be administered will vary depending upon the severity of symptoms and the hematocrit or hemoglobin level. Transfusion intervals (the time between one transfusion and the next) may vary from every few months in lower risk MDS to every 2 to 6 weeks in higher risk disease. In some MDS patients, the transfusion interval may be as often as once every 1 to 2 weeks. MDS patients who require a series of transfusions of red blood cells are considered to be transfusion-dependent. Transfusion-dependence is a common trigger to consider disease modifying treatment (treatment directed at the abnormalities in the bone marrow) to improve production of normal blood cells, including red blood cells and limit continued exposure to excess iron (iron overload).

What are the risks associated with red blood cell transfusion?

There are some potential risks associated with red blood cell transfusion. Most side effects are mild and are easily managed with medications. More serious reactions can happen, but are rare. The side effects can be divided into two time frames: *short-term risks* and *long-term risks*.

Short-term risks

- Fever, rash, itching, and/or hives are common side effects that you may experience and usually are mild.
- A severe allergic reaction may occur, but is rare.
- Difficulty breathing is uncommon, but can happen with severe allergic reactions or a build-up of fluid in your lungs.
- Nurses will be monitoring you throughout your transfusion to identify any reactions early.

Long-term risks

Transmission of an infection (such as HIV or hepatitis) through a blood transfusion is very low. Although blood products are tested for diseases, it will never be possible to guarantee that a transfusion will not transmit an infection. After many transfusions of blood, you may develop antibodies to donor blood which will make it more difficult for the blood bank to "match" your blood. Iron overload may occur if you have received 10-20 units of blood.

Other concerns related to red cell transfusions include the risk of retaining excess fluid which may cause or exacerbate shortness of breath. Fortunately, the fluid build-up can usually be managed by administration of a diuretic like furosemide (Lasix®). Transmission of viruses through blood transfusions is another concern. However, screening tests that can detect viruses in donated blood are used to keep the blood supply as safe as possible. The risk of transmittal of viruses, such as HIV, hepatitis B virus, and hepatitis C, is extremely low. Despite the concerns and risks, supportive therapy with regular red cell transfusions has been shown to improve the quality of life for patients with symptomatic anemia.



A platelet transfusion is defined as the intravenous (IV, through a vein) infusion of platelets. Whole blood is collected from donors and then separated into various blood components. Platelets are one component of whole blood.

Why are platelets given?

Platelet transfusions are a common way to provide temporary relief of the symptoms of thrombocytopenia associated with MDS or its treatment. They are most often given when the risk of bleeding is increased. Platelet transfusions are given much less frequently than red blood cell transfusions in patients with MDS.

How are platelets administered?

Platelets are administered through an intravenous (IV) catheter in the arm, a peripherally inserted central catheter in the upper arm (PICC line) or an implanted central catheter in the chest (port-a-cath or Hickman catheter).

How do I know if I need a platelet transfusion?

Most patients with MDS will have regular blood tests to monitor their disease. Your provider will notify you if your platelet count is at a level that may require a platelet transfusion. You may also notice symptoms of thrombocytopenia (low platelets) such as increased bruising, petechiae, or episodes of bleeding. These symptoms should be reported to your health care team (see: *Quick Tips: Thrombocytopenia*). The decision to transfuse platelets will be based on your symptoms as well as your blood counts.

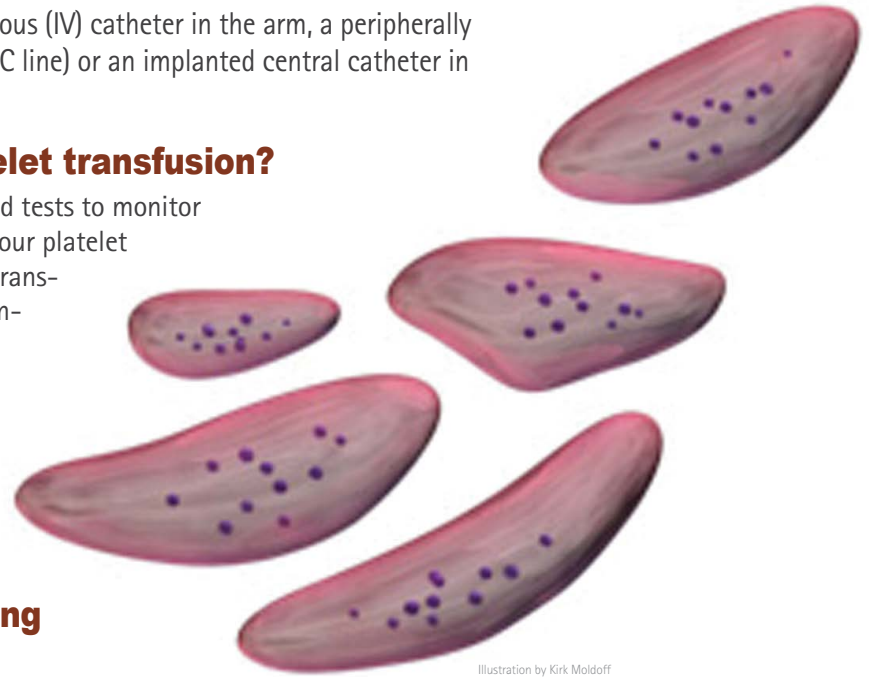


Illustration by Kirk Moldoff

What is the process for receiving a platelet transfusion?

Once the decision is made to transfuse, you will need a laboratory test (blood sample) to “crossmatch” your blood to available units of platelets in your nearest blood bank. This can take a few hours to several days depending on blood availability and your individual blood profile.

You will have a wrist band (usually red) placed on your wrist when the sample is taken. This should not be removed until after you have received the transfusion. The blood identification band will be used to verify the blood match prior to you receiving the transfusion.

What can I expect on the day that I receive the transfusion?

The process for obtaining platelets and infusing them may require more than one day. Each facility has its own policy for the transfusion of platelets. Platelets may be either random donor units (the platelet component from multiple units of whole blood) or single donor units (individual donors donate a single unit of platelets). Most often, 1 unit of single donor platelets or 4-6 units of random donor platelets are administered based on the patient's symptoms and platelet count. Platelets are infused over 15-30 minutes depending on the volume of each unit. You will need to have an IV catheter placed for the transfusion unless you have an existing intravenous access device. Transfused platelets do not last long (hours to a couple days). The frequency of transfusions will be determined on how well your bone marrow is able to produce platelets, your symptoms and your platelet count.

What are the risks associated with platelet transfusion?

There are some potential risks associated with platelet transfusion. Most side effects are mild and are easily managed with medications. More serious reactions can happen, but are rare.

Short-term risks

- Fever, rash, itching, and/or hives are common side effects you may experience and usually are mild.
- A severe allergic reaction may occur, but is rare.
- Difficulty breathing is uncommon, but can happen with severe allergic reactions.
- Nurses will be monitoring you throughout your transfusion to identify any reactions early.

Long-term risks

- The development of antibodies would make it more difficult to find suitable donor units.
- Transmission of an infection (such as HIV or hepatitis) through a platelet transfusion is very low.

Growth factors are synthetically produced proteins that mimic the normal proteins needed for hematopoiesis (normal development of blood cells). There are growth factors that stimulate the production of red blood cells, granulocytes (a type of white blood cell) and platelets. These growth factors are considered a form of supportive care.

Red blood cell growth factors (Erythropoietin stimulating agents or ESAs)

Red blood cell growth factors may improve anemia by improving red blood cell production. Red blood cell growth factors contain the protein erythropoietin. Erythropoietin (EPO) is a natural hormone produced by the kidneys to help red blood cells develop fully so that they can carry oxygen. The level of erythropoietin in the blood can be measured. Patients with a serum erythropoietin level <500 IU/L who require fewer than two units of packed red blood cells (PRBCs) every 4 weeks have been shown to benefit most from the administration of synthetic erythropoietin stimulating proteins.

Available agents:

Erythropoietin (EPO) (Procrit®) is a synthetic form of EPO. It is administered as a subcutaneous (under the skin) injection once weekly in low-risk MDS patients to improve red cell production. Doses are based on individual response and regional guidelines for use.

Darbepoetin (Aranesp®) is a longer acting synthetic form of EPO. It is administered as subcutaneous injection (under the skin) every 2-3 weeks in low-risk MDS patients to improve red cell production. Doses are based on individual response and regional guidelines for use.

ESAs in the United States must be administered under the APPRISE safety program known as a REMS program.

White blood cell growth factors

MDS patients often have cytopenias resulting in low neutrophil counts and an increased risk of infection. White blood cell growth factors are synthetic proteins used to stimulate the bone marrow to produce more neutrophils to fight infection in patients with bone marrow diseases or undergoing chemotherapy.

Available agents:

Filgrastim (Neupogen®) Short acting synthetic form of granulocyte colony-stimulating factor (GCSF).

Pegfilgrastim (Neulasta®) PEGylated (long-acting) synthetic form of GCSF.

Sagramostim (Leukine®) Recombinant granulocyte macrophage colony-stimulating factor functions to increase white cell production.

Platelet growth factors

Platelet growth factors are agents used to promote platelet production (thrombopoiesis) to prevent thrombocytopenia and bleeding. These agents are not currently approved for use in MDS.

Available agents: *(currently not approved for use in MDS)*

Eltrombopag (Promacta®) is currently in clinical trials and also belongs to the class of drugs known as thrombopoietin-receptor agonists, working to stimulate receptors located on the megakaryocytes to increase platelet counts. It appears to significantly improve platelet counts in patients with severe thrombocytopenia. Eltrombopag is administered orally as a tablet once daily and is currently in phase III clinical trials for the treatment of patients with chronic idiopathic thrombocytopenic purpura.

Oprelvekin (Neumega®), a recombinant platelet growth factor, is approved for the treatment of patients with severe thrombocytopenia. Oprelvekin increases platelet production by stimulating the growth of immature platelets in the bone marrow. Oprelvekin has limited activity in some MDS patients. In a phase II study of 32 MDS patients receiving oprelvekin at a dose of 10 micrograms/kilogram/day, 9 patients (28%) had increases in their platelet count, but only 5 of these platelet responses were clinically meaningful. The increase in platelet counts lasted an average of 9 months. Oprelvekin use is associated with side effects, the more common being edema, malaise, and low-grade fevers, which are problematic for MDS patients with symptomatic anemia.

Romiplostim (Nplate™) received FDA approval for thrombocytopenia in patients with chronic immune thrombocytopenia purpura, a disorder characterized by increased platelet destruction or inadequate platelet production. Romiplostim is a recombinant protein given by subcutaneous injection weekly. It belongs to a class of drugs known as thrombopoietin-receptor agonists, and works by stimulating these receptors located on specific cells in the bone marrow called megakaryocytes, which leads to increased platelet counts. In a study of low-risk MDS patients with thrombocytopenia, romiplostim produced a durable platelet response in 18 (41%) of patients that lasted an average of 23 weeks. Several ongoing phase II studies in MDS patients are evaluating the benefit of romiplostim on thrombocytopenia. At present, it is not recommended for use in patients with blood cancer or a precancerous condition such as MDS.

Disease Modifying Agents

Disease Modifying Agents are treatment with the potential to affect the underlying abnormalities that cause MDS. They have the potential to change the natural history of the disease and extend survival. The decision to start treatment with a disease modifying agents is based on common treatment triggers such as transfusion dependence, increasing blasts, higher risk MDS, and progressive or symptomatic cytopenias.

FDA Approved Agents for Treatment of Myelodysplastic Syndromes

	Azacitidine	Decitabine	Lenalidomide
Indication	All 5 FAB subtypes (RAa, RARSa, RAEB, CMML, RAEB-t)	Int-1/Int-2/high risk per IPSS, as well as MDS	Transfusion-dependent MDS low-int-1 MDS with del(5q) with or without additional chromosomal abnormalities
Drug class	Hypomethylating agent	Hypomethylating agent	Immunomodulatory agent (IMiD)
Key clinical trials	CALGB 9221, phase I/II CALGB 8421 phase II continuation (2000) Established efficacy and safety AZA-001, phase III international, multicenter Int-2, high-risk MDS First survival data for active therapies in MDS	D-0007, phase I/II (2003) Established efficacy and safety ADOPT trial (2007) phase III randomized, multicenter trial Established new dosing guidelines Decitabine 20 mg/m ² IV given over 1 h days 1–5 Outpatient treatment feasible	MDS-001, phase I/II (2002) Established efficacy and safety MDS-003, phase II multicenter trial, lenalidomide in del(5q) led to FDA approval based on efficacy and safety MDS-002, phase II multicenter trial, lenalidomide in non-del(5q) low-Int-1 MDS. Confirmed activity in non-(del)5q MDS; confirmed safety and efficacy
Primary end points met (IWG)	Improved overall survival Hematologic improvement Transfusion independence Cytogenetic response Safety and efficacy	Hematologic improvement Transfusion independence Cytogenetic response Safety and efficacy	Hematologic improvement Transfusion independence Cytogenetic response Safety and efficacy
Common side effects	Myelosuppression is most common Injection site reactions Nausea and vomiting Constipation Contraindicated in patients with hepatic tumors Use with caution in renal impairment May cause fetal harm	Myelosuppression is most common Nausea and vomiting Constipation Hyperbilirubinemia Use with caution in renal impairment May cause fetal harm	Myelosuppression is most common Rash Diarrhea Requires renal dose adjustment Nonteratogenic in animal studies Analog of thalidomide Must be prescribed through Revassist program for safety
Mode of use	SC or IV x 7 days Every 28 days Outpatient regimen Treat until unacceptable toxicity or disease progression	IV daily for 5 days over 1 hour Every 28 days Outpatient regimen Treat until unacceptable toxicity of disease progression	10 mg orally days 1–21 Every 28 days Treat until unacceptable toxicity of disease progression

Hypomethylating agents

Hypermethylation, the accumulation of compounds called methyl groups on portions of DNA, has been identified as one of the contributing factors in the development of MDS and leukemia. These compounds silence or turn off genes that are necessary for the normal development and maturation of blood cells. Hypermethylation is a constant process. Hypomethylating agents, drugs that block the methyl compounds, have been shown to improve normal blood cell development (hematopoiesis) in patients with MDS by allowing the silenced genes to be turned back on. There are currently two hypomethylating agents available: 5-azacytidine (azacitidine) and 5-aza-2-deoxycytidine (decitabine).

Azacitidine (Vidaza®) www.vidaza.com

Azacitidine was the first drug approved by the FDA specifically to treat MDS. It is administered by subcutaneous (under the skin) or by intravenous injection. The intravenous and subcutaneous dosing schedules are the same. Several clinical trials showed that, compared with patients who did not receive azacitidine, MDS patients treated with one subcutaneous injection of azacitidine daily for 7 days every four weeks had durable hematologic improvements: increases in red blood cells and transfusion independence, increase in hemoglobin, increases in white blood cell or platelet numbers, and/or decrease in bone marrow blast percentage. All patients in the clinical trials received supportive care regardless of whether or not they received azacitidine. In some clinical trials, the time to onset of AML was significantly delayed in azacitidine-treated patients when compared with patients who did not receive azacitidine. Results of a large phase III study in 358 high-risk MDS patients (IPSS of Intermediate-2 or High) showed that compared with conventional care (either low dose chemotherapy plus supportive care or standard chemotherapy plus supportive care), treatment with azacitidine significantly prolonged overall survival (24.4 months versus 15 months). More convenient dosing schedules (5-day subcutaneous schedules) and a short intravenous infusion for azacitidine have also been investigated. The most common side effects seen with azacitidine are myelosuppression, nausea, constipation, and injection site reactions. An oral formulation has been developed and is currently in clinical trials.

Decitabine (Dacogen®) www.dacogen.com

Decitabine, (also called 5-deoxyazacytidine), is a DNA hypomethylating agent like azacitidine and works like azacitidine. In other words, decitabine reduces DNA methylation, and restores the normal functioning of tumor suppressor genes in MDS. Positive findings from a major phase III clinical trial that compared decitabine with supportive care in MDS patients revealed that of 170 patients with intermediate to high-risk MDS who participated in the trial, a significantly higher overall response rate was seen in patients receiving decitabine with the responses lasting for about 10 months: 17% response for decitabine-treated patients versus 0% for patients receiving standard of care. Patients who responded to decitabine became or remained transfusion independent. In addition, patients who had a response (complete or partial) to decitabine had a longer time to progression to AML and extended survival compared with patients receiving supportive care alone. The most common side effects seen with decitabine are myelosuppression, nausea, and constipation.

Immunomodulatory agents www.revlimid.com

Immunomodulatory agents are a form of disease modifying treatment targeted at the bone marrow microenvironment and elements of the abnormal MDS cells (malignant clone). Revlimid® (lenalidomide). Lenalidomide is approved in the U.S for anemic MDS patients with Low- or Intermediate-1 risk MDS, particularly those with 5q- who are transfusion-dependent. Lenalidomide is taken orally and is available in capsule form. The findings of a landmark study in MDS patients with symptomatic anemia and chromosome 5q deletion treated with lenalidomide showed that 67% of patients who were initially red blood cell transfusion-dependent achieved transfusion independence, and another

9% had their transfusion requirement decreased by 50% or more. Also, a complete cytogenetic response (i.e., chromosome abnormalities were no longer detectable) was achieved in 45% of patients. In this study, the response to lenalidomide was rapid, with an average time to response of 4.6 weeks and durable. Most of the patients received continuous daily dosing with 10 mg of lenalidomide. Some patients experienced side effects, such as rash, itching, fatigue, diarrhea, and nausea. Because lenalidomide is an analog (chemical look-alike) of thalidomide, there is a potential for birth defects with its use. Because of this potential, the manufacturer of lenalidomide, Celgene Corp., has set up a restricted distribution program called RevAssistSM. Only patients that enroll in and meet all of the conditions of the program are able to receive the drug. In a study of MDS patients without chromosome 5q-, lenalidomide was shown to reduce the red blood cell transfusion need in 43% of patients and eliminate the transfusion need in 26% of patients. The majority of patients had a heavy transfusion burden (two or more red blood cell units/month).

Immunosuppressive agents

Immunosuppressive agents, although not currently FDA approved for the treatment of MDS, may be used in patients with low-risk MDS or hypocellular MDS in the clinical trial setting or in selected clinical settings.

Cyclosporine: Used primarily to inhibit immune rejection. In low doses, it can be used for the treatment of hypocellular MDS and MDS with refractory anemia (RA).

Antithymocyte Globulin (ATG): A T cell depleting agent that exists in two forms: rabbit or equine. It is used in selected cases of MDS but must be administered in the inpatient setting with close surveillance for anaphylaxis reaction.

Alemtuzumab (Campath): An antibody to the CD52 receptor found on many mature immune cells, including T and B cells is being used primarily in the clinical trials setting.

Induction chemotherapy

A patient with higher-risk MDS has a higher probability of disease progression to AML. For this reason, your physician may recommend intensive, high-dose, or induction chemotherapy that may "induce" control of MDS by killing the myelodysplastic cells. Induction or intensive chemotherapy for MDS refers to cytotoxic ("cell-killing") combination regimens like those used to treat AML. Intensive chemotherapy may also be appropriate for Low- and Intermediate-1 Risk patients with progressive disease, 60 years of age or younger, and in good physical condition.

Chemotherapy treatment has significant side effects. Commonly recognized side effects include hair loss, mouth sores, nausea, vomiting, diarrhea and infections. There are a number of different chemotherapy drugs and combinations of drugs that may be used. All of these regimens affect normal cells of the body in addition to the MDS cells. For this reason, this type of treatment generally requires hospitalization for days to weeks depending on how well it is tolerated and how quickly the bone marrow and other cells in the body recover. Aggressive supportive care including transfusions, intravenous fluids, antibiotics, nutritional support, pain management, and psychosocial support are necessary during the hospitalization.

Once there is evidence of bone marrow recovery (improved counts) and improvement of any side effects of treatment, you will be discharged to be followed up in the outpatient setting. A bone marrow biopsy and aspirate will be repeated either while hospitalized or after discharge to evaluate the effectiveness of the treatment. As normal cells proliferate, the frequency of transfusions will decrease and the risk of infection will lessen. Unfortunately, the chance of controlling MDS with induction chemotherapy is only about 30%. Even in successful cases, the disease often returns within twelve months. Thus, aggressive chemotherapy is given to a minority of MDS patients.

References:

- Kurtin, S. (2011) *J Adv Pract Oncol*, 2 (Suppl. 2), 7-18
Ridgeway, J. et. al. (2012) *Clin J Oncol Nurs*, 16 (3, Suppl. 1), 9-22

Palliative care focuses on relieving the pain and suffering of individuals with illness. The benefits of palliative care are recognized and accepted by the American Board of Medical Specialties.

What is palliative care for MDS?

Myelodysplastic Syndromes (MDS) can affect the body, the mind, and the spirit. Patients with MDS, their caregivers, and families may have trouble in one or more of these areas during any stage of the illness. Palliative care for patients with MDS can be started as soon as they are diagnosed with the disease. The majority of oncology health care professionals will incorporate the elements of palliative care into your day-to-day care. Palliative care offer assistance with:

- Difficult treatment decisions
- Physical symptoms: for example pain, nausea and vomiting, diarrhea, constipation, fatigue, nutritional needs, etc.
- Emotional needs such as depression or anxiety
- Social needs
- Financial direction
- Spiritual support

The palliative care team

The palliative care team will work with the patient and their caregivers to identify his or her needs, goals and fears. Palliative medicine utilizes a multidisciplinary approach to patient care, relying on input from physicians, pharmacists, nurses, chaplains, social workers, psychologists, and other allied health professionals in formulating a plan of care to relieve suffering in all areas of a patient's life. This multidisciplinary approach allows the palliative care team to address physical, emotional, spiritual, and social concerns that arise with advanced illness or incurable diseases. Some cancer centers or clinics have designated palliative care teams; other centers may have access to trained individuals upon request. A palliative care team may include one or more of the following:

- Physician(s)
- Nurse practitioners (NP) or physician assistants (PA)
- Oncology nurse specialist
- Social worker
- Pain service
- Chaplain service or other spiritual support services
- Nutritionist
- Physical therapist
- Financial counselor

Patients with lung cancer who received palliative care starting in the early stages of the illness had a better quality of life, less depression, and lived longer than those that did not receive palliative care. Though more research with MDS patients is needed, this study suggests that palliative care starting in the early stages of disease, such as MDS, may benefit patients. Although palliative care is not intended as a cure for MDS, it may increase the chances of survival by preparing the patient for the road ahead and supporting them and their families.

References:

- Loscalzo, M.J. (2008) *Palliative Care: An Historical Perspective*, doi: 10.1182/asheducation-2008.1.465
ASH Education Book January 1, 2008 vol. 2008 no. 1 465
- Termel, J.S., et. al. (2010) *Early Palliative Care for Patients with Metastatic Non-Small-Cell Lung Cancer*,
NEJM 363:8 nejm.org august 19, 2010

What is a bone marrow transplant?

A bone marrow transplant (BMT), also known as a stem cell transplant or hematopoietic stem cell transplant (HSCT) involves treatment with high dose chemotherapy and possibly radiation followed by the infusion of stem cells (progenitor cells). These stem cells have the capacity to restore bone marrow function (see: *What does bone marrow do?*). There are significant risks with this procedure. Therefore, although blood or marrow transplantation offers a potential cure for MDS, this procedure is available to only a small proportion of adult MDS patients.

Bone marrow transplant

Allogeneic bone marrow transplantation offers the only currently available treatment option with the potential to completely remove the malignant MDS clone (MDS factory cells) from the bone marrow. Removal of the MDS clone is necessary to "cure" MDS. As the only proven cure for MDS, allogeneic hematopoietic stem cell transplantation (HSCT) should be considered for transplantation-eligible patients with high-risk disease (see: *Am I a candidate for a bone marrow transplant?*). Allogeneic bone marrow transplants represent the most aggressive treatment option and are not suitable for most patients with MDS.

There are different types of transplants: autologous and allogeneic. Autologous stem cells are obtained from the patient and used for the same patient's transplant. Allogeneic stem cells are obtained from another individual who is genetically as similar to the patient as possible. This is usually a brother or a sister, but may be an unrelated volunteer donor. For MDS, allogeneic stem cell transplant is most common.

The allogeneic stem cells are usually obtained from the blood stream of the donor after the donor receives a medication to stimulate production of stem cells. We call these mobilized peripheral blood stem cells. On rare occasion, we collect cells from the bone marrow of the donor, called bone marrow stem cells.

You will be human leukocyte antigen (HLA) typed to determine your profile. This is a simple blood test but it is the most critical component of finding a perfect "match" for your transplant. HLA antigens are proteins or markers found on the surface of most cells in your body. Your immune system uses these markers to recognize which cells belong in your body and which do not. Human leukocyte antigen (HLA) typing is used to match patients and donors for stem cell and bone marrow transplants.

Am I a candidate for a bone marrow transplant?

The first step toward a bone marrow transplant is to determine if you are a candidate for this type of treatment. Your provider and health care team will evaluate several factors known as eligibility criteria. The most common eligibility criteria include:

- Age less than 65 years (some exception may be made at some centers)
- Availability of a HLA identical matched donor
- Good heart, lung, liver, and kidney function
- Physically active and able to perform daily activities independently

Am I a BMT candidate?



There are many resources available to help you understand blood and bone marrow transplantation for MDS.

- National Marrow Donor Program (NMDP) www.marrow.org
- Blood and Marrow Transplantation Information Network www.bmtinfonet.org
- National Coalitions for Cancer Survivorship www.canceradvocacy.org/toolbox
- Be The Match www.marrow.org

The Bone Marrow Transplant Process



Blood or bone marrow transplantation is a complex multi-step process. It is important for you and your caregiver(s) to familiarize yourselves with each step in the process. This will help you in planning your time, resources, and areas where you may need assistance.

1. **Pre-transplant treatment** — It is always best if your MDS is well-controlled prior to proceeding to transplant. This will require disease modifying therapy.
2. **Transplant evaluation** — (see: *Bone Marrow Transplant Evaluation*)
3. **Donor search** — During your transplant evaluation, you will be asked about possible sibling donors. If there are no sibling matches, a donor search will be initiated. This may take days to months; and, in some cases, a suitable donor cannot be located. The best donor will match all of your DNA markers. In some cases, donors who match most, but not all, of the DNA markers will be considered. This type of transplant (mismatched) carries greater risks.
4. **Pre-admission consent signing** — After a donor has been located, you will return to the transplant center with your designated caregiver(s) for a pre-hospitalization visit. This visit usually takes more than 1 hour and will include a detailed discussion of the possible risks and benefits of the transplant for you. It is important to prepare any questions that you or your caregivers may have prior to this visit. If you wish to proceed with the transplant, you will sign a consent form prior to being hospitalized for the transplant.
5. **Conditioning regimen** — Prior to proceeding with the transplant, you will need to have high-dose chemotherapy to remove the remaining elements of your bone marrow which carry the MDS clone. This will make room for the new stem cells from your donor that will repopulate your bone marrow with new factory cells (progenitor or stem cell). This treatment phase requires hospitalization at the bone marrow transplant center for several weeks.
6. **Stem cell infusion** — The day of infusion, or transplant, is commonly referred to as "Day 0." The donor stem cells are infused via central venous access. The actual infusion can take as long as an hour depending on the number of frozen bags of HSC product. There may be other activities as part of the infusion, such as hydration, that will result in a day-long procedure.
7. **Engraftment** — Blood count recovery, or "engraftment," will be the first sign that the transplanted stem cells have populated your bone marrow and are starting to produce the elements of blood. Engraftment is established when absolute neutrophils are >500 cells/dL for three consecutive days or >1,000 for one day, and platelets remain >20,000 independent of transfusion for at least 7 days.
8. **Transplant side effect management** — Allogeneic stem cell transplants are associated with considerable treatment-related side effects, both during and after the transplant. These side effects will be discussed with you and your caregiver(s) at the pre-transplant visit.

Selecting a transplant center

Once you and your health care team have determined a blood or bone marrow transplant is a good treatment option for your MDS, there are a number of things for you and your caregiver(s) to consider.

How do I choose a bone marrow transplant center?

There are more than 200 transplant centers in the United States alone. Finding one that best suits your needs may seem like an overwhelming task. The choice of centers may be based on a number of factors:

- The recommendations made by your primary oncologist.
- The transplant centers under contract with your insurance plan.
- The rating of the individual center.
- The proximity of the center to your home.

A directory of blood and bone marrow transplant centers can be found online:

- BMT Information Network www.bmtinfonet.org
- The National Marrow Donor Program (NMDP) www.marrow.org
- The Center for International Blood and Marrow Transplant Research www.cibmtr.org

The bone marrow transplant evaluation

Once you have identified the transplant center, you will be referred for a formal consultation and evaluation. This process may take several days and will include a number of blood tests, radiology examinations, breathing tests, and a bone marrow biopsy and aspirate. You will meet with members of the transplant team including the transplant physician, nurses, social workers, and dietitians. The screening visit is to be certain that a bone marrow transplant is the best treatment option for you.

What questions should I ask my bone marrow transplant physician?

There are a number of questions that you and your caregiver(s) may want to ask when you meet with the members of the transplant team:

1. Is the facility approved by your insurance company for transplant?
2. Is the program accredited by the Foundation for Accreditation of Cellular Therapy (FACT)? (This agency conducts rigorous inspections of transplant programs and certifies a program if it offers high quality care.)
3. What tests will I need before the transplant?
4. Is housing available in the area for post-transplant care and what is the recommended/required duration to reside locally?
5. What is the experience of the transplant team in treating patients with MDS?
6. Is there extra financial support available from the institution for non-insurance costs?
7. What is the usual length of hospital stay during transplant?
8. How often will I need to be seen in the clinic after discharge?
9. Does the transplant program have a long-term follow-up program to help you with medical issues that may come up months or years after transplant?
10. Are there emotional support services for me, my donor, my caregiver and my family?
11. What is the center's success rate with stem cell transplants?
12. What are the expectations for the caregiver(s)?

What are clinical trials?

Clinical trials offer an option for treatment under the guidance of a research protocol. Clinical trials provide several important benefits:

1. Are an important part of developing new treatments for MDS and other diseases
2. Help to improve diagnostic techniques
3. Identify new targets for treatment
4. May offer treatment options which are not otherwise available
5. Help to refine treatment strategies, such as refinement of the IPSS tool for MDS which is now the IPSS-R (see: *My IPSS-R score*)
6. Help to improve side effect management
7. Offer a way to research quality of life while studying a disease or the treatment of disease

About clinical trials



A clinical trial falls into one of four phases:

Phase I	This is the first time a drug is used in humans. The trial is designed to determine dosage, route of administration (oral, intravenous, or by injection), and schedule of administration (how many times a day or week). In this phase, researchers also begin to determine the drug's safety. The Phase I trial is normally conducted in healthy adults and enrolls only a small number of people (15-30).
Phase II	Patients with the disease receive the drug at dose levels determined in the earlier phase. The Phase II trial begins to determine the effectiveness of the drug and provides more information about its safety. Phase II trials usually include less than 100 people.
Phase III	The drug is tested alone or against an approved standard drug. The typical Phase III trial enrolls a large number of patients (100-thousands). If it is a comparison trial, patients may be randomly assigned to receive either the new drug or the standard intervention.
Phase IV	In Phase IV, the drug, already approved by the FDA and available to the public, undergoes continued evaluation in a large number of patients (several hundreds to several thousands). The Phase IV designation is rare.

Some trials, screening trials, and studies evaluating supportive care or prevention are not conducted in phases. In this type of trial, a group following a certain strategy to combat disease, such as a detection method or a behavioral change, is compared to a control group.

How is a clinical trial conducted?

Clinical trials may be conducted at a specific institution or as a part of a collaborative group. Each trial is assigned a lead researcher, known as the Primary Investigator (PI). You may meet some of the other members of the research team when participating in a clinical trial. They all work to be certain that your treatment follows the guidelines set out by the trial and that your safety is maintained.

Members of the research team

1. Lead physician, scientist, or nurse researcher – primary investigator (PI)
2. Other clinicians: physicians, nurse practitioners, or scientists (Sub-Investigators)
3. Statisticians
4. Research nurses
5. Data managers

How are clinical trials monitored?

Clinical trials for cancer treatment are overseen by a number of groups. The primary goals are to ensure patient safety and maintain rigorous scientific standards. These groups will review each clinical trial before the trial can be open for patient enrollment.

- **Institutional Review Boards (IRB):** A group of experts from the institution conducting the trial or representing a cooperative group of institutions who review each trial for patient safety and scientific merit. The IRB will continue to monitor the conduct of the trial until it is completed along with the Primary Investigator and the research team.
- **Scientific Review Panels:** A panel of experts who review clinical trials to ensure that they are based on sound scientific principles.
- **Data and Safety Monitoring Boards:** An independent committee of physicians, researchers, statisticians, and other experts.
- **National Cancer Institute (NCI) and National Institutes of Health (NIH):** Oversee selected clinical trials and maintain a list of registered trials. www.clinicaltrials.gov

Key elements of a clinical trial

Patient protection: Patient safety is a primary focus for all clinical trials. The potential risks and benefits of each trial are reviewed carefully by a number of groups. You will be given a consent form which discusses the risks and benefits of the clinical trial in detail. Patient privacy is also a key component of patient safety. Data collected for the clinical trial will list patients by a study number and will only be shared with members of the research team who have signed a confidentiality agreement.

Informed consent: Before you can participate in a clinical trial, the research team must provide detailed information about the trial including the purpose of the trial, potential benefits and risks, the treatment plan (protocol and schedule), and your right to withdraw from the study at any time. You are encouraged to ask questions during this discussion so that you feel you understand the trial. You will then sign a consent form which provides this information and documents your informed consent.

Am I a candidate for a clinical trial?

Each clinical trial has specific criteria for participation. These criteria ensure the specific research goals of the trial and patient safety criteria are being met. You will be screened for the trial before being enrolled to be sure these criteria are met. Additional testing will be conducted after you have signed the consent form for the trial. In some cases, after these tests are obtained, a patient may not meet the criteria for the trial and cannot proceed to treatment.

What questions should I ask about participating in a clinical trial?

These are most often answered during the informed consent process.

1. Why is the trial being done?
2. What are the potential benefits of the trial?
3. What is the potential risk of the trial?
4. What can I expect from day to day while I am on the trial? (Frequency of visits, types of testing, length of visits)
5. If I experience side effects, whom should I contact?
6. What are the costs of participating in the trial?
7. What other treatment options do I have if I do not participate in the clinical trial?
8. How long will I be in the trial?
9. What happens if the treatment is not working?

Clinical trials and drug approval information

European Medicines Agency

Decentralized agency of the European Union, located in London; responsible for the scientific evaluation of medicines developed by pharmaceutical companies for use in the European Union

www.ema.europa.eu

Health Canada

Provides a notice of compliance (NOC) for full approval of a new drug or an NOC with conditions in Canada

www.hc-sc.gc.ca

National Cancer Institute, National Institutes of Health

Registry and results database of federally and privately supported clinical trials conducted in the United States and around the world

www.clinicaltrials.gov

National Institute of Health and Clinical Excellence

Guidance for cost effectiveness of treatments for England and Wales

www.nice.org.uk

Nordic MDS Group

Provides Nordic guidelines for MDS management online and patient information in all Nordic languages

www.nmds.org

Pharmaceuticals and Medical Devices Agency

Regulation of drug availability in Japan

www.pmda.go.jp

Therapeutic Goods Administration

Division of the Australian government's Department of Health and Aging; responsible for regulating therapeutic goods including medicines, medical devices, blood, and blood products

www.tga.gov.au

U.S. Food and Drug Administration

Approval required for commercial availability of therapy in the United States

www.fda.gov

An expanding number of experimental, or investigational, drugs are being evaluated for their potential use in treating MDS. Many trials are designed to find new targets in the MDS clone or the bone marrow microenvironment (see: *What Happens to the Bone Marrow in MDS?*). Other trials are investigating ways to combine currently available treatments with other novel agents. By using combinations of drugs that act at more than one target site, it is hoped that a more effective treatment than any one of the agents used alone will be produced. Participation in a clinical trial may offer you a treatment option that would otherwise not be available to you. Some of the active clinical trials for MDS are included in the table below. Ask your provider if there are clinical trials that might be an option for you. The MDS Foundation's Centers of Excellence provide options for clinical trial participation. Trials available at each center may vary. Additional information about clinical trials can be obtained by contacting the MDS Foundation, Inc. www.MDS-Foundation.org or The National Institutes of Health. www.clinicaltrials.gov.

Active Clinical Trials in MDS

Agent	Mechanism of Action	Phase	Indication
Arry-614	P38MAPK inhibitor	I	Lower risk
Gimatecan	Topoisomerase inhibitor	I	Lower and higher risk that have failed prior treatment
Alemtuzumab	Anti-CD52 immune modulation	II	Lower risk, hypoplastic
Oral azacitidine	Hypomethylating agent	II	Lower risk
Clofarabine	Nucleoside analog	II	Intermediate and higher risk
Vatalanib	Oral VEGF tyrosine kinase inhibitor	II	Primary or secondary MDS, any FAB subtype
Sapacitabine	Nucleoside analog	II/III	Intermediate and higher risk
Lenalidomide	IMiD® immunomodulatory agent	III	Lower risk, non-del(5q)
Rigosertib	Dual inhibitor of PI-3K and PLK	II/III	Higher risk by injection, oral in lower risk

FAB—French-American-British; MAPK—mitogen-activated protein kinase; MDS—myelodysplastic syndromes; VEGF—vascular endothelial growth factor

Note: based on information from www.ClinicalTrials.gov (2012)

References:

Kurtin, S. et. al. (2012) *Clin J Oncol Nurs*, 16S, 3, 58-64
 National Institutes of Health @ www.clinicaltrials.gov

How common is MDS in children?

MDS is primarily a disease of the elderly (most patients are older than age 65), but MDS can affect younger patients, as well. MDS in children is rare (1–4 cases per million per year). The median age at presentation in children is 6.8 years. It occurs equally in male and female children.

What causes MDS in children?

MDS can appear in an otherwise healthy child. Some evidence suggests that certain children are born with a tendency to develop MDS. This tendency or pre-existing factor can be thought of as a switch that can be triggered by external factors. The most common pre-existing factors in MDS are congenital (present at birth) and genetic (programmed in the cells) syndromes. These are present in about 50% of pediatric patients. If the external factor cannot be identified, then the disease is referred to as "primary MDS."

MDS may also develop in a child with a known pre-existing condition, and is therefore called "secondary MDS." Secondary MDS can be seen in children after chemotherapy or radiation therapy for another cancer. Children who take chemotherapy drugs or who receive radiation therapy for potentially curable cancers are at risk of developing secondary MDS for up to 10 years following treatment.

Secondary MDS is also seen with inherited bone marrow failure disorders such as Fanconi anemia or Diamond–Blackfan anemia, with acquired aplastic anemia, as well as with familial MDS. While this is extremely rare, some families seem to have a predisposition to develop MDS. It is a very rare occasion when family members, including siblings, are diagnosed with MDS. Factors that have been linked to the development of childhood MDS are listed below.

Factors and conditions that may predispose children to MDS

- Constitutional bone marrow failure abnormalities
- Fanconi anemia
- Kostmann syndrome
- Diamond–Blackfan syndrome
- Shwachman syndrome
- Down syndrome (trisomy 21)
- Neurofibromatosis type 1 (NF1) mutations
- Trisomy 8 mosaicism (some, but not all cells have an extra copy of chromosome 8)
- Congenital severe neutropenia
- Bloom syndrome
- Noonan syndrome
- Dubowitz syndrome
- Mitochondria cytopathy
- Familial MDS or leukemia
- Idiopathic aplastic anemia
- Prior chemotherapy (treatment-related MDS)

There are no known food or agricultural products that cause MDS. Children and their families often worry that MDS might be contagious. No evidence exists to suggest that a virus causes MDS, and MDS cannot be "transmitted" to loved ones.

What are the symptoms of MDS in children?

In the early stages of MDS, children may experience no symptoms at all. A routine blood test may reveal cytopenias (low blood counts). Sometimes the white cell and platelet counts may be low while the hematocrit remains normal. Children with MDS may present with nonspecific symptoms such as a pale complexion, fatigue, petechiae (tiny red or purple spots on the skin), or recurrent infections. In some cases, more severe symptoms such as shortness of breath, weakness, or bleeding may be present.

Is MDS fatal?

Failure of the bone marrow to produce mature healthy cells is a gradual process and therefore, MDS is not necessarily a terminal disease. However, some children do succumb to the direct effects of the disease and gradual bone marrow failure. A small number of the children diagnosed with MDS may progress to acute myeloid leukemia (AML).

Pediatric MDS can be quite variable in both the disease course and the outcomes. For example, some children with refractory cytopenia or low-grade RAEB can remain stable for many months or years, while others may rapidly become worse. Monosomy 7 in children is not associated with poor prognosis, unlike in adults; however, a few studies have suggested that children with monosomy 7 progress earlier to AML.

How severe is my child's MDS?

Accurate classification of MDS is very important to help predict the course of your child's disease, and is essential in guiding your child's hematologist in selecting the best treatment. Because the disease course of MDS can vary widely from patient to patient, classification systems for grouping various "subtypes" of the myelodysplastic "syndromes" have been developed, and several classification systems are available that have been developed from those used for the adult forms of MDS (see: *How Severe is My MDS?*).

The adult World Health Organization (WHO) classification system has been revised to make it more applicable to pediatric MDS. The Modified WHO Classification for Pediatric MDS classifies myelodysplastic and myeloproliferative disorders into three major groups: (1) adult-type MDS, (2) Down syndrome-related disorders, and (3) juvenile myelomonocytic leukemia (JMML).

Revised World Health Organization Classification of Childhood Myelodysplastic Syndromes (2008)

Myelodysplastic Syndromes

- Refractory cytopenia (RC)—blood blasts <2%, bone marrow blasts <5%
- Refractory anemia with excess blasts (RAEB)—blood blasts >2%, bone marrow blasts 5-19%
- Refractory anemia with excess blasts in transformation (RAEB-t)—bone marrow blasts 20-29%
- AML with MDS-related changes—peripheral blood or bone marrow blasts >20%

Myelodysplastic/Myeloproliferative Disease

- Juvenile myelomonocytic leukemia (JMML)

Down Syndrome Disease

- Transient abnormal myelopoiesis
- Myeloid leukemia of Down syndrome

Down syndrome disease

Approximately 10% of newborns with Down syndrome develop transient myeloproliferative disorder (TMD). In TMD there is an abnormally high number of immature white blood cells in the blood stream. Most children with TMD recover on their own within several weeks. A minority of children progress to a form of acute myeloid leukemia (AML) called M7-AML. Myeloid leukemia in children with Down syndrome is related to MDS, but has its own distinct features.

Blast cells from nearly all of these children have a specific abnormality in the gene that controls normal development of red blood cells and platelets. This mutation may prove to be useful in diagnosing the disease. M7-AML is very sensitive to chemotherapy. Children with TMD who develop M7-AML have a good response to AML chemotherapy.

Juvenile myelomonocytic leukemia (JMML)

The term JMML includes other childhood leukemias that were previously known as juvenile chronic myeloid leukemia, chronic myelomonocytic leukemia, and infantile monosomy 7 syndrome. JMML typically occurs at a very young age (less than 2 years) and is more common in boys. It is thought to represent about 25% of all pediatric MDS patients. JMML is often associated with other inherited diseases and other bone marrow failure syndromes. In JMML, many bone marrow stem cells develop into two types of white blood cells: monocytes and myelocytes. Some of these cells remain immature, or blast cells, and cannot carry out their normal functions. These excess build up in the bone marrow and get in the way of the manufacture of red and white blood cells, which can lead to anemia and infection.

Patients with JMML can have varying outcomes based on factors such as, age at diagnosis, number of blood platelets, level of fetal hemoglobin, or any changes in the chromosomes.

How do you treat MDS in children?

There are many considerations in the treatment of childhood MDS (see: *General Principles of Treatment of MDS*). Many of the strategies used to treat adults with MDS are being investigated in pediatric clinical trials (see: *Clinical Trials*). Allogeneic hematopoietic stem cell transplantation (HSCT) provides the best option for a cure (see: *Bone Marrow Transplant*).

How is MDS in children different than MDS in adults?

Criteria	Adult MDS	Childhood MDS
Incidence (million/yr)	>30	0.5-4
Refractory anemia with ring sideroblasts (RARS)	20%-25%	<2%
Cytogenetic aberrations	30%-50%	50%
Mutation of Ras gene	Common	Rare
5q- chromosomal aberration	20%	<2%
Monosomy 7 abnormality (seen in)	8%-10%	30%
Aim of therapy	Usually palliative	Usually curative

Pediatric Information Resources— MDS and Childhood Cancers



Alex's Lemonade Stand

Raises money and awareness for pediatric cancer causes, primarily for research into new cures and treatments

www.alexlemonade.org

American Cancer Society

250 Williams Street, NW
Atlanta, GA 30303

800-ACS-2345

www.cancer.org

American Society of Pediatric Hematology/Oncology (ASPHO)

4700 W. Lake Avenue
Glenview, IL 60025

847-375-4716

847-375-6475 fax

www.aspho.org

Aplastic Anemia & MDS International Foundation

100 Parl Avenue, Suite 108
Rockville, MD 20850

301-279-7202

800-747-2820

www.aamds.org

Blood & Marrow Transplant Information Network

2900 Skokie Valley Road, Suite B
Highland Park, IL 60035

847-433-3313 or 888-597-7674

847-433-4599 fax

www.bmtinfonet.org

Candlelighters Childhood Cancer Foundation

Provides information and awareness to support children with cancer and their families, and supports research

www.candlelighters.org

Childhood Leukemia Foundation

Supports children with cancer and their families

www.clf4kids.com

EWOG (European Working Oncology Group)

www.ewog-mds.org

JMML Foundation

9921 Carmel Mountain Road #170
San Diego, CA 92129

858-243-4651

www.jmmlfoundation.org

National Marrow Donor Program

3001 Broadway Street N.E., Suite 100
Minneapolis, MN 55413

800 MARROW2 (800-627-7692)

www.marrow.org

National Cancer Institute's Physician Data Query (PDQ) Comprehensive Cancer Database

Includes disease and treatment summaries for major types of pediatric cancers, including MDS

www.cancer.gov/cancertopics/pdq/cancerdatabase

National Cancer Institute's Clinical Trials Database

Listing of clinical trials for all types of cancer, including MDS

www.cancer.gov/clinicaltrials

Pediatric Myelodysplastic and Bone Marrow Failure Registry

Children's Hospital Boston
Department of Hematology

Fegan 7

300 Longwood Avenue
Boston, MA 02115 USA

Phone: 888-5-PediMDS

Email: MDS@childrens.harvard.edu

www.pedimds.org

Pediatric Oncology Resource Center

Resources for parents, friends, and families of children with cancer

www.acor.org/ped-onc

The Leukemia & Lymphoma Society

1311 Mamaroneck Avenue, Suite 130
White Plains, NY 10605

800-955-4572

www.leukemia.org

The MDS Foundation, Inc.

4573 South Broad Street, Suite 150
Yardville, NJ 08620

800-MDS-0839 (within US only)

609-298-1035 (outside US)

609-298-0590 fax

www.mds-foundation.org





QUICK TIPS

There are a number of symptoms that you (or your loved-one) may experience while living with MDS. The quick-tips offered in this section of the Building Blocks of Hope include guidelines for monitoring your symptoms and reporting them to your health care provider when necessary. You will also be provided with very practical strategies for preventing more severe symptoms.

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Definition: Anemia is a decrease in the number of red blood cells that are available in the blood to carry oxygen to all the tissues of the body. Oxygen is needed by all of the body's cells to grow, carry out their specific functions, and divide. When the number of red blood cells falls below a certain level, the amount of oxygen also falls, such that cells and tissues do not receive enough oxygen. Without oxygen to provide the energy to carry out specific functions, cells become less efficient and fatigued.

Anemia is a common finding in patients with MDS due to the ineffective blood cell development in the bone marrow. Anemia may affect each person differently based on their general state of health, age, and the severity of the anemia. Anemic patients generally experience fatigue and report that they are tired much of the time and have no energy. Anemia varies in its severity. In mild anemia, patients may feel well or just slightly fatigued. In moderate anemia almost all patients experience some fatigue, which may be accompanied by heart palpitations, shortness of breath, and pale skin. In severe anemia, almost all patients appear pale and report chronic overwhelming fatigue and shortness of breath. Because severe anemia reduces blood flow to the heart, older patients may be more likely to experience cardiovascular symptoms, including chest pain. Although chronic anemia is seldom life threatening, it can drastically reduce a patient's quality of life.

Symptoms of anemia:

- Shortness of breath (especially during exercise)
- Palpitations (feeling skipped or irregular heart beat)
- Pale skin
- Mental confusion or difficulty concentrating
- Lightheadedness or dizziness, especially when standing
- Feeling tired (fatigue) and/or weak
- Rapid heart rate (tachycardia)
- Chest pain
- Headache

How is anemia measured?

Anemia is characterized by a persistently low hematocrit (a measure of the body's red blood cell volume) or persistently low levels of hemoglobin (the blood protein that carries oxygen to the body's tissues).

Hemoglobin is measured from a blood sample and the amount present is expressed in units of grams per deciliter, abbreviated g/dL. The normal value for hemoglobin varies by age and gender. Anemia occurs when hemoglobin concentrations fall below 12 g/dL for women and 13 g/dL for men. The severity of anemia is categorized by the following hemoglobin concentration ranges:

- **Mild anemia**—hemoglobin between 9.5–13.0 g/dL
- **Moderate anemia**—hemoglobin between 8.0–9.5 g/dL
- **Severe anemia**—hemoglobin below 8.0 g/dL

Like hemoglobin, hematocrit is measured from a blood sample. The hematocrit is the fraction of blood composed of red blood cells and is expressed as a percentage. People with a high volume of plasma (the liquid portion of blood) may be anemic even if their blood count is normal because the blood cells have become diluted. Like hemoglobin, a normal hematocrit percentage depends on age and gender. In adults, anemic ranges for hematocrit generally fall below 39% in men and below 36% in women.

Things your health care provider may recommend:

- Your health care provider may recommend red blood cell transfusion to improve the symptoms you are experiencing from the anemia. Red blood cell transfusions are considered a form of supportive care. They do not change the characteristics of the MDS. The benefits of red blood cell transfusion are temporary so that repeated transfusions may be needed. The number and frequency of red blood cell transfusions will vary for each person based on the severity of symptoms, the characteristics of the MDS, and what other treatments are being used.
- Your doctor may recommend growth factors such as erythropoietin to try to stimulate your bone marrow to produce more red blood cells. You can discuss this with your doctor. If the injections are prescribed, be sure to have the injections on schedule.

Things you can do:

1. Let your doctor know if you experience increasing shortness of breath, chest pain or palpitations.
2. Keep all of your appointments as scheduled.
3. Record and track your blood counts, blood type and any antibodies, transfusion dates, and any symptoms before and after transfusions or growth factor administration (see: *My MDS Plan*).
4. Balance rest with activity.
5. Ask for help from family and friends.

Your health care providers will discuss the risks and benefits of each treatment option with you. Be sure that you discuss any concerns with your health care team. Based on your symptoms and how you feel, some changes to your care may be made to make you more comfortable.

**Staying Healthy—Living
with low blood counts**



Definition: Neutropenia (*noo-troh-PEE-nee-uh*) is a decrease in the number of neutrophils. Neutrophils are a type of white blood cell (WBC) that help to fight common infections. When the neutrophils or the WBCs are below normal, you may be at an increased risk of infection.

Neutropenia is less common in patients with MDS than is anemia at the time of diagnosis. In patients receiving disease modifying treatments for MDS, the WBC count and in turn the absolute neutrophil count (ANC) are commonly reduced in the early months of treatment.

How is neutropenia measured?

Neutrophils are the most common type of white blood cell, normally 60-70% of the WBC. The severity of neutropenia is estimated based on the absolute neutrophil count (ANC). The normal WBC is 3,500-10,000 cells/microliter (μL). The normal ANC is 1500-8,000 cell/ μL . The ANC is calculated using the following formula:

$$\text{ANC} = \text{WBC} \times \% \text{ neutrophils}$$

The ANC is often included in the laboratory report. You can ask your health care provider to help you with finding or calculating this number. The severity of neutropenia (based on the ANC) is measured by results obtained from peripheral blood:

- **Mild neutropenia:** ANC 1,000-1500/ μL
- **Moderate neutropenia:** ANC 500-1,000/ μL
- **Severe neutropenia:** ANC less than 500/ μL

Febrile neutropenia is considered a medical emergency and should be reported to your health care provider immediately. Febrile neutropenia is present when the ANC is less than 1,000/ μL and you have a body temperature $>38.5^\circ\text{C}$ (101.4°F) or a sustained temperature $>38.0^\circ\text{C}$ (100.4°F) for more than one hour. Ask your health care team who to contact, how to contact them, and when you should seek urgent or emergency care.

Symptoms of neutropenia:

- Elevated body temperature (fever)
- Low blood pressure
- Frequent infections or infections that linger
- Shaking chills

Things your health care provider may recommend:

- Your health care provider may recommend the administration of WBC growth factors to reduce the severity or duration of neutropenia.
- The administration of antibiotics for prevention is not commonly recommended for most patients, but may be recommended for patients at greater risk.
- If neutropenia is severe, it may be necessary to modify your MDS treatment by changing the dose or holding the medication temporarily until the neutrophil count recovers.

Things you can do:

1. Let your doctor know if you develop a fever when your ANC is $<1,000/\mu\text{L}$. If you are not sure what your ANC is, ask your health care team for guidelines on when you should report a fever.
2. Keep all your appointments as scheduled.
3. Have a working thermometer at home.
4. Record and track your blood counts, including the WBC and ANC, any symptoms including fevers, chills, or infections.

5. Wash your hands frequently.
6. Avoid people who are obviously ill.
7. Avoid crowded, enclosed places—this does not mean you can't go out—ask your health care team for places to avoid, such as buffets, crowded shopping areas, or concerts.
8. Avoid uncooked or unpasteurized meat or dairy products.
9. Wash all fruits and vegetables before eating them.
10. Maintain good hygiene—bathe daily, have good oral hygiene, cleanse after bowel movements or urination, wash hands frequently.
11. Stay hydrated.
12. Ask for help from family and friends.

Your health care providers will discuss the risks and benefits of each treatment option with you. Be sure that you discuss any concerns with your health care team. Based on your symptoms and how you feel, some changes to your care may be made to ensure safety and make you more comfortable.

Definition: Thrombocytopenia (THROM·boh·sy·toh·PEE·nee·uh) is a decrease in the number of platelets in the blood. Platelets help stop bleeding by clumping and forming plugs in blood vessel holes (clotting). Platelets also help maintain normal blood vessel health in the body. When a patient develops thrombocytopenia, the risk of bleeding or bruising increases.

Thrombocytopenia is less common than anemia in patients with MDS. Platelets are produced in the bone marrow from the same factory cell (myeloid stem cell). The myeloid stem cell produces megakaryocytes (MEGA·care·EE·oh·sy·t), which, in turn, produce thousands of platelets each day. In MDS, the megakaryocytes are often abnormal (dysplastic) and may produce too few platelets (thrombocytopenia), too many platelets (thrombocytosis), or platelets that do not function normally. Megakaryocytes are present only in the bone marrow and cannot be measured by a peripheral blood count.

The primary concern for patients with thrombocytopenia is bleeding. The risk of bleeding is related to the severity of the thrombocytopenia. Certain medications may increase the risk of bleeding, such as blood thinners, aspirin, and other anti-inflammatory medications.

How is thrombocytopenia measured?

Thrombocytopenia is characterized by a platelet count below normal. Normal platelet levels are between 150,000–450,000/ μL . The severity of thrombocytopenia is measured by following platelet counts obtained from peripheral blood:

- **Mild thrombocytopenia:** platelet count of 50,000–100,000/ μL
- **Moderate thrombocytopenia:** platelet count of 25,000–50,000/ μL
- **Severe thrombocytopenia:** platelet count less than 25,000/ μL

Symptoms of thrombocytopenia:

- Excessive bruising with normal daily activities
- Bleeding gums
- Bloody nose
- Cuts that won't stop bleeding
- Petechiae—pinpoint red dots on the skin
- Coughing up blood
- Blood in the urine or stool

Things your health care provider may recommend:

- Your health care provider may recommend platelet transfusions when the platelets are below 10,000/ μL or at higher levels for patients with additional risk factors, such as a recent surgery. Platelet transfusions may be given to reduce the risk of bleeding. Platelet transfusions are considered a form of supportive care. They do not change the characteristics of the MDS. The benefits of platelet transfusions are temporary (hours) so that repeated transfusions may be needed. The number and frequency of platelet transfusions will vary for each person based on the severity of symptoms, the characteristics of the MDS, and what other treatments are being used.
- Your doctor will recommend that you stop taking any medications that interfere with platelet function (aspirin) or prevent clotting through other mechanisms (blood thinners such as Coumadin, Plavix, and Heparin). These medications are generally held when the platelet count is below 50,000/ μL .

- There are currently no FDA approved growth factors for the treatment of thrombocytopenia in patients with MDS. There are medications used for thrombocytopenia resulting from other causes that are being studied in clinical trials for patients with MDS and thrombocytopenia.
- If thrombocytopenia is severe, it may be necessary to modify your MDS treatment by changing the dose or holding the medication temporarily until the platelet count recovers.

Things you can do:

1. Let your doctor know if you experience unusual bruising, uncontrolled bleeding, or develop petechiae.
2. Keep all of your appointments as scheduled.
3. Record and track your blood counts, transfusion dates, and any symptoms before and after transfusions.
4. Avoid excess alcohol, which may contribute to platelet dysfunction.
5. Avoid injuries (falls, cuts, scrapes) and activities that can cause bruising or bleeding, such as contact sports and heavy lifting.
6. Avoid constipation or straining to have a bowel movement.
7. Use a soft tooth brush.
8. Ask for help from family and friends.

Your health care providers will discuss the risks and benefits of each treatment option with you. Be sure that you discuss any concerns with your health care team. Based on your symptoms and how you feel, some changes to your care may be made to ensure safety and make you more comfortable.

Definition: Body temperature above normal. Fever may be a result of infections or may be a side effect of certain chemotherapy agents used to treat MDS. Ask your health care providers when you should report a fever and what type of thermometer is best to use. It is essential to treat MDS patients with fevers quickly to avoid the possibility of developing more serious infections (see: *Quick Tips: Neutropenia*). Normal body temperatures increase up to 1° higher in the evening.

Signs and symptoms of a fever

The most common recommendations for checking a temperature:

- Feeling warmer than normal
- Shaking chills (can't get warm even with blankets, chattering teeth)
- Flushing (red in the face)
- Feeling lightheaded or dizzy
- Low blood pressure
- Temperature higher than normal (normal = 98.6°)

Things your health care provider may recommend:

- Take your temperature if you are having any of the symptoms listed above.
- Medications to reduce fevers (Acetaminophen is most common) should only be taken after discussion with the health care team.
- It is important to drink plenty of fluids and get plenty of rest.

Things you can do:

1. Have a working thermometer at home. Discuss which type of thermometer is best for you to use with your health care team.
2. Stay hydrated.
3. Record and track your blood counts, including the WBC and ANC, any symptoms including fevers, chills, or infections (see: *My MDS Plan*).
4. Let your doctor know if you develop a fever when your WBC or ANC are $<1,000/\mu\text{L}$. If you are not sure what your ANC is, ask your health care team for guidelines on when you should report a fever.
5. Notify the physician for any fever $\geq 101.4^\circ\text{F}$ or 38.5°C .
6. Shaking chills at any body temperature in patients with neutropenia (see: *Quick Tips: Neutropenia*) should be reported immediately.
7. Keep all of your appointments as scheduled.
8. Ask for help from family and friends.

Your health care providers will discuss the risks and benefits of each treatment option with you. Be sure that you discuss any concerns with your health care team. Based on your symptoms and how you feel, some changes to your care may be made to ensure safety and make you more comfortable.

Low blood counts (cytopenias) are a common finding in MDS. Anemia is the most common cytopenia, and the majority of patients with MDS will require blood transfusions as a result of their anemia (see: *Quick Tip: Anemia*). Transfusion dependence (requiring repeated transfusions) is often a trigger to discuss the use of disease modifying treatments or additional supportive care strategies. A reduction in the number of transfusions in an eight-week period [hematologic improvement, as defined by the International Working Group (IWG) criteria] may be the first indication of response to treatment. Each patient with MDS will have variable transfusion requirements and frequency. Patients receiving treatments for MDS will have variable rates of response.

A system for tracking blood counts, transfusions, and other treatments can help you see your individual trends and progress. You may have laboratory evaluations, clinical visits, and blood transfusions performed in many different settings.

The Complete Blood Count (CBC), Differential and Platelet Count

Blood Count	Normal Range	
White Blood Cells (WBC)	4.5–13.0 1,000/ μ L	
Absolute Neutrophil Count (ANC) (WBC x % Segs + Bands)	\geq 1,500 /mm ³	
Hemoglobin (Hgb)	Men: 13.5–17.5 g/dL	Women: 12.0–16.0 g/dL
Hematocrit (Hct)	Men: 41–53%	Women: 36–46%
Platelets (Plt)	150,000–350,000/mm ³	

Things you can do:

1. You can take your tracking tool with you as a part of your MDS Plan (see: *My MDS Plan*) to each visit.
2. Ask your health care providers for copies of your blood results. Enter the key results in your tracking tool.
3. Make note of the dates of transfusion, the number of units, and level of hemoglobin or platelets at that time.
4. Make a note of any symptoms experienced before and after receiving transfusions or growth factor injections.
5. See also *Quick Tips for: Anemia, Neutropenia, and Thrombocytopenia*.

Definition: Diarrhea is defined as frequent and watery bowel movements. Diarrhea may be caused by medications, changes in diet, or in some cases infections. The severity of the diarrhea is generally determined by the number of liquid stools passed per day. Moderate diarrhea is defined as 4–6 stools per day. Severe diarrhea is defined as greater than 7 liquid stools per day, or incontinence (not making it to the bathroom in time). Frequent liquid or watery stools can lead to dehydration, weakness, and loss of electrolytes needed for normal body functions, and damage to the kidneys.

Symptoms of diarrhea:

- Liquid stools
- Cramping with explosive liquid stools
- Abdominal pain
- Foul smelling liquid stools

Things your health care provider may recommend:

- Staying hydrated—drinking 2–3 liters of fluid per day. Liquids with electrolytes may be recommended.
- Avoid high sugar sports drinks or fruit juices—these often make the diarrhea worse.
- Anti-diarrhea medications may be recommended. Discuss which medications are right for you with your health care team. Be sure to ask how many of these medications are safe to take each day.
- Meeting with a dietician may be helpful in finding a diet that works best for you.

Things you can do:

1. Drink 2–3 liters of fluid a day—avoid caffeine or high sugar drinks.
2. Report any blood in the stool, severe abdominal cramping, fevers, or symptoms of severe diarrhea to your health care team immediately.
3. Eat small frequent meals.
4. The BRAT diet is often recommended until more severe symptoms improve: Bananas, Rice, Applesauce, and Toast.
5. Foods to avoid: dietary fiber (brown rice, fruits, vegetables, popcorn, whole grain breads and pasta), alcohol, caffeine, chocolate, greasy foods, dairy products containing lactose.
6. Increase the intake of foods and fluids high in sodium and potassium, such as broths, soups, low-sugar sports drinks, potatoes and crackers.
7. Probiotic supplements or foods containing probiotics (natural gut bacteria) may improve diarrhea.
8. Keep all of your appointments as scheduled.
9. Keep a log of symptoms that you are concerned about—discuss these with your health care team.
10. Soak in a warm bath—be sure that you feel safe and able to get in and out of the bath on your own. If you do not feel safe, ask for help.
11. Wash your hands after using the bathroom.
12. Maintain good hygiene—bathe daily, have good oral hygiene, cleanse after bowel movements or urination, wash hands frequently.
13. Ask for help from family and friends.

Your health care providers will discuss the risks and benefits of each treatment option with you. Be sure that you discuss any concerns with your health care team. Based on your symptoms and how you feel, some changes to your care may be made to ensure safety and make you more comfortable.

Definition: Constipation is an unpleasant, sometimes painful, condition characterized by infrequent and difficult passing of stool. Constipation may result from a number of causes including dehydration, medications (narcotics in particular), other illnesses such as diabetes or irritable bowel syndrome, changes in diet, immobility, and changes in bowel function common in older adults. Patients with MDS may experience constipation as result of treatment with disease modifying agents and medications used to prevent or treat nausea.

Symptoms of constipation:

- Bloating
- Pain with bowel movements
- Decreased appetite
- Nausea
- Small hard stools
- A feeling that you cannot completely empty the bowel
- Straining with bowel movements
- Low-back or abdominal pain
- Fatigue
- Small amounts of liquid stool without formed stools

Things your health care provider may recommend:

- Daily exercise—even walking can improve bowel motility.
- Staying hydrated—drinking 2–3 liters of fluid per day.
- Adding fruits and other natural sources of fiber to your diet may improve bowel motility.
- Laxatives and stool softeners may be recommended. Discuss the best options for you with your health care team.
- Fiber supplements are not generally recommended for constipation. They may make the symptoms worse.
- Probiotic supplements or foods containing probiotics (natural gut bacteria) may improve constipation.
- Suppositories and enemas are not recommended if you have a low white blood cell count (neutropenia) or have low platelets (thrombocytopenia) due to the risk of infection or bleeding.
- Meeting with a dietician may be helpful in finding a diet that works best for you.

Things you can do:

1. Stay active.
2. Drink 2–3 liters of fluid a day.
3. Eat a diet rich in fruits, vegetables, and natural fibers.
4. Don't let more than 3 days go by without a normal bowel movement—discuss this with your health care team.
5. Let your doctor know if you have pain with bowel movement, any blood in the stool, severe abdominal pain, persistent nausea, or vomiting.
6. Keep all of your appointments as scheduled.
7. Keep a log of symptoms that you are concerned about—discuss these with your health care team.
8. Soak in a warm bath—be sure that you feel safe and able to get in and out of the bath on your own. If you do not feel safe, ask for help.
9. Wash your hands after using the bathroom.
10. Maintain good hygiene—bathe daily, have good oral hygiene, cleanse after bowel movements or urination, wash hands frequently.
11. Stay hydrated.
12. Ask for help from family and friends.

Your health care providers will discuss the risks and benefits of each treatment option with you. Be sure that you discuss any concerns with your health care team. Based on your symptoms and how you feel, some changes to your care may be made to ensure safety and make you more comfortable.

Definitions: Nausea is a symptom that is often described as an unpleasant feeling associated with flushing, tachycardia, and the urge to vomit.

Vomiting is a physical phenomenon that involves contraction of the abdomen, chest wall muscles, and movement of the diaphragm followed by expulsion of the stomach contents.

Nausea and/or vomiting may be caused by a number of problems including:

- Constipation
- Medications including chemotherapy
- Hiccups
- Dry mouth
- Dehydration
- Migraines
- Heart disease
- Odors
- Infections
- Dehydration
- Stomach acid
- Anxiety

Symptoms often associated with nausea or vomiting:

- feeling hot and cold
- sore throat
- sweating
- fatigue
- headache
- dizziness
- weakness
- bloating
- sleep disturbance

Things your health care provider may recommend:

- Staying hydrated—drinking 2–3 liters of fluid per day. Liquids with electrolytes may be recommended.
- There are a number of medications commonly used to prevent and or treat nausea and vomiting, these are called anti-emetics. These may be administered prior to your chemotherapy or may be prescribed for use at home. Anti-emetics may be given as an intravenous or subcutaneous injection or may be taken by mouth. Discuss which medications might be best for you.
- Eating small, frequent meals will reduce bloating and stomach acid.
- Meeting with a dietician may be helpful in finding a diet that works best for you.

Things you can do:

1. Avoid exposure to strong odors including perfumes.
2. Keep all of your appointments as scheduled.
3. Ask for help.
4. Discuss how many of each type of anti-emetic you are able to safely use each day and what side effects they may cause.
5. Some of the medications used to treat or prevent nausea and vomiting may increase the risk of developing constipation. Refer to the *Quick Tips: Constipation* page to review strategies to prevent this.
6. Make a note of any symptoms of nausea that you have or episodes of vomiting. Discuss these with your health care provider at your next visit.
7. If you experience vomiting more than 5–6 times in a 24 hour period, notice any blood when you vomit, or are not able to keep food or liquids down, and be sure to contact your health care provider immediately. Talk with your health care provider about when and how to call in case of more severe symptoms.
8. Drink 2–3 liters of fluid a day—avoid caffeine or high sugar drinks.

9. Eat small, frequent meals.
10. Foods to avoid: fatty foods, greasy foods, spicy foods, foods that are hard to digest (hard fruits, meats, hard cheese, popcorn), alcohol, caffeine, chocolate.
11. Avoid foods with strong odors.
12. Increase the intake of foods and fluids high in sodium and potassium, such as broths, soups, low-sugar sports drinks.
13. Brush your teeth more frequently and use non-alcohol-based mouth washes to reduce the symptoms of dry mouth and bad taste.
14. Peppermint and ginger supplements have been found to helpful for some patients.
15. Relaxation, imagery, and meditation may help some patients. Ask your health care team about any resources available.
16. Ask for help from family and friends.

Your health care providers will discuss the risks and benefits of each treatment option with you. Be sure that you discuss any concerns with your health care team. Based on your symptoms and how you feel, some changes to your care may be made to ensure safety and make you more comfortable.

Definitions: Local irritation at the site of a subcutaneous (SC) injection.

Medications that are injected into the subcutaneous tissue (fatty layer under the skin) are referred to as subcutaneous (SC) injections. Subcutaneous injection of medications may cause burning pain while being injected and may cause local irritation or inflammation in the skin and soft tissue. In most cases, the reactions are mild and are not painful. More severe reactions may include painful lumps, or involvement of a larger area of the skin. The severity of the reactions can be minimized with the proper technique for administration and care of the skin. Most injection site reactions clear completely with time. This type of reaction is not considered a true allergic reaction.

Injection site reactions are common when Azacitidine (Vidaza®) is administered SC. Mild redness of the skin which fades with time is the most common reaction. More severe reactions may occur in some patients.

Mild injection site reactions have also been reported in patients receiving SC growth factors, including Neupogen® (filgrastim), Neulasta® (pegfilgrastim), and Procrit® (erythropoietin). Most skin reactions clear completely with time.

All medications, including medications given by SC injection, may cause allergic reactions. Skin changes commonly seen with allergic reactions to medications include widespread (systemic) redness (erythema) and pruritus (itching). When severe, the skin can blister and peel. This type of reaction requires stopping the suspected medications and may require hospitalization in more severe cases.

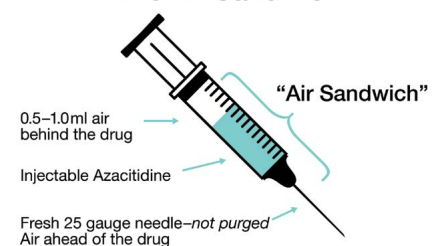
Symptoms of injection site reactions:

Mild skin reaction	Localized dry, red, soft skin. Not painful. May have pruritus (itching).
Moderate skin reaction	Localized redness and swelling. May be painful, firm, and include a large area around the injection site. May have pruritus (itching).
Severe skin reaction	Larger area of redness and swelling may have blistering, ulceration, or peeling of skin at the injection site. Most often painful.
Allergic reaction to SC injection of medication	Widespread (systemic) redness that commonly involves the torso and extremities.

Selecting a site for injection of medication

- Subcutaneous injections are given in areas with adequate adipose (fatty) tissue, where you can pinch an inch: abdomen, the back of the upper arms, and the outer portion of the upper thighs.
- Rotating the sites during your treatment will limit the severity at any one site and allow previous sites to heal.
- Avoiding areas prone to friction, such as the seat belt region or the belt-line, will also reduce the severity of injection site reactions.
- Areas with scarring, birth marks, inflammation, or breaks in the skin should be avoided.
- Using a technique called the "Air Sandwich" may also limit the amount of medication in contact with the adipose tissue.

Injection Technique: The Air Sandwich



Things your health care provider may recommend:

- Your health care provider may recommend oral antihistamines to reduce the itching and the urge to scratch.
- Local administration of antihistamines or topical steroid creams may be recommended to reduce the local inflammation.
- Application of a cool compress may minimize any burning. You should not apply heat or ice to the injection site for up to 4 hours after the injection. This may interfere with proper absorption of the medication and make it less effective.
- Oral anti-inflammatory medications may be recommended. Discuss which medication is right for you with your health care team.
- Review of all medications, environmental exposures (soaps, detergents, perfumes, lotions etc.), sun exposure, and transfusions to evaluate possible causes.
- Referral to a dermatologist, a physician specializing in the treatment of skin disorders, may be recommended in more severe cases.

Things you can do:

1. Let your health care team know if you develop injection site reactions. The nurse administering your medication will check the sites prior to administering your next dose.
2. Avoid friction to site: wear loose fitting clothing, avoid rubbing the site immediately after receiving an injection.
3. Ice or heat should not be applied to the injection site immediately after injection. Heat may cause increased irritation and ice may limit the absorption of the medication. A cool compress may be applied within two hours of the injection. Ice can safely be applied 4 hours after the injection.
4. Wear loose fitting, cotton clothes.
5. Avoid scratching, rubbing, or picking at the skin.
6. Keep all of your appointments as scheduled.
7. Ask for help from family and friends.

Your health care providers will discuss the risks and benefits of each treatment option with you. Be sure that you discuss any concerns with your health care team. Based on your symptoms and how you feel, some changes to your care may be made to ensure safety and make you more comfortable.

Definition: A rash is a change of the skin which affects its color, appearance, or texture. A rash may be localized in one part of the body, or affect all of the skin. Rash is generally caused by a skin irritation that can result from chemotherapy, allergy, infection, or skin problem.

Signs and Symptoms

A rash can be as mild as red or discolored skin, with or without bumps, or fluid-filled lesions (pustules). A rash can be localized (in one area of the body) or systemic (covering multiple areas of the body). With certain chemotherapy drugs, such as Lenalidomide (Revlimid®) it is not unusual to experience patches of dry skin, itchiness, mild swelling and redness (Kurtin & Sokol, 2009). This type of rash will often resolve gradually without discontinuing the drug. In rare cases, skin rashes can be more severe and may require hospitalization.

Things your health care provider may recommend:

- Your health care provider will need to evaluate the rash to determine the most likely cause and level of severity.
- Topical antihistamines or steroid creams may be prescribed to reduce irritation and itching.
- If you get any kind of rash, call your health care professional to discuss the best way to treat it. It is important that all skin rashes are correctly identified.



Skin rash from Revlimid (Lenalidomide)

Things you can do:

1. Examine your skin daily.
2. Avoid sun exposure and use sunscreens with a sun protection factor of at least 15.
3. Wear hats, sunglasses, and cover skin as much as possible.
4. Use mild, non-perfumed, non-deodorant soaps, such as Dove, Aveeno, or Neutrogena soaps.
5. Take showers or short, cool baths instead of long, hot showers.
6. Use lanolin-based creams, lotions and ointments regularly to keep your skin well hydrated.
7. Avoid perfumes.

Managing the side effects of treatment



Definition: An unusual tiredness that interferes with normal activities and is not relieved by resting or a good night's sleep. Fatigue may be more severe in patients with MDS who also have anemia. Insomnia (difficulty sleeping) is common in older adults and may contribute to fatigue. Other things that can contribute to fatigue include: inactivity, pain, emotional distress, poor nutrition, and other illnesses that are not well controlled such as diabetes or thyroid disorders.

Symptoms of fatigue:

- Physical weakness
- Difficulty concentrating or making decisions
- Difficulty performing normal activities, such as preparing food, cleaning house, paying bills, and working
- Drowsiness, or feeling wiped out
- Withdrawal from social activities
- Increased time to perform basic activities, such as bathing and grooming

Things your health care provider may recommend:

- Your health care provider may order laboratory tests to determine possible contributing factors for fatigue, such as anemia, thyroid disorders, dehydration, or diabetes.
- If you are anemic and the symptom of fatigue is felt to be a result of the anemia, your provider may order a red blood cell transfusion.
- There are some medications that have been used to treat severe fatigue. However they do have other side effects, so they may not be right for you. Discuss your fatigue with your provider to determine which treatments may be best for you.

Things you can do:

1. Stay active as much as possible to maintain muscle strength and improve stamina. Consider starting an exercise routine, such as daily walks with caregiver or friend.
2. List the activities for each day. Set priority activities for the day, and schedule priority activities for periods of highest energy level.
3. Limit naps during the day to less than 1 hour to prevent problems with nighttime sleeping.
4. Talk to your health care team if you are experiencing difficulty with anxiety or overwhelming sadness.
5. Stay hydrated.
6. Eat small, frequent meals.
7. Check with health care provider regarding the need for transfusion based on symptoms and hemoglobin level.
8. Ask for help from family and friends.

Your health care providers will discuss the risks and benefits of each treatment option with you. Be sure that you discuss any concerns with your health care team. Based on your symptoms and how you feel, some changes to your care may be made to ensure safety and make you more comfortable.

Definitions: Anxiety is a common reaction to learning that one has MDS. It is described as a vague, unpleasant, and uneasy feeling of potential harm or distress. Many individuals have trouble understanding why they have these feelings, but certainly find them uncomfortable. Anxiety can range from a mild and vague feeling that something may be wrong, to an overwhelming feeling that interferes with a person's ability to function.

All people experience periods of anxiety in their lives. Starting a new job, going off to college, or moving to a new city can all cause some amount of anxiety. Receiving a diagnosis of a disease that you have likely not heard of before, can also cause some amount of anxiety.

Because MDS is an uncommon illness, there is less information known about the disease. Uncertainty about the diagnosis of MDS, what treatments might be right for you, how they will work, and what side effects you may experience may contribute to your anxiety.

Anxiety can interfere with one's ability to concentrate, to remember, and to eat or sleep. Many people find it difficult to make decisions or solve problems, and may be more irritable. Headaches, diarrhea, shortness of breath, or palpitations can occur if the anxiety is severe.

Things you can do:

1. Explore **Building Blocks of Hope**. There are a number of resources to help you understand your diagnosis, treatment options, and strategies to take an active part in your journey.
2. Allow yourself time to adjust to the diagnosis.
3. Evaluate other parts of your life where you have been successful in mastering control—use those techniques to help you meet the challenge you face while living with MDS.
4. Try to simplify your life. Eliminate or reduce the activities that are not essential to your physical and emotional well-being.
5. Ask for help. This can be from family, friends, or professionals. Counseling from a psychologist or social worker can also be useful.
6. Consider joining a support group—in person, or by computer. Others living with MDS may have good suggestions for how to better cope with this disease. There are many active MDS support groups. You can contact the MDS Foundation for more information.
7. Explore resources that will help you with relaxation such as meditation, massage, yoga, or listening to relaxing music.
8. Try to eat well, and maintain some sort of activity.
9. Avoid excess amounts of alcohol or caffeine.
10. You may find it difficult to remember instructions, or to concentrate when hearing information, so write them down.
11. Talk to your health care team about other options for managing your anxiety. Ask if an anti-anxiety medication might be helpful.

Definition: Depression is a common consequence of living with cancer, including MDS. The ability to adjust to the diagnosis of MDS affects each person differently. While some people are able to continue to live a full and rewarding life, others may find the stress of coping with MDS more challenging.

There are a number of things that may contribute to feeling that you are not able to continue to do the things that you enjoy or need to do each day including: decreased energy (fatigue), frequent doctor or clinic visits, treatment, low-blood counts, and finances. These challenges are real and important. They are often the cause of situational depression. Yet, another cause of depression is an imbalance in some of the chemicals that normally affect how our brain drives our emotions. Regardless of the cause, you may feel that your life is less meaningful or that you are a burden to others.

Things you can do:

1. Recognize some of the common signs of depression: A lack of interest or pleasure in doing things; feeling down, depressed, or hopeless; difficulty sleeping; decreased appetite; tearfulness. If you are having any of these symptoms, you may have clinical depression. It may also be helpful to ask someone who knows you well if they think that you may be depressed. Severe depression can cause people to lose interest in life, and feel that life is no longer worth living.
2. Give yourself time to adjust to the diagnosis and changes in your daily routines. While you may not be able to return to as active a lifestyle as you once had, you may be able to substitute those activities with less strenuous ones that are still enjoyable.
3. Set priorities for activities that are necessary to maintain your physical and emotional health.
4. Try to find some activity that you can still enjoy—such as listening to music or watching a ball game. These activities can help you keep a positive outlook.
5. Continue with a diet and exercise routine that will help you to stay healthy. Get enough rest.
6. Avoid alcohol—it can make depression worse.
7. Talk with your health care team about resources available to help you: nurses or advanced practice nurses, social workers, or a psychologist can help you work through your concerns and identify the best resources to help you.
8. Prayer or meditation can also be very useful to provide peace.
9. Consider joining a support group—in person, or by computer. Others living with MDS may have good suggestions for how to better cope with this disease.
10. Ask your provider about trying an anti-depressant medication. These medications may be helpful in restoring the chemical imbalance in the brain. These medications may take 4-6 weeks before you notice improvement. Anti-depressant medicines should not be stopped suddenly.
11. Talk with your health care provider about any herbal or natural remedies for depression. Some of these drugs—St. John's Wort, for example—can interfere with your other medication.

It is very important to talk with your health care team about symptoms that require immediate medical care.

Ask when you should call, who to call during normal business hours, who to call after business hours, and what symptoms may require emergency medical care.

- Fevers above 101.4°F (38.5°C)
- Shaking chills at any temperature
- Sudden onset of shortness of breath or chest pain (call 911)
- Skin changes including:
 - Unusual bruising
 - Tiny red, pinpoint spots on your skin (petechiae)
 - A new or worsening rash
- Severe headache
- Sudden changes in vision
- Bleeding that does not stop after a few minutes
- Changes in bowel or bladder function:
 - Visible blood or a red to pink color of the urine
 - Uncontrolled diarrhea or constipation
 - Black or bloody stools
- Uncontrolled nausea or vomiting

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IRON OVERLOAD

Iron overload is a possible outcome of receiving repeated red blood cell transfusions. Iron overload is a potentially dangerous condition because excess iron can damage tissues. Some of the questions discussed in this section include: Why red blood cell transfusions are necessary in MDS? What is iron overload and how can iron overload be monitored and treated?

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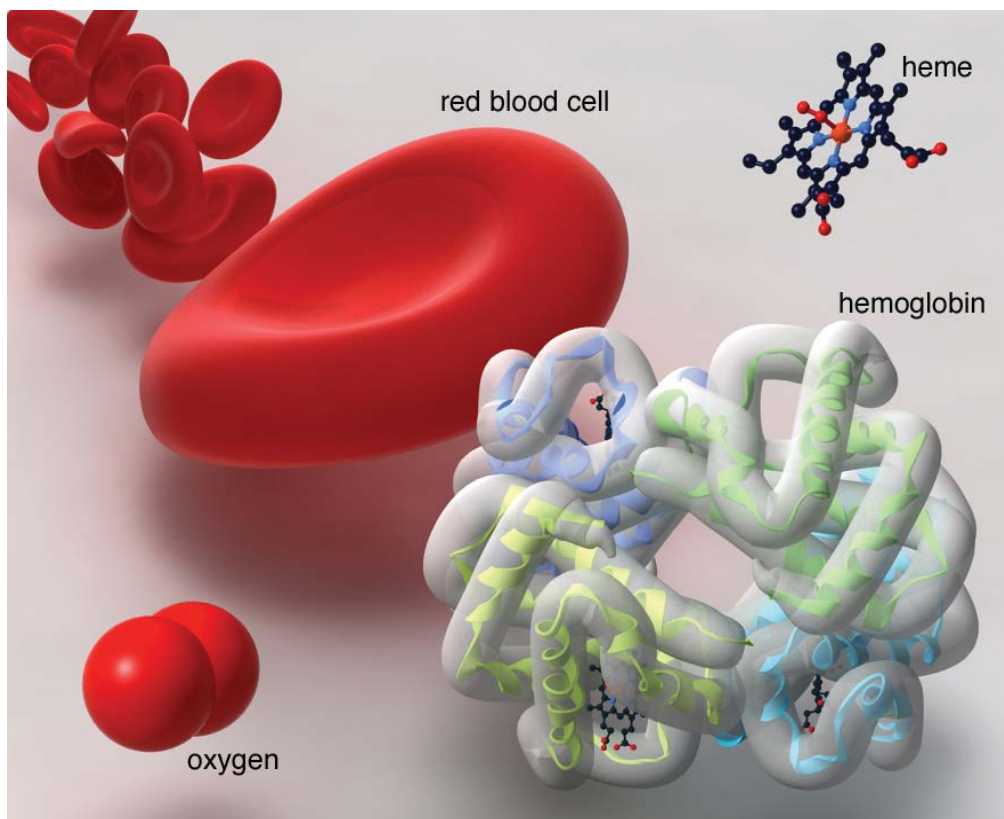
Why are blood transfusions necessary for patients with MDS?

Myelodysplastic Syndromes are a group of bone marrow disorders in which not enough mature red blood cells, white blood cells and platelets are produced by the bone marrow. Roughly 80% of MDS patients have anemia (low red blood cell counts and corresponding low hemoglobin levels) when they are initially diagnosed with MDS. Red blood cells transfusions are often used to treat the symptoms of anemia. Although chronic anemia is seldom life threatening, it can reduce a patient's quality of life.

Red blood cells contain hemoglobin, a large iron-containing protein that gives blood its red color and carries oxygen from the lungs to all body tissues. Oxygen is needed by all of the body's cells to grow, divide, and carry out their specific functions. When the number of red blood cells falls below a certain level, the amount of oxygen also falls, such that cells and tissues do not receive enough oxygen. Without oxygen to provide the energy to carry out specific functions, cells become less efficient and fatigued.

The level of anemia may affect each person differently depending on the person's age and general health. Some of the symptoms you may notice when you are anemic include a pale complexion, fatigue, weakness, and sometimes shortness of breath.

Blood transfusions are a common way to provide temporary relief of the symptoms of anemia. Thus, blood transfusions are sometimes referred to as symptomatic or supportive care. However, red blood cells carry iron and, after repeated transfusions, a patient may end up with elevated levels of iron in the blood and other tissues. There are other possible side effects associated with blood transfusions that your health care provider will discuss with you. Most often, two units of packed red blood cells are given during each transfusion session.



General Guidelines for Transfusion of PRBCs

- Requires informed consent
- Asymptomatic patients: transfuse to maintain Hgb 7-9g/dL
- Symptomatic with hemorrhage: transfuse to maintain hemodynamic stability
- Symptomatic with Hgb < 10g/dL: transfuse to maintain Hgb 8-10g/dL
- Acute coronary syndromes with anemia: transfuse to maintain Hgb > 10g/dL

BENEFITS

- Rapid increase in hemoglobin (Hgb), may reduce fatigue in some patients

RISKS

- Viral transmission: HIV: 3.1/100,000, Hepatitis C: 5.1/100,000, Hepatitis B: 3.41-3.43/100,000
- Transfusion-related acute lung injury (TRALI): 0.81/100,000
- Transfusion associated circulatory overload (TACO): 1-6% - ↑ in ICU and post-operative settings
- Fatal Hemolysis: 1.3-1.7/million transfused units
- Febrile non-hemolytic reactions: 1.1-2.15%
- Transfusion-related iron overload (hemosiderosis)

How frequently transfusions need to be administered will vary depending upon the severity of symptoms and the hematocrit or hemoglobin level. Transfusion intervals (the time between one transfusion and the next) may vary from every few months in low-risk MDS to every 2 to 6 weeks in high-risk disease. In some MDS patients, the transfusion interval may be as often as once every 1 to 2 weeks. MDS patients who require a series of transfusions of red blood cells are considered to be transfusion-dependent. Transfusion dependence is a common trigger to consider disease modifying treatment (treatment directed at the abnormalities in the bone marrow) to improve production of normal blood cells, and limit continued exposure to excess iron (see: *General Principles of Treatment of MDS*).

Transfusions and iron overload



What Is Iron Overload?

Red blood cell transfusions may provide temporary relief from the symptoms of anemia, but they also add extra iron to the body. While there are a few therapies that can restore the production of red blood cells so that patients become transfusion-independent, they are not appropriate for all MDS patients. For many MDS patients, transfusions are the only option to treat the symptoms of anemia. Supportive therapy with repeated red blood cell transfusions can lead to elevated levels of iron in the blood and other tissues. Thus, MDS patients who receive transfusions for their anemia are at risk for excess iron or iron overload.

Your body contains about 3 to 4 grams of the element iron (Fe). Nearly two-thirds of the body's iron is found in the oxygen-carrying protein in the blood called hemoglobin. The remainder is found in myoglobin (found in muscle cells) and other proteins. The amount of iron in the body is tightly controlled and most of it is recycled. The very small amounts that are lost daily (1 to 2 milligrams) are balanced by absorption from the diet.

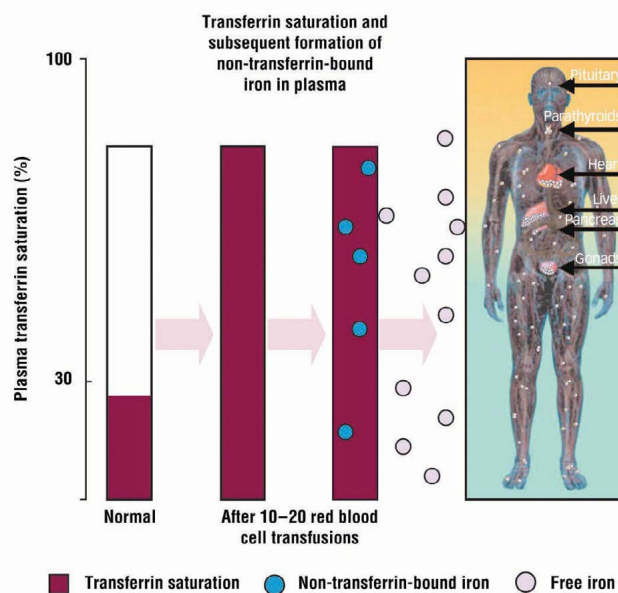
Red blood cell transfusion and iron overload

Each unit of packed red blood cells contains about 250 milligrams of iron. Over the course of therapy with repeated blood transfusions, iron builds up in the body's tissues and organs. After approximately 20 transfusions, a patient will receive an additional 5 grams of iron, nearly doubling the amount of iron in their body.

Normally, iron binds to plasma protein called transferrin, which circulates in the body, accumulating within cells in the form of ferritin. Iron overload occurs when transferrin becomes saturated, increasing the concentration of non-transferrin-bound iron—a toxic substance to cells. As levels of non-transferrin-bound iron accumulate in the blood, they are absorbed into the surrounding tissues, leading to increased levels of unbound iron in the liver, heart, pancreas, pituitary gland, and other glands.

How do I know if I have iron overload?

The onset of iron overload is variable. As a general rule, iron overload occurs after you receive 20 units of red blood cell transfusions. However, iron overload may occur after as few as 10 units of transfused blood in some patients and may not be present in some patients who have received more than 60 units of blood. In addition to developing iron overload as a result of multiple transfusions, MDS patients with sideroblastic anemia may develop iron overload as a result of excessive absorption of iron from food or supplements. You may not know that excess iron is building up in your body because there may be no symptoms. Other MDS patients considered to be at risk for iron overload are transplant recipient candidates who have already received more than 20 to 30 red blood cell transfusions, those with a serum ferritin level greater than 1000–2500 ng/mL, and those with an IPSS risk of "Low-Intermediate-1" who require continued transfusions.



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How Serious Is Iron Overload? Is Iron Overload Treatable?

Iron overload is a potentially dangerous condition because excess iron can damage tissues. Excess iron may accumulate in the heart, liver, lungs, brain, bone marrow, and endocrine organs, putting you at risk for a number of conditions. Many of these are not reversible and may be life-threatening, including heart failure, cirrhosis and fibrosis of the liver, gallbladder disorders, diabetes, arthritis, depression, impotence, infertility, and cancer. Much of the data on the damaging effects of iron overload are from other blood disorders such as sickle cell anemia and thalassemia which are also associated with transfusion-dependent anemia.

Studies in patients with MDS have shown that iron overload resulting from regular red blood cell transfusions is associated with poorer overall survival and a higher risk of developing leukemia. This negative effect on survival depends on the number of red blood cell transfusions received per month. The negative effect on survival is also related to the severity of MDS (see: *How Severe is My MDS?*). Management of iron overload and treatment of iron toxicity by iron chelation (*key-LAY-shun*) therapy in patients with MDS and transfusion-dependent anemia have been shown to reduce iron burden and may improve survival in some patients with MDS.

How is iron overload diagnosed?

Although many tests are available to assess iron overload, the most commonly used one today is a simple blood test called a ferritin test. The ferritin level indirectly estimates iron overload. Ferritin is a protein in the serum that binds iron and helps to store iron in the body. Because it is a simple blood test, it is easy to perform repeatedly to obtain ferritin readings over time, and a trend can be observed and monitored. Serum ferritin levels are generally checked in MDS patients at the time of diagnosis and repeated every 3–4 months when regular blood transfusions are required (transfusion-dependent MDS). Keeping track of your serum ferritin level along with your transfusions and hemoglobin levels can help you understand your risk of iron overload (see: *My MDS Plan*).

In MDS patients, serum ferritin levels have been shown to be related to the number of red blood cell units received. A serum ferritin value of 1,000 ng/mL may be reached after as few as 20 units of red blood cells have been transfused. One disadvantage to the ferritin test is that the results are affected by inflammation, infection, and ascorbic acid (vitamin C) deficiency. Therefore, the trends in the ferritin levels over a period of time are most useful in monitoring iron overload.

Ferritin Values

Normal serum ferritin levels	Low serum ferritin levels	High serum ferritin level	Iron Overload
12–300 ng/mL for men 12–150 ng/mL for women	A low serum ferritin level typically means reduced iron stores. Lower than normal levels of ferritin are a sign of iron-deficiency anemia.	May indicate hemolytic anemia, megaloblastic anemia, or iron overload.	Serum ferritin levels greater than 1,000–2,500 ng/mL indicate iron overload in patients with transfusion-dependent anemia.

How Serious Is Iron Overload? Is Iron Overload Treatable?

Is iron overload treatable?

Fortunately, iron overload can be treated with chelation therapy using iron-chelating drugs. The goal of therapy is to keep the body's iron level low enough to prevent the development of organ damage. Even after organ toxicity has developed, chelation therapy can reverse some of the complications of iron overload. Drugs called chelating agents that bind to iron so that it can be removed from the body are the most common way to treat iron overload in patients with transfusion-dependent MDS. Ultimately, transfusion dependence is a trigger to consider disease modifying treatments to improve bone marrow function and avoid additional red blood cell transfusions (see: *General Principles of Treatment of MDS*).

Phlebotomy

Some MDS patients who no longer require red blood cell transfusions as a result of treatment for their MDS may be candidates for phlebotomy (*fla-BOT-ame*). Phlebotomy involves removing a unit of blood—similar to donating blood—which, like iron-chelating agents, removes the iron carried in red blood cells, as well as unbound iron in the blood. Many patients with MDS do not have adequate hemoglobin levels to allow this approach for removing excess iron.

Tests for Iron Overload

TEST	ADVANTAGES	DISADVANTAGES
Ferritin test <i>(Most common method)</i>	<ul style="list-style-type: none"> • Noninvasive • Widely available • Useful in deciding when to initiate therapy • Useful in monitoring treatment effectiveness 	<ul style="list-style-type: none"> • Measurement values are altered by inflammation, infection, and ascorbic acid (vitamin C) deficiency • Does not correlate well with total body iron
Liver biopsy liver iron concentration <i>(Limited use due to risk)</i>	<ul style="list-style-type: none"> • Correlates well with total body iron burden • Allows for assessment of liver histology • High levels predict risk for cardiac disease, endocrine complications, and death 	<ul style="list-style-type: none"> • Invasive • Accuracy affected by sample size • Sampling errors due to fibrosis and uneven distribution of iron • Cardiac disease may be present when liver iron is low
MRI Magnetic Resonance Imaging <i>(Used to evaluate abnormal liver enzymes in patients with elevated ferritin)</i>	<ul style="list-style-type: none"> • Noninvasive • More widely available • Correlates well with liver iron concentration by biopsy 	<ul style="list-style-type: none"> • Expensive • Variety of techniques and analytic programs may limit comparability • Cardiac disease may be present when liver iron is low
Cardiac iron loading by MRI <i>(Used primarily to evaluate cardiac symptoms in patients with elevated ferritin)</i>	<ul style="list-style-type: none"> • Noninvasive • Correlates with risk for cardiac disease 	<ul style="list-style-type: none"> • Expensive • Difficult to validate without biopsy specimen

Chelating agents

Currently there are three iron chelating drugs available for MDS patients: Desferal® (generic name: deferoxamine), Exjade® (generic name: deferasirox), and Ferriprox® (generic name: deferiprone).

Property	Deferoxamine (Desferal®)	Deferasirox (Exjade®)	Deferiprone (Ferriprox®)
Route of administration	Subcutaneous, intramuscular, or intravenous	Oral	Oral
Dose	25–50 mg/kg	Starting dosage: 20 mg/kg	75 mg/kg
Schedule	Administered over 8–24 hours daily for 3–7 days per week	Daily	Three times per day
Main route of excretion	Urine/feces	Feces	Urine

How long will I receive iron chelation therapy?

Chelation therapy is continued until your serum ferritin level is less than 1,000 ng/mL. This may take several months to several years. For patients who remain transfusion-dependent, chelation therapy may continue indefinitely. After beginning iron chelation therapy, your iron level will be monitored every 3–4 months. The ferritin test is used to evaluate your response to iron chelation therapy. If you are receiving therapy, your health care provider will monitor the number of red blood cell transfusions you receive as well as your serum ferritin level. If your serum ferritin level falls below 500 ng/mL during the course of treatment or if you are no longer receiving transfusions, chelation therapy may be discontinued. However, your iron level will continue to be monitored.

What are the side effects of iron chelating drugs?

Some, but not all, patients experience side effects while on iron chelation therapy. Most side effects can be prevented or effectively managed by working closely with your health care team. In some cases, the side effects can be managed by a dose adjustment or dose interruption. Such medication changes should only be made after talking with your health care provider.

Iron Chelating Drugs: Common Side Effects

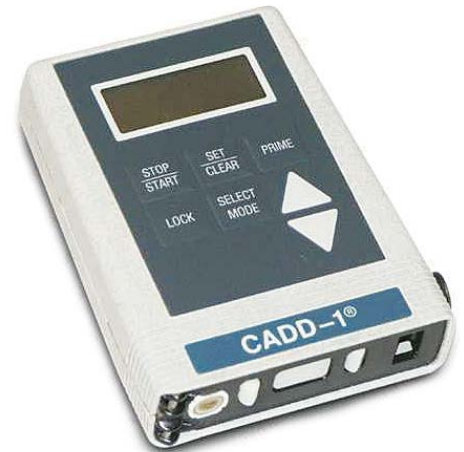
Desferal® (deferoxamine)	Exjade® (deferasirox)	Ferriprox® (deferiprone)
Local infusion site reactions	Gastrointestinal disturbances	Neutropenia (very low neutrophil count) and agranulocytosis
Neurological toxicity	Elevated liver enzymes	Gastrointestinal abnormalities
Growth and skeletal disturbances	Elevated serum creatinine	Musculoskeletal and joint pain
Allergic reactions		Elevated liver enzymes

Discuss any symptoms you have after starting chelation therapy with your health care team. Ask about when you should notify them, how to call, what phone number to call, and who you should talk to if you are having symptoms. Find out what symptoms need to be reported immediately so that they can be managed promptly.

Desferal® (deferoxamine)

Desferal® is administered by injection anywhere from 3–7 times a week. Some patients receive twice-daily subcutaneous (beneath the skin) injections. Others receive slow intravenous infusion by way of a portable, battery-operated pump worn over a period of about 8 hours, often overnight. Desferal® can also be given by injection into muscle (intramuscular administration). The most effective route of administration is different for each patient. Less frequent injections (1–2 times per week) may be possible when the ferritin level is reduced. Typically, a physician will initiate treatment with one gram, gradually adjusting the dose upward until it reaches no more than three grams a day. Desferal® is slow acting, removing only 6 to 10 mg of iron per infusion; however, it can maintain negative iron balance even when blood transfusions continue.

The most common reported side effects of Desferal® include rash, hives, itching, pain or swelling at the infusion site, vomiting, diarrhea, stomach or leg cramps, bloody urine, blurred vision, fever, rapid heartbeat, and dizziness. Potential long-term adverse reactions include kidney or liver damage, loss of hearing, or cataracts.



Exjade® (deferasirox)

Exjade® is an oral treatment for iron overload that is taken once daily at a dose of 20 milligrams per kilogram of body weight (20mg/kg/day). Exjade® should be taken dissolved in liquid once a day on an empty stomach, at least 30 minutes before food, preferably at the same time every day. Clinical trials in patients with beta thalassemia, sickle cell disease, and other forms of transfusion-dependent anemia including MDS, have shown that Exjade® significantly reduced liver iron concentration (LIC), an indicator of iron content in the body, and led to the maintenance or reduction of iron burden in transfused patients. Because Exjade® may cause certain adverse reactions that impair kidney or liver function, its use is closely monitored by blood tests every month or more frequently if a patient is at increased risk for these complications. You should not receive Exjade® if you have impaired kidney or liver function, or have a hypersensitivity to deferasirox, or any component of Exjade®. Exjade® must be used with caution in patients with low platelet or white blood cell counts.

The most common side effects associated with Exjade® use include diarrhea, nausea, vomiting, headache, abdominal pain, fever, cough, and mild nonprogressive increases in serum creatinine. Potential long-term adverse reactions to Exjade® include kidney or liver damage, loss of hearing, or cataracts. Keep all appointments with your doctor and the laboratory.

Your doctor will order certain laboratory tests to monitor the effects of your chelation therapy. Keep this medication in the container it came in, tightly closed, and out of reach of children. Store it at room temperature and away from excess heat and moisture (not in the bathroom). Throw away any medication that is outdated or no longer needed.



How to take Exjade®

1. Place Exjade® tablets in a glass of orange juice, apple juice, or water.
2. Allow to dissolve completely. You may stir or shake the mixture until dissolved and the solution is evenly mixed.
3. The solution may have a thick consistency and this may take several minutes.
4. Drink as you would a regular glass of water or juice. It is important to finish any of the remaining Exjade® in the glass by adding a little more liquid to the glass and stirring.
5. Exjade® should not be chewed or swallowed whole, and should not be taken at the same time as antacids medicines that contain aluminum, such as Maalox®.

Ferriprox® (deferiprone)

Ferriprox® is not licensed for use in MDS patients, although the manufacturer is seeking approval for iron overload in MDS in several countries. Ferriprox® is currently used to treat iron overload in patients with thalassemia who are unable to use Desferal® because of intolerability or lack of effectiveness. It is taken by mouth as a tablet or as an oral solution. The usual dose is 25 mg/kg, three times per day, or a total daily dose of 75 mg/kg/day. In clinical studies and in clinical practice, Ferriprox® has been shown to be effective in removing iron from the body. Ferriprox® has a side effect profile similar to that of Desferal®. Ongoing clinical trials are evaluating the use of Ferriprox® alone and in combination with Desferal® in patients with transfusion-dependent iron overload. The use of combination chelation therapy would allow Desferal® to be infused less frequently, and help facilitate medication adherence (taking both therapies as prescribed at recommended doses on time every time). The most common side effects associated with Ferriprox® use include nausea, vomiting, heartburn, stomach pain, diarrhea, increased or decreased appetite, weight gain, pain in the arms, legs, back or joints. Deferiprone may cause a decrease in the number of white blood cells made by your bone marrow. White blood cells help your body fight infection, so if you have a low number of white blood cells, there is a higher risk that you will develop a serious or life-threatening infection.

Keep all appointments with your doctor and the laboratory. Your doctor will order certain laboratory tests to monitor the effects of your chelation therapy. Keep this medication in the container it came in, tightly closed, and out of reach of children. Store it at room temperature and away from excess heat and moisture (not in the bathroom).

What practical measures can I take to help reduce iron overload?

Keeping track of the number of transfusions you have received and certain laboratory results, such as hemoglobin and ferritin levels, can help you in a number of ways. You will be able to monitor the level of hemoglobin that causes you symptoms and how often you need transfusions. Knowing how many transfusions you've had will help in talking with your doctor, nurse, and other health care providers about your risk for iron overload and how best to treat your symptoms. The Treatment and Transfusion Tracker (see: *My MDS Plan*) provides a useful tool to track laboratory results, transfusions, other treatments for your MDS, and any symptoms you may be having. Regardless of whether or not you're receiving treatment for iron overload, you should keep a record of all transfusions, your blood type, and any antibodies in the blood. If you're receiving iron chelation therapy, keep track of your transfusions, ferritin levels, and any testing for iron overload or chelation therapy (see: *My MDS Plan*). Keep all appointments with your doctor and the laboratory. Your doctor will order certain laboratory or radiology tests to monitor the effects of your chelation therapy.

Test	Frequency
Auditory Testing	Baseline and then yearly or for any changes in symptoms
Granulocytes	Monthly
Serum Ferritin	Baseline and every three to four months
Serum Transaminase	Monthly
Serum Creatinine	Monthly
Liver Iron Stores (T2MRI)	May be ordered based on serum ferritin levels and other clinical signs (elevated liver enzymes)
Myocardial Iron Stores (T2MRI)	May be ordered based on serum ferritin level and any signs of heart problems
Ophthalmic Testing (eye exam)	Baseline and then yearly or with any changes in symptoms

Avoiding iron overload: diet and medications

In addition to iron chelation therapy for transfusion-dependent iron overload, there are some everyday guidelines you can follow to decrease your dietary intake of iron:

To decrease the absorption of iron:

- Consume milk products, eggs, certain high fiber foods, and tea which contains polyphenols.

To help prevent further increase of iron levels:

- Avoid alcohol and tobacco smoke.
- Avoid taking iron supplements or iron-containing medications (vitamins with iron).
- Avoid excess sugars.
- Limit intake of foods with very high iron content: beef, lamb, and venison contain the highest amounts of iron as compared to pork and chicken which contain lower amounts of iron.
- Certain fish are thought to be high in iron content.

To reduce infections:

- You should also avoid eating raw shellfish, particularly oysters, because they carry bacteria that thrive in plasma-containing high iron levels and therefore can increase your susceptibility to a serious bacterial infection.

References:

Kurtin, S. (2011) *Current Approaches to the Diagnosis and Management of Myelodysplastic Syndromes*. *J Adv Pract Oncol* 2(suppl): 7-18

absolute neutrophil count

A measure of the number of neutrophils, a type of white blood cells, in the blood; abbreviated ANC. A low ANC indicates an increased risk for serious infections.

anemia

A condition that results from not enough red blood cells; may produce a variety of symptoms and is detected by measuring RBC count and hemoglobin in the blood.

antibodies

Proteins produced by certain cells of the immune system in response to the presence of foreign or “non-self” substances called antigens. Each type of antibody is unique, responds to a specific antigen, and signals other immune system cells to rid the body of the foreign substance or microorganism or aberrant cell. Also called immunoglobulins.

blood type

The four main blood types are based on the presence of two proteins on the surface a person’s red blood cells—the A antigen and the B antigen. The four main blood types are A, B, AB, or O, with type A blood indicating that the A antigen is present on red blood cells and type B blood indicating that the B antigen is present on red blood cells. Type AB indicates the presence of both A and B antigens on red blood cells and type O indicates that neither A nor B antigens is present on red blood cells.

bone marrow

The spongy tissue in the center of bones that produces blood cells and platelets.

cirrhosis

Scarring of the liver that results from injury or inflammation; also called liver fibrosis.

ferritin

A protein in plasma that binds iron and helps to store iron in the body.

fibrosis

The formation of scar tissue that results from injury or inflammation.

granulocyte

A type of white blood cell that helps the body fight infection.

hematocrit

The fraction of the blood that is composed of red blood cells.

hemoglobin

The iron-containing protein in the blood that carries oxygen to the body’s tissues.

neutrophil

A type of white blood cell that plays a key role in protecting the body against infection. The absolute neutrophil count, or ANC, is a common blood test that is a measure of the number of neutrophils.

plasma

The liquid portion of the blood that contains salts (electrolytes), hormones, and proteins.

platelet

Cell fragment found in blood that is involved in blood clotting

red blood cell

A type of blood cell that contains the protein hemoglobin that carries oxygen to the tissues of the body; also called erythrocytes; abbreviated RBC.

serum

The liquid portion of the blood that contains salts (electrolytes), hormones, and proteins but not the clotting protein fibrinogen; identical in composition to plasma but without fibrinogen.

serum creatinine

A blood test used to evaluate kidney function; creatinine is removed from the body by the kidneys and excreted in the urine. If kidney function is suboptimal, creatinine levels will increase in the blood because less creatinine is released in the urine.

serum transaminase

A blood test used to evaluate liver function. High levels of enzymes called transaminases are found in the liver and are released into the blood when the liver is injured.

sideroblastic anemia

An anemia in which developing red blood cells in the bone marrow (erythroblasts) do not produce enough hemoglobin and become loaded with iron (called ringed sideroblasts).

thalassemia

A blood disease caused by abnormal hemoglobin production that results in anemia.

transferrin

A protein found in plasma that binds iron and circulates it throughout the body.

white blood cell

A type of blood cell of which there are five subtypes, including neutrophils and granulocytes. White blood cells, or WBC, also called leukocytes, play a central role in immunity.

Foundations and Organizations Specific to MDS

Myelodysplastic Syndromes Foundation www.mds-foundation.org

The MDS Beacon www.mdsbeacon.com

Foundations or Organizations Specific to Iron Overload

Iron Disorders Institute www.irondisorders.org

Iron Overload Diseases Association, Inc. www.ironoverload.org

Other Foundations or Organizations

Aplastic Anemia & MDS International Foundation www.aamds.org

American Cancer Society www.cancer.org

American Society of Hematology www.hematology.org

Caring Bridge www.caringbridge.org

National Anemia Action Council www.anemia.org

National Heart, Lung and Blood Institute www.nhlbi.nih.gov

The Leukemia & Lymphoma Society www.lls.org

Drug Specific Resources

Desferal® (deferoxamine) www.desferal.com

Exjade® (deferasirox) www.exjade.com

Ferriprox® (deferiprone) www.ferriprox.com

General Information

Medline Plus www.nlm.nih.gov/medlineplus/medlineplus.html

The Merck Manual Home Edition for Patients and Caregivers www.merckmanuals.com/home/index.html

Additional reading from the medical literature

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Malcovatti, L. *Red blood cell transfusion therapy and iron chelation in patients with Myelodysplastic Syndromes*. Clin Lymphoma Myeloma. 2009;9:S305-S311

National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology. Myelodysplastic Syndromes. Version 2. 2012* Available online at www.nccn.org/professionals/physician_gls/f_guidelines.asp

Shander, A., & Sweeney, J.D. *Overview of current treatment regimens in iron chelation therapy*. US Hematol. 2009;2:59-62

Steensma, D. *The role of iron chelation therapy for patients with Myelodysplastic Syndromes*. J Natl Compr Canc Netw. 2011;9:65-75

Financial assistance

Exjade® Patient Assistance and Support Services (EPASS™)

Complete Care for patients residing in the United States.

www.us.exjade.com/patient/epass-advantage.jsp

888-903-7277

Novartis Patient Assistance Foundation

www.pharma.us.novartis.com/about-us/our-patient-caregiver-resources/pafenrollment.shtml

800-277-2254

Diplomat Specialty Pharmacy Co-Pay Assistance Navigator Program

<http://diplomatpharmacy.com/en/financial-assistance>

877-977-9118 ext.10184

How to contact the Myelodysplastic Syndromes Foundation

The MDS Foundation, Inc.

4573 South Broad Street, Suite 150

Yardville, NJ 08620

800-MDS-0839 (within US only)

609-298-1035 (outside US)

Living with Iron Overload



video testimonial

My name is Bob Weinberg. I was diagnosed in 1998 at age 48 with MDS-RARS (refractory anemia with ringed sideroblasts). Here are my numbers: Since then, I have received over 850 units of packed red blood cells. My white blood cells hover around 2.0, my absolute neutrophil count (ANC) between 500 and 700 and my platelets between 30,000 and 40,000. My blast count is under 5%. My current transfusion frequency is 7-8 days. I take 2,500 mg of Exjade® daily. My ferritin level, checked monthly, ranges from 450 to 700.

I will discuss my experience with preventing iron overload as a consequence of all of these transfusions. For about a year after my diagnosis in May of 1998, I needed transfusions on a monthly basis. In February of 1999, I received a call from my hematologist asking me to come into his office to meet with a professional from a home health service to discuss iron chelation. My ferritin level had hit 1,000, far above the normal range of 22 to 322. He explained that each time I received a transfusion I was receiving new iron with the blood and that my body has no natural way to rid itself of excess iron. Eventually, the iron will build up to the point where it will enter my organs, and it will break down the heart, liver and other tissue to the point that it becomes fatal. Iron chelation, he said, was a way to introduce a drug called deferoxamine (with the trade name Desferal®) that binds with the iron and causes the body to excrete in my urine.

So I met with the people from the home health agency and they showed me a pump, like an insulin pump, that had a reservoir of deferoxamine for an 8 hour infusion, drop by drop, subcutaneously into my skin. The only problem is that I had to stick myself in the gut with a needle and then tape it to me and leave it there for 8 hours. They noted with sorrow that there was no "oral chelator." The drug caused a skin reaction that turned the infusion site bright red and painful. Night after night, 7 days a week, I would stick myself and then try to sleep with this pump lying next to me and the tube coming from it wrapping around me. I did this from February 1999 to January 2007, every night. Sometimes the small tube from the drug reservoir to the infusion site would become occluded, and a high-pitched beep would wake me up. But the worst was the skin reaction at the numerous infusion sites. It was like I was wearing a painful belt of red boils around my gut. I am amazed that I could tolerate the process, but I did.

After becoming desperate with the pain and agony of the infusion pump, I started hearing about an oral chelator being developed. My ferritin level was then 1,700. I searched for an international expert, not in MDS, but in transfusional iron overload. He ordered an MRI of my heart and liver, and every year since, I have had these annual tests taken. After the oral chelator, Exjade®, was approved by the

FDA, I gave up the hateful pump and switched to Exjade®. This drug comes in the form of a disc about the size of a quarter, each with 500 mg. The dosage is based on body weight. I put 5 of these discs (2,500 mg) in 7 oz. of orange juice every night before bed. I use a 12 oz. plastic beverage container with a tight lid and a tight rubber band showing me the line for 7 oz. I then allow the medicine to dissolve overnight in the orange juice and, after a hard shake or two, drink the mixture in the morning as soon as I wake up. You need to drink the mixture on an empty stomach and wait 30 minutes after that before eating anything. I make the mixture before bed so I don't need to wait 15 to 20 minutes in the morning for it to dissolve and then wait another 30 minutes before eating anything. I need my coffee sooner than that, and that extra 15 to 20 minutes gets my caffeine addiction satisfied sooner.

The one downside with Exjade® that I have experienced is gastro-intestinal distress. It is amazing how fast the drug triggers my need to move my bowels. Diarrhea is common, and sometimes intense. It is a good idea not to wander at any time of day too far from a toilet. But as those of us with MDS know far too well, some things we just have to put up with. MDS patients have told me of other side effects; some of which are far more severe than what I have experienced.

In the spring of 2007, I began taking Vidaza® to raise my blood counts. In July of that year, my hemoglobin began to rise, eventually hitting 14.5. I cannot express my excitement when I saw that number on my CBC report without an "L" after it (for low). I was transfusion-free for a period of 5 months. During that period, even though I did not have a single transfusion. I continued taking Exjade® daily. Once the Vidaza® stopped working, and I needed transfusions again, my ferritin level had dropped from 1,700 to just under 400. In the almost six years since that time, even with transfusion frequency now down to 7-8 days, my ferritin generally holds between 500-700. Clearly, in addition to being much easier to administer, Exjade® appears to be much more efficacious than deferoxamine.

There appears to be some controversy among physicians as to whether to prescribe iron chelation to MDS patients at all. I believe that is because patients with high-risk MDS will probably never live to see the effects of iron overload. However, for me, who started with a lower risk IPSS score, the chance that I could live many years on transfusions raised the probabilities that I could live long enough to die from iron overload. I am thankful for that telephone call from my hematologist less than one year from diagnosis, starting me on chelation. It has enabled me to continue with transfusions for 14 and a half years.

Bob Weinberg





MY MDS PLAN

Understanding the diagnosis of MDS will help you and your caregiver take an active part in your individual treatment plan. My MDS Plan provides several tools to allow you to create an individualized profile about your MDS diagnosis, your health profile, and the members of your health care team. Tools for tracking your progress are included.

contributing authors

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The diagnosis of MDS

The Myelodysplastic Syndromes represent a group of bone marrow diseases that have variable prognoses, treatment options, and expected survival rates. Being told that you have MDS can bring on many emotions including fear and uncertainty. Uncertainty about the diagnosis of MDS, what treatments might be right for you, how they will work, and what side effects you may experience may contribute to your fear and anxiety. Understanding your MDS diagnosis will help you and your caregiver take an active part in your individual treatment plan, as well as help you make an informed decision on the best treatment options.

Explore the Building Blocks of Hope

Allow yourself time to adjust to the diagnosis. Take time to explore *Building Blocks of Hope* which provides a number of resources to help you better understand your diagnosis and offers strategies to take an active part in your MDS journey. Forming a partnership with your health care team, caregivers, and friends can help you LIVE with MDS. Ask for help from family, friends, or professionals. Consider joining a support group either in person or online. Others living with MDS may have good suggestions for how to better cope with this disease.

Daily activities

Eat well, stay active, and spend time with loved ones. Eating right, exercising, sleeping well, and participating in activities with friends and family help improve overall wellness.



Tracking Your Treatment

Initial Laboratory Results

Diagnostic Test	Normal Result	My Result	Date	Notes
Hemoglobin	Women: 12.5–16.5 gm/dL			
	Men: 13.5–17.5 gm/dL			
White Blood Cell Count	3,500–10,000/mm ³			
Absolute Neutrophil Count	1,500–8,000/mm ³			
Platelet Count	150,000–450,000/mm ³			
Serum Erythropoietin	2.6–18.5 IU/ml			
Serum Iron	50–170 mcg/ml			
Serum Folate	> 2.76 ng/ml			
Serum B12	239–931 pg/ml			
Thyroid Stimulating Hormone	0.35–4.00			
Diagnostic Test	Normal Result	My Result	Date	Notes
WHO Classification				
FAB Classification				
Blast %				
Cytogenetics				
IPSS/IPSS-R Score				

Normal ranges may vary amongst different laboratories.

WHO – World Health Organization Classification System FAB – French-American-British Classification System
 IPSS – International Prognostic Scoring System IPSS-R – Revised International Prognostic Scoring System
 (see: *How Severe Is My MDS?* and the *IPSS-R calculator*)

patient identification sticker

My Health Profile



MY HEALTH PROFILE		
Name		
Date of Birth	Social Security #	
Address		
City	State	ZIP Code
Home Phone	Cell Phone	
Work Phone	Email	
Caregivers		
Name/Relationship		Phone
Emergency contacts		
Marital status/Living situation		

My Health Profile



EMPLOYMENT INFORMATION		
Employer	Job Title	
Address	Supervisor	
City	State	ZIP Code
Phone		

INSURANCE INFORMATION		
Insured or Guarantor <input type="radio"/> self <input type="radio"/> spouse <input type="radio"/> parent		
Date of Birth	Social Security #	
Employer	Phone	
Address		
City	State	ZIP Code
Insurance Name		ID Number
Contact		

Insured or Guarantor <input type="radio"/> self <input type="radio"/> spouse <input type="radio"/> parent		
Date of Birth	Social Security #	
Employer	Phone	
Address		
City	State	ZIP Code
Insurance Name		ID Number
Contact		

What is MDS? *(MDS Foundation, 2011)*

MDS is a group of bone marrow disorders. The bone marrow is the factory for the production of blood cells including red blood cells, white blood cells, and platelets. In MDS, the bone marrow is abnormal because of a variety of malignant changes. The result is ineffective production of normal mature blood cells, resulting in low blood counts (cytopenias). Various subtypes of the disease exist with variable prognoses, treatment options, and risk of developing leukemia.

Is MDS cancer? *(Bejar et. al., 2011)*

The diagnosis of MDS requires a bone marrow biopsy and aspirate. The specimen is analyzed by pathologists specializing in blood disorders. The diagnosis of MDS requires specific malignant features such as dysplasia or cytogenetic abnormalities. Research has identified molecular abnormalities thought to play a role in the development of MDS. Given the underlying malignant features of the disease, MDS is considered a form of blood cancer.

What causes MDS? *(Greenberg et. al., 2011; Sekeres, 2011; Sekeres et. al., 2011)*

The cause of MDS is unknown in more than 80% of diagnosed patients. It is more common in men (male to female ratio is 4.5:2 per 100,000). As with many types of cancer, older age is a predisposing factor. The majority (86%) of patients with MDS are older than age 60. Exposure to chemicals such as benzene and other solvents and tobacco smoke are known to increase the risk of developing MDS. Patients who receive certain types of chemotherapy or radiation treatment for other cancers may be at increased risk of developing treatment-related MDS.

Is MDS inheritable? *(Sekeres, 2011)*

Inherited genetic predisposition for developing MDS and congenital abnormalities is rare. Before 1973, only 143 cases of MDS were reported. Today, based on data analysis techniques, the estimated incidence varies from 15,000–162,000 *(USA data)* cases per year. The wide variation in this data highlights the challenging diagnostic features of MDS. As diagnostic features of MDS become more familiar to clinicians, MDS is detected more often in patients presenting with cytopenias (low blood counts). The development of therapeutic options may increase the number of patients considered for diagnostic evaluation. Increasing numbers of patients are being treated with cytotoxic therapies, raising the potential for secondary malignancies, including MDS (Cogle, et. al., 2011; Ma, et. al., 2007; Sekeres, 2011).

What are the symptoms of MDS? *(Kurtin, 2011)*

Many patients are asymptomatic and are diagnosed on routine screening. Others present with vague symptoms associated with one or more cytopenias (low blood counts).

- Fatigue, shortness of breath, palpitations (common anemia symptoms)
- Fever, recurrent or prolonged infections (common neutropenia symptoms)
- Bruising, petechiae, or bleeding (common thrombocytopenia symptoms)

How is MDS diagnosed? *(Kurtin, 2011; National Comprehensive Cancer Network, 2011)*

The initial patient evaluation most often includes a complete blood count (CBC), which reveals normocytic or macrocytic anemia, normal to decreased numbers of neutrophils, and variable platelet counts. Anemia is observed in 90% of patients with MDS, either at initial presentation or during the course of their disease. A careful history and additional laboratory analysis should be pursued to exclude other causes of cytopenias.

What are my treatment options? *(Greenberg et. al., 2011)*

Treatment selection for MDS is individualized based on recognized disease characteristics and risk analysis. Treatment options vary by region based on approval mechanisms. The goals of therapy for MDS are based on individualized disease characteristics, patient characteristics, and risk category. In the United States, the International Prognostic Scoring System (IPSS) categorizes the MDS subtypes into two major groups: low- and intermediate-1 risk or intermediate-2 or high-risk. The goal of therapy for each category differs based on expected survival and risk of leukemic transformation. A revised IPSS (IPSS-R) is being developed to further refine these risk categories and guide treatment selection. The World Health Organization Prognostic Scoring System, with similar treatment guidelines, is commonly used in Europe.

Are blood transfusions dangerous? *(Kurtin, 2011; National Comprehensive Cancer Network, 2012)*

The normal body mechanism for control of iron stores is highly efficient. Each unit of transfused blood delivers iron in excess of the normal daily requirements. After repeated transfusions, excess iron storage exceeds the levels that can be controlled by normal iron homeostatic mechanisms, leading to the formation of toxic iron storage and subsequent cellular damage.

A strong correlation exists between transfusion intensity (number of units received over time) and organ damage. Iron accumulation may result in end-organ damage.

heart - congestive heart failure

endocrine glands - diabetes

liver - elevated liver function tests, hepatomegaly, pain

bone marrow - dysfunctional hematopoiesis

Based on this data, and the concern for increasing bone marrow failure, transfusion dependence is considered an indication to initiate disease modifying treatment for MDS.

How likely am I to get better with the treatment?

The response to treatment for patients with MDS varies according to IPSS risk categories as well as other prognostic indices. Allogeneic bone marrow transplantation remains the only potential cure to date. However, patients may benefit from currently available therapies, and durable responses have been reported.

How long will the treatment take to work?

A minimum of four to six months of treatment is required to evaluate initial response, and the best response may not be evident until after as many as nine months of therapy.

How long can I expect to be treated? *(Kurtin, 2011)*

Because of the limited number of treatment options and the incurable nature of the disease, disease modifying treatments for MDS are continued until disease progression or unacceptable toxicity.

What are the common side effects of treatment, and what can be done to control them?

(Kurtin, 2011; Kurtin & Demakos, 2010)

- The most common side effect for all therapies for MDS is myelosuppression, including anemia, neutropenia, and thrombocytopenia.
 - Weekly complete blood count, differential, and platelet counts are recommended for the first eight weeks of treatment.
 - Cytopenias are expected to get worse before they get better.
 - Supportive care strategies are encouraged, including growth factors and transfusions.
 - Drug-specific guidelines for dose modifications or holidays are provided by each drug manufacturer based on clinical trials.

- **Nausea and vomiting:** all agents
 - Administration of anti-nausea medication is an effective strategy to minimize nausea and vomiting.
- **Constipation:** hypomethylating agents—also thought to be related to administration of 5HT3 antagonist anti-emetics
 - A regular bowel regimen that includes a stool softener and laxatives, as needed, will reduce the severity of constipation associated with treatment.
 - In addition, a good diet management and exercise routine will help.
- **Renal and hepatic toxicities**—more common in older adults
 - Baseline and ongoing laboratory analysis will allow early identification and prompt intervention for potential renal and hepatic toxicities associated with treatment.
- **Drug-specific adverse events**
 - Azacitidine: injection-site reactions
 - Lenalidomide: rash, pruritus, diarrhea, safety program for lenalidomide
- **Iron overload**
 - Chelation therapy may be associated with cytopenias and renal and hepatic toxicities.

What new treatments are on the horizon to treat patients with MDS? *(Garcia-Manero, 2011, Kurtin, 2011)*

Clinical trials continue to explore treatment options for MDS and are always recommended for diseases that have limited treatment options, such as MDS. These trials offer hope to patients who have had limited benefit from approved therapies or have high-risk disease thought to have limited potential for benefit from these therapies. Each country has approved mechanisms for clinical trial oversight and drug approval.

How do I select a bone marrow transplantation center? *(National Marrow Donor Program, 2011)*

There are many factors to consider when choosing a transplantation center. Some patients look at a center's experience with certain diseases or ages of patients. Other patients choose a center close to their family and friends. Some things that you and your referring doctor can find out about transplantation centers are the following.

- What experience does this transplantation center have?
- What do transplantation center survival statistics mean?
- How does the number of transplantations conducted for your disease at this center compare with other centers?
- What are the patient- and donor-matching levels required at this center?
- What are some of the pre-transplantation costs at this center?
- Is this center covered under your insurance plan?

What can I do to keep myself healthy?

The general principles of a healthy lifestyle remain important. A balanced diet, daily activity and exercise as tolerated, and participation in activities of enjoyment are important to maintain optimal health and well-being. Ongoing management of other health conditions is important to optimal health and continued eligibility for future treatment options.

Living with low
blood counts



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Eating healthy

Healthy eating begins with a plan. By eating the proper foods, your body receives nourishment and energy to get through the day. A balanced diet can help combat fatigue and illness. Adequate intake of food and fluids also helps individuals tolerate treatment. The key pieces of a healthy diet are hydration, fruits and vegetables, whole grains, low-fat dairy products, and limited amounts of sugar and processed foods.

Being diagnosed with MDS affects people's nutrition differently. Some have a difficult time eating, and lose weight, while others do not. Each person has a unique cancer experience, with varying goals for nutrition. A registered dietitian can help work through your goals to eat well and maintain your weight.

Another good place to start is with the Dietary Guidelines for America 2010 at www.dietaryguidelines.gov.



Do I need to follow a special diet with MDS?

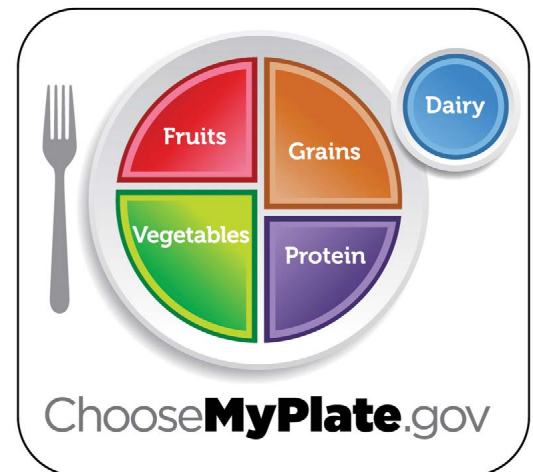
People with MDS may need to follow a special diet if they have a very low white blood cell count or are undergoing a stem cell transplant. Check with your health care provider to see what they recommend because the guidelines for a neutropenic diet vary by cancer center.

General dietary guidelines

The most important thing to keep in mind is to maintain a balanced diet and adequate hydration. Each person will have unique needs based on their normal diet (vegetarian, vegan, kosher, gluten-free, diabetic, etc.), and any additional individual needs (previous bowel surgeries, dental health, irritable bowel syndrome, food allergies, etc.). It is helpful to meet with a registered dietitian to determine your daily caloric needs and how you might get these in the foods you like to eat.

Guidelines for healthy eating

- Eat fruits and vegetables.
 - They can be fresh, frozen, or canned.
 - Eat more dark green vegetables like leafy greens or broccoli and orange vegetables like carrots and sweet potatoes.
 - Wash all fruits and vegetables well prior to eating.
- Vary your protein choices with more fish, beans, and peas.
- Eat at least three ounces of whole-grain cereals, breads, crackers, rice, or pasta every day.
- Have three servings of low-fat or fat-free dairy (milk, yogurt or cheese) that are fortified with vitamin D to help keep your bones healthy.
- Make the fats you eat healthy ones (polyunsaturated and monounsaturated fats).
- If you are undergoing a stem cell transplant—you may need to follow a specific neutropenic diet (a diet for patients with very low blood counts due to stem cell transplants or leukemia treatment).
 - Avoid raw or rare meat and fish and uncooked or undercooked eggs. Cook meat until it's well done. Thoroughly cook eggs (no runny yolks).



- Avoid salad bars and deli counters. Buy vacuum-packed lunch meats instead of freshly sliced meats.
- Consume only pasteurized milk, yogurt, cheese, and other dairy products.
- Avoid soft mold-ripened and blue-veined cheeses such as Brie, Camembert, Roquefort, Stilton, Gorgonzola, and Bleu.
- Avoid well water or boil it for one minute before drinking. At home, it's okay to drink tap water or bottled water.

Hydration

Fluids are an essential part of a healthy diet. Your body needs fluids to function properly, like a car needs gas to run. Adequate hydration varies from one person to another. The goal of hydration is to avoid dehydration without drinking too many fluids. The following tips can help you improve hydration.

- Carry fluids with you wherever you go.
- If drinking a full glass causes bloating, take small sips throughout the day.
- Drink most of your fluids between meals.



Exercise

The most frequently reported symptom in MDS patients is fatigue. One of the best strategies for fighting fatigue is exercise, so move to improve your fatigue! In several studies, exercise has been shown to decrease fatigue and emotional distress. Exercise improves functioning and overall quality of life. A variety of exercise interventions have been studied in cancer patients during different phases of treatment, including aerobic exercise, strength training, and stretching. Examples of studied aerobic exercises are walking and bicycling.

Prior to starting a new exercise program, it is a good idea to discuss your plans with a health care provider to make sure that it is safe for your condition. Individual exercise programs can be designed to fit most needs. An exercise program



can be modified to fit each person based on their age, sex, type of MDS and treatment, and physical fitness level. Blood counts should be taken into account prior to exercise. If neutropenic, it is best to avoid community swimming pools and hot tubs. For severe anemia, aerobic exercise should be performed following a transfusion, when the hemoglobin is in a safe range. When the platelets are less than 50,000 high impact sports should be avoided, in order to prevent problems with bleeding. When in doubt, discuss with your health care team. In general, the primary objective is to get moving. Start slowly and try to make progress by setting realistic goals along the way. Recruit the support of family and friends.

Sleep

Wellness begins with a good night's rest, which can be challenging when diagnosed with MDS. It may be reassuring to know that you are not alone in having a difficult time sleeping. One-third to one-half of cancer patients experience changes in their sleep patterns. Difficulty sleeping has been linked to physical illness, pain, hospitalization, medications, and the psychological impact of being diagnosed with cancer. Poor sleep interferes with your ability to function well and increases the likelihood of depression and anxiety. Sleep deprived states have also been linked with decreased pain tolerance. It is clear that adequate sleep improves quality of life.



How much sleep is enough?

The general rule of thumb is 7-9 hours of sleep per night, according to the National Sleep Foundation. However, like exercise, sleep needs are individual. One person may function well with 7 hours of sleep, while another may need 10 hours. Research also supports that each person has basal sleep needs and sleep debt. Basal sleep needs are the normal amounts of sleep needed nightly, and sleep debt is the amount of sleep lost due to work, illness, or other reasons. When sleep is consistently short, it affects all areas of life, and can lead to illnesses.

Make sleeping well a priority.

This begins with an evaluation of the current sleep habits including number of sleep hours, quality of sleep, and environment. If sleep is altered by symptoms related to MDS, discuss these symptoms with the health care team. There are various strategies and medications that can improve the quality and quantity of sleep. The following suggestions may be helpful:

- Keep regular bedtime and awakening hours.
- Avoid stimulants and caffeine 2 hours prior to bedtime.
- Exercise for 30 minutes three to five times per week.
- Limit day time napping to 30 minutes.
- Spend 30 minutes to an hour of quiet time prior to going to bed.
- Discuss problems sleeping with the health care team. Medications for anxiety, depression, and insomnia may be necessary.

Going out

Being diagnosed with MDS changes your life. Like many other cancers, there is a lot of uncertainty. How long do I have to live? The next question is usually how MDS will affect your quality of life. Changes in the blood counts can limit the activities that you are able to participate in. This is a frequent question posed to health care providers.

What can I safely do when I am neutropenic?

Remember, neutrophils are a type of white blood cell that protect the body from infection. Neutrophils are a part of the total white blood cell count. The number of neutrophils can be found in the differential section of the complete blood cell count (CBC). Neutropenia refers to a neutrophil count of less than 1,000. If your total white blood cell count is only 1,000, then you have neutropenia. Your nurse can help you understand your blood work.

Guidelines for activities while neutropenic are related to the risk of being exposed to people or things that would increase the chance of developing an infection. As expected, crowded places with close personal contact creates the opportunity for catching an illness. However, whether an infection occurs depends on many factors. The majority of

Infections that neutropenic patients experience are not related to exposure to other people or places. Instead, most infections are from bacteria that already live inside the body that turn into problems when the neutrophils are low. Most cancer centers have neutropenic precautions, which vary.

Listed below are common recommendations that can be used as a guideline to follow when neutropenia occurs. These are only guidelines, and quality of life should be weighed against the benefit of "following the rules."

- Common sense: Avoid people who are obviously ill, avoid crowded enclosed places when your counts are low, maintain a healthy lifestyle.
- Avoid exposure to people with respiratory infections—this does not mean that you can't go out, just avoid close contact with individuals who are ill.
- Avoid areas of large crowds if your counts are very low. This does not apply to all patients with MDS, only those undergoing stem cell transplants, leukemia therapy, or who have very low blood counts.
- Carry hand sanitizer—use it in public places or when using phones, toilets, etc.
- Wash hands frequently.

Being around children

The time spent enjoying the company of family, including children, is important. Most patients with MDS can enjoy their family without restrictions. Discuss any recommendations for limiting contact with children with your health care team.

Specific recommendations for contact with children are recommended for patients undergoing a stem cell transplant, leukemia therapy, or who have very low white blood cell counts (neutropenia). These guidelines include avoiding exposure to:

- Any child that is running a fever, or showing signs of infection, such as runny nose or cough. Viral infections are common in children who attend daycare and increases the chance of transferring infections to their close contacts.
- Children receiving live vaccines (e.g., polio vaccine) may shed the virus in the first few hours following immunization. Check with your health care provider when you have questions concerning risk of infection.
- You should be aware that small children might be incubating chicken pox or measles. If you find that you have been in contact with a child who goes on to get chicken pox or measles soon after, you should notify your health care provider.

Medications

It is important to keep a current list of all medications, who prescribed them, the dose and frequency of administration, and any medications that have been discontinued and why (see: *My MDS Plan*). This includes over the counter medications and any "natural medicines."

All medications, whether prescribed, over the counter, or "natural," have potential and, in some cases, serious side effects. Some of the common over the counter medications that should be used with caution include:

- **Acetaminophen (Tylenol):**
 - Most commonly used over-the-counter medication in the United States.
 - Very often included in combination medications. Check labels to see if the names Acetaminophen or Tylenol appear in the list of active ingredients.
 - Doses in excess of 3gm per 24 hours may be toxic to the liver.
 - Check with your health care team about the use of Acetaminophen for fevers when your white blood cell count is low—this may interfere with monitoring any fevers.

- **Anti-inflammatory medications** are commonly used to alleviate pain from arthritis, headache, and fever. Examples include ibuprofen, aspirin, Naprosyn, and meloxicam.
 - This class of drug can cause problems by masking fevers during periods of neutropenia, and interfere with platelet function.
 - When the platelet count is less than 50,000, medications in this class should not be taken. This can increase the risk of bleeding.
- **Antihistamines:** Diphenhydramine (Benadryl) is often used prior to transfusion of packed red blood cells and platelets to help prevent transfusion reactions. The main side effect reported by patients is sedation. It can also cause problems with restless legs and agitation with higher doses of the medication. If you experience unpleasant side effects, discuss alternative medications or dose adjustments with your health care team.

Complementary therapies

Complementary therapy is treatment used in addition to standard therapy, that is assumed to be safe, and not a risk for causing harm. Common forms of complementary therapies include:

- Acupuncture
- Aromatherapy
- Art therapy
- Biofeedback
- Labyrinth walking
- Massage therapy
- Meditation
- Music therapy
- Prayer and spirituality
- Tai chi
- Yoga

Other alternative treatments

Wheat grass juice has been studied for its ability to remove excess iron in patients with MDS, and found to provide a benefit. The study was small, with only 20 patients. The participants drank a tablespoon of fresh wheat grass juice daily for 6 months. There was noted to be a reduction in their ferritin levels, on average from 2,250 to 950 ng/mL. There were no reported negative side effects.

Evening primrose oil has also been found to decrease injection site reactions for patients who are receiving subcutaneous azacitadine. This was tested on ten patients by German researchers. Six of the ten patients experienced a reduction in the injection site redness and irritation. The oil was applied to the injection sites every evening. It is relatively inexpensive, and can be purchased in many health food stores. Side effects that were mentioned are headache and stomach upset.

Staying well



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Insurance and Reimbursement Resources for MDS Patients and Caregivers



Cancer treatments may be given in a variety of ways: by mouth (oral) or as an intravenous (in the vein) or subcutaneous (in the fatty tissue) injection. Insurance coverage for each of these methods of treatment delivery may vary. We have assembled a listing of financial assistance programs available to MDS patients in the United States. We hope that this new resource will be beneficial in helping you with your medical needs.

Medicare

Medicare Part A (hospital insurance)

Part A covers inpatient hospital stays, care in a skilled nursing facility, hospice care, and some home health care.

Medicare Part B (medical insurance)

Part B covers certain doctors' services, outpatient care, medical supplies, and preventive services. Medicare covers services (such as lab tests, surgeries, and doctor visits) and supplies (such as wheelchairs and walkers) considered medically necessary to treat a disease or condition.

If you're in a Medicare Advantage Plan or other Medicare plan, you may have different rules, but your plan must give you at least the same coverage as Original Medicare. Some services may only be covered in certain settings or for patients with certain conditions.

Medicare Part B covers 2 types of services

Medically necessary services: Services or supplies that are needed to diagnose or treat your medical condition and that meet accepted standards of medical practice.

Preventive services: Health care to prevent illness (like the flu) or detect illness at an early stage, when treatment is most likely to work best.

How will Medicare B work for treating MDS?

Infused drugs

Medicare covers drugs infused through an item of durable medical equipment, such as an infusion pump or nebulizer.

Oral anticancer drugs and oral supportive care medications

Oral drugs used for cancer treatment should be covered under Medicare part B provided they are approved by the Food and Drug Administration for the treatment of cancer (such as MDS) or other illnesses (such as iron overload or nausea). Medicare helps pay for oral anti-nausea drugs used as part of an anti-cancer treatment. You must take the drugs immediately before, at, or within 48 hours of chemotherapy, and use them as a full therapeutic replacement for intravenous anti-nausea drugs you would otherwise take. Most plans include co-pays. The amount of these co-pays may vary according to your individual plan.

Erythropoietin (EPO)

Erythropoietin agents are injectable medication covered for the treatment of anemia for persons with chronic renal failure who are undergoing dialysis when given in the dialysis center or when given "incident to" a physician's service for other approved uses. Coverage for use in patients with anemia due to MDS is restricted to individuals who meet specific criteria including: low bone marrow blasts (<5%), no other identified cause of the anemia (iron, B12, or folate deficiency), and who have a low serum erythropoietin level.

Durable medical equipment (DME) supply drugs

Drugs that require administration with an infusion pump in the home if medically necessary such as some chemotherapeutic agents.

Drugs furnished “incident to” a physician’s service

Drugs that are prescribed under Medicare Part B and administered at the time of a provider visit (incident to a provider visit).

For covered Part B prescription drugs that you get in a doctor’s office or pharmacy, you pay 20% of the Medicare-approved amount. They must accept assignment for Part B drugs, so you should never be asked to pay more than the co-insurance or co-payment for the drug itself.

For covered Part B prescription drugs you get in a hospital outpatient setting, you pay a co-payment. If you get drugs not covered under Part B in a hospital outpatient setting, you pay 100% for the drugs, unless you have Part D or other prescription drug coverage. What you pay depends on whether your drug plan covers the drug, and whether the hospital is in your drug plan’s network.

Medicare Part D: supplemental prescription drug coverage

If you want broader prescription drug coverage, you must also join a Medicare Prescription Drug Plan (Medicare Part D). There are several different types of Medicare Part D plans, each with different levels of coverage and different drugs as a part of their formulary (preferred drugs for the plan). These plans are voluntary except for people who have both Medicaid and Medicare. It is important to consider the costs of prescription medications and co-pays needed during your treatment when deciding on participation in these plans. Out-of-pocket expenses can be quite high. Discuss this with your health care team to assist you in making an informed choice.

Medicare Advantage Plan (Part C)

If you join one of the Part C programs, much like and HMO or PPO group insurance plans they will generally include a prescription drug plan. In most cases, you must take the drug coverage that comes with the Medicare Advantage Plan. These programs must be approved by Medicare.

Original Medicare

Your yearly income and the amount of assets you have (not including the home you live in or your car) determine how much of the Part D costs Medicare will pay. The doughnut hole occurs when Medicare stops paying for part of your drug costs and you pay all of this yourself. Most states have many, many plans from which to choose, making it difficult to make a decision. All plans have to offer what Medicare calls a basic package, but some companies will offer more than one plan. You should pick a plan carefully. Compare plan formularies. Research drug plans to take advantage of lower co-pays. You may pay a little more each month, but you will probably save money in the long run. About 40 states have assistance programs to help low-income patients, who can also get help with Medicare Part D costs, either through their state or Medicare. Check with your Area Agency on Aging (to find your local agency call 800-677-1116).

Write Your Legislators

Letters do make a difference — There is power in numbers

To locate your legislator: www.house.gov/writerep/

For a Representative of the House:

The Honorable *(First and Last Name)*
United States House of Representatives
Washington, DC 20515

Dear Representative *(Last Name)*:

For a Member of the Senate:

The Honorable *(First and Last Name)*
United States Senate
Washington, DC 20515

Dear Senator *(Last Name)*:

Tips for writing Congress

1. State your purpose for writing in the first sentence of the letter. For example: As your constituent, I am writing to urge your support for increased funding for [health care concern].
2. Include personal information about why the issue matters to you to make your point.
3. If your letter pertains to a specific piece of legislation, identify it. Make sure that you are referencing the correct legislation to the correct body of Congress.
 - House bills are H.R._____.
 - Senate bills are designated as S._____.
 - It is also important to know the status of the bill.
4. Be courteous.
5. Close your letter with a restatement of your purpose and indicate the response that you expect.



Medicare

www.medicare.gov Official Medicare website

www.mymedicarematters.org Questions and answers to help explain Medicare

www.medicarerights.org Resources for the Medicare consumer

www.ssa.gov Website of the Social Security Administration. Apply here for Part D extra help.

Formulary finder

The Formulary Finder for Prescription Drug Plans tool will allow you to find plans in your state that match your required drug list. This site is maintained by the Centers for Medicare and Medicaid Services. This document also available in Spanish.

www.medicare.gov/find-a-plan/questions/home.aspx

General prescription assistance programs

Medicare and Medicaid Prescription Drug Programs 800-633-4227

Centers for Medicare and Medicaid Services
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, DC 20201

Information about prescription drug coverage:

www.medicare.gov

www.cms.hhs.gov/home/medicaid/asp

Social Security Disability Programs 800-772-1213

The Social Security and Supplemental Security Income disability programs are the largest of several federal programs that provide assistance to people with disabilities.

www.ssa.gov/disability

Medication & Underinsured Assistance

Chronic Disease Fund: 877-968-7233

This program provides assistance to those underinsured patients who are diagnosed with chronic or life-altering diseases.

www.cdfund.org

HealthWell Foundation 800-675-8416

This charitable organization offers co-pay assistance for MDS medications.

Hours are Monday to Friday from 9:00am to 5:00pm EST.

www.healthwellfoundation.org

National Organization for Rare Diseases 800-999-6673 or 203-744-0100

Medication Assistance Program

www.rarediseases.org/programs/medication

Needy Meds 978-281-6666

A resource for people who cannot afford medicine or other health care costs. Needy Meds has information on over 600 programs.

www.needy meds.org

Partnership for Prescription Assistance 888-4PPA-NOW (888-477-2669)

Prescription assistance programs, often sponsored by drug makers, to help patients who qualify based on financial need. Search this website for a comprehensive listing of more than 475 public and private patient assistance programs including nearly 200 programs offered by pharmaceutical companies.

www.pparx.org

Patient Access Network Foundation 866-316-PANF (866-316-7263)

This foundation assists patients with their coinsurance associated with MDS treatments/medications.

Hours are Monday to Friday from 9:00am to 5:00pm EST.

www.patientaccessnetwork.org

Patient Advocate Foundation 800-532-5274

This program provides direct copayment assistance for pharmaceutical products to insured Americans who financially and medically qualify.

www.patientadvocate.org

Patient Services, Inc. 800-366-7741

A nonprofit charitable organization primarily dedicated to subsidizing the high cost of health insurance premiums and pharmacy copayments for persons with specific chronic illnesses and rare disorders.

www.uneedpsi.org

RxAssist 401-729-3284

This program provides a comprehensive database of patient assistance programs.

www.rxassist.org

Together Rx Access 800-444-4106

This program is free and offers savings of 25–40% on over 300 brand name and generic prescription drugs.

www.togetherrxaccess.com

Specialty pharmacies that carry MDS medications

Accredo Nova Factor 866-289-7577

Offers specialized care and support for patients. Their clinical, educational and reimbursement services are tailored to meet each patient's individual needs. They will even help untangle your insurance coverage.

www.accredonovafactor.com

BioPlus 888-292-0744

This is a free service to assist patients in obtaining medicines. This service also works with various prescription funding programs, pharmaceutical manufacturers, and other resources to find financial assistance for patients.

www.bioplusrx.com

BioScrip 866-807-0516

Your complete source for effective specialty pharmacy solutions, from personalized patient support services to medication management programs for health plans.

www.bioscrip.com

Diplomat Specialty Pharmacy 877-977-9118

Provides clinical and reimbursement solutions to patients with oncologic and hematologic disorders. Diplomat's Oncology Navigator Program provides a dedicated team to help patients and health care professionals gain access to required oncology medications.

www.diplomatpharmacy.com

US Bioservices 877-263-7089

Delivers nationwide specialty pharmacy and nursing services that meet the unique needs of patients.

www.usbioservices.com

Pharmaceutical company assistance

Amgen

Amgen Assist Online 888-4ASSIST (888-427-7478)

Amgen's patient assistance programs provide replacement product for uninsured or underinsured qualifying patients with limited financial resources. Program includes Aranesp[®], Neulasta[®], NPlate[®], Epogen[®], Vectibix[®], and XGEVA[™].

www.AmgenAssistOnline.com

Centocor Ortho Biotech, Inc.

ProcritLine 800-553-3851

Resources to help patients or caregivers learn more about treatments or financial programs.

Hours of operation are Monday to Friday from 9:00am to 8:00pm EST.

www.procritline.com

Celgene Corporation

Celgene Patient Support[™] 800-931-8691

A dedicated central point of contact helping providers and patients identify resources to gain access to Celgene products, including Revlimid[®] and Vidaza[®]. Available to answer your questions Monday to Friday from 8:00am to 7:00pm EST.

www.CelgenePSC.com

www.Revlimid.com

www.Vidaza.com

The RevAssist[®] Program 888-423-5436

A proprietary risk-management education and restrictive distribution program for patients who have been prescribed Revlimid[®]. Information about Revlimid[®] can be obtained by calling the Celgene Customer Care Center toll free Monday to Friday from 8:00am to 8:00pm EST and Saturday from 9:00am to 3:00pm EST.

RevAssist[®] registration may be completed by visiting RevAssist Online[®] or by calling the Celgene Customer Care Center.

www.Revassistonline.com

www.Revlimid.com

Eisai, Inc.

Dacogen® Patient Assistance and Reimbursement Program 877-644-6270

Provides information on Dacogen® reimbursement services. Available Monday to Friday from 8:00am to 8:00pm EST.

www.Dacogen.com

Genzyme

Leukine® Reimbursement Program 888-479-5385

Provides answers to reimbursement and coverage policy questions. Hours of operation are Monday through Friday from 9:00am to 7:00pm EST.

www.leukine.com

Novartis Oncology

EPASS™ Advantage® 888-90 EPASS (888-903-7277)

EPASS (EXJADE® Patient Assistance and Support Services)

EXJADE® prescription and reimbursement program helps ensure that patients receive their prescriptions on time at home or the location of their choice. The EXJADE® ScriptAssist Program provides assistance and support services hotline for patients already receiving EXJADE®. Contact your specialty pharmacy to determine your eligibility and to enroll in this cost savings program. Eligible patients can receive up to \$100 toward out-of-pocket expenses for prescriptions. Contact EPASS Advantage Monday through Friday 9:00am to 8:30pm EST.

www.epassrx.com

www.us.exjade.com

Living with MDS



video testimonial

My name is Bob Weinberg. I was diagnosed in 1998 at age 48 with MDS–RARS (refractory anemia with ringed sideroblasts). Here are my numbers: Since then I have received over 850 units of packed red blood cells. My white blood cells hover around 2.0, my absolute neutrophil count (ANC) between 500 and 700, and my platelets between 30,000 and 40,000. My blast count is under 5%. My current transfusion frequency is 7–8 days. I take 2,500 mg of Exjade® daily. My ferritin level, checked monthly, ranges from 450 to 700. I have an MRI every year on my heart and liver, looking for embedded iron in those organs.

My MDS story began in the water. During my 30's and 40's, I was an avid swimmer. Every morning before going to work at a large high-pressure law firm in Philadelphia, I would sleepwalk my way to the local Y to swim my daily mile—thirty-six laps. I was only one of a group of groggy people who began their day with a swim. Side by side, we would glide through the water, and being competitive by nature, we each knew which swimmers would pass us and which swimmers we would pass. Until the winter and spring of 1997–98. That is when I found the morning swim's natural order of things out-of-whack. Those I usually passed started passing me. Those who would pass me once every four laps would pass me twice as often. So to build-up my stamina, I thought that I should jog, as well. After running less than a city block, I had to stop, almost keeling over with a sharp pain in my chest, severe breathlessness, aching calves, a pounding heart and dizziness. Something was wrong, so I gave up jogging after one try and went back to the pool. Over a couple of months, my stamina and strength declined to where every one of my fellow swimmers passed me. I could not even swim six laps. I started to need a nap in the afternoon—at 48 years old. It was time to see the doctor and have my first ever physical.

That was on a Friday, and by Tuesday morning I learned the words “myelodysplasia” and “sideroblastic anemia.” I went right to Google. The first thing item that came up was an article on Carl Sagan. I knew I was in for a game-changer. My siblings were tested for a bone marrow match and both failed. My internist called to ask me if “my affairs were in order.” That is when the hematologist at the local hospital told me that he had patients like me with low hemoglobin, but manageable platelets and white cells, who lived on transfusions for 15 years. I then visited a specialist in MDS at a major university medical center for a second opinion. He said that I should not expect to live more than five years. I told him that I had a better offer from the hematologist at my local community hospital, and he said he could not match that. So, of course, I took the higher offer and my community hospital is where I have been treated for the last 14 and one-half years.

Not that I didn't visit the best of best in experts over the next 10 years—Stanford University, Memorial Sloan Kettering, Moffitt Cancer Center, University of Rochester, Mt. Sinai. I remember my first visit with an international expert. I asked him what causes MDS. He quickly replied, “Bad luck.” I took Revlimid® on a clinical trial, but all it did was lower my blood counts, cause boils and make my hair itch. I took Vidaza® , and it worked for 5 months, but within less than a year of starting it, I was back on a 14-day transfusion frequency.

So the family flew to Seattle in early 2006. We visited the Fred Hutchinson Cancer Center, which I was told was the place for MUD (matched unrelated donor) transplants. The doctor sat my wife, my 23-year-old daughter, and me down at a small round table in a small windowless conference room and told us that I had only six months to live unless I submitted myself to a *mismatched* unrelated donor bone marrow transplant. Chances of surviving 5 years were 65%. So I gave notice at work and my wife and I leased an apartment in Seattle. But first, I took a 10-day motorcycle trip in Europe, where I conveniently broke my ankle when my Ducati spilled on gravel and landed on my foot. That set back the transplant schedule. Bones won't heal when your immune system is suppressed as it is in a BMT. By the time my ankle had healed, however, I decided against the unrelated mismatched procedure. That was 6 and half years ago. I recently had the donor search re-run, and I learned that with the donors available and the billions of antibodies I have garnered from so many past transfusions, I should consider a BMT only if it is my very last option. So I am sticking with the transfusions.

By year 2009, transfusion frequency was down to 10 days, and I was faltering in meeting the pressures at work what with the interruptions for blood tests, feeling lousy and transfusions. So I cut my workload by 80%, became further involved in the MDS Foundation and spent much more time walking my dog. Meanwhile, antibodies seem to be destroying the transfused blood more quickly and preventing me from getting quite the same energy lift I used to get from a transfusion. But time marches on, and I have no sense that anything is coming to a close.

Recognizing that MDS comes in many shapes and sizes, I have lived by the following points.

- Don't worry about something that may happen in the future. I can worry about it when it happens.
- Do everything I can to be informed so that I can make intelligent choices.
- Don't get caught up thinking that I am in a battle in which I have some control over whether I win or lose. We are in the realm of those things over which we don't have control.
- If things don't work out, it is not because I did not fight enough, or I did not have faith enough, or others weren't praying for me enough.

Bob Weinberg



Living with MDS



video testimonial

Hello. My name is William Pearson. I am 76 years old and live in Hamilton, Ontario, Canada. I was born and raised in Nelson, British Columbia. Following school, I played hockey for two years and after that worked in the steel manufacturing sector for 45 years. Following my retirement, I started up a consulting business. My consulting projects took me to different parts of Canada, Germany, and Poland. When I was in Krakow, Poland our office was within walking distance from our hotel and then arranged transportation to different steel plants in that area. One week into the project, I started to labor in my morning walk to the office. At this point I found it difficult and started to taxi back and forth. Walking about the steel plants became more difficult. Climbing stairways to operating decks became difficult. I found myself having to stop every 5 or 6 stairs before I could continue.

On my return to Canada, my first visit was to my family doctor who ordered blood tests. She called me after receiving the results. My hemoglobin was 88mg/dL (or 8.8 g/dL), well below the normal range. She referred me to a hematologist. Thankfully, I wasn't going to a stranger as I had seen the hematologist in the past with other problems. I find it more comfortable if you know the doctor you're about to see. The hematologist repeated the blood tests and at the next visit, I had a bone marrow biopsy and aspiration. (January/2003 hg.81 (8.1)

In a follow-up appointment 6 weeks later, she indicated that the results didn't look good. She also needed to repeat the bone marrow test to get more information to compare. I still kid her that she bent the needle during the second bone marrow aspiration on purpose but she maintained it was my bone structure being so hard nothing to do with her. At this point I started red blood cell transfusions to maintain my hemoglobin. (March 19, 2003)

On the next visit, she indicated the results of the two bone marrow procedures indicated a diagnosis of MDS. I don't remember any fear or concern other than what's next. We discussed the option of a stem cell transplant. If that was to proceed, my sister would be the most suitable candidate. I called my sister to discuss this with her. My sister Jane lives on the west coast, about 5 hours by plane, her response was, "How soon do you want me there?" Bone marrow transplants take time to plan and not all patients are able to have an allogeneic bone marrow transplant. My age at the time being 60+ was a factor, just outside the range recommended for this type of transplant. So, the doctor suggested a pill, Danazol®, which might help my bone marrow function better. She indicated that based on her experiences, it was working in about 5% of her patients.

After a period of time, the drug stopped working and I was being transfused 2 units of blood at two-week intervals (between April 2007 and January 2008). I had developed iron overload as a result of all of these transfusions. She referred me to a major cancer hospital in Toronto, about 60 kilometer away. The hospital (Princess Margaret Hospital) has the reputation of being one of the top cancer hospitals in the world. My first appointment was early in September 2007. I was referred to this hospital in hopes of being fit into a clinical trial for new treatments for MDS. After another bone marrow procedure and several visits, it was determined that I did not meet the criteria for any of the drug trials.

In December 2007, she wanted to try a drug called Cyclosporine (autoimmune suppressant). After reading all of the literature on the drug, I determined it was not for me. Big mistake on my part. My wife and I got to know the doctor very well, seeing her every 2 weeks for 3 months. We developed an admiration and a deep respect for her. When she said it was the best treatment for me at that time and that we needed to consider it, our "yes" came very quickly. The results were very positive. At one of my appointments, the doctor and Janet (wife) said phlebotomy in unison. I had a total of 3 which brought my iron overload out of the critical area.

Today I am still on cyclosporine and it is holding my hemoglobin in the range of 105 mg/dL (10.5g/dL). We can't increase the dosage because it has affected my kidney function.

How is my quality of life?

To sum it up, for the most part there has been little change. Some days are worse than others. An example is walking a kilometer one day without stopping and others having to stop for a moment every 5 meters. Lifting is also a chore, house work exhausts me—sometimes my excuse works but not too often as Janet knows it is a poor excuse to avoid it.

We still travel. In 2010, we went to Scotland for a holiday in conjunction with the MDS Foundation International Symposium. Janet and I spoke at an MDS forum for patients and their caregivers from all the European countries. We travel across Canada to the west coast yearly. I still play golf with the use of a power cart. The golf club puts a flag on my cart to allow me to take it to as close to my ball as possible excluding the greens.

What are my fears?

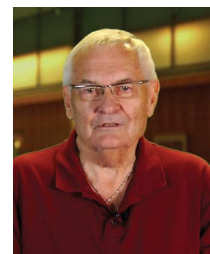
I am apprehensive about my life with MDS. I don't dwell on it and, for the most part, have little fear. The only time I get a bit edgy is after blood tests while I am waiting for results.

Early in my diagnosis, I enrolled in the Leukemia Lymphoma Society first connection program (until about a year ago). The LLS would contact me that X person would like to talk to someone with MDS. Being the only name in the databank, I would be asked if I would contact a person regarding MDS—95% of the folks were from the United States. I think that my sense of helping someone else took away my anxieties.

I have seen a major change in the past 1½ years. MDS is no longer in the closet, so to speak. A significant example is Robin Roberts, anchor for ABC Good Morning America. Robin went public on her show, and many stories about MDS were in newspapers across the country. ABC continues with updates.

What are my hopes for the future? I'm not sure how a 76-year-old man should feel, quality of life and longevity of life are my biggest hopes and I would be satisfied with status quo. I do hope in my lifetime I see research that would treat and maintain MDS of all types.

William Pearson



Living with MDS



video testimonial

My name is Janet Pearson and my husband William has Myelodysplastic Syndrome.

The initial diagnosis was 10 years ago (the internet description and prognosis of MDS was more frightening than hopeful). In 2002, William was in Poland for two weeks and on his return he saw his family doctor. The blood work from that visit showed hemoglobin of 88mg/dL (8.8g/dL). He was then referred to a hematologist.

A bone marrow aspiration was done in January 2003. William's hemoglobin at that time was 81mg/dL (8.1g/dL). We spoke with the hematologist about a bone marrow transplant, but his age was a concern.

The doctor put William on a drug which maintained his hemoglobin counts, and sustained his and my quality of life for about 4½ years.

Our lives carried on as if nothing was threatening our longevity together. We played golf together, vacationed, and socialized. William travelled to Europe on business trips, and his life was visibly unaltered. I was working, playing piano, painting, going to yoga and enjoying the daily activities that were a part of a relaxing lifestyle.

In April of 2007, our lives were altered with a 4:00 am, hospital visit. William's hemoglobin was 80mg/dL, which meant another bone marrow aspiration, transfusions and other diagnostic testing to check for a possible source of bleeding.

Diagnostic tests proved normal. The bone marrow confirmed MDS had evolved to a more critical level, a more aggressive treatment would be required. Transfusions continued every two weeks. An appointment was arranged at a major cancer centre in September of 2007. This initial appointment required another bone marrow test, and weekly appointments which were then followed by biweekly appointments. These bone marrow results confirmed that this type of MDS did not fit the criteria for any of the drug trials that were currently in place. This information was expressed to us at one of our October meetings. The hematologist at that time talked about Cyclosporine being an option; however, it would require approval from the government for insurance coverage. Treatment was approved and William began the medication in January 2008. The side effects were frightening.

This was a very difficult time for me. I would call home from work several times a day to check on him. If he didn't answer the phone, I would call my neighbor so that she could reassure me, and let me know that he was okay. Often times she would find him asleep in his chair in the yard. He was so pale that she would check to see if he was breathing. She would call his name to stir him awake. Everyone noticed a difference in William.

When William had iron overload I spoke with a dietician and asked about diet and foods to avoid. Tea was something she recommended and if eating red meat always have a glass of cab-sauvignon wine, not Merlot, not Shiraz but cabernet sauvignon. When William's hemoglobin reached 140 (14.0) I thought of phlebotomy and shared this with him and the hematologist. He had three phlebotomy sessions to help remove the excess iron. I also believe in movement, the importance of getting out for maybe 3/10 minute walks a day, keep moving. When creatinine starting creeping up, drinking more water was important. I still bug him about drinking water.

I am not here to tell his story but that's what I find I am doing, MDS has consumed so much of me. How has it affected me? I work, I worry. Fear sometimes consumes me. Fear of being alone, fear of what he has to go through, fear of the unknown. I know I cannot do anything about it. It is difficult to share this fear with others who do not understand MDS. You see on the outside, I project a well put together woman. I appear to be calm, but my insides are continually racing. I have been told that I am a patient and kind person, and I care so much.

I feel that I have been compromised out of fear. We used to walk for miles, chatting and laughing. Walking at a good pace, and in all kinds of weather, be it sun, rain or snow. We would sit out on summer evenings, but West Nile Virus has precipitated a fear in William and me. Walking is now a slow to medium pace. Distance depending on the day may be very short. This past Sunday evening William initiated a walk, he said, "Let's go down to the lake." We walked for 2 kilometers. It was a beautiful evening. The following night however was different. Walking any distance was impossible and he was sure it was from the walk the night before. So you see, I grab impulsive and special moments.

Last year in September, (this is usually when we vacation), we did not travel. William had an old sports injury that flared up and restricted his mobility. Therefore, rest, ice and heat were in order. During that time I started walking with my neighbor from 7-8am Monday to Friday for 3 weeks. It felt great. We are still walking on the days that I have off from work. This is my time.

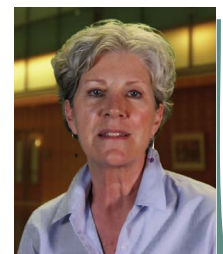
I have written letters to William regarding my fears and my frustration, but have never shared them with him.

I love my life with William; I grab the moments that we share together. I enjoy the little things like cooking together, shopping, short walks, and whatever vacation time that we can have.

My job is in the Intensive Care unit in an administrative position. Due to the fact that this is a high risk floor in the hospital, I feel the daily stresses that encompass the patients and their families also contribute to my fears.

With the fears, frustration and uncertainty, it is important to take care of yourself as a caregiver. Take time for yourself. I like to read, have lunches with friends, knit, walk and have started a quilt. I will be starting a yoga class in November with a friend.

Janet Pearson



Living with MDS



video testimonial

Hello, my name is Ryan Szanto. I am 74 years old and have been an MDS patient for 15 years. I hope to convey to you my experiences with MDS. I also hope my longevity with MDS will give you hope and encouragement as you live with MDS.

During a routine wellness check, I was diagnosed with anemia in July 1996. I was a very active outdoor person and did not feel that there was anything wrong with me, so I did nothing about it. The next year, during another routine wellness check, the doctor wrote in red pen and circled: Significant Anemia. He recommended that I see my primary doctor. I saw him on August 1997, and had blood tests run over a 5-week period. I was told that they didn't know what was wrong with me. My doctor recommended that I see a hematologist/oncologist, which I did.

A bone marrow biopsy was performed and it was determined that my anemia was due to MDS. This doctor had me come in once a week for a CBC for the next 15 months. In January 1999, I started on Procrit injections, 30,000 units once a week. During the next 5 years and 9 months, the Procrit injections increased gradually from 30,000 to 80,000 units to keep my hemoglobin at healthy levels. In December 2005, I was switched from weekly Procrit to bi-weekly Aranesp® injections. This was a blessing. The Aranesp® dosage started at 300mcg for 28 injections and now continues at 400mcg. I have had a total of 176 Aranesp® injections as of October 2012.

In June 2001, I started on blood transfusions. As of October 2012, I have received 377 units of blood. By June 2004, I was in iron overload. My ferritin was 2,990 due to the number of blood transfusions, so I started iron chelation with a drug called Desferal®, which is dispensed with an infusion pump for 12 hours a day, 5 days a week. I continued this treatment for 1½ years.

In the fall of 2005 the MDS Foundation notified me that there was a new oral drug, Exjade®, used to treat iron overload. Exjade® was up for FDA approval in Washington, DC and I was asked to testify as to why the drug should be approved. I was thrilled to go. It would be wonderful to get off that pump. I went with 14 other patients who also developed iron overload as a result of chronic transfusions for MDS, Aplastic Anemia, and Thalassemia. Thankfully, it was approved. I started taking Exjade® 1,500mg daily in January 2006. Hurray!!! This was another blessing. Every morning, I dissolve the Exjade® tablets in water and drink it. I've been on Exjade® ever since, except for 6 months when the Ferritin level went low enough (312) for me to come off. The dosages have varied over the last 7 years. I am currently taking 1,000mg a day.

In September 2004, Dr. Alan List of the Moffitt Cancer Research Center stopped the Procrit injections so my system would be clean to start the CC5013 (Revlimid®) drug trial. My diagnosis was MDS sub-type Refractory Anemia with Ringed Sideroblasts or RARS. The drug did not work for me. It did work for patients with 5q- chromosome malfunction. Results for these patients were amazing. Most of the patients with the 5q- had a significant reduction in their transfusion needs; some no longer needed transfusions at all. Halfway through the trial, I had a sense it wasn't working for me, but I went ahead and completed the trial because I knew that the research collected from me might benefit other MDS patients later on.

During these past 15 years, I have had 7 bone marrow biopsies. MDS is classified as high or low risk. I am in the low risk category and my biopsies have not changed during these 15 years.

During my first 3 years, I could not find any non-MDS specialists who knew anything about the disease. Also during this time, there wasn't much or any research on MDS. The first research that took place was for high-risk patients. I totally agree with this because they are at greater risk to come down with Leukemia. There is now research taking place for high and low-risk patients. The good news is that there is 100+ MDS research centers worldwide.

When I was first diagnosed with anemia and then with MDS, I was in denial. This went on for 1½ years. As time went on, I realized that not many people knew about this disease, so I decided to find out all I could and I began to keep detailed records of what was going on. I knew that my body was the temple of the Lord and I had a responsibility to take care of it. This is when my denial shifted to a positive attitude. I started by reading everything I could, looking up on the Internet, talking to my doctor, and attending the MDS patient forums put on by the MDS Foundation. In fact, I continue to try to attend one or two a year. These forums have been very educational; we hear from doctors and nurses in the field and from patients who share their experiences, ask, and discuss questions.

I have also done several videos for the drug manufacturer of Exjade®. This involvement has caused me to realize how much I appreciate what was taking place to find better ways to deal with iron overload.

I joined "data for national MDS registry" in June 2008. This is a registry that collects detailed information on MDS patients nationwide. Their goal is to help MDS patients by determining what the similarities and differences are in patients. (What works and what doesn't work.)

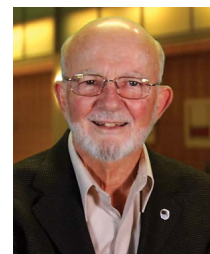
Besides learning all that I can about MDS from multiple avenues and getting involved, I have also used my faith to pray for and encourage other patients. Each time that I get out of my vehicle to enter the Oncology Center or Infusion Center, I pray the Lord will put someone in my path that He wants me to speak to, encourage, or pray for. He honors this request each time. I also thank the nurses who attend to me and if they need to pray, I pray with them. When I go to the blood bank, I introduce myself to the donors and thank them for keeping me alive.

I believe that this involvement is what is keeping me going. My positive attitude and faith has been strengthened every day.

To summarize, I would say, learn all that you can about MDS, stay up to date on the research, stay positive, be motivated, and get involved especially in patient forums. Ask questions of your doctor and nurses, and, most of all, keep God as your pilot.

Yes, it is true, I have not been healed physically, but God has healed me spiritually and my spirit is what will live on for eternity. I thank the MDS Foundation for allowing me to share this time with you. May God bless you now and forever.

Ryan Szanto





THE MDS FOUNDATION


The MDS Foundation is an international publicly supported organization dedicated to serving the MDS patient, their caregivers, and the professionals that are working to improve the lives of patients living with MDS. The MDS Foundation provides a number of resources which support the Building Blocks of Hope program.

contributing authors

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Sandra Kurtin
Deborah Murray
Bob Weinberg

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About the MDS Foundation

The Myelodysplastic Syndromes Foundation was established by an international group of physicians and researchers to provide an ongoing exchange of information relating to MDS.

Until the Foundation was set up, no formal working group had been devoted to MDS. Since its inception, we have conducted 11 international symposia in Austria, the United Kingdom, the United States, Spain, Czech Republic, Sweden, France, Japan, Italy, Greece, and Scotland. The 12th International Symposium was held in Berlin, Germany, on May 8-11, 2013.

A major Foundation effort is our international information network. This network provides patients with referrals to Centers of Excellence, contact names for available clinical trials, sharing of new research, and treatment options between physicians, and extension of educational support to physicians, nurses, pharmacists, and patients.

In response to the needs expressed by patients, families, and health care professionals, we have established patient advocacy groups, research funding, and professional education for physicians, nurses, pharmacists, and other health care professionals.

The MDS Foundation is a publicly supported organization.



contact us

800-MDS-0839 *(within the US)*
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Director of Operations

Susan Hogan

Susan has been with the MDS Foundation for ten years, originally as Office Manager. Susan came to the Foundation with 15 years of prior pharmaceutical experience in the Medical and Scientific Affairs, Finance, and Marketing Research areas. At the Foundation, Susan oversees all daily business activities, including finances, staffing, and staff projects. She works with the MDS Board of Directors and Board Committee members on strategic planning for meeting the ongoing needs of MDS patients and education of MDS health care professionals.

Grants Director/Project Manager

Tracey Iraca

Tracey joined the MDS Foundation in 2004 as a part-time Patient Coordinator, assisting with patient education programs. Presently, Tracey manages the corporate grants program and is responsible for all corporate relations. She also coordinates Scientific Symposia, serves as liaison to the Foundation's International Nurse Leadership Board and International Working Group for Prognosis in MDS (IWG-PM), as well as serving as the primary contact for the volunteer Development Committee.

Production Coordinator

Janice Butchko

Janice joined the Foundation in 2008 and is responsible for the coordination, quality control, and production of printed and electronic Foundation material. Janice also manages exhibit shipment needs, coordinates mailings, is responsible for patient information inquiries and membership renewals, as well as administrative bookkeeping services.

Patient Liaison

Audrey Ann Hassan

Audrey joined the MDS Foundation ten years ago as the Patient Liaison. She came to the MDS Foundation with over 14 years' experience in patient services working in the Medical Affairs Department of a leading pharmaceutical company. Her primary role is to provide international support to patients, families, and caregivers touched by MDS. Whether it is face-to-face or by telephone or email, Audrey responds to questions regarding MDS, including information about treatment options, clinical trials, financial assistance, as well as providing patients with a priority referral to any MDS Center of Excellence worldwide.

Patient Coordinator

Deborah (Dee) Murray

Dee assists the Foundation in the patient awareness development area. An important part of this development is Dee's coordination and management of the Foundation's Patient Forum meetings. These meetings bring together patients, caregivers, and family members throughout the US, for the purpose of education and to offer an opportunity to share their experience with others whose lives are also affected by Myelodysplastic Syndromes. In addition to this responsibility, Dee manages the Foundation's donation database, ensuring the acknowledgment of support in a timely manner.

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Haematological Medicine
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University of Arizona
Tucson, Arizona, United States

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Teamleader, Anemia Leukemia Team
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Sahlgrenska University Hospital
Goteborg, Sweden

Arno Mank, RN
President EBMT Nurses Group
European Group for Blood and Marrow Transplantation
Nurse Researcher
Academic Medical Centre
Amsterdam, The Netherlands

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Cambridge, United Kingdom

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Department of Hematology Oncology
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The Beatson West of Scotland Cancer Centre
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Palo Alto, California, United States
Associate Clinical Professor
University of California, San Francisco
San Francisco, California, United States

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Malignant Hematology Nurse Practitioner
H. Lee Moffitt Cancer Center
Tampa, Florida, United States

To be recognized as a Center of Excellence, an institution must have:

- An established university (or equivalent) program
- Recognized morphologic expertise in MDS
- Available cytogenetics and/or molecular genetics
- Ongoing research, including Institutional Review Board–approved clinical trials
- Documentation of peer-reviewed publications in the field

Please contact the Foundation for further information.

MDS Centers of Excellence within the United States

Arizona

Mayo Clinic Hospital
Phoenix, Arizona
Ruben Mesa, MD
James Slack, MD

The University of Arizona Cancer Center
Tucson, Arizona
Ravi Krishnadasan, MD, FACP

California

Cedars–Sinai Medical Center
UCLA School of Medicine
Los Angeles, California
H. Phillip Koeffler, MD

City of Hope National Medical Center
Duarte, California
Stephen J. Forman, MD

Moore's Cancer Center at the
University of California, San Diego
Rafael Bejar, MD, PhD
Peter Curtin, MD

Stanford University Medical Center
Stanford, California
Peter L. Greenberg, MD
<http://med.stanford.edu/clinicaltrials>

UCLA Center for Health Sciences
Los Angeles, California
Gary J. Schiller, MD

University of Southern California
Keck School of Medicine
Los Angeles, California
Casey L. O'Connell, MD

Florida

All Children's Hospital
St. Petersburg, Florida
Gregory Hale, MD

Mayo Clinic
Jacksonville, Florida
Alvaro Moreno–Aspitia, MD
James M. Foran, MD

Sylvester Comprehensive Cancer Center
University of Miami Miller School of Medicine
Miami, Florida
Stephen D. Nimer, MD

University of Florida
Shands Hospital
Gainesville, Florida
Christopher R. Cogle, MD

University of South Florida
H. Lee Moffitt Cancer Center
Tampa, Florida
Alan F. List, MD

Georgia

Emory Winship Cancer Institute
Emory University School of Medicine
Atlanta, Georgia
Amelia Langston, MD

The Blood and Marrow Transplant Program
at Northside Hospital
Atlanta, Georgia
Asad Bashey, MD

Illinois

Loyola University Chicago
Cardinal Bernardin Cancer Center
Maywood, Illinois
Scott E. Smith, MD, PhD

Robert H. Lurie Comprehensive Cancer
Center of Northwestern
University Feinberg School of Medicine
Chicago, Illinois
Olga Frankfurt, MD

Rush University Medical Center
Chicago, Illinois
Stephanie A. Gregory, MD
Jamile Shammo, MD
<http://www.rush.edu>

University of Chicago Medical Center
Chicago, Illinois
Richard A. Larson, MD
http://webres.uccrc.org/clinical_trials

Indiana

Indiana University Simon Cancer Center
Indianapolis, Indiana
Larry Cripe, MD
Hamid Sayar, MD, MS

Maryland

Johns Hopkins University School of
Medicine
Baltimore, Maryland
Steven D. Gore, MD
<http://www.hopkinsmedicine.org>
<http://trials.johnshopkins.edu?ctg=mds%20AND%20onconova>

University of Maryland
Greenebaum Cancer Center
Baltimore, Maryland
Maria R. Baer, MD
<http://www.umgcc.org>
<http://data.umms.org/scripts/trials/listing.cfm?criteria=1910&tx=13&ty=5>

Massachusetts

Children's Hospital Boston
Harvard Medical School
Boston, Massachusetts
Inga Hofmann, MD
<http://www.pedimds.org>

Dana-Farber Cancer Institute
Boston, Massachusetts
Richard M. Stone, MD/David P. Steensma, MD
<http://www.dana-farber.org>
<http://www.dana-farber.org/Research/Clinical-Trials/Clinical-Trial.aspx?tid=2330>

Tufts University School of Medicine
Tufts Medical Center
Boston, Massachusetts
Kellie Sprague, MD

Michigan

Barbara Ann Karmanos Cancer Institute
Wayne State University
Detroit, Michigan
Charles A. Schiffer, MD

William Beaumont Hospital Cancer Center
Royal Oak, Michigan
Ishmael Jaiyesimi, DO

Minnesota

Mayo Clinic
Rochester, Minnesota
Mark R. Litzow, MD
<http://www.mayoclinic.org>

University of Minnesota Medical Center, Fairview
University of Minnesota Medical School
Minneapolis, Minnesota
Erica D. Warlick, MD

Missouri

Washington University School of Medicine
Siteman Cancer Center
St. Louis, Missouri
John F. DiPersio, MD, PhD

Nebraska

University of Nebraska Medical Center
Omaha, Nebraska
Lori Maness, MD

New Jersey

The Cancer Center of Hackensack University Medical Center
Hackensack, New Jersey
Stuart Goldberg, MD
<http://www.humc.com>

New York

Albert Einstein College of Medicine Cancer Center
Bronx, New York
Amit Verma, MD
<http://www.mdstreatment.com/investigational-therapy-2>

Columbia University Medical Center
New York, New York
Azra Raza, MD

Memorial Sloan-Kettering Cancer Center
New York, New York
Virginia M. Klimek, MD

Mount Sinai School of Medicine
New York, New York
Lewis R. Silverman, MD
<http://msccc.com>

New York Medical College/Westchester Medical Center
Zalmen A. Arlin Cancer Center
Valhalla, New York
Karen Seiter, MD

North Shore University Hospital
Lake Success, New York
Steven L. Allen, MD

Roswell Park Cancer Center
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James E. Thompson, MD

University of Rochester Cancer Center
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Carlos M. deCastro, MD

Wake Forest University School of Medicine
Comprehensive Cancer Center
Winston-Salem, North Carolina
Bayard L. Powell, MD

Ohio

Cleveland Clinic Foundation
Taussig Cancer Center
Cleveland, Ohio
Jaroslaw Maciejewski, MD, PhD
<http://my.clevelandclinic.org/default.aspx>
http://my.clevelandclinic.org/research/clinical_trials/nct01241500.aspx

The Ohio State Comprehensive Cancer Center
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Kimmel Cancer Center
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University of Pennsylvania Cancer Center
Philadelphia, Pennsylvania
Selina Luger, MD

UPMC Cancer Centers
University of Pittsburgh Cancer Institute
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Vanderbilt University Medical Center
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Madan Jagasia, MD
Stephen Strickland, MD

Texas

Cancer Care Centers of South Texas
San Antonio, Texas
Roger Lyons, MD
<http://cancercareouthtexas.com>
<http://cancercareouthtexas.com/clinical-trials/category/myelodysplastic-syndromes-mds-chronic-myelomonocytic-leukemia-cmml-acute-my/>

Southwest Regional Cancer Center
Austin, Texas
Richard Helmer, III, MD

University of Texas
MD Anderson Cancer Center
Houston, Texas
Guillermo Garcia-Manero, MD
Hagop Kantarjian, MD
<http://utm-ext01a.mdacc.tmc.edu/dept/prot/clinicaltrialswp.nsf/Index/2010-0209>

Washington

Fred Hutchinson Cancer Research Center
University of Washington
Seattle Cancer Care Alliance
Seattle, Washington
Joachim Deeg, MD/Elihu Estey, MD

Washington, DC

Georgetown University Hospital
Lombardi Comprehensive Cancer Center
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Wisconsin

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MDS Centers of Excellence outside of the United States

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University of Melbourne
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Royal Hobart Hospital
Hobart, Tasmania, Australia
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Dublin, Ireland
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Valencia, Spain
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Hwei-Fang Tien, MD, PhD

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Pathumwan, Bangkok, Thailand
Tanin Intragumtornchai, MD

Tunisia

Hôpital Aziza Othmana
Tunis, Tunisia
Balkis Meddeb, MD

Turkey

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Ankara, Turkey
Osman Ilhan, MD

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Research Center for Radiation Medicine
Kiev, Ukraine
Dimitry Bazyka, MD

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Aberdeen University
School of Medicine
Foresterhill, Aberdeen, Scotland
Dominic Culligan, MD

Addenbrookes Hospital
Cambridge University Hospitals
NHS Foundation Trust
Cambridge, United Kingdom
Alan J. Warren, PhD, FRCP, FRCPath

Christie NHS Foundation Trust
Manchester, United Kingdom
Mike Dennis, MD
<http://www.christie.nhs.uk/research/themes/dg/htu/default.aspx>

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London, United Kingdom
Ghulam J. Mufti, MD

Queen Elizabeth Hospital
University Hospital Birmingham NHS Trust
Birmingham, United Kingdom
Charles Craddock, MD

Radcliffe Hospitals
and University of Oxford
Oxford, United Kingdom
Paresh Vyas, MD

Royal Bournemouth Hospital
Bournemouth, United Kingdom
Sally Killick, MD

St. James's University Hospital
St. James's Institute of Oncology
Leeds, United Kingdom
David T. Bowen, MD

University Hospital of Wales
Cardiff, Wales
Jonathan Kell, MD

MDS–specific organizations

Life Beyond Limits

Brings together an independent group of MDS experts to raise awareness of ageism in access to care for patients with MDS

www.mdslifebeyondlimits.org

MDS Beacon

Objective and unbiased news and other information related to MDS; mission is to be a key Internet resource and online community for patients with MDS, their families, and others interested in MDS

www.mdsbeacon.com

MDS Foundation

Multidisciplinary, international, nonprofit organization dedicated to the education of professionals, patients, and caregivers; facilitation and support of clinical trials; and development and support of patient advocacy groups

www.mds-foundation.org

United Kingdom MDS Patient Support Group

Offers support, information, referral advice, and patient information in the United Kingdom

www.mdspatientsupport.org.uk

Organizations that include MDS within the scope of hematologic malignancies

Aplastic Anemia and MDS Foundation

Nonprofit health organization dedicated to supporting patients and families living with aplastic anemia, MDS, paroxysmal nocturnal hemoglobinuria, and related bone marrow failure disease

www.aamds.org

Leukaemia and Lymphoma Research Foundation

Programs for support of all of the different blood cancers for patients and their families

www.leukaemialymphomaresearch.org

Leukaemia Care

Resources for people affected by Hodgkin, non-Hodgkin, and other lymphomas; myeloma; MDS; aplastic anemia; and myeloproliferative disorders

www.leukaemiacare.org.uk

Leukemia and Lymphoma Society

Mission is to cure leukemia, lymphoma, Hodgkin disease, and myeloma and improve the quality of life of patients and their families

www.lls.org

General resources

American Cancer Society

www.cancer.org

American Society of Clinical Oncology

www.asco.org and www.cancer.net

American Society of Hematology

www.hematology.org

CancerCare

www.cancercare.org

Medline Plus®

www.nlm.nih.gov/medlineplus/medlineplus.html

Merck Manual Home Edition for Patients and Caregivers

www.merckmanuals.com/home/index.html

National Anemia Action Council

www.anemia.org

National Heart, Lung and Blood Institute

www.nhlbi.nih.gov

National Marrow Donor Registry

www.marrow.org

For more resources also see: *Chapter 2: Seeking Treatment, MDS in Children, and Pediatric Information Resources*

The MDS Foundation provides a number of patient and caregiver services globally. These include referrals to an MDS Foundation Center of Excellence, referral to MDS patient and caregiver support services, and a number of print and online patient and caregiver educational materials.

To learn more, contact our Patient Liaison. The Patient Liaison speaks with newly diagnosed patients and their family members daily and can offer support in various forms, including:

- **Referrals to our Centers of Excellence.** Our Patient Liaison will connect newly diagnosed patients with an MDS specialist in their area of the world and work closely with the patient and referral institution to coordinate a proprietary appointment convenient for the patient.
- **Provide information on current treatment options and available clinical trials.** Our Patient Liaison will answer general questions and offer information regarding current treatment options in MDS and clinical trials open to MDS patients.
- **Provide responses to email and social media inquiries.** Our Patient Liaison will monitor our social media sites and provide timely responses to inquiries submitted on Facebook, Twitter, and via email.
- **Provide a connection between MDS patients.** Our Patient Liaison will maintain a list of patients worldwide that have offered the distribution of their contact information to newly diagnosed patients in need of support and guidance from someone who is currently being treated for MDS.
- **Referral to the MDS Foundation Patient and Family Forums coordinator.**

Patient and family forums

These events are free one-day conferences for MDS patients and their families.

- Registration is required to attend. Learn the latest on the diagnosis and treatment of MDS from leading experts in the field. Complimentary breakfast and lunch.
- Visit the MDS Foundation website for our Calendar of Events and further details.

MDS Foundation Patient Liaison

Audrey Hassan

800-MDS-0839 (*within the US*)

609-298-1035 (*outside the US only*)

609-298-0590 fax

email: patientliaison@mds-foundation.org

MDS Foundation Patient Coordinator

Deborah Murray

800-MDS-0839 (*within the US*)

609-298-1035 (*outside the US only*)

609-298-0590 fax

email: dmurray@mds-foundation.org

The MDS Foundation support group guidelines

The purpose of a support group is to bring individuals together to meet others with similar challenges, discuss feelings, gather information, and socialize.

Here are some ideas on how you can start your own active and thriving support group.

Planning the meeting

- Locate meeting place, determine date and time. Most libraries, churches, and hospitals have meeting rooms that are often free to non-profit groups.
- Book guest speaker (specialist from one of the MDS Centers of Excellence). They will speak for free if you ask them. The Foundation is happy to help you in any way.
- Place posters or flyers in doctors' offices, pharmacies, on hospital bulletin boards, libraries, church halls, grocery stores, etc.
- Advertise the group in local newspapers. Most newspapers have a health section with a datebook, calendar or an area for support groups. It's a free service the paper offers.
- Get local newspapers and health newspapers to write stories on Myelodysplastic Syndromes.
- Local hospitals have a health calendar. Call hospitals and get on their list of support groups.
- Post information about your support group on the MDS Foundation website.
- The MDS Foundation may mail invitations to all known MDS patients and their families. Note that these lists are confidential.
- Contact the MDS Foundation for patient information handouts.
- Plan refreshments.

How can the MDS Foundation support your group?

- We can advertise your group in our printed and electronic newsletters.
- We can distribute meeting flyers to our health care and patient members.
- If needed, we can provide sample flyers, forms, letters, etc.
- We can assist in recruiting members, providing patient handouts, and serving in a general advisory capacity.
- We can contact our MDS Center of Excellence in your area to secure space for your meeting.
- We can assist in selecting a group facilitator for your group.
- We can assist in booking guest speakers (i.e., leading experts, hematologists, researchers or drug company representatives).
- We can provide an MDS Foundation representative to assist and guide your inaugural meeting.
- We can provide financial support to defray start-up fees or apply toward coffee and refreshments.

These are some of the ways in which the MDS Foundation can assist you. If you have a request not listed above, please do not hesitate to contact us.

Suggested format for the meeting

You may select a group facilitator in advance (the MDS Foundation will be happy to assist you). The facilitator will welcome everyone to the meeting and ask those in attendance to introduce themselves.

The facilitator will then introduce the guest speaker who will provide a short presentation about MDS, the MDS Foundation, the programs and services available, and the structure and benefits of forming a support group.

Hold a facilitated question-and-answer period following this presentation. Issues that you will want to cover include:

- What are the main areas the support group should concentrate on? For instance:
 - Information forums
 - Support meetings
 - Assisting individuals to access services and treatments
 - Fundraising to help raise funds for research and patient services
 - Public awareness events
 - Buddy scheme—to help newly diagnosed patients and their families
- Who is available to assist with organizing/conducting these services and events?

Position description

Support group facilitator

Overview

The Facilitator of support group meetings is responsible for organization of the meetings. The Support Group Facilitator is there to guide the group, stimulate discussion, manage the group dynamics, and encourage interaction.

Responsibilities

- Arranges meeting place
- Identifies topics for meetings
- Coordinates speakers as required
- Introduces and thanks speakers at meetings
- Provides for refreshments
- Ensures security of location
- Provides information to the MDS Foundation for any newsworthy items

Suggestion for time required

- One meeting per month (approx. two hours/month)
- Speaker coordination (approx. two hours/month)

Suggested meeting activities

- Hold sessions for caregivers to discuss their concerns, issues, and frustrations, and share ideas for rest, relaxation, and coping with stress.
- Discuss available resources—government programs, transportation, respite programs, community hospices, life insurance, travel insurance.
- Discuss the fear of dying and coping with what lies ahead, both for the patient and his or her family.
- Discuss research updates (invite a hematologist, researcher, or drug company representative).
(Note: Caution the speaker not to recommend a certain therapy or drug to individuals.)
- Hold a video/book review evening. Ask participants to review a book or video and present to the group.
- You may contact the Patient Liaison for the MDS Foundation for contacts from other support groups to discuss topics and activities for your group.

Support Group Evaluation

Ongoing evaluation of a support group is imperative to keep it fresh and up-to-date. When you pick a speaker and topic for a meeting, discuss the objective with the speaker then set some goals for what information is to be imparted. From those goals, develop a quick evaluation form to be completed at the end of the meeting. This feedback will help to set the agenda for the next meeting.

Remember...

The support group is there to support those living with MDS and their families. Feel free to survey them to find out what they would like to discuss or learn during a meeting.

It is worth noting that not all topics will be appropriate for all participants. For instance, talking about death and dying may upset newly diagnosed individuals.

Global patient support groups

For a complete listing of global support groups for MDS visit the MDS website at <http://www.mds-foundation.org/global-patient-support-groups/>.

Creating a national group

Stage 1

- Start with setting up one patient forum day in your own city/hospital
- Invite your local nurse/physician—maybe also your Primary Care Provider (PCP)
- Invite nurses from other regions, who will also advertise the forum in their own hospital

At the Patient Forum—Set aside time for the following:

- Identify patients, family members, and friends willing to contribute to a long-term patient group
- Elect the following people (if possible):

- | | | |
|-----------------------------|--------------------------|----------------------|
| 1. Chairman | 4. Treasurer | 7. Nurse Consultant |
| 2. Deputy Chairman | 5. Web Manager | 8. Newsletter Editor |
| 3. Secretary/contact person | 6. Scientific Consultant | 9. Fundraiser |

You may not identify all people at the first meeting—some members may have to take on several roles until a suitable candidate is found later on. Just 3 or 4 people are enough to start the committee for a support group.

- Set up regular committee meetings to discuss future plans
- Establish priorities for your own region/country
- Plan expenses and costs for the year
- Get charity status for your group
- Create a leaflet and a poster for distribution in your country's hospitals
- Request stock of information booklets in your language from MDS Foundation for distribution to patients who request information

Stage 2

- Involve caregivers, relatives, friends, colleagues—all may have time and good ideas—as well as energy.
- Anyone willing to help—ask them for their skills and contacts—they may have connections in the printing industry, catering, event organizing, etc.
- Establish contacts to the pharmaceutical industry—they are a great resource for information, assistance, contacts—but make sure that you follow ethical guidelines for your own country—and do feel free to say no to suggestions if they are not suitable for your group. Nobody will be offended. Feel free to check with the MDS Foundation for feedback and additional advice if you are unsure.
- Plan fundraising activities to pay for future patient forum events.
- Consider appointing a Patient Liaison—or someone willing to take on this role part-time (some groups work very well on that basis—having someone available for a few hours a week).
- If relevant for your own country—and part of your priorities—establish contacts with people in government responsible for health, access to treatment, cancer issues, etc.
- Establish contacts with European groups such as ECPC—European Cancer Patient Coalition and EPF—European Patient Forum, Eurordis, rare cancers groups in your own country.
- Create a paper newsletter for distribution in hospitals for patients who do not use the Internet. Approximately 50% of MDS patients do not use computers or the Internet!

Finally, don't get frustrated at slow progress, or lack of immediate volunteers—it takes time to find the right members and the right contacts, but it will happen. Other groups in various countries are proof that it can work. Don't give up—as it represents invaluable help for many people, and the patient voice and patient choices are becoming very important.

A guide to charitable financial planning—finding a cure for MDS

Those of us in the MDS community (patients and their family members, doctors, medical personnel, and researchers) recognize all too well the enormity of the task before us to conquer this disease. Although great strides have been made over the past three decades in understanding the types of MDS and developing prognostic guidelines, the financial base underlying the research is minimal. The MDS Foundation has taken numerous steps to overcome the disabling effects of MDS, including:

- Biannual International Symposia meetings concentrating on bringing state-of-the-art MDS information to the world's physicians
- Sponsorship of the study resulting in the recently revised International Prognostic Scoring System (IPSS-R)
- Patient forums both in person and electronically
- Provision of written materials for patients and caregivers
- Availability of a Patient Liaison by telephone to provide information and guide patients and caregivers with their questions
- Establishment of patient support groups internationally
- Awarding of Young Investigators Grants
- Serving as a clearinghouse for clinical trials

The Foundation can implement this program, however, only if it has sufficient financial resources. This requires individual and corporate donations. It is to this end that the Foundation has initiated its Planned Giving Program.

Planned Giving is a way for individuals to make charitable donations that optimize the financial and tax benefits for the donors. It should be an important part of estate and financial planning for persons who wish to assist in finding an effective cure for MDS. The MDS Foundation has the capacity to provide potential donors with professional advice to assist them in maximizing for themselves the benefits of their donations. Among the techniques for donating funds that the Foundation would like to suggest are the following:

Outright lifetime charitable gifts

Undoubtedly, the simplest yet most effective way to aid the Foundation is to make an outright charitable gift. This provides a dollar-for-dollar charitable income tax deduction for persons who itemize their deductions. The gift may be in the form of cash, or it may be in the form of stock or other property. With today's rising stock values, there is a tax advantage for the donor to contribute appreciated stock rather than cash to the Foundation. The donor would receive a full income tax deduction for the value of the stock without paying a tax on the capital gain. Meanwhile, as a tax-exempt entity, the Foundation may sell the stock without paying tax. If the stock had been sold by the donor, the sales proceeds would have been reduced by the capital gains tax.

Outright bequests

Persons who have a special desire to help in developing a cure for MDS may wish to provide for the Foundation at their deaths. This is especially so in light of federal and state death tax rates. A bequest to the Foundation in a will can convert dollars that otherwise would go to estate taxes to help in the fight against MDS. Because insurance proceeds may be subject to estate tax as well, it is also tax efficient to name the MDS Foundation as a beneficiary of all or a portion of an insurance policy. If the ownership of an insurance policy is transferred to the Foundation, in addition to the estate tax benefit, the donor may take an income tax deduction for both the value of the policy at the time of the transfer and for the annual premiums paid.

Charitable Lead Trusts

A powerful tax savings technique is the Charitable Lead Trust (or CLT). This is a trust that allows a donor to eliminate taxable income while saving estate or gift taxes for his or her family. The CLT is created during lifetime, or at death, and would provide for an annuity or specified percentage of the value of the trust to be paid to the MDS Foundation for a fixed term of years or for the life of the donor. The principal remaining at the end of the trust is then distributed to family members. The estate or gift tax on the principal passing ultimately to the family is reduced to reflect a "time value of money" discount for its delayed receipt. Hence, the gift or estate tax is calculated on a much smaller amount than may actually be received by the family at the end of the trust (depending on the investment performance of the trust).

The CLT can be a very effective estate tax reduction technique for individuals who have MDS but have a 50% probability of surviving more than one year. In that case, the trust would provide that the MDS Foundation receive an annual payment for the life of the individual, with the principal passing at the individual's death to the family. Under IRS rules, the gift and estate tax deduction is determined by assuming that the donor will live a normal life expectancy. This causes the charitable deduction to be much larger than would be the case if the actual life expectancy were taken into account. The result is that the estate tax is significantly reduced.

The CLT can be designed so that the donor will be entitled to a one-time income tax deduction at the time of the funding of the trust equal to the present value of the stream of annuity payments paid to the Foundation. This deduction can offset any extraordinary amounts of income in a particular year (such as capital gain on the sale of a major asset). On the other hand, the trust may be designed so that there is no initial income tax deduction, but income generated by the trust is not included in the donor's gross income for tax purposes.

Charitable Remainder Trust

A Charitable Remainder Trust (or CRT) is the reverse of a charitable lead trust. It also provides a charitable deduction for income, as well as gift or estate, tax purposes. A CRT is a trust created during lifetime, or at death, from which a fixed dollar amount (i.e., an annuity payment) or a fixed percentage of the net fair market value of its assets (i.e., a "unitrust" payment) is paid at least annually to the donor or to family members. At the termination of the trust, the remaining principal is payable to the MDS Foundation. Income and gift tax deductions are available for the present value of the remainder that will pass to charity. The shorter the term of the trust, the greater the available deduction.

Because a CRT is exempt from income taxes, an individual may contribute significantly appreciated stock or real estate which, if sold, would create a large taxable capital gain. The trust is then able to sell the stock or real estate without tax. This leaves a greater pool of funds to generate income for the benefit of the donor or the family members.

Conclusion

By incorporating Planned Giving into our estate and financial plans, each of us may contribute to the fight against MDS in a way that improves our own or our family's financial circumstances. This allows us, as a group, to create a funding base to finance the research that will eliminate the disease. The Foundation has at its disposal expert resources to answer tax and estate planning questions related to charitable contributions and would be pleased to assist you, and work with your own tax and legal counsel, in developing a Planned Giving Program.



Building Blocks of Hope is a global print and online patient advocacy initiative providing a personalized educational program for patients and caregivers to prepare, participate, and **LIVE** with MDS. The colors of the Building Blocks of Hope include Tucson Teal, Navajo Red, and Desert Sand. They are reminiscent of a Southwest landscape with the beauty of the night sky over the sand swept deserts and stunning mountain ranges. The colors represent welcoming, warmth, stability, healing, passion, and protection. These colors form the base for the Building Blocks of Hope logo constructed in a wave-like pattern indicating the fluidity of life, health and illness. The single red band which continues up into the plant symbolizes strength and improvement in bone marrow function. The idea of hope for the future and extension of life is emulated in the sprouting plant.

Building Blocks of Hope was created by Sandra Kurtin, Nurse Practitioner and Clinical Assistant Professor of Medicine at The University of Arizona Cancer Center, Board Member of the MDS Foundation, and advocate for patients and caregivers **LIVING** with hematological malignancies. The individual pages have been developed in collaboration with members of the International Nurse Leadership Board of the MDS Foundation and members of the MDS Foundation Board of Directors. Creative and technical support was provided by Adam Nichols and his team at Markations. Organizational and communications support was provided by Tracey Iraca, Sue Hogan and the MDS Foundation staff. Bone marrow illustrations by Kirk Moldoff.

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We hope this project will provide a useful tool for health care professionals working with MDS patients. Most importantly, we hope the Building Blocks of Hope will empower MDS patients and their caregivers to **LIVE** with MDS.



Best regards and best wishes,
Sandy Kurtin



The Building Blocks of Hope is a registered trademark of Sandra Kurtin:
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