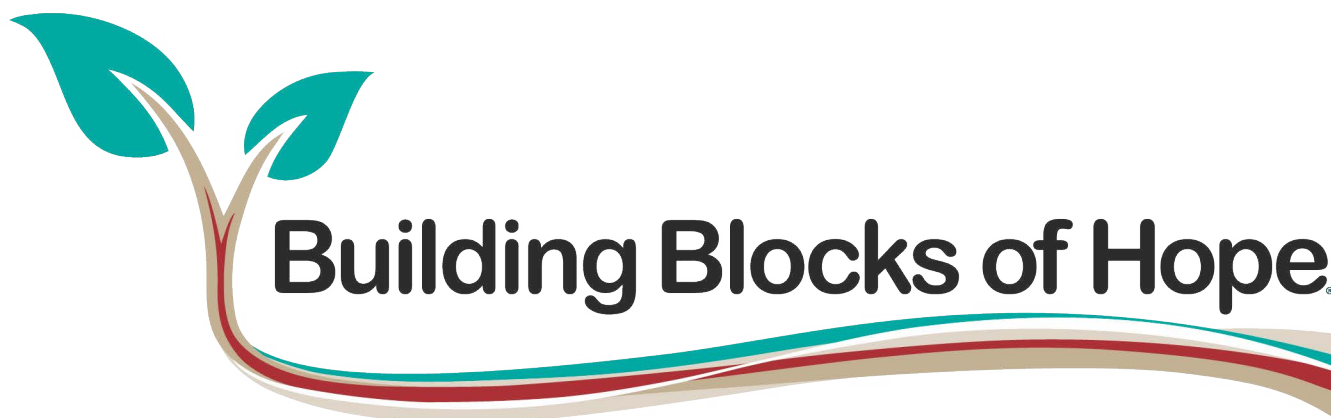


English Edition
(USA)



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 education program for the patient and caregiver to prepare, participate, and **LIVE** with MDS.



MDS Foundation
The Myelodysplastic Syndromes Foundation, Inc.

Published by the Myelodysplastic Syndromes Foundation, Inc.

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® resource. It is designed to help get you the information that you need to take an active part in your MDS journey.

There are five chapters and a glossary of MDS terms included in the Building Blocks of Hope®:

- **Chapter 1 – Understanding MDS:** A complete description of the disease process of MDS and answers to common questions.
- **Chapter 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.
- **Chapter 3 – General Resources for Living with MDS:** This chapter will provide you with strategies for staying well, managing your health and your MDS. Quick-Tips are provided to help you recognize and manage common symptoms or problems experienced by patients and caregivers living with MDS. Each Quick-Tip includes links to several digital resources that may help you manage your health. This chapter also includes a glossary of terms that will help you to understand the complex language used to describe these diseases.
- **Chapter 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.
- **Chapter 5 – 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 slides 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 pdf format at <https://www.mds-foundation.org/bboh>. 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 (see 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® resource will provide you and your caregivers with tools and strategies for LIVING with MDS.

The MDS Foundation, Inc.

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UNDERSTANDING MDS

Myelodysplastic Syndromes (MDS) are a group of bone marrow failure disorders. There are several subtypes of MDS. Each subtype 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 your subtype is determined are included. Understanding your MDS diagnosis will help you and your caregiver take an active part in your individual treatment plan.

UNDERSTANDING MDS

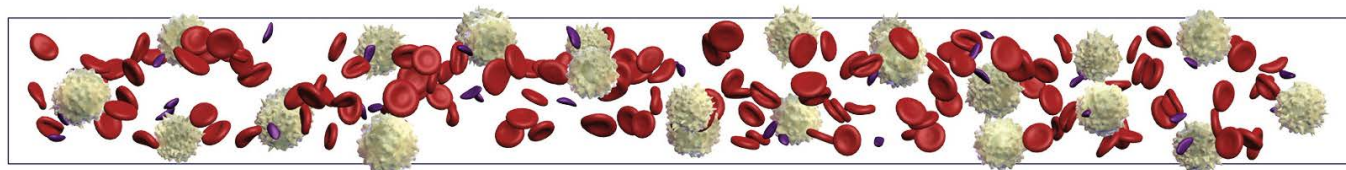
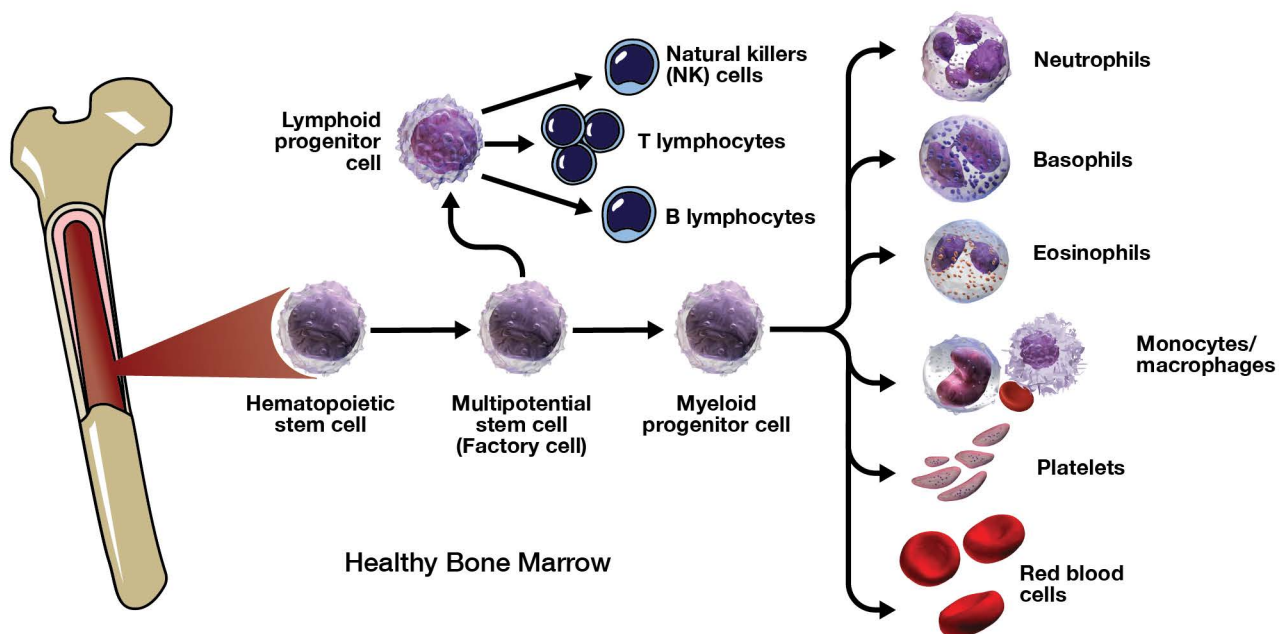
Chapter 1 provides general information about Myelodysplastic Syndromes (MDS) and other related myeloid diseases, including what we currently know about what happens in the bone marrow when MDS develops, how MDS is diagnosed, and how to determine whether you have lower risk MDS or higher risk MDS.

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What Does Bone Marrow Do?

What does bone marrow do?

- All blood cells begin as hematopoietic (hee-muh-toh-poi-et-ik) stem cells in the bone marrow. The bone marrow is the factory for these stem cells. In healthy persons, hematopoietic stem cells develop and mature (differentiate) in the bone marrow to form all the different blood cells that can be found in the bloodstream.
- 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.



normal hematopoiesis

Illustration by Kirk Moldoff

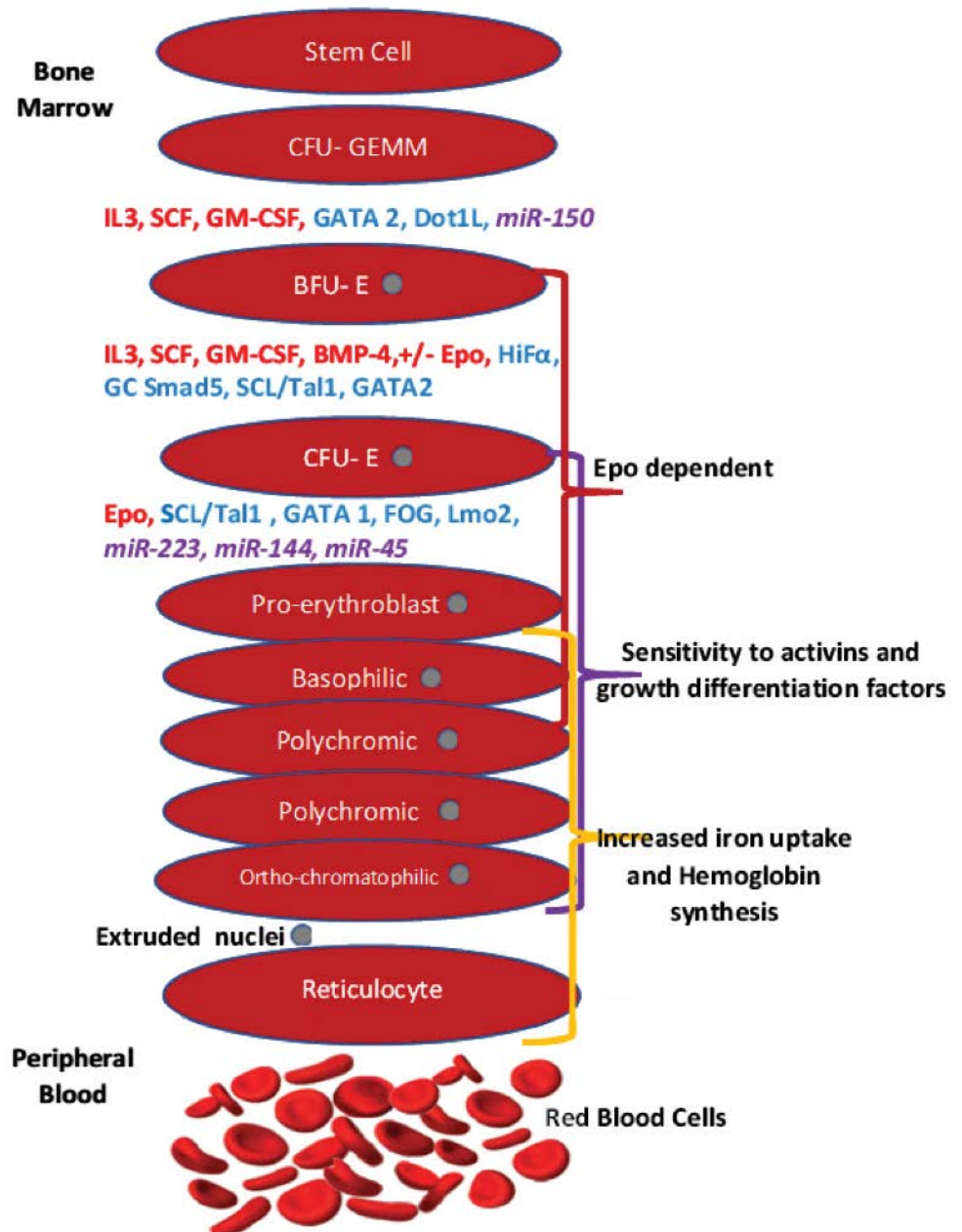
References:

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

How are Red Blood Cells Produced?

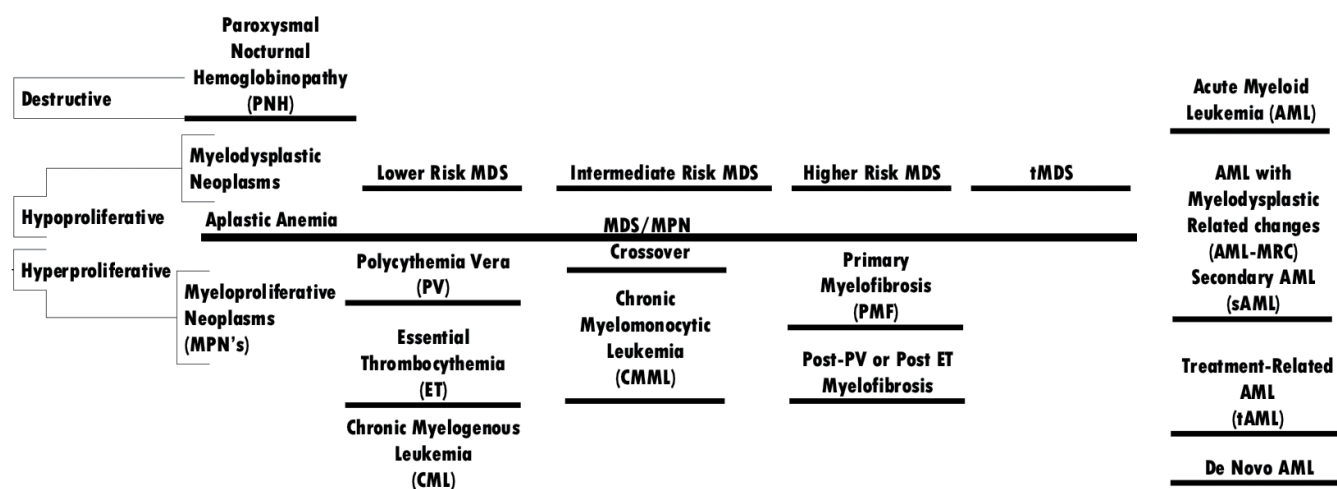
Erythropoiesis - Red Blood Cell Production

- Erythropoiesis is the process of developing red blood cells (RBCs).
- Development of RBCs takes 21-23 days and includes several steps. Early stage erythropoiesis involves the proliferation of RBC progenitor cells.
- RBCs originate from the myeloid progenitor cells (CFU-GEMM -colony forming unit granulocyte, erythrocyte, monocyte, megakaryocyte) in the bone marrow.
- The CFU-GEMM can produce RBCs, platelets or granulocytes (a type of white blood cell).
- RBC progenitor cells transition to erythroid burst forming units (BFU-E), then to colony forming units (CFU), and on to proerythroblasts.
- Late phase erythropoiesis is focused primarily on the differentiation (continued normal development) and maturation of erythroblasts.
- Each step requires support of a complex network of substances that regulate differentiation and maturation of RBCs. These include transcription factors, cytokines, hormones, vitamins, copper, iron and iron metabolism regulators, various proteins and erythroid receptors.
- Abnormalities in the proliferation and differentiation of red blood cells is common in MDS resulting in ineffective erythropoiesis (production of red blood cells) and anemia.
- Treatments for MDS may target one or more of the steps or substances needed to produce RBCs.



The Myeloid Continuum of Diseases

Myeloid malignancies include diseases that may decrease production of blood cells or increase production of blood cells. Each disease has specific criteria for diagnosis, estimated prognosis and options for treatment. All of these diseases have the potential to evolve into acute leukemia. The focus of this issue of the Building Blocks of Hope® is on Myelodysplastic Syndromes (MDS).



What Is MDS? Is MDS Cancer?

Yes, MDS is cancer

The diagnosis of MDS requires a 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 can be a gradual process where patients have minimal to no symptoms for years or can be a rapid process where symptoms are severe. 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).

For more information <http://www.youandmds.com/en-mds/home>

What is MDS?

Definition: The Myelodysplastic Syndromes (MDS) are a group of blood cancers that are characterized by low blood counts. Because MDS occurs due to acquired changes in the bone marrow factory, it is considered a type of bone marrow failure disorder. Various subtypes of the disease exist with variable onsets, prognoses, treatment options, and risks of developing leukemia.

What happens to the bone marrow in MDS?

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)



normal bone marrow



Abnormal bone marrow with dysplastic blood cells and abnormal chromosomes

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

What Causes MDS? Is MDS Hereditary?

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.
 - 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. **A personal history of autoimmune disease has been associated with the development of MDS, although the presence of the autoimmune disease did not affect MDS survival. Autoimmune diseases found to be associated include: hypothyroidism, thyroiditis, rheumatoid arthritis, pernicious anemia, inflammatory bowel disease (Crohn's, ulcerative colitis), and systemic lupus erythematosus (SLE). Although the mechanism of these associations has not been fully established, possible explanations include: a) shared genetic or environmental risk factors, b) treatment for autoimmune diseases that may damage the bone marrow or cause chronic immunosuppression, and c) inflammatory changes that may be linked to an increased risk of clonal hematopoiesis and autoimmune disease. Patients with Cardiovascular disease have also been known to have a chronic inflammatory state and are more likely to develop clonal hematopoiesis.**
4. **Patients with other hematologic malignancies, specifically cancers of the lymphoid lineage, (e.g.) Monoclonal gammopathy of uncertain significance, Myeloma, selected types of Lymphoma, although rare, may be predisposed to developing second or concurrent cancers, including MDS.**
5. **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.
6. **Inherited genetic predisposition for developing MDS and congenital abnormalities are present in less than 10% of cases.** Therefore, the chance of passing MDS to children or grandchildren is rare.
7. **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.

What are the Signs & Symptoms of MDS?

What are the signs and 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



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.

The Bone Marrow Biopsy & Aspirate

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. Spicules of the bone marrow contain small collections 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.

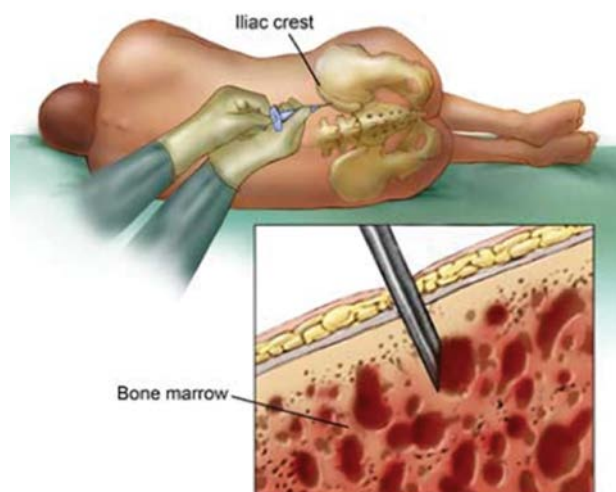
Processing the sample

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 healthcare 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.



The Bone Marrow Biopsy & Aspirate

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 healthcare 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 caregiver travel home with them. The patient should not drive.

What Happens to Bone Marrow in MDS?

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.

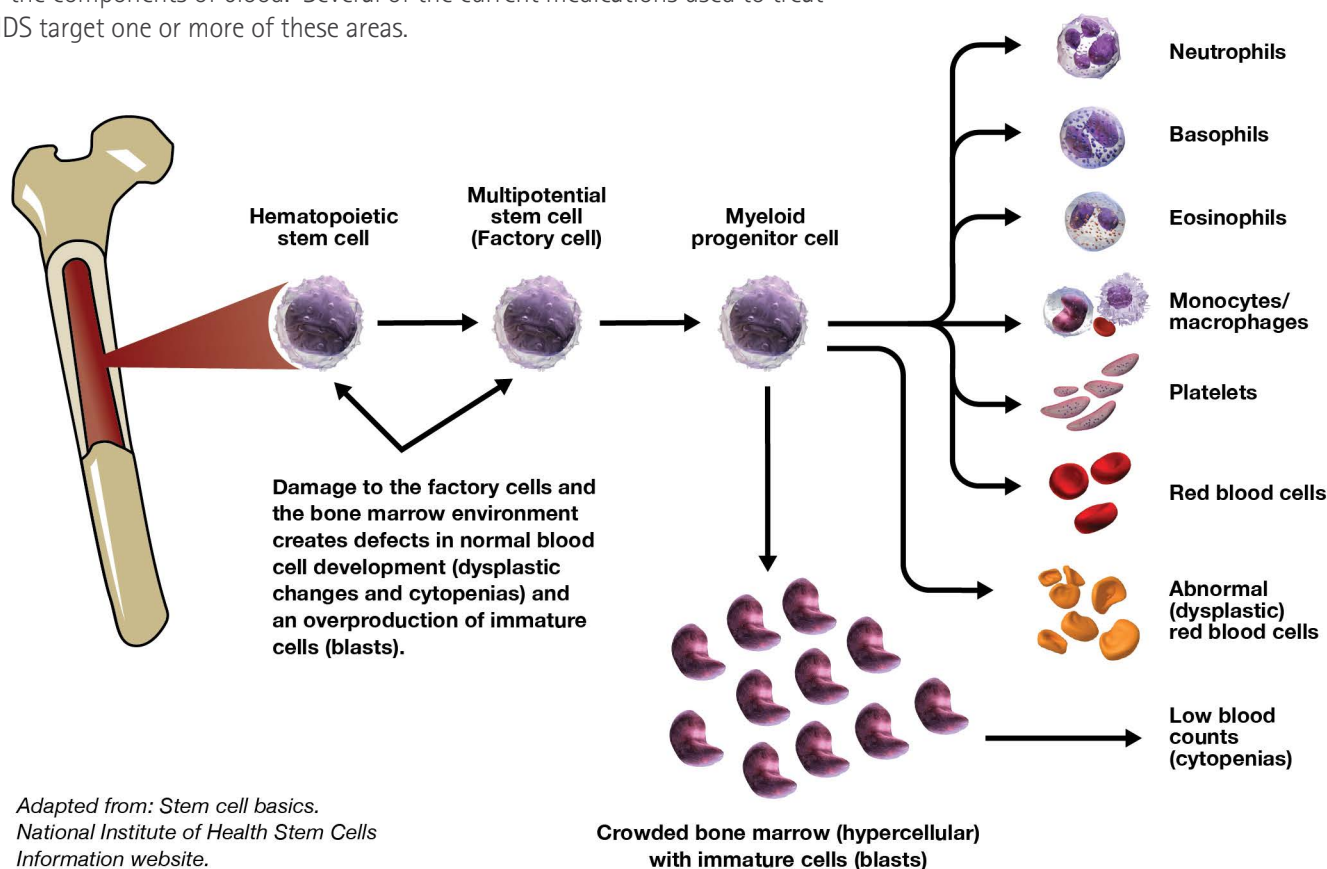
Red blood cells, white blood cells, and platelets all come from the same myeloid factory cell (progenitor cell). These are the cells that we can measure in the peripheral blood. In MDS, these cells are often low in number (cytopenias) and do not function normally.

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.

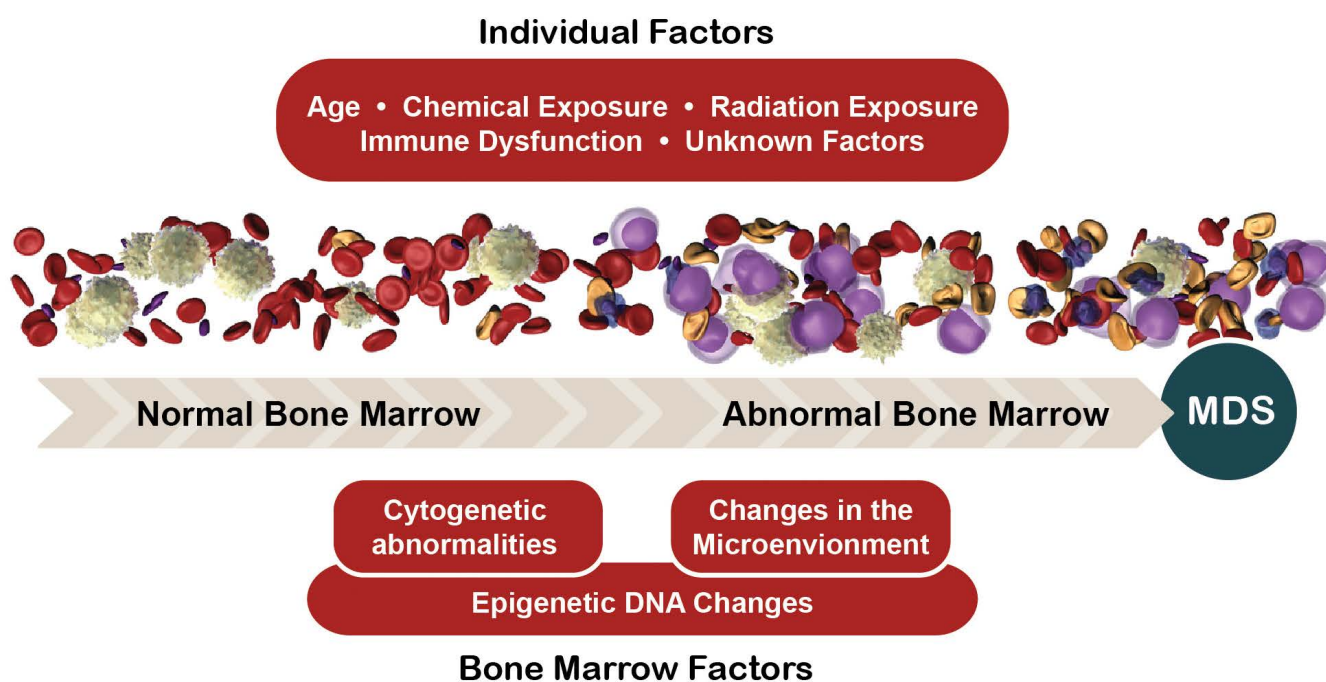


Adapted from: Stem cell basics.
National Institute of Health Stem Cells
Information website.

Genetic and Epigenetic Changes in MDS

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 groups (chemical complexes) may be abnormally attached 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. Hyper-methylation is common in MDS. It is a constant process and is associated with disease progression, including the development of acute myeloid leukemia. Recent discoveries have shown that abnormal epigenetic mechanisms are largely secondary to mutations (changes) in several genes in patient MDS cells (see below). Some treatments for MDS, known as hypomethylating agents, block the methyl groups to allow the transfer of information needed for normal blood cell development. Research continues to identify mutations that contribute to the development and progression of MDS, including ways to target those mutations for therapeutic benefit.

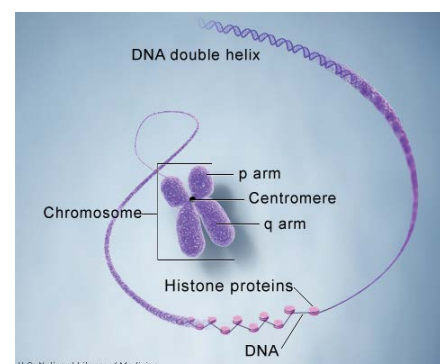


What happens to the bone marrow in MDS

Chromosomes in MDS

Cells are the fundamental working units of every living system. The instructions needed to direct cellular development and activity are contained within the DNA and RNA. The DNA, a combination of proteins, provides a blueprint for making each type of 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.

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, 2 X chromosomes for females (one from father and one from mother) 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 center called the centromere, which divides the chromosome into two sections, or "arms". The short arm of the chromosome is labeled the "p". The long arm of the chromosome is labeled the "q".



Cytogenetic abnormalities are present in approximately 40% of all cases of primary MDS, and in the majority of cases of secondary MDS. 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).

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 revised International Prognostic Scoring System (IPSS-R) risk category.

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®). As previously mentioned, targeting genes associated with MDS for therapeutic benefit is currently under study (see clinical trials).

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.

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)

Understanding Genetics and Molecular changes in MDS

Molecular study is gaining importance in MDS. It is estimated that 90% of patients with MDS harbor one or more genetic mutations. Chromosomes contain several thousand genes. Genes are shorter sections of DNA. Each gene acts as a code or set of instructions for making a specific protein. These proteins control the cell's activity, telling the cell what to do. Genes can become mutated (altered, faulty). In most cases, the cause of these mutations is not fully understood. Some of these genes, when mutated, are known to cause or promote the development of MDS. In some cases, the gene can be targeted to interrupt the abnormal production of blood cells and cytokines common in MDS.

Genetic mutations are currently identified by sequencing the DNA, commonly using a technique called "next generation sequencing" (NGS) using the material from a bone marrow sample. Today, the genetic profile is used primarily for estimating prognosis. Several clinical trials are exploring the potential therapeutic benefit of targeting genes known to promote MDS. Importantly, the genetic profile may change over time. This is why it is important to re-characterize MDS at points of progression. These tests require a bone marrow sample.

The International Working Group for Prognosis in MDS (IWG-PM) has recently released a new risk estimation model based on analysis of 2957 MDS patient bone marrow samples from 24 international MDS Foundation Centers of Excellence. All patient samples were obtained prior to receiving any MDS treatment. The International Prognostic Scoring System - Molecular (IPSS-M) also allows for risk stratification for patients who may be missing molecular data. Future clinical trials using the IPSS-M will build on the work of the the International Working Group for Prognosis in MDS in validating this model in clinical practice.

Common Gene Mutations and Potential Therapeutic Targets in patients with MDS

Gene Abbreviation	Gene Name	Chromosome location	Frequency in MDS	Significance
NRAS	Neuroblastoma RAS oncogene	1p13.2	1-10%	More common in AML; Targeted agents in clinical trials
DNMT3A	DNA-methyltransferase 3 alpha	2p23	>10%	Related to mechanism or action for hypomethylating agents.
SF3B1	Splicing factor 3b, subunit 1	2q33.1	>10% (up to 40%)	Favorable Agents in clinical trials
IDH1	Isocitrate dehydrogenase 1	2q33.3	1-10%	More common in AML FDA approved targeted treatment: Ivosidenib
GATA2	GATA binding protein 2	3q21.3	<1%	Agents in clinical trials
KIT	V-kit oncogene homolog	4q11-12	1-10%	More common in AML
TET2	Tet methylcytosine deoxygenase 2	4q24	>10%	More likely to respond to hypomethylating agents when a sole abnormality
NPM1	Nucleophosim	5q35.1	<1%	More common in AML
EZH2	Enhancer of zeste homolog 2	7q35-36	1-10%	Unfavorable; histone deacetylation agents in clinical trials
JAK2	Janus Kinase 2	9p24	1-10%	More common in overlap syndromes
KRAS	Kirsten sarcoma viral oncogene	12p12-11		Agents in clinical trials
FLT3	Fms-related tyrosine kinase 3	13q12	<1%	More common in AML
IDH2	Isocitrate dehydrogenase 2	15q26.1	<1%	More common in AML FDA approved targeted treatment: Enasidenib
TP53	Tumor protein p53	17p13.1	1-10%	Unfavorable; Targeted agents in clinical trials
SRSF2	Serine/arginine-rich splicing factor 2	17q25.1	>10%	Agents in clinical trials
CEBPA	CCAA/enhancer binding protein A	19q13.1	<1%	Lower response for hypomethylating agents
ASXL1	Additional sex combs like 1	20q11	>10%	Lower response for hypomethylating agents
RUNX1	Runt-related transcription factor 1	21q22.12	1-10%	Unfavorable
BCL2	B-Cell Lymphoma 2	mitochondria	-	Agents in clinical trials

References:

Valent, P., Orazi, A., Steensma, D. P., Ebert, B. L., Haase, D., Malcovati, L., . . . Bennett, J. M. (2017). Proposed minimal diagnostic criteria for myelodysplastic syndromes (MDS) and potential pre-MDS conditions. *Oncotarget*, 8(43), 73483-73500. doi:10.18632/oncotarget.19008; Aleshin, A., & Greenberg, P. L. (2018). Molecular pathophysiology of the myelodysplastic syndromes: insights for targeted therapy. *Blood Adv*, 2(20), 2787-2797.

How Is MDS Classified?

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 results of bone marrow biopsy and aspirate, cytogenetics, and results of the CBC, differential and aspirate drawn from the peripheral blood.

Do you know your MDS subtype?

Knowing your MDS subtype can guide discussions with your healthcare team about the best treatment options for you.

MDS is classified into several different subtypes based on the following features: blood cell counts; percentage of blasts in the bone marrow; and cytogenetics.

French-American-British (FAB)* classification system

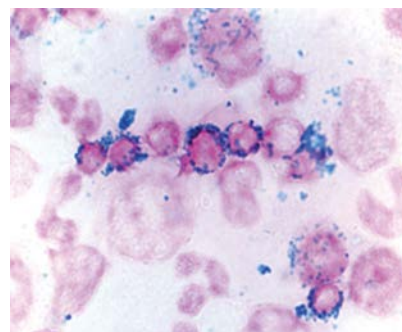
The FAB Classification was developed in the early 1980s by a group of physicians with expertise in diagnosing MDS. These experts were from France (F), America (A), and Great Britain (B); the central criterion for classification in the FAB system was the percentage of blast cells in the bone marrow. The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

Refractory Anemia (RA)

Is low red blood cell counts that do not respond to iron or vitamin therapy. This subtype may be accompanied by mild to moderate thrombocytopenia (low platelets) and/or neutropenia (low white blood cells).

Refractory anemia with Ringed Sideroblasts (RARS)

Is low red blood cell counts that do not respond to iron or vitamin therapy. These red blood cells contain abnormal iron deposits in a "necklace" pattern (ringed sideroblasts). This subtype may also be accompanied by mild to moderate thrombocytopenia (low platelets) and/or neutropenia (low white blood cells).



ringed sideroblasts

Refractory Anemia with Excess Blasts (RAEB)

Is low red blood cell counts that do not respond to iron or vitamin therapy with excess blasts (immature blood cells). This subtype is further divided into two subtypes, distinguished by the number of blasts.

- RAEB-1 – 5 to 9% blasts in the bone marrow
- RAEB-2 – 10 to 19% blasts in the bone marrow

Refractory Anemia with Excess Blasts in Transformation (RAEB-t)

Is low red blood cell counts that do not respond to iron or vitamin therapy. This subtype is defined by more than 20% blasts in the bone marrow and at least 5% blasts in the bloodstream. This subtype may also be accompanied by mild to moderate thrombocytopenia (low platelets) and/or neutropenia (low white blood cells).

Chronic myelomonocytic leukemia (CMML)

Is distinguished by persistent elevated levels of monocytes (a type of white blood cell) in the bloodstream with blasts (immature blood cells) less than 20%.

**The FAB Classification has been replaced by the World Health Organization Classification System and is largely used for historic reference and comparison.*

References:

Arber, D. A., Orazi, A., Hasserjian, R., Thiele, J., Borowitz, M. J., Le Beau, M. M., . . . Vardiman, J. W. (2016). The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*, 127(20), 2391-2405. doi:10.1182/blood-2016-03-643544

How is MDS Classified?

The World Health Organization (WHO) classification system

The WHO classification of MDS was updated in 2016. The WHO classification system has incorporated the key parts of the FAB classification system. The categories are largely based on morphology (how the cells look under the microscope), the presence of blasts (immature cells), how many cell lines are involved, and specific cytogenetic or molecular findings. The current classification of MDS includes:

MDS with single lineage dysplasia (MDS-SLD)

Is a low number of one to two types of blood cells in the bloodstream and one type of blood cell looks abnormal (dysplasia) in the bone marrow. For the affected cell type, at least 10 percent of the cells look abnormal. Less than 5% of cells in the bone marrow are blast (immature) cells with no blasts in the bloodstream.

MDS with multilineage dysplasia (MDS-MLD)

Is a low number of one or more types of blood cells in the bloodstream and two or more types of blood cells look abnormal in the bone marrow. Of the affected cell types, at least 10 percent of the cells look abnormal. Less than 5% of cells in the bone marrow are blast cells with no blasts in the bloodstream.

MDS with ring sideroblasts (MDS-RS)

Is a low number of one or more types of blood cells in the bloodstream and bone marrow. At least 15% of young red blood cells in the bone marrow show rings of iron with special staining and are called ring sideroblasts. Less than 5% of cells in the bone marrow are blast cells. No blast cells are found in the bloodstream. There are 2 types with:

- MDS-RS and single lineage dysplasia (MDS-RS-SLD) – same characteristics as MDS-SLD but with ring sideroblasts
- MDS-RS and multilineage dysplasia (MDS-RS-MLD) – same characteristics as MD-MLD but with ring sideroblasts

MDS with excess blasts (MDS-EB)

Is a low number of one or more types of blood cells in the bloodstream that also look abnormal in the bone marrow with an increased number of blast (immature) cells.

- MDS-EB1 – less than 5% of cells in the bloodstream are blasts. In the bone marrow, 5-9% of cells are blast cells.
- MDS-EB2 – 5-19% of cells in the bloodstream are blast cells and 10-19% of cells in the bone marrow are blast cells.

MDS with isolated del(5q)

Is identified when part of chromosome 5 is missing (deleted), this change is called del(5q). One additional chromosome abnormality is also permitted as long as it does not involve chromosome 7. There is a low number of red blood cells in the bloodstream and the number of platelets is normal or high. Less than 5% of cells in the bone marrow are blast (immature) cells and the platelet producing cells may look abnormal.

MDS, unclassifiable (MDS-U)

Is when the features of the blood and bone marrow don't fit any of the other subtypes. One or more types of blood cells are low in the bloodstream, but less than 10% of that cell type may look abnormal in the bone marrow. Very few or no blast (immature) cells are found in the bloodstream on at least 2 occasions and less than 5% of the cells in the bone marrow are blasts. Sometimes the diagnosis is made solely based on the presence of a typical chromosome abnormality that is linked with MDS.

Provisional entity: Refractory cytopenia of childhood (RCC)

Is characterized by persistent cytopenia with less than 5% blasts in bone marrow and less than 2% blasts in the bloodstream. It is the most common subtype of childhood MDS.

How is MDS Classified?

The World Health Organization (WHO) classification system

The WHO classification of MDS was updated in 2022. The WHO classification system for MDS has proposed the new term, Myelodysplastic Neoplasms (still abbreviated MDS) to reflect the malignant nature of MDS. This revised classification system divides MDS into two major groups:

1. MDS with defining genetic abnormalities
2. MDS that are morphologically defined (how the cells look under the microscope). The threshold for dysplastic changes in all cell lines has been set at >10%.

Classification and defining features of myelodysplastic neoplasms (MDS)

MDS with defining genetic abnormalities	Blasts	Cytogenetics	Mutations
MDS with low blasts and isolated 5q deletion (MDS-5q)	<5% bone marrow and <2% peripheral blood B	5q deletion alone, or with 1 other abnormality other than monosomy 7 or 7q deletion	
MDS with low blasts and SF3B1 mutation (MDS-SF3B1)		Absence of 5q deletion, monosomy 7, or complex karyotype	SF3B1 Detection of ≥15% ring sideroblasts may substitute for SF3B1 mutation
MDS with biallelic TP53 inactivation (MDS-biTP53)	<20% bone marrow and peripheral blood	Usually, complex	Two or more TP53 mutations, or 1 mutation with evidence of TP53 copy number loss or cnLOH

MDS morphologically defined	Blasts
MDS with low blasts (MDS-LB)	<5% bone marrow and <2% peripheral blood
MDS, hypoplastic (MDS-h) (≤25% age adjusted bone marrow cellularity)	N/A
MDS with increased blasts (MDS-IB)	
MDS-IB1	5–9% bone marrow or 2–4% peripheral blood
MDS-IB2	10–19% bone marrow or 5–19% peripheral blood or Auer rods
MDS with fibrosis	5–19% bone marrow; 2–19% peripheral blood

The Revised International Prognostic Scoring System (IPSS-R)

The prognosis and disease course may vary widely among patients with MDS 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 Revised International Prognostic Scoring System (IPSS-R). The IPSS-R may be used to estimate life expectancy (survival) for a patient newly diagnosed with MDS without treatment and estimate the risk of developing acute myelogenous leukemia (AML).

The bone marrow biopsy and aspirate, the cytogenetics and the peripheral blood (CBC, differential and platelet count) are used to determine the risk category. The impact of molecular features is not yet included in this system. 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.

Do you know your IPSS-R Score?

Knowing your IPSS-R Score can guide discussions with your healthcare team about the best treatment options for you.

Prognostic Values for Determining IPSS-R Score

Value/Score	0	0.5	1	1.5	2	3	4
Cytogenetics Risk Group	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 Group	Cytogenetic Abnormalities	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 overall risk scores in 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

To access the online IPSS-R calculators or download the IPSS-R mobile applications, please use the following link:

The Revised International Prognostic Scoring System - Molecular (IPSS-M)

The International Prognostic Scoring System - Molecular (IPSS-M) is the newest MDS prognosis calculator. The model is based on analysis of 2957 MDS patient bone marrow samples from 24 international MDS Foundation Centers of Excellence. All patient samples were obtained from previously untreated patients. This model builds on the work of the IPSS-R. The IPSS-M also allows for risk stratification for patients who may be missing molecular data.

This updated model improves the risk stratification of patients with MDS and provides a valuable tool for clinical decision-making, offering the prospect of tailoring diagnosis and therapeutic interventions to each patient's molecular profile. Future clinical trials using the IPSS-M will build on the work of the IWG-PM in validating this model for broader use. You can access the calculator on the MDS Foundation website at <https://www.mds-foundation.org/mds-iwg-pm/>.

Data you will need for the calculator includes:

1. Your age
2. From peripheral blood report:
 - a. Hemoglobin
 - b. Platelet count
 - c. Absolute Neutrophil count
3. From bone marrow biopsy and aspirate report, cytogenetic and molecular reports.
 - a. % Bone marrow blasts
 - b. IPSS-R cytogenetic risk categories
 - c. Next generation sequencing or other molecular testing methods.

Gene mutation status is weighted by the estimated risk of adverse outcomes. The genes noted here are listed from the most adverse to the most favorable with a choice of non-mutated, mutated, or not assessed. As with cytogenetics, the presence of multiple mutated (driver) genes is associated with a worse prognosis.

- | | | |
|-------------------------------|---------|----------|
| • TP53 – number of mutations | • RUNX1 | • U2AF1 |
| • TP53 loss of heterozygosity | • NRAS | • SRSF2 |
| • MLLPTD | • ETV6 | • DNMT3A |
| • FLT3ITD+TKD | • IDH2 | • ASXL1 |
| • SF3B1-5q | • CBL | • KRAS |
| • NPM1 | • EZH2 | • SF3B1α |

- d. Additional information regarding the number of residual gene mutations with adverse effects but weighted lower based on statistical measures. These genes are also rated as non-mutated, mutated, or not assessed:

- | | | |
|----------|---------|----------|
| • BCOR | • GNB1 | • PRPF8 |
| • BCORL1 | • IDH1 | • PTPN11 |
| • CEBPA | • NF1 | • SETBP1 |
| • ETNK1 | • PHF6 | • STAG2 |
| • GATA2 | • PPM1D | • WT1 |

The Revised International Prognostic Scoring System - Molecular (IPSS-M)

The collective data are used to generate one of six overall risk scores to estimate survival and median risk of AML transformation (AML-t): VL = Very Low; L = Low; ML = Moderate Low; MH = Moderate High; H = High; VH = Very High

Six IPSS-M Risk Categories (N=2701)		VL	L	ML	MH	H	VH
Characteristics / Values	N per group	381	889	302	281	379	469
Distribution by risk group (%)		14%	33%	11%	11%	14%	17%
Median Leukemia free survival (years) 25–75% range		9.7	5.9	4.5	2.3	1.5	0.76
Median Overall survival (years) 25–75% range		10.6	6.0	4.6	2.8	1.7	1.0
AML transformation (AML-t) %	Time from MDS diagnosis						
	% by year 1	0.0	1.7	4.9	9.5	14.3	28.2
	% by year 2	1.2	3.4	8.8	14.0	21.2	38.6
	% by year 4	2.8	5.1	11.4	18.9	29.2	42.8
Death without AML %	Time from MDS Diagnosis						
	% by year 1	2.2	8.5	12.0	18.0	19.3	30.6
	% by year 2	7.0	16.2	19.8	31.1	39.8	45.6
	% by year 4	15.9	29.5	33.6	51.1	54.2	51.3

To access the online IPSS-M calculators or download the IPSS-M mobile applications, please use the following link:

www.mds-foundation.org/additional-tools



Adapted from:

Bernard, E., et al., Molecular International Prognostic Scoring System for Myelodysplastic Syndromes. NEJM Evidence, 2022. 0(0): p. EVID0a2200008.

Chronic Myelomonocytic Leukemia (CMML)

Chronic myelomonocytic leukemia (CMML) is a clonal hematopoietic stem cell cancer. It has features of both myelodysplastic syndromes (MDS) and myeloproliferative neoplasms (MPN). It is considered an "overlap" or "crossover" disease within the myeloid continuum of diseases.

- Patients may have CMML with features more common in MDS. These patients tend to experience cytopenias, fatigue, bruising and infections. This type of CMML is associated with transfusion dependence.
- Patients may have CMML with features more common in MPNs. These patients tend to present with elevated blood counts, enlarged liver and/or spleen, and tend to experience fatigue, night sweats, early satiety (getting full fast after eating), pain in the upper abdomen, bone pain, and weight loss.

Like most myeloid malignancies there is a risk of developing leukemia, otherwise known as leukemic transformation. The risk of leukemic transformation in CMML is 15%-20% over 3-5 years.

- The diagnosis of CMML requires evaluation of both peripheral blood and bone marrow.
- Cytogenetic abnormalities are present in ~ 30% of patients with CMML. The most common cytogenetic changes include trisomy 8, - Y, abnormalities of chromosome 7 (monosomy 7 and del7q), trisomy 21, and complex karyotypes.
- Genetic mutations are present in more than 90% of patients with CMML and aid in the diagnostic process. These include: TET2 (~60%); SRSF2 (~50%); ASXL1 (~40%); RAS (~30%). Additional genetic mutations are known to negatively impact survival including ASXL1, DNMT3A, or the absence of TET2

The prognosis and disease course may vary widely among patients with CMML based on the type of CMML and the risk category (estimate of severity).

2016 World Health Organization (WHO) diagnostic criteria for CMML		
Peripheral Blood	the presence of sustained monocytosis	>3 months
Peripheral blood monocytosis	> 1 x10 ⁹ /L and >10% of monocytes	< 20% blasts
Bone Marrow	evidence of bone marrow dysplasia in one or more myeloid cell lineages. If myelodysplasia is absent or minimal, the diagnosis of CMML may still be made if the other requirements are met	< 20% blasts
Genetic Mutations	No evidence for PDGFRA or PDGFRB rearrangements Absence of FGFR1 rearrangements or the PCM1-JAK2 fusion in the context of concomitant eosinophilia	
An acquired clonal cytogenetic or molecular genetic abnormality (TET2, ASXL1, SRSF2, and SETBP1) is present in hemopoietic cells.		

Chronic Myelomonocytic Leukemia (CMML)

There are a number of risk models being used to estimate prognosis and the risk of transformation to AML in patients with CMML. The Mayo Molecular Model (MMM) and the CMML specific prognostic scoring system (CPSS-mol) are two of the most recent prognostic scoring systems. Each model places patients into low-risk, Intermediate-1 risk, Intermediate-2 risk, or High-risk categories. Each category is associated with an estimated survival in months and the probability of developing AML.

Prognostic Models Studied in CMML

Model and Variables Included in the Model	Median Survival in Months				
	low risk	Int1 risk	Int2 risk	High risk	AML transformation
Mayo Molecular Model <ul style="list-style-type: none"> Increased absolute monocyte count >10 x 10⁹/L Presence of circulating blasts Hemoglobin <10 gm/dL Platelet count <100 310⁹/L Frameshift and nonsense ASXL1 mutations 	97	59	31	16	At a median follow up of 23 months, 16% leukemic transformations occurred.
CMML specific prognostic scoring system <ul style="list-style-type: none"> Genetic risk groups as defined by *CPSS cytogenetic risk stratification and gene mutations involving ASXL1, NRAS, SETBP1, and RUNX1. Bone marrow blasts >5%. WBC count > 13 x 10⁹/L Red blood cell transfusion dependency 	Not reached	64	37	18	48 months cumulative incidence of AML evolution; 0%, 3%, 21%, and 48%, respectively

Treatment of CMML is evolving with better understanding of the disease, including risk features. The most common approach to treatment includes the use of agents commonly used to treat both MDS and MPNs. Allogeneic hematopoietic stem cell transplantation is recommended for those patients eligible for this intensive therapy.

References:

1. Patnaik MM, Tefferi A. Chronic myelomonocytic leukemia: 2018 update on diagnosis, risk stratification and management. American journal of hematology. 2018;93(6):824-840.
2. McCullough KB, Patnaik MM. Chronic Myelomonocytic Leukemia: a Genetic and Clinical Update. Current hematologic malignancy reports. 2015;10(3):292-302.

Acute Myelogenous Leukemia (AML) is a clonal hematopoietic stem cell cancer within the myeloid continuum of diseases. Like other myeloid diseases, AML originates in the factory cells of the bone marrow (see: [What Does Bone Marrow Do](#)). There are different types of AML, each with variable time to onset, prognosis, and treatment options.

How is AML Diagnosed?

The diagnosis of AML requires evaluation of both peripheral blood and bone marrow. The presence of at least 20% myeloid blasts (immature cells) in the blood or bone marrow is required for the diagnosis of AML. The process used for diagnosis is like the process used to diagnose MDS.

The disease is then categorized based on the way the cells look on a slide (morphology) when reviewed by a pathologist, and the genetic signature of the disease. AML is a complex, dynamic disease, characterized by multiple genetic abnormalities. There can be more than one genetic abnormality present at any time during the disease and these abnormalities may change over time.

Types of AML: There are three main types of AML

De-novo AML

De-novo (or at the start) AML occurs in patients of all ages. The onset is usually abrupt with symptoms progressing over days to a few weeks. Most patients present with fevers, infections, bruising or bleeding, fatigue, bone pain, and in some cases skin nodules. This type of AML is uncommon in patients with MDS, MPNs or CMML.

Secondary AML (sAML)

These subtypes of AML are found in patients with a prior history of a myeloid malignancy, most often MDS, CMML, or an MPN, or in a patient with prior exposure to anti-cancer treatments (chemotherapy or radiation). The two common subtypes include Treatment-related AML (tAML) and AML with Myelodysplasia-related Changes (AML-MRC). The risk of developing secondary AML is variable and is largely related to the risk of the underlying myeloid malignancy and the complexity of genetic changes, or the intensity and type of treatment for other cancers. Genetic abnormalities are present in more than 90% of patients with these subtypes of AML and most carry an unfavorable prognosis. Most patients with secondary AML, develop progressive cytopenias (low-blood counts) over weeks or months. The presenting signs and symptoms are most often related to these cytopenias.

Treatment related (tAML) AML

Patients who are receiving treatment with chemotherapy or radiation for other types of cancer may experience damage to the bone marrow cells and microenvironment that pre-dispose them to the development of AML. The time to onset is highly variable and is largely dependent on the specific drugs and doses used or the amount and of location of radiation. Although it is possible that patients with MDS may have more than one type of cancer requiring treatment, this type of MDS is less common in patients with MDS.

AML with Myelodysplastic Changes (AML-MRC)

All patients with MDS carry some risk of developing AML-MRC. This risk is related to the subtype of MDS, the genetic profile of the disease and the IPSS-R risk category. Patients with higher-risk MDS are at an increased risk of developing AML-MRC. The time to onset is highly variable. Some patients may present with what appears to be De Novo AML based on the number of blasts (>20%) in the peripheral blood or bone marrow and are later found to have AML-MRC.

How is AML Treated

The goals of treatment for all types of AML are to eradicate the myeloid blasts to the lowest level possible (remission), generally < 5% blasts in the marrow with no evidence of genetic mutations. Like MDS, allogeneic stem cell transplantation is the only potential for cure. Determining transplant eligibility (see: [Am I a candidate for a bone marrow transplant?](#)) and fitness for aggressive treatment is the first step.

High-intensity treatment

Patients eligible for high intensity treatment receive chemotherapy, usually in two phases.

- **Induction therapy:** Patients receive chemotherapy with the goal of reducing the number of blasts in the bone marrow to <5%. This most often requires hospitalization due to the potential risks associated with this type of treatment, including infections and bleeding. Some patients require more than one cycle of induction therapy if they do not reach the goal of <5% blasts.
- **Consolidation:** Once the bone marrow has recovered from induction therapy, additional cycles of chemotherapy are administered to improve the depth of response and reduce the chance that the AML will come back (relapse). The number of cycles is determined by the type of AML, the age and fitness of the patient, and whether the patient is eligible for an allogeneic stem cell transplant. This can be administered in the outpatient setting/clinic in some cases.

Chemotherapy used for Induction and Consolidation

Cytarabine and Daunorubicin (7+3) is the most common induction chemotherapy regimen used to treat DeNovo AML. This combination is administered in the inpatient setting. Vyxeos, a liposomal formulation combining Cytarabine and Daunorubicin is approved for induction and consolidation therapy for tMDS and MDS-MRC. You can learn more about the treatment of tAML and AML-MRC at www.youandaml.com.

Low-intensity treatment

- Patients not eligible for high intensity treatment may be treated with treatments commonly used to treat MDS, including the hypomethylating agents Azacitidine and Decitabine (see disease modifying agents for MDS). There are several new treatments that are targeted toward genetic mutations that play a role in the development or progression of AML including Venetoclax, Enasidenib and Ivosidenib. Patients receiving low-intensity treatment may continue treatment indefinitely if they are benefitting and do not experience serious side effects. Low-intensity treatments are not curative. Most of these treatments are administered in the outpatient/clinic setting.

You can find out more about AML at:

www.mds-foundation.org/wp-content/uploads/2021/06/BBOH.AML_Handbook_061121_ebook.pdf

SEEKING TREATMENT

The goals of treatment for MDS are based on the specific subtype 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 also 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.

SEEKING TREATMENT

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Preparing for the Initial Visit

Once the diagnosis of MDS has been established, you will meet with your oncology team 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 healthcare team.

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.

1. Make a list of other health problems, any surgeries and dates, and any family history of cancer or blood disorders.
2. Create a current list of medications including any over-the-counter medications.
3. 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.
4. Prepare your questions for your doctor visits. It is helpful to write them down before the visit. On the next page is a list of questions you can use during your MDS journey – from diagnosis to treatment options to clinical trials.
5. Have a caregiver take notes during the visit so that you can concentrate on what the provider is telling you.
6. Understanding some of the principles of treatment for MDS will help you to prepare for your visit.
7. 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.
8. 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.

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.

References:

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

This is a list of commonly asked questions you may use in your MDS diagnosis and treatment journey.

Frequently, patients may get overwhelmed by the information provided by the treatment team and may not think of specific questions during consultations or clinic visits. This is perfectly normal as these visits are often stressful, with complex disease and treatment related information. Having this list will help you prepare for your visit and may help you better understand your diagnosis, treatment options, and strategies for wellness.

This list was compiled by MDS patient groups in collaboration with clinicians.^{1,2} This list has been updated by the MDS Foundation Nurse Leadership Board. Not all questions may apply to your unique MDS journey.

Diagnosed with MDS

- Are you sure I have the diagnosis of MDS?
- Can you explain what MDS is? Is it a form of cancer?
- Can I get a copy of the reports from my blood and bone marrow tests?
- What type of MDS do I have?
- Are there stages in MDS?
- Which risk group does my MDS fall into (IPSS-R)?
- What is the prognosis for my survival?
- What factors could affect my prognosis or treatment options?
- Where can I get information about MDS?
- Are there MDS support groups available?
- Who can I see to get a second opinion?

Deciding on a MDS Physician

Support groups and MDS experts recommend seeking an opinion from an MDS expert when it comes to rare blood cancers like MDS, as not all hematologists are MDS specialists. This can be particularly helpful to gain access to clinical trials.

- Are you part of a multidisciplinary team or do you have access to a recognized MDS expert?
- Can you suggest an MDS Center of Excellence?

Deciding on a Treatment Plan

- Which treatment, if any, do you recommend, and why?
- What would happen if I do not receive treatment?
- How is the treatment given? How often is it given? How long does each treatment take?
- What are the risks or side effects of the treatments that you recommend? How long are they likely to last?
- Will treatment affect my daily activities?
- How will I know that treatment is working?
- How and when will you re-assess my MDS disease?
- Am I a candidate for a bone marrow transplant?

Clinical Trials

- Am I a candidate for a clinical trial?
- What are the advantages or disadvantages of participating in a clinical trial?
- Are there any clinical trials I should consider now?
- Is travel required?
- Am I able to travel by plane, both domestically and internationally?
- Will I have additional responsibilities or additional doctor visits if I participate in a clinical trial?

While on Treatment

Once treatment begins, you'll need to know what to expect, how you can manage your health, and how your response to treatment will be evaluated.

- How will we know if the treatment is working?
- What type of follow-up will I need during treatment?
- Is there anything I can do to help manage side effects?
- What symptoms or side effects should I tell you about right away?
- How can I reach a healthcare professional with knowledge of MDS on nights, holidays, or weekends?
- Are there any food restrictions or dietary changes I need to make?
- Should I exercise? What type of exercise is recommended?
- What would my options be if this treatment isn't working?

Other support

- Can you suggest a mental healthcare professional?
- What other support services do you recommend for me and my caregivers?

Visit Recommendations

- Take a pen and paper or use your smart phone or tablet to take notes.
- Bring a family member/caregiver to all of your visits, have them take notes. With the permission of your physician, you may be able to record the visit.
- Ask about team members that can provide additional information about your diagnosis or treatment plan. These may be Advanced Practitioners, Nurses, Social Workers, Nutritionists, or other health care professionals.
- Explore resources in the Building Blocks of Hope®.
www.mds-foundation.org/bboh

References:

¹ Completed by French MDS experts in France, Leukaemia Foundation of Australia, Melbourne, Australia, CCM – Connaître et Combattre les Myélodysplasies, Paris, France. <https://www.ncbi.nlm.nih.gov/pubmed/25850728>

² Original article from MDS UK Patient Support Group, June 2019

Treatment Selection

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?](#) and [How is MDS classified?](#))

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

1. Your general health and ability to be independent in the activities of daily living
2. Other illnesses, how well they are controlled and what medications are needed to manage them
3. Your individual social and emotional profile
4. Insurance coverage and finances
5. The characteristics of your MDS
6. The IPSS-R risk category Lower risk vs. Higher risk
7. The IPSS-M risk category that incorporates the presence of certain genetic mutations.
8. The presence of certain genetic markers
9. Currently available treatment options including clinical trials (these may be based on geographical location)
10. Eligibility for a bone marrow transplant
11. The availability of a caregiver
12. Proximity to the healthcare setting
13. Your personal goals and how the individual treatment may affect your quality of life and lifestyle

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.

What are the Goals of Treatment?

The general goals of treatment vary based on the specific subtype of MDS you have, the risk category (low risk vs. high risk), how the disease is affecting you, what treatments are available for you. There can be variation in the way MDS is managed based on the unique needs of each patient.

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

IPSS-R	Very Low	Score of <1.5
	Low	Score of >1.5 - 3.0
	Intermediate	Score of >3.0 - 4.5

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-R score or selected high-risk features.

IPSS-R	High	Score of 4.5 - 6.0
	Very High	Score of >6.0

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
 Ridgeway, J. et. al. (2012) Clin J Oncol Nurs, 16(3, suppl. 1), 9-22
 Komrokji, R., Skeres, M. & List, A.F. (2011) Curr Hematol Malig Rep, doi: 10.1007/s11899-011-0086-x
 Garcia-Manero, G. (2011) Semin Oncol 38:658-666
 Greenberg, et. al. (2012) Blood, 120:2454-2465; doi:10.1182/blood-2012-03-420489

General Principles of Treatment of MDS

Treatment for MDS can be grouped into four primary types: Observation, Palliative Care, 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 lower risk MDS who have not required blood transfusions or who require them very infrequently.

Supportive and Palliative Care

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. 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.

Palliative care may help 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

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.

General Principles of Treatment of MDS

A palliative care team may include one or more of the following:

- Physician(s)
- Advanced Practice Providers (APP): Nurse Practitioner or Physician Assistant
- Oncology nurse specialist
- Clinical Pharmacist
- Social worker
- Pain service
- Chaplain service or other spiritual support services
- Nutritionist
- Physical therapist
- Financial counselor

Throughout the disease course, counseling is directed at maintaining or improving quality of life. For example, yoga and regular exercise have been studied and found to help alleviate symptoms, improve fatigue, anxiety, and depression in patients with MDS.

Open communication with the healthcare team helps align treatment with patient and family-centered goals for care. It is important to discuss the goals of the proposed treatment, including impact on survival and quality of life.

Supportive Care

Supportive care in MDS may include 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.

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.

Red Blood Cell Transfusion

Whole blood is collected from volunteer 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 over the course of their disease.

MDS patients who require a series of RBC transfusions are considered to be transfusion dependent. Transfusion-dependence is a common trigger to consider disease modifying treatment to improve production of normal red blood cells and limit continued exposure to excess iron (iron overload).

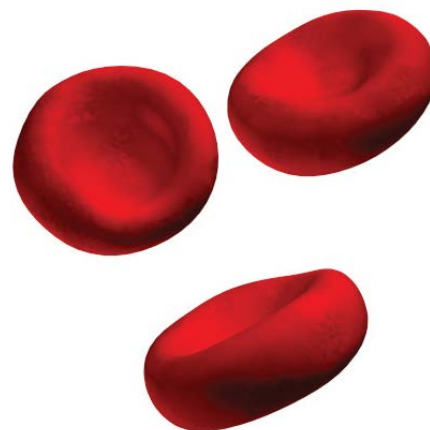


Illustration by Kirk Moldoff

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. The decision to transfuse RBCs will be based on your symptoms (anemia such as increasing fatigue, a pale complexion, shortness of breath with exertion, or a faster heart rate), as well as your blood counts. You should report symptoms associated with anemia to your healthcare team.

How often will I receive red blood cell transfusion?

The frequency of RBC transfusions will vary depending upon the severity of symptoms and your hemoglobin level. Transfusion intervals (the time between one transfusion and the next) may vary from every few months in lower risk MDS to every 1 to 2 weeks in higher risk MDS.

What are the risks associated with red blood cell transfusion?

There is the potential for both short term or long term risks with red blood cell transfusion. Most side effects are mild and are easily managed with medications. More serious reactions are possible but are rare.

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.
- Fluid retention or transfusion associated cardiovascular overload (TACO). Fortunately, the fluid build-up can usually be managed by administration of a diuretic like furosemide (Lasix®).

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. Antibodies can develop after each blood transfusion, requiring regular screening.

The blood sample will be sent to the designated blood bank in your area for testing. The blood bank will then search the available donor units that match 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. The process for obtaining matched red blood cells and infusing them may require more than one day.

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

Each facility has its own policy for the rate of red blood cell transfusion. Most often, 1 unit of PRBCs is administered based on the patient's symptoms and hemoglobin level. For Hgb levels below 6, you may require more than 1 unit of PRBCs.

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. The transfusion of 2 units of PRBCs may take anywhere from 4-5 hours once the blood is obtained.



Platelet Transfusion

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 may provide temporary relief of the symptoms of thrombocytopenia (low platelets) 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 healthcare team will notify you if your platelet count is at a level that requires a platelet transfusion or if you experience excessive bruising or uncontrolled bleedings. Ask your healthcare team about symptoms that need to be reported.

What is the process for receiving a platelet transfusion?

Platelets, unlike RBC do not need to be crossmatched unless you specifically require matched platelets. You will need a blood band to check the platelet unit(s) to ensure they are intended for you. You should not remove the blood band until you have safely received your 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.

Platelet Transfusion

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 (alloimmunization), making it more difficult to find suitable donor units.
- Transmission of an infection (such as HIV or hepatitis) through a platelet transfusion is very low

Disease Modifying Treatment of MDS

Disease Modifying Agents are treatment with the potential to affect the underlying abnormalities that cause MDS. Disease modifying treatments have the ability to change one or more of the abnormal features responsible for the ineffective production of blood cells and platelets (hematopoiesis) in MDS. As a result, disease modifying treatment may change the natural history of the disease and extend survival.

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?](#)).

References:

Kurtin, S. (2012) J Adv Pract Oncol, 3, 209-224

Disease Modifying Agents for MDS: 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 and has been associated with the development of AML.

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)

Drug class: Azacitidine is a hypomethylating agent

FDA Approval: Indicated for the treatment of intermediate to high-risk MDS

Several clinical trials showed that, compared with patients who did not receive azacitidine, MDS patients treated with azacitidine daily for 7 days every four weeks had durable hematologic improvement: 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-days once a month) have also been investigated and may be an option for selected patients.

How administered: Azacitidine is an injectable medicine that can be administered either subcutaneously using a syringe and a small needle inserted under the skin in the stomach or legs, like the technique used to administer insulin or intravenously. Azacitidine is given for 7 days each month for most patients.

The most common side effects include:

- Decreased bone marrow activity (myelosuppression)
- Constipation
- Fatigue
- Nausea or diarrhea
- Injection site irritation

You can learn more about Azacitidine at: <http://chemocare.com/chemotherapy/drug-info/azacitidine.aspx>

Disease Modifying Agents for MDS: Hypomethylating Agents

Decitabine (Dacogen)

Drug class: Decitabine is a hypomethylating agent

FDA Approval: Indicated for the treatment of higher-risk MDS

A study of MDS 170 MDS patients with intermediate to high risk disease were treated with Decitabine and experienced responses lasting for about 10 months: 17% response for decitabine-treated patients versus 0% for patients receiving standard of care. Those responding 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.

How administered: Decitabine is administered intravenously for five days once a month. For patients with higher risk disease, such as those with the TP53 mutation, Decitabine may be given for 10 consecutive days once every 28 days.

The most common side effects include:

- Decreased bone marrow activity (myelosuppression)
- Constipation
- Fatigue
- Nausea or diarrhea
- Injection site irritation

You can learn more about Decitabine at: <http://chemocare.com/chemotherapy/drug-info/decitabine.aspx>

References:

Steensma, D. (2011) Semin Oncol 38:635-647

Disease Modifying Agents for MDS: Hypomethylating Agents

INQOVI (decitabine 35mg and cedazuridine 100mg)

Drug Class: Hypomethylating agent

FDA approval: Indicated for the treatment of adult patients with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS, including:

- refractory anemia
- refractory anemia with ringed sideroblasts
- refractory anemia with excess blasts
- chronic myelomonocytic leukemia (CMML)
- intermediate-1, intermediate-2, and high risk IPSS groups.

The approval of Inqovi was based on a phase 3 study evaluating the standard of care Decitabine given intravenously five consecutive days every 28 days, compared to the oral formulation of decitabine and cedazuridine. Among 133 patients treated, at a median follow-up of 5.2 months, 101 patients were available for evaluation. Results of this trial showed similar drug concentrations between intravenous decitabine and Inqovi. Additionally, about half of the patients who were formerly dependent on transfusions were able to no longer require transfusions during an 8-week period. The safety profile of Inqovi was also similar to intravenous decitabine.

How administered:

- One tablet orally once daily on day 1-5 of each 28-day cycle for a minimum of 4 cycles until disease progression or unacceptable toxicity. A complete or partial response may take longer than 4 cycles.
- Should be taken on an empty stomach at the same time each day. Avoid eating 2 hours before and 2 hours after each dose.
- Tablets should not be crushed, cut, or chewed.
- If a dose is missed, take the missed dose as soon as possible within 12 hours. If more than 12 hours from the normal time you are scheduled to take the dose, take the dose on the following day at the usual time.
- If you experience nausea or vomiting after taking a dose, do not repeat that dose on the same day. Contact your health care team.

The most common side effects are:

- Low blood counts (cytopenias, including anemia, thrombocytopenia, or neutropenia)
- Infections, including pneumonia, urinary tract infections and more serious infections including febrile neutropenia and sepsis
- Fatigue/tiredness
- Constipation or diarrhea
- Nausea
- Elevation of liver function tests
- Muscle or joint pain
- Embryo-fetal toxicity
- Rash
- Decreased appetite

You can find out more about Inqovi at: www.inqovi.com

Disease Modifying Agents for MDS: Immunomodulatory and Immunosuppressive Agents

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 (Revlimid)

Drug Class: Immunomodulatory agent

FDA approval: Treatment of transfusion-dependent myelodysplastic syndrome (MDS) patients with deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.

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., chromo- some abnormalities were no longer detectable) was achieved in 45% of patients. In this study, the average time to response was an average of 4.6 weeks with many long-term responders.

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).

How administered: Lenalidomide is taken orally and is available in capsule form. It can either be given continuously (once daily) or for 21 of 28 days. 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 drug distribution is regulated by a REMs safety program and must be dispensed by specialty pharmacies.

The most common side effects are:

- Rash
- Itching
- Fatigue
- Diarrhea
- Nausea

You can find out more about Lenalidomide at: <http://chemocare.com/chemotherapy/drug-info/Revlimid.aspx>

Disease Modifying Agents for MDS: Differentiation Agents

Luspatercept (REBLOZYL)

Drug Class: Luspatercept binds to proteins, called ligands, that may interrupt the normal production of red blood cells. Certain proteins, such as the Smad 2/3 signaling molecules, play a role in the normal production of hematopoietic stem cells, including the production of red blood cells. Smad 2/3 is commonly overexpressed (uncontrolled production) in some cases of MDS resulting in the interference of normal red blood cell development (differentiation and maturation). Luspatercept may restore differentiation and maturation of red blood cells (normal development) in the last phase of erythroid cell (red blood cell) development in some patients with lower risk MDS.

FDA approval: Indicated for the treatment of anemia without previous erythropoiesis stimulating agent use (ESA-naïve) in adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS) who may require regular red blood cell (RBC) transfusions.

- REBLOZYL® (luspatercept-aamt) is indicated for the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions.
- REBLOZYL® (luspatercept-aamt) is indicated for the treatment of anemia without previous erythropoiesis stimulating agent use (ESA-naïve) in adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS) who may require regular red blood cell (RBC) transfusions.
- REBLOZYL® (luspatercept-aamt) is indicated for the treatment of anemia failing an erythropoiesis stimulating agent and requiring 2 or more red blood cell (RBC) units over 8 weeks in adult patients with very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T).

REBLOZYL® is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia.

How administered: Luspatercept is administered subcutaneously (an injection under the skin) once every three weeks.

The most common side effects are:

- | | |
|---|---|
| • High blood pressure (hypertension) | • Stomach (abdominal) pain |
| • Fatigue | • Upper respiratory infections |
| • Syncope | • Urinary tract infection |
| • Musculoskeletal pain (joint, bone or muscle pain) | • Dyspnea (trouble breathing) |
| • Dizziness | • Blood clots in the arteries, veins, brain, and lungs happened in patients with beta thalassemia during treatment with REBLOZYL. |
| • Diarrhea | |
| • Nausea | |
| • Headache | |

The severity of the majority of side effects improved over the course of treatment.

You can find out more about Reblozyl at: <https://media2.celgene.com/content/uploads/reblozyl-patient-info.pdf> or www.reblozyl.com

Disease Modifying Agents for MDS: Immunomodulatory and Immunosuppressive agents

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.

Allogeneic hematopoietic stem cell transplant for MDS

Allogeneic hematopoietic stem cell transplant is the only treatment that is potentially curative treatment for MDS.

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](#)).

Allogeneic stem cells are obtained from another individual who is genetically like the MDS patient. Donors may be related (brother, sister, child) or may be an unrelated volunteer donor. Human Leukocyte Antigen (HLA) testing is required from the MDS patient (recipient) and the donor to find the best match. Transplant is not an option without an identified donor.

There are significant risks associated with this procedure. Therefore, although this procedure offers a potential cure for MDS, it is available to only a small proportion of adult MDS patients.

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 healthcare team will evaluate several factors known as eligibility criteria.

The most common eligibility criteria include:

1. Age less than 70 years (some exception may be made at some centers)
2. Availability of a HLA identical matched donor
3. Good heart, lung, liver, and kidney function
4. Physically active and able to perform daily activities independently
5. Consistent availability of a caregiver

There are many resources available to help you understand blood and bone marrow transplantation:

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

While transplants are not recommended for patients with lower risk disease, it is a consideration for patients with higher risk MDS because the risk of death from the disease may be higher than the treatment-related mortality of transplant.

Long-term survival with an allogeneic transplant is in the range of 40-50%, but factors such as patients age, prognostic risk group, and type of donor, may all impact outcomes. Higher treatment-related mortality is observed in myeloablative compared to reduced intensity conditioning transplants; however, higher rates of relapse are observed in reduced intensity conditioning transplants vs. myeloablative transplants. While transplants are not recommended for patients with lower risk disease, it is a consideration for patients with higher risk MDS because the risk of death from the disease may be higher than the treatment-related mortality of transplant.

The risk of relapse is based on multiple factors, including the donor source, the type of transplant, the health and MDS profile of the transplant recipient to name a few. Strategies to reduce the risk of relapse or progression may include maintenance treatment following transplant, salvage treatments that may include donor lymphocyte infusions given together with a hypomethylating agent. You can find out more about post-transplant care at the resources listed above.

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.

Additional Resources:

Be the Match: Find the latest references, outcomes, and referral timing guidelines by disease. Access patient-friendly handouts. Order or download the updated 2019 HCT Guidelines for Referral Timing and Post-Transplant Care.

Download the guidelines in our free mobile app, access them online, or order your free print copy.

<https://bethematchclinical.org/Catalog/Details?id=3522>

HCT Guidelines: Referral Timing and Post-Transplant Care <https://bethematchclinical.org/resources-and-education/>

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 is the center's success rate with stem cell transplants?
4. What is the experience of the transplant team in treating patients with MDS?
5. What tests will I need before the transplant?
6. Is housing available in the area for post-transplant care and what is the recommended/required duration to reside locally?
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 are the expectations for the caregiver(s)

About clinical trials

Clinical trials offer an option for treatment under the guidance of a research protocol. Clinical trials provide several important benefits. In addition to developing new treatments for MDS and other diseases, clinical trials may:

1. Help to improve diagnostic techniques
2. Identify new targets for treatment
3. Offer treatment options which are not otherwise available
4. Help to improve side effect management

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.

ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.
<https://clinicaltrials.gov>

References:

US Department of Health and Human Services, National Institutes of Health, publication No. 07-6249, 2007

Clinical Trials

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.

Clinical Trials

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

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

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

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

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.

MDS in Children

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.

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 (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.

MDS in Children

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 Park Avenue, Suite 108

Rockville, MD 20850

301-279-7202 or 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 for children with Cancer

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

www.candlelightersoregon.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

<https://www.cancer.gov/publications/pdq>

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

888-5-PediMDS

MDS@childrens.harvard.edu

www.pedimds.org

Pediatric Oncology Resource Center

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

www.ped-onc.org

The Leukemia & Lymphoma Society

1311 Mamaroneck Avenue, Suite 130

White Plains, NY 10605

800-955-4572

www.lls.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

GENERAL RESOURCES FOR LIVING WITH MDS

This chapter will provide you with strategies for staying well, managing your health and your MDS and includes several Quick-Tips to recognize and manage common symptoms or problems experienced by patients and caregivers living with MDS. Each Quick-Tip includes links to several digital resources that may help you manage your health. This chapter also includes a glossary terms that will help you to understand the complex language used to describe these diseases.

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What can you do to stay healthy?

- Take an active role in managing your health
- Continue to enjoy the things you love – focus on living
- Ask for help when needed
- Be an active participant in your care. Feel empowered.
- Have honest, open discussions with your healthcare team. Ask questions.
- Make your wishes clear
- Share in decision making
- Prepare for each visit
- Learn all you can about your treatment
- Learn to manage and report symptoms
- Take advantage of patient portals to improve communication with your healthcare team and track your results
- Consider participating in a clinical
- Stay well

The Quick tips listed in this section will provide a brief summary of common challenges faced by patients and caregivers living with MDS. Links to additional resources are included.

Bleeding and Bruising

Bleeding or bruising may be a result of faulty platelet function, acquired bleeding disorders, or too few platelets (thrombocytopenia) in patients with MDS. 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.

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.

Things you can do:

1. Record and track your blood counts, transfusion dates, and any symptoms before and after transfusions, then bring the results with you to your next healthcare provider appointment to discuss the results.
2. Keep all your appointments as scheduled.
3. Keep a current list of all of your medications, including over the counter medications. Review this list with your healthcare team at each visit.
4. Let your healthcare providers know if you experience unusual bruising, uncontrolled bleeding, or develop petechiae.
5. Avoid excess alcohol, which may contribute to platelet dysfunction.
6. Avoid injuries (falls, cuts, scrapes) and activities that can cause bruising or bleeding, such as contact sports and heavy lifting.
7. Avoid constipation or straining to have a bowel movement.
8. Use a soft toothbrush.
9. Ask for help from family and friends.

Additional Resources:

Cancer.net: Thrombocytopenia www.cancer.net/coping-with-cancer/physical-emotional-and-social-effects-cancer/managing-physical-side-effects/low-platelet-count-or-thrombocytopenia

Oncolink: Low Platelet Count www.oncolink.org/support/side-effects/low-blood-counts/low-platelet-count-thrombocytopenia

Caregiving: Resources for managing each day

Caregivers are an essential part of the healthcare team. They are most often family members or close friends but may also be professionals that assist with organizing and delivering care. There are many distinct roles for caregivers. Many involve everyday activities such as home management, shopping, and running errands. When you are living with a diagnosis of MDS either yourself or with your loved one, these daily routines may be more difficult to maintain. In addition, there are several other tasks that will be necessary to accommodate the treatment routine.

Common roles for a caregiver:

- Providing support and encouragement
- Giving medications
- Helping manage symptoms and side effects
- Coordinating medical appointments
- Providing a ride to appointments
- Assisting with meals
- Helping with household chores
- Handling insurance and billing issues

Caring for or 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 healthcare team. Specific recommendations for contact with children are recommended for patients undergoing a stem cell transplant, leukemia therapy, or who have a very low white blood cell counts (neutropenia).

Things you can do:

1. Focus on your needs, too. Ask for Help. Build a support team. Strike a balance each day.
2. Maintain a healthy lifestyle: nutrition, exercise, sleep
3. Practice relaxation or meditation
4. Make an appointment to see your healthcare provider for a wellness check.
5. Seek help if you are feeling anxious or depressed
6. Talk with a financial counselor and your certified public accountant for financial guidance

Additional Resources:

Cancer.net: Being a Caregiver www.cancer.net/coping-with-cancer/caring-loved-one

Cancer.net: Sharing Responsibilities: www.cancer.net/coping-with-cancer/caring-loved-one/sharing-responsibilities

Family Caregiver Alliance: Community Resources www.caregiver.org/caregiving-home-guide-community-resources

Be the Match: Caregivers and Bone Marrow Transplant

<https://bethematch.org/for-patients-and-families/caregivers-and-transplant/>

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.

Talk with your healthcare team prior to starting any complementary or alternative therapies to ensure safety.

Additional Resources:

Chemocare is a patient friendly website with a focus on drug information and the management of side effects of chemotherapy. Included are handouts on specific oral and intravenous agents and are updated frequently when new drugs are approved. www.chemocare.com

Cancer Care: Our comprehensive services include [counseling](#) and [support groups](#) over the phone, online and in-person, [educational workshops](#), [publications](#) and [financial and co-payment assistance](#). All CancerCare services are provided by oncology social workers and world-leading cancer experts. www.cancercare.org/about

ASCO People Living with Cancer: Trusted, compassionate information for people with cancer and their families and caregivers, from the American Society of Clinical Oncology (ASCO), the voice of the world's cancer physicians and oncology professionals. www.cancer.net

<https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs>

Constipation

You may experience either constipation or diarrhea because of your illness(s) or medications. There are several things you can do to prevent or treat changes in bowel function.

Things you can do for Constipation

1. Keep a log of symptoms that you are concerned about. Discuss these with your healthcare team.
2. Keep all your appointments as scheduled.
3. Let your doctor know if you have pain with bowel movement, any blood in the stool, severe abdominal pain, persistent nausea, or vomiting.
4. Don't let more than 3 days go by without a normal bowel movement—discuss this with your healthcare team.
5. Stay active.
6. Drink 2-3 liters of fluid a day.
7. Eat a diet rich in fruits, vegetables, and natural fibers.
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.
9. Cleanse after bowel movements or urination.
10. Wash your hands after using the bathroom.

Additional Resources:

Cancer.net: Constipation www.cancer.net/coping-with-cancer/physical-emotional-and-social-effects-cancer/managing-physical-side-effects/constipation

Cancer Care: Constipation www.cancercare.org/publications/218-coping_with_constipation

Oncolink: Constipation www.oncolink.org/support/side-effects/gastrointestinal-side-effects/constipation

Depression

Depression is a common consequence of living with cancer, including MDS. Adjusting to the diagnosis of MDS affects each person differently. While some people can continue to live a full and rewarding life, others may find the stress of coping with MDS more challenging. These challenges are real and important. Regardless of the cause, there are things that can help you manage the emotions of Living with MDS.

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
2. 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.
3. 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.
4. Set priorities for activities that are necessary to maintain your physical and emotional health.
5. Try to find some activity that you can still enjoy—such as listening to music or watching a ball game.
6. These activities can help you keep a positive outlook.
7. Continue with a diet and exercise routine that will help you to stay healthy. Get enough rest.
8. Avoid alcohol—it can make depression worse.
9. Talk with your healthcare team about resources available to help you.
10. Prayer or meditation may be useful to provide peace.
11. 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.
12. 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.
13. Anti-depressant medicines should not be stopped suddenly.

Additional resources:

Cancer.net: Managing emotions: www.cancer.net/coping-with-cancer/managing-emotions

American Cancer Society: www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/changes-in-mood-or-thinking/depression.html

Oncolink: Managing Practical and Emotional Concerns www.oncolink.org/support/practical-and-emotional

Diarrhea

You may experience either constipation or diarrhea because of your illness(s) or medications. There are several things you can do to prevent or treat changes in bowel function.

Things you can do for Diarrhea:

1. Keep a log of symptoms that you are concerned about. Discuss these with your healthcare team.
2. Keep all your appointments as scheduled.
3. Report any blood in the stool, severe abdominal cramping, fevers, or symptoms of severe diarrhea to your healthcare team immediately.
4. Drink 2-3 liters of fluid a day. Avoid caffeine or high sugar drinks.
5. Eat small frequent meals.
6. The BRAT diet is often recommended until more severe symptoms improve: Bananas, Rice, Applesauce, and Toast.
7. Foods to avoid dietary fiber (brown rice, fruits, vegetables, popcorn, whole grain breads and pasta), alcohol, caffeine, chocolate, greasy foods, dairy products containing lactose.
8. Increase the intake of foods and fluids high in sodium and potassium, such as broths, soups, low-sugar sports drinks, potatoes and crackers.
9. Probiotic supplements or foods containing probiotics (natural gut bacteria) may improve diarrhea.
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. Cleanse after bowel movements or urination.
12. Wash your hands after using the bathroom.

Additional Resources:

Cancer.net: Diarrhea www.cancer.net/navigating-cancer-care/side-effects/diarrhea

Cancer Care: Diarrhea www.cancercare.org/tagged/diarrhea

Oncolink: Diarrhea www.oncolink.org/support/side-effects/diarrhea

A balanced diet, daily activity and exercise as tolerated, and participation in activities of enjoyment are important to maintain optimal health and well-being. A balanced diet can help combat fatigue and illness. Adequate intake of food and fluids also helps individuals tolerate treatment.

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.

People living 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. Ask your healthcare providers if there are specific restrictions for you.

Things you can do:

1. The Dietary Guidelines for America 2015-2020 (www.dietaryguidelines.gov) provide the basic principles of a healthy diet.
2. Meet with a registered dietician to determine your daily caloric needs and how you might get these in the foods you like to eat.
3. Stay hydrated: 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.
4. Eat a balanced diet
5. Eat fruits and vegetables. Wash all fruits and vegetables well prior to eating. Eat dark green vegetables like leafy greens or broccoli and orange vegetables like carrots and sweet potatoes.
6. 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.
7. 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. Consume only pasteurized milk, yogurt, cheese, and other dairy products.
8. Make the fats you eat healthy ones (polyunsaturated and monounsaturated fats).

Additional Resources:

Cancer.net: Nutrition Recommendations During and After Treatment www.cancer.net/survivorship/healthy-living/nutrition-recommendations-during-and-after-treatment

Cancer.net: Food Safety: www.cancer.net/survivorship/healthy-living/food-safety-during-and-after-cancer-treatment

Anxiety

Anxiety is a common reaction to learning that one has MDS. 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. Uncertainty about the diagnosis of a MDS, what treatments might be right for you, how they will work, and what side effects you may experience may contribute to your anxiety.

Things you can do:

There are several resources to help you understand your diagnosis, treatment options, and strategies to take an active part in your journey. Explore the Building Blocks of Hope® www.mds-foundation.org/bboh, the MDS Foundation website www.mds-foundation.org.

1. Evaluate other parts of your life where you have been successful in mastering control—use those techniques to help you meet the challenges you face while living with MDS
2. Try to simplify your life. Eliminate or reduce the activities that are not essential to your physical and emotional well-being.
3. Ask for help. This can be from family, friends, or professionals. Counseling from a psychologist or social worker can also be useful.
4. 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.
5. Explore resources that will help you with relaxation such as meditation, massage, yoga, or listening to relaxing music.
6. Try to eat well and maintain some sort of activity.
7. Avoid excess amounts of alcohol or caffeine.
8. You may find it difficult to remember instructions, or to concentrate when hearing information, so write them down or bring a caregiver or advocate with you to appointments.
9. Talk to your healthcare team about other options for managing your anxiety. Ask if an anti-anxiety medication might be helpful.

Additional resources:

Cancer.net: Managing emotions: www.cancer.net/coping-with-cancer/managing-emotions

American Cancer Society: www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/changes-in-mood-or-thinking/anxiety-and-fear.html

Cancer Care: Anxiety www.cancercare.org/tagged/anxiety

Oncolink: Managing Practical and Emotional Concerns www.oncolink.org/support/practical-and-emotional

Employment

Many patients or caregivers LIVING with MDS continue to work.

Ask your healthcare provider how to plan for the time off you will need to make sure you are receiving your treatment in the safest and most effective way possible. Understand that these recommendations may change unexpectedly due to disease or treatment related factors. It will be important to set up a network of support for these unexpected events. Ask your healthcare provider to write a letter describing your schedule for treatment or clinic visits.

It is important to ask about your employers' options for sick-leave and family medical leave. The [Family and Medical Leave Act](#) (FMLA) provides certain employees with up to 12 weeks of unpaid, job-protected leave per year. It also requires that their group health benefits be maintained during the leave.

For some patients, there may a need to pursue Social Security Disability. Ask if there is a Social Worker that might help guide you through this process. The process for approval can take several weeks.

Social Security Disability Insurance pays benefits to you and certain members of your family if you are "insured," meaning that you worked long enough and paid Social Security taxes.

[Supplemental Security Income](#) pays benefits based on financial need.

When you apply for either program, we will collect medical and other information from you and decide about if you meet [Social Security's definition of disability](#).

Use the [Benefits Eligibility Screening Tool](#) to find out which programs may be able to pay you benefits.

Ask your certified public accountant about options you may have to access any retirement savings early

Additional resources:

Cancer Care: Workplace resources www.cancercare.org/tagged/workplace_issues

Cancer.net: Balancing work and caregiving www.cancer.net/blog/2015-08/balancing-work-and-caregiving

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.

Things you can do:

1. Prior to starting a new exercise program, it is a good idea to discuss your plans with a healthcare provider to make sure that it is safe for your condition.
2. An exercise program can be modified to fit each person based on their age, sex, type of MDS and treatment, and physical fitness level.
3. Ask about a referral to a physical therapist or trainer to develop a tailored program
4. Strength training can even be done in a chair using resistance bands or light weights
5. Even light cardio such as walking will add benefit
6. Blood counts should be considered prior to exercise.
 - If neutropenic, it is best to avoid community swimming pools and hot tubs.
 - If you are severely anemic, you may need to avoid aerobic exercise.
 - Listen to your body, if you experience severe pain or shortness of breath, stop the exercise.
 - When the platelets are less than 50,000 high impact sports should be avoided to prevent problems with bleeding.
 - When in doubt, discuss with your healthcare team.
 - Start slowly and try to make progress by setting realistic goals along the way.
 - Recruit the support of family and friends.

Fatigue

Fatigue is defined as 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.

Things you can do:

1. Keep a log of symptoms that you are concerned about. Discuss these with your healthcare team.
2. Keep all your appointments as scheduled.
3. Exercise is the best way to treat fatigue. Stay active as much as possible to maintain muscle strength and improve stamina. Consider starting an exercise routine, such as daily walks with a caregiver or friend. Your healthcare provider will provide you with recommendations to maintain or increase your activity safely.
4. List the activities for each day. Set priority activities for the day, and schedule priority activities for periods of highest energy level.
5. Limit naps during the day to less than 1 hour to prevent problems with nighttime sleeping.
6. Talk to your healthcare team if you are having trouble with anxiety or overwhelming sadness.
7. Stay hydrated.
8. Eat small, frequent meals.
9. Ask for help from family and friends.
10. Be sure to discuss any concerns with your healthcare 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.

Additional resources:

Cancer.net: Fatigue: www.cancer.net/navigating-cancer-care/side-effects/fatigue

Oncolink: Fatigue: www.oncolink.org/support/side-effects/fatigue-and-cancer

American Cancer Society: Fatigue: www.cancer.org/treatment/survivorship-during-and-after-treatment/staying-active/nutrition/nutrition-and-physical-activity-during-and-after-cancer-treatment.html

Fever and infections

Fever may be a result of infections or may be a side effect of certain chemotherapy agents used to treat MDS. The Absolute Neutrophil Count (ANC) is used to determine your risk of infection. 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. Ask your healthcare providers when you should report a fever, who to call and when you might need emergent treatment. It is essential to treat MDS patients with fevers quickly to avoid the possibility of developing more serious infections.

Things you can do:

1. Keep a log of symptoms that you are concerned about. These can be tracked in the MDS Manager Symptom Tracker. Discuss these with your healthcare team.
2. Record and track your blood counts, including the WBC and Absolute Neutrophil Count (ANC) and any symptoms including fevers, chills, or infections. You can use the MDS Manager to keep track of your counts and your temperature.
3. Keep all your appointments as scheduled.
4. Notify your healthcare team immediately for any fever $\geq 101.4^{\circ}\text{F}$ or 38.5°C or shaking chills at any body temperature
5. Have a working thermometer at home. Discuss which type of thermometer is best for you to use with your healthcare team.
6. Avoid people who are obviously ill, avoid crowded enclosed places when your counts are low, maintain a healthy lifestyle. This does not mean that you can't go out, just avoid close contact with individuals who are ill.
7. Wash your hands frequently. Carry hand sanitizer. Use it in public places.
8. Talk with your healthcare providers about what immunizations are right for you.
9. Stay hydrated.

Additional resources:

Cancer.net: Neutropenia www.cancer.net/navigating-cancer-care/side-effects/neutropenia

Cancer Care: Infections: www.cancercare.org/publications/216-neutropenia_and_infections_what_you_need_to_know

Cancer.net: Infection: www.cancer.net/navigating-cancer-care/side-effects/infection

Oncolink: Neutropenia: www.oncolink.org/support/side-effects/low-blood-counts/neutropenia

Finances and insurance

Living with any illness and its treatment, including MDS, can place a financial burden on you and your family. There are several resources that may be useful in seeking assistance with financial concerns you may have.

The first step is to ask members of your healthcare team who you can talk to about your financial concerns. There may be a financial counselor or social worker that can assist you. Financial counselors work directly with your providers and your insurance company to obtain authorization for treatments, procedures or certain tests. If you need treatment, the Financial Counselor can discuss your anticipated cost of the treatment prescribed by your provider. A social worker can often identify services and resources within your community to help with transportation, disability or Medicaid enrollment, home care, and other needs.

Drug Assistance Programs

Many of the pharmaceutical companies sponsor drug assistance programs. These programs aim to provide medications used to treat your MDS at a reduced fee, or in some cases for free. This is generally based on financial need. Check with your pharmacist or healthcare team for the availability of these programs.

General Finances

We encourage you to speak to an advisor at your bank and your certified public accountant about things you can do to manage your finances and avoid any penalties.

Additional Financial Resources:

Good Days

877-968-7233 www.mygooddays.org

Health Well Foundation

800-675-8416 www.healthwellfoundation.org

Provides aid to underinsured patients who are diagnosed with chronic or life-altering diseases.

National Organization for Rare Diseases Medication Assistance Program

800-999-6673 or 203-744-0100

<https://rarediseases.org/for-patients-and-families/help-access-medications/patient-assistance-programs-2/>

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

PhRMA's Medicine Assistance Tool (MAT)

<https://medicineassistancetool.org/>

A search engine designed to help patients, caregivers and healthcare providers learn more about the resources available through the various biopharmaceutical industry programs. MAT is not its own patient assistance program, but rather a search engine for many of the patient assistance resources that the biopharmaceutical industry offers.

Patient Access Network Foundation

866-316-PANF (866-316-7263)

www.panfoundation.org

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

Patient Advocate Foundation

800-532-5274 www.patientadvocate.org

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

Patient Services, Inc.

800-366-7741 www.patientservicesinc.org

A non-profit 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.

Additional Resources:

Cancer.net: www.cancer.net/navigating-cancer-care/financial-considerations

American Cancer Society: www.cancer.org/treatment/finding-and-paying-for-treatment/understanding-health-insurance.html

American Cancer Society: www.cancer.org/treatment/finding-and-paying-for-treatment/understanding-financial-and-legal-matters.html

Home management

Living each day in health or faced with the challenge of illness requires organization and planning. When faced with illness or other unexpected events, it is even more important to organize your resources.

1. We encourage you to build a support team. This can include family, friends, and community resources as well as resources suggested to you by your healthcare team or those included in the Building Blocks of Hope.
2. Consider using online care organization services like Lotsa Helpings Hands <http://lotsahelpinghands.com>
3. Make a list of all your service providers such as phone, internet, water, electricity, gas, waste management and any other individuals that provide you with services. If you are experiencing financial difficulties or having trouble managing your bills, this will help you to get in touch with them to alert them to your situation.

Additional resources:

Cancer.net: Coping with Cancer

www.cancer.net/navigating-cancer-care/financial-considerations/tips-organizing-financial-information

Cancer.net: Finding Support and Information www.cancer.net/coping-with-cancer/finding-support-and-information

Cancer Care: Doctor-Patient Communications www.cancercare.org/tagged/doctor-patient_communication

Immunizations are an important strategy in avoiding infections, particularly the flu or pneumonia. The Center for Disease Control (CDC) provides updated guidelines for immunizations on adults who are considered to be immunocompromised due to cancer or cancer treatment.

Things you can do:

1. Get a flu shot every year
2. Pneumonia Vaccine
 - a. Two pneumococcal vaccines are recommended for adults:
 - 13-valent pneumococcal conjugate vaccine (PCV13, Prevnar13®)
 - 23-valent pneumococcal polysaccharide vaccine (PPSV23, Pneumovax®23)
3. Shingles Vaccines
 - a. Only attenuated Shingles vaccines are recommended for patients who are immunocompromised – ask your provider before you get a Shingles vaccine
4. Talk with your healthcare provider about which vaccines you should receive (CDC recommendations for age >65, immunocompromised)

Additional resources:

CDC Immunizations Guidelines by Age:

<https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html>

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 healthcare provider may recommend:

- Your healthcare 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 healthcare 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 healthcare 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 healthcare providers will discuss the risks and benefits of each treatment option with you. Be sure that you discuss any concerns with your healthcare 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.

The diagnosis of MDS is often unexpected and filled with both immediate and long-term challenges. Assisting patients and their caregivers to live with the highest quality of life possible, despite the diagnosis of MDS, is the primary mission of The Myelodysplastic Syndromes Foundation.

Cancer patients need both specialized medical care and support services to address a range of issues that can affect their health and well-being. There are many excellent resources to aid in managing day to day challenges. Organizing your resources and asking for help is the first step. There are many resources that may help you manage each day.

1. First, it is important to make the most of your relationship with your healthcare team. This will improve your participation in making decision about your health and treatment.
2. Enter each of the members of your healthcare team into MDS Manager or your smart-phone. This will allow you to access the information quickly. The contact information can be saved to the contact list on your device.
3. Communication among and between the members of your healthcare team will improve your health.
4. Keeping track of symptoms or problems you are experiencing between visits to your healthcare provider using the MDS Manager symptom tracker will help you track day to day events. Making notes about questions to ask at your next visit will help prioritize the items you would like to discuss.
5. Explore the BBoH-MDS to learn more about MDS and the resources available for each specific disease or symptom.
6. We have included links to specific resources from several well-respected cancer advocacy organizations that provide general information for cancer patients.

Additional Resources:

Be the Match: Information for patients undergoing bone marrow transplant <https://bethematch.org/>

American Cancer Society: www.cancer.org/about-us/what-we-do.html

Helpline 800-227-2345

Cancer Care: www.cancercare.org/contact

Services: 800-813-HOPE (4673) https://media.cancercare.org/publications/original/178-helping_hand.pdf?1442411382

Cancer.net: The American Society of Clinical Oncology (ASCO) patient information website www.cancer.net

Oncolink: Online links to cancer resources www.oncolink.org

Problems with attention, thinking and memory are common in patients with cancer. These may vary in severity and I'll often make it hard to complete daily tasks. If you're experiencing any changes in attention, thinking or memory, be sure to discuss this with your healthcare team. We want you to remain safe and encourage you to ask for help.

Organizing health information by using the MDS Manager app can help you in organizing your thoughts. The symptom tracker may help you keep track of symptoms you're experiencing in between visits to your healthcare provider.

Things you can do:

1. Keep a log of symptoms that you are concerned about. These can be tracked in the MDS Manager Symptom Tracker. Discuss these with your healthcare team.
2. Keep all your appointments as scheduled.
3. Get enough sleep.
4. Maintain a healthy lifestyle.
5. Stay active.
6. Stay connected to friends and family and community activities
7. Exercise your mind. Use crossword puzzles, reading, and other mind exercise program such as Luminosity: Memory and Concentration Exercises www.lumosity.com/sign_up
8. Involve as many senses as possible.
9. Reduced background noise during conversations.

Additional resources:

Cancer.net: Attention, Thinking or Memory Problems www.cancer.net/navigating-cancer-care/side-effects/attention-thinking-or-memory-problems

Cancer Care: Chemo Brain www.cancercare.org/publications/72-chemobrain_what_you_need_to_know

Oncolink: Chemo Brain www.oncolink.org/support/side-effects/chemo-brain

Out-of-home mobility is necessary for accessing commodities, making use of neighborhood facilities, and participation in meaningful social, cultural, and physical activities. Mobility also promotes healthy aging as it relates to the basic human need of physical movement. You may have limited mobility because of your MDS or other illnesses. We want you to remain safe and encourage you to ask for help.

Things you can do:

1. Keep a log of symptoms that you are concerned about. These can be tracked in the MDS Manager Symptom Tracker. Discuss these with your healthcare team.
2. Keep all your appointments as scheduled.
3. Talk with your healthcare team about home safety evaluations and other resources to help you maintain or improve your mobility.
4. Ask your healthcare team if physical therapy might be helpful to improve strength and mobility.
5. Consider installation of assistive devices, such as shower bars, an elevated toilet seat or bars next to the toilet.
6. Make sure there is good lighting in hallways and bathrooms.

Additional resources:

Cancer.net: Nutrition, Physical Activity and You

www.cancercare.org/connect_workshops/256-nutrition_physical_activity_and_you_2011-11-15

American Cancer Society: www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/weakness.html

Sores or swelling in the tissue in the mouth (mucositis) can occur because of cancer treatment, other illnesses, certain medications, or poor dental health. Patients with MDS who have had a bone marrow transplant may experience graft-versus-host disease in the mouth that may be painful.

Things you can do:

1. Keep a log of symptoms that you are concerned about. These can be tracked in the MDS Manager Symptom Tracker. Discuss these with your healthcare team.
2. Keep all your appointments as scheduled.
3. If you are experiencing pain in the mouth making it difficult to chew or swallow, or if there is any bleeding from the mouth, contact your healthcare providers immediately. You may need medication.
4. See your dentist regularly, however, speak to your healthcare team prior to any dental procedures.
5. Rinse with saltwater and baking soda and water. You can make this at home by simply combining a tablespoon of salt to a quart of water in one solution and a tablespoon of baking soda and water in a second solution. Rinse with the saltwater first and then spit it out. Follow-up with a rinse of baking soda and water and spit it out. You can do this several times a day. Avoid alcohol-based mouth washes.
6. Use a soft toothbrush.
7. Stop using dental floss if your mouth is painful. Dental floss can be continued unless your blood counts are too low. Speak to your healthcare team about when to stop using dental loss.
8. Avoid alcohol.
9. Avoid eating coarse or acidic foods.

Additional resources:

Cancer.net: Mouth sores or mucositis

www.cancer.net/navigating-cancer-care/side-effects/mouth-sores-or-mucositis

Cancer Care: Mouth sores www.cancercare.org/tagged/mouth_sores

American Cancer Society: Mouth sores

www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/mouth-problems/mouth-sores.html

Oncolink: Mucositis www.oncolink.org/support/side-effects/mucositis

Nausea is a symptom that is often described as an unpleasant feeling associated with 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.

Things you can do:

1. Meeting with a dietician may be helpful in finding a diet that works best for you.
2. Make a note of any symptoms of nausea that you have or episodes of vomiting. Discuss these with your healthcare provider at your next visit.
3. 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 healthcare provider immediately. Talk with your healthcare provider about when and how-to call-in case of more severe symptoms.
4. Discuss how many of each type of anti-emetic you can safely use each day and what side effects they may cause. Some of the medications used to treat or prevent nausea and vomiting may increase the risk of developing constipation.
5. Drink 2-3 liters of fluid a day—avoid caffeine or high sugar drinks.
6. Eat small, frequent meals.
7. Avoid: fatty foods, greasy foods, spicy foods, foods that are hard to digest (hard fruits, meats, hard cheese, popcorn), alcohol, caffeine, chocolate, and foods with strong odors.
8. Brush your teeth more frequently and use non-alcohol-based mouth washes to reduce the symptoms of dry mouth and bad taste.
9. Peppermint and ginger supplements have been found to be helpful for some patients.
10. Relaxation, imagery, and meditation may help some patients. Ask your healthcare team about any resources available.
11. Ask for help from family and friends.

Additional resources:

American Cancer Society: Nausea

<https://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/nausea-and-vomiting.html>

Cancer Care: Nausea and Vomiting from Chemotherapy

www.cancercare.org/publications/7-coping_with_nausea_and_vomiting_from_chemotherapy

Oncolink: Nausea and Vomiting <https://www.oncolink.org/support/side-effects/gastrointestinal-side-effects/nausea-and-vomiting>

Many patients experience pain during and after cancer treatment. It may help to know that cancer pain can be treated successfully for most patients. It is important to focus on managing pain during all phases of cancer treatment.

Things you can do:

1. Keep a log of symptoms that you are concerned about. These can be tracked in the MDS Manager Symptom Tracker. Discuss these with your healthcare team.
2. Keep all your appointments as scheduled.
3. If you are experiencing severe pain contact your healthcare providers immediately. You may need medication, changes in your medications, or other treatments.
4. If you are experiencing chest pain, contact emergency services (911) immediately.
5. If you are taking pain medication, make sure you are also following a bowel regimen to avoid constipation.
6. There are several other strategies for managing pain including acupuncture, biofeedback, breathing exercises and meditation, massage, and physical therapy. Discuss options for managing your pain with your healthcare team.

Additional resources:

Cancer.net: Pain www.cancer.net/navigating-cancer-care/side-effects/pain

ASCO Managing Cancer-related Pain: A Guides for Patients, Families and Caregivers
www.cancer.net/sites/cancer.net/files/managing_pain_booklet.pdf

American Cancer Society: Facts About Cancer Pain
www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/pain/facts-about-cancer-pain.html

Cancer Care: Pain www.cancercare.org/tagged/pain

Oncolink: Pain www.oncolink.org/support/side-effects/pain-management

Sexuality is an important part of your overall well-being and should be discussed with your healthcare provider. Do not be concerned about bringing up the topic of sexuality to your healthcare provider. There may be some safety precautions necessary if your blood counts are low to prevent infection or bleeding.

Questions you should ask your healthcare provider:

1. How can MDS or the side effects of treatment affect my sexual activity?
2. Describe any changes in your sexual function.
3. What could be causing the change in my sexual ability?
4. Decreased sexual drive: not wanting sex
5. Dryness with intercourse: vaginal dryness
6. Fear of sexual contact: scared to be touched
7. Lack of erection: unable to obtain or maintain penis fullness during sex
8. Lack of orgasm: lack of complete satisfaction
9. Are there any precautions I need to take while on treatment?
10. Pain with intercourse: pain that occurs during sexual activity
11. What referral might be helpful in addressing my sexuality and intimacy concerns?
12. Is it safe to get pregnant?

Additional resources:

Cancer.net: Sexual health <http://cancer.net/blog/2017-03/your-sexual-health-and-cancer-what-know-what-do>

Oncolink: Women's guide to sexuality

<https://www.oncolink.org/support/sexuality-fertility/sexuality/women-s-guide-to-sexuality-during-after-cancer-treatment>

Oncolink: Men's guide to sexuality

<https://www.oncolink.org/support/sexuality-fertility/sexuality/men-s-guide-to-sexuality-during-after-cancer-treatment>

The feeling that you are not able to get a good breath or are not getting enough oxygen can be alarming and uncomfortable. Shortness of breath, or dyspnea, may be a result of several underlying problems. In patients with MDS, anemia may predispose you to feeling short of breath with activity. Deconditioning due to inactivity may also predispose you to shortness of breath with activity.

Things you can do:

1. Keep a log of symptoms that you are concerned about. These can be tracked in the MDS Manager Symptom Tracker. Discuss these with your healthcare team.
2. Track your blood counts using MDS Manager. Discuss when a transfusion may be of benefit to you if you are anemic with your healthcare team.
3. Keep all your appointments as scheduled.
4. If you experience shortness of breath suddenly and this does not resolve with rest, there may be a more severe problem, and this will need to be reported immediately to your healthcare provider.
5. Stay active.
6. Get enough rest.
7. Practice deep breathing exercises.

Additional resources:

Cancer.net: Shortness of Breath or Dyspnea

www.cancer.net/navigating-cancer-care/side-effects/shortness-breath-or-dyspnea

American Cancer Society: Shortness of Breath

www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/shortness-of-breath.html

Oncolink: Shortness of Breath <https://www.oncolink.org/support/side-effects/pulmonary-side-effects/shortness-of-breath-dyspnea>

Skin Changes including rash, pruritus

The most common skin changes for patients with MDS are injection site reactions due to the administration of Azacitidine. It is also possible to experience a rash with Lenalidomide.

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 the skin. Rash is generally caused by a skin irritation that can result from chemotherapy, allergy, infection, or skin problem.

Certain skin changes may indicate more severe skin infections, such as shingles.

Things you can do:

1. Examine your skin daily.
2. Report changes in your skin to your healthcare provider as soon as you notice them.
3. Avoid sun exposure and use sunscreens with a sun protection factor of at least 30.
4. Wear hats, sunglasses, and cover skin as much as possible.
5. Use mild, non-perfumed, non-deodorant soaps, such as Dove, Aveeno, or Neutrogena soaps.
6. Take showers or short, cool baths instead of long, hot showers.
7. Use lanolin-based creams, lotions and ointments regularly to keep your skin well hydrated.
8. Avoid perfumes.
9. Talk with your healthcare team about other supportive medications such as anti-histamines.

Additional resources:

Cancer.net: Rash www.cancer.net/sites/cancer.net/files/asco_answers_rash.pdf

American Cancer Society: Getting help for skin changes

www.cancer.org/content/dam/cancer-org/cancer-control/en/booklets-flyers/getting-help-for-skin-changes-english.pdf

Cancer Care: Rash: www.cancercare.org/tagged/rash

Oncolink: Nail and Skin Changes: <https://www.oncolink.org/support/side-effects/skin-hair-nail-side-effects>

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 tough 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.

How much sleep is enough? The general recommendation 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.

Things you can do:

1. Keep a log of symptoms that you are concerned about. These can be tracked in the MDS Manager Symptom Tracker. Discuss these with your healthcare team.
2. Keep all your appointments as scheduled.
3. Discuss problems sleeping with the healthcare team. Medications for anxiety, depression, and insomnia may be necessary.
4. If sleep is altered by symptoms related to MDS, discuss these symptoms with the healthcare team.
5. Keep regular bedtime and awakening hours.
6. Avoid stimulants and caffeine 2 hours prior to bedtime.
7. Eat light before bed
8. Avoid reading a backlit device in bed
9. Create dark, quiet and comfortable sleeping conditions
10. Help your body relax
11. Exercise for 30 minutes three to five times per week.
12. Limit daytime napping to 30 minutes.
13. Spend 30 minutes to an hour of quiet time prior to going to bed.

Additional resources:

Cancer.net: Sleep www.cancer.net/blog/2016-05/8-steps-restful-nights-sleep

American Cancer Society: Sleep Problems

www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/sleep-problems.html

Cancer Care: Sleep www.cancercare.org/tagged/sleep

Oncolink: Sleep disturbances www.oncolink.org/support/side-effects/insomnia

Spirituality is an important aspect of living with cancer, including MDS. There is a growing body of evidence indicating that spiritual practices are associated with better health and wellbeing.

Spirituality is a broad concept that is defined in several ways. In general, it includes a sense of connection to something larger than us, and it typically involves a search for meaning in life. As such, it is a universal human experience—something that touches us all.

Some may find that their spiritual life is intricately linked to their association with a church, temple, mosque, or synagogue. Others may pray or find comfort in a personal relationship with God or a higher power. Still others seek meaning through their connections to nature or art or other aspects of their life or environment.

Things you can do:

1. Discuss your spirituality and beliefs with your healthcare provider. They may direct you to other resources within the care environment to help you.
2. Many cancer centers have programs for supportive care or integrative medicine that include classes for meditation, yoga, and mindfulness.
3. Journaling may help you with reflection.
4. If you are a member of a church, temple, mosque, synagogue or other religious organization, speak to the leaders of your organization about resources available to you.
5. Maintain friendships and activities as much as possible. Connections to others is important to your overall health. This can be by phone, using digital media, or in person.

Additional resources:

American Cancer Society: Sources of Support

www.cancer.org/treatment/understanding-your-diagnosis/advanced-cancer/sources-of-support

Cancer Care: Spirituality www.cancercare.org/tagged/spirituality

Oncolink: Spirituality

<https://www.oncolink.org/support/practical-and-emotional/integrative-therapies-spirituality/addressing-spiritual-concerns-across-the-cancer-continuum>

Cancer Care

www.cancercares.org/publications/303-transportation_resources

Here are other organizations that provide transportation resources for individuals affected by cancer.

Air Charity Network

877-621-7177 www.aircharitynetwork.org

Air Charity Network serves all 50 states and provides free flights to people in need of medical treatment.

American Cancer Society's Road to Recovery Program

800-227-2345 <https://www.cancer.org/treatment/support-programs-and-services/road-to-recovery.html>

Some local chapters of the American Cancer Society may offer volunteers to drive patients to and from treatment.

Angel Wheels to Healing

800-768-0238 www.angelwheels.org

Angel Wheels to Healing provides non-emergency, long distance ground transportation to financially disadvantaged patients for treatment.

Fisher House Foundation

www.fisherhouse.org

Fisher House Foundation operates a network of comfort homes where military and veterans' families can stay at no cost while a loved one is receiving treatment. Their Hero Miles program uses donated frequent flyer miles to bring family members to the bedside of ill service members.

Good Days

877-968-7233 www.mygooddays.org

Good Days helps patients with chronic medical conditions who have limited financial means with transportation.

The Patient Travel Referral Program

www.patienttravel.org

The Patient Travel Referral program, a program of Mercy Medical Angels, provides information about all forms of charitable, long-distance medically-related transportation and provides referrals to all appropriate sources of help available in the national charitable medical transportation network.

The most common urinary symptoms in older adults are incontinence, difficulty urinating or pain with urination. These symptoms may indicate an underlying problem such as infection, or prostate enlargement. In some cases, these are normal changes of aging.

Things you can do:

1. Keep a log of symptoms that you are concerned about. These can be tracked in the MDS Manager Symptom Tracker. Discuss these with your healthcare team.
2. Keep all your appointments as scheduled.
3. If you are experiencing severe pain with urination, are unable to urinate, or have blood in your urine, contact your healthcare provider immediately.
4. If you're experiencing urinary incontinence or need to get up frequently during the night to urinate, ask about a referral to a urologist.
5. If you are getting up frequently during the night to urinate, be certain that there is a night light and that hallways are well lit. Make sure there are no throat drugs or other items that you may trip over when getting up to the bathroom.

Additional resources:

Cancer.net: Urinary incontinence www.cancer.net/navigating-cancer-care/side-effects/urinary-incontinence

Oncolink: Incontinence www.oncolink.org/support/side-effects/incontinence

It is very important to talk with your healthcare 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

Acute

Sudden, such as a sudden onset of symptoms or diseases.

Acute Myeloid Leukemia (AML)

A cancer of blood cells. AML happens when very young blood cells (blasts) in the bone marrow fail to mature normally. More blast cells are produced than needed, so there is not enough room within the marrow for other normal blood cells to develop, such as red blood cells or platelets. Some cases of MDS may develop into AML. However, most do not.

Synonyms: acute myeloblastic leukemia, acute myelocytic leukemia

Allogeneic Stem Cell Transplant

A procedure where bone marrow stem cells are taken from a genetically matched donor (a brother, sister, or unrelated donor) and given to the patient through an intravenous (IV) line. Over time, donated stem cells start making new, healthy blood cells.

Anaphylaxis

A very severe allergic reaction to a foreign protein, such as in a bee sting, or to a medicine. This reaction causes the blood pressure to drop and may cause difficulty breathing. Emergency treatment is required to manage these symptoms. If very severe, anaphylaxis can progress to shock.

Synonym: anaphylactic shock

Anemia

A condition in which the number of red blood cells is below normal. This may result in fatigue, generalized weakness and shortness of breath.

Antibiotics

Medications used to treat bacterial infections and other similar microorganisms.

Antibodies

Proteins produced by plasma cells in response to foreign substances in the body.

Anticoagulant

See blood thinner.

Anti-thymocyte globulin (ATG)

An extract of the serum of horses and rabbits that have been immunized against certain human cells; used in the treatment of aplastic anemia.

Apheresis

A procedure in which blood is taken from a person, and part of that blood component (such as white blood cells, red blood cells, or plasma) is separated out, and the remaining blood components are reinfused back into the donor.

Aplastic Anemia

A rare and serious condition in which the bone marrow does not make enough blood cells: red blood cells, white blood cells, and platelets. Anemia is a condition that happens when the red blood cell count is low. Most scientists believe that aplastic anemia happens

when the immune system attacks the bone marrow stem cells.

Aplastic anemia can be acquired (begin any time in life) or can be hereditary (less common, passed down from parent to child).

Synonyms: acquired aplastic anemia, hereditary aplastic anemia

Apoptosis

Programmed cell death. This means, if cells are no longer needed, they commit suicide by activating an intracellular death program. This is a natural process.

Autoimmune Disease

Any condition that happens when the immune system attacks the body's own normal tissues. The immune system is a complex organization within the body that is designed normally to "seek and destroy" invaders of the body, including infectious agents.

Basic Research

The study of a subject to increase knowledge and understanding about it. The goal of basic research in medicine is to better understand disease. In the laboratory, basic research scientists study changes in cells and molecules linked to disease. Basic research helps lead to better ways of diagnosing, treating, and preventing disease.

Basophil

A type of white blood cell that plays a role in allergic reactions.

Benzene

A chemical that is widely used by the chemical industry to make plastics, resins, nylon and synthetic fibers. Benzene is found in tobacco smoke, vehicle emissions, and gasoline fumes. Exposure to benzene may increase the risk of developing a bone marrow failure disease. Benzene can affect human health by causing bone marrow stem cells not to work correctly.

Bilirubin

(bil-i-ROO-bun) A reddish yellow substance formed when red blood cells break apart. It is found in the bile and in the blood. Yellowing of the skin and eyes can occur with high levels of bilirubin. Also called total bilirubin.

Biologic Agent

A substance made from a living system, such as a virus, and used to prevent or treat disease. Biological drugs include antibodies, globulin, interleukins, serum, and vaccines. Also called a biologic or biological drug.

Synonyms: biologic, biological drug

Blast Cells

Immature blood cells that would normally become fully functional mature red cells, white cells, or platelets. The number of blast cells in the bone marrow helps define how severe MDS is in a person. When 20 or more out of 100 cells in the bone marrow are blasts, this is considered acute myeloid leukemia (AML).

Synonym: precursor cell

Blood Clot

A clot or small cluster of blood cells that forms when platelets stick together. A combination of platelets and fibrin that form a mesh with the intention of preventing bleeding in response to an injury or illness. The term thrombus describes a blood clot that develops and attaches to a blood vessel. Blood clots are more common in Paroxysmal Nocturnal Hemoglobinuria (PNH) or in people with blood clotting disorders.

Synonym: thrombus

Blood Tests

Blood samples drawn from a vein, usually the arm, that are evaluated for cell counts (red cells, white cells [and their subtypes], and platelets). The blood is also evaluated for the shape and size of the different blood cells and for how various organs are functioning such as the kidneys and liver.

Blood Thinner

A medicine used to treat or prevent blood clots. Also called anticoagulants. Some common blood thinners are enoxaparin or clexaine (Lovenox or Clexane), heparin (Calciparine or Liquaemin), and warfarin (Coumadin).

Synonyms: anticoagulant, anti-clotting

Blood Transfusion

A procedure in which whole blood or one of its components is given to a person through an intravenous (IV) line into the bloodstream. A red blood cell transfusion or a platelet transfusion can provide temporary improvement for some patients with low blood counts.

Bone Marrow

The soft, sponge-like tissue in the center of bones that functions like a factory to produce white blood cells, red blood cells, and platelets.

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.

Bone Marrow Aspiration

The process of removing bone marrow from a specific area using a small needle and syringe. Used for diagnostic purposes. Tests may also be run on the bone marrow cells to look for any genetic abnormalities.

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. 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.

Synonym: Bone Marrow Trephine Biopsy

Bone Marrow Failure

A condition that occurs when the bone marrow stops making enough healthy blood cells. The most common of these rare diseases are myelodysplastic syndromes (MDS), aplastic anemia, and paroxysmal nocturnal hemoglobinuria (PNH). Bone marrow failure can be acquired (begin any time in life) or can be hereditary (less common, passed down from parent to child).

Bone Marrow Transplant (BMT)

A procedure where bone marrow stem cells are collected from the donor and given to the patient through an intravenous (IV) line. In time, donated stem cells start making new, healthy blood cells.

CD 55 and CD 59

Protein antibodies

Cellularity

How much of the bone marrow volume is occupied by various types of blood cells.

Chemotherapy

The use of medicines that kill cells (cytotoxic agents). People with high-risk or intermediate-2 risk myelodysplastic syndrome (MDS) may be given chemotherapy. Chemotherapy may also hurt healthy cells causing side-effects. If chemotherapy works in controlling abnormal cells, then relatively normal blood cells will start to grow again. Chemotherapy agents include: cytarabine (Ara-C) and hydroxyurea (Hydrea), daunorubicin (Cerubidine), idarubicin (Idamycin), and mitoxantrone (Novantrone).

Chronic Illness

A medical condition that lasts a long time. A chronic illness can affect a person's lifestyle, ability to work, physical abilities and independence.

Chromosomes

A structure that contains your genetic information, or DNA. Normally each person has 23 pairs of chromosomes.

Clinical Trial

A type of research study that tests how a drug, medical device, or treatment approach works in people. There are several types of clinical trials. Treatment trials test new treatment options. Diagnostic trials test new ways to diagnose a disease. Screening trials test the best way to detect a disease or health problem. Quality of life (supportive care) trials study ways to improve the comfort of people with chronic illness. Prevention trials look for better ways to prevent disease in people who have never had the disease. Trials are in four phases:

- **Phase I** tests a new drug or treatment in a small group to see if it is safe.
- **Phase II** expands the study to a larger group of people to find out if it works.
- **Phase III** expands the study to an even larger group of people to compare it to the standard treatment for the disease.
- **Phase IV** takes place after the drug or treatment has been licensed and marketed to find out the long-term impact of the new treatment.

Glossary

Clone

To make copies. Bone marrow stem cells clone themselves all the time. The cloned stem cells become mature blood cells that leave the bone marrow and enter the bloodstream. Abnormal clones are associated with cancers, such as MDS.

Coagulate

To thicken. Normal blood platelets cause the blood to coagulate and stop bleeding.

Combination Chemotherapy

The use of more than one drug during cancer treatments.

Comorbidities

Additional medical conditions beyond MDS.

Complement System

A group of proteins that move freely in the bloodstream. These proteins support (complement) the work of white blood cells by fighting infections.

Complete Blood Count (CBC)

The CBC measures the number of white blood cells (WBC) and the number and size of red blood cells, the total amount of hemoglobin, and the fraction of the blood made up of red blood cells.

Complex Karyotype

Three or more abnormalities in the chromosomes being evaluated.

Conditioning Treatment

Chemotherapy used to kill all remaining cancer cells before stem cell transplantation.

Cytogenetics

Testing that is performed on bonemarrow samples and examines the chromosomes of the cells. 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. Common abnormalities include:

- **Deletion 5q-** – deletion of chromosome 5
- **Deletion 20** – deletion of chromosome 20
- **Deletion Y** – deletion of the Y chromosome
- **Monosomy 7** – loss of one of the two 7 chromosomes
- **Trisomy 8** – addition of a third chromosome 8

Synonyms: Chromosomes, Karyotype, DNA

Cytogenetic Remission

No sign of previously detected abnormal chromosomes are found. This represents a response to treatment. When a bone marrow test is performed on a patient with 5q deletion MDS, and there are no signs of an abnormal chromosome 5, then that patient has achieved a cytogenetic remission. Also called cytogenetic response.

Cytokines

Proteins

Cytopenia

A deficiency of (or too few) mature cells in the blood. Deficiencies can occur in red cells, white cells, and/or platelets.

Cytotoxic Agent

A medicine that kills certain cells. Chemotherapy for MDS patients often involves the use of cytotoxic agents.

D-dimer

A test that helps doctors find out if a person has a problem with blood clotting.

del(5q)

Deletion in the long (q) arm of chromosome 5.

De Novo

The original source of disease, something present at the start. MDS may be de novo, the original source of disease, or treatment related, caused from chemotherapy or radiation given for other forms of cancer.

Differentiation

The process of cells maturing to become healthy adult cells of a particular type (i.e. red cells, white cells, and platelets).

Dietary Supplement

Vitamins, minerals, herbs and other substances meant to improve your nutritional intake. Dietary supplements are taken by mouth in the form of a pill, capsule, tablet or liquid.

DNA Methylation

A process that helps control gene activity, resulting in blockage of cell growth.

Dysplasia

Abnormal shape and appearance or morphology, of a cell.

Synonym: dysplastic

Embolus

A blood clot or other foreign matter that gets into the bloodstream and gets stuck in a blood vessel.

Engraftment

Refers to how well a graft (donor cells) is accepted by the host (the patient) after a bone marrow or stem cell transplant. Several factors contribute to better engraftment – physical condition of the patient, how severe the disease is, type of donor available, age of patient. Successful engraftment results in new bone marrow that produces healthy blood cells.

Epidemiology

The study of patterns and causes of disease in groups of people. Researchers who study how many people have a disease, how many new cases are diagnosed each year, where patients are located, and environmental or other factors that influence disease, are known as Epidemiologists.

Erythroid Response

- In patients who have not received red blood transfusions—hemoglobin increase of 1.5 g/dl
- In those who have had transfusions—reduction in transfusions by at least four units of packed red blood cells over 8 weeks compared with the 8 weeks before treatment

Erythrocyte

(i-RITH-ruh-site) See red blood cell.

Erythropoietin (EPO)

A protein substance naturally manufactured by the kidneys in response to low oxygen levels in body tissues. Erythropoietin stimulates the production of red blood cells in the bone marrow.

Erythropoietin-stimulating Agent (ESA)

A medicine used to help the bone marrow make more red blood cells. Epoetin alfa (Epogen, Procrit) and darbepoetin alfa (Aranesp) are erythropoiesis-stimulating agents that can help boost the red blood cell count of some bone marrow failure patients. These medicines are given via an injection. Also called red blood cell growth factor.

Eosinophil

A type of white blood cell that kills parasites and plays a role in allergic reactions.

Etiology

The cause or origin of a disease.

FAB Classification

A criteria used for classifying different types of myelodysplastic syndromes (MDS). The FAB (French, American, British) Classification System was developed by a group of French, American and British scientists. This system is based on 2 main factors: the percentage of blast cells in bone marrow, and the percentage of blast cells in the bloodstream. The FAB system is somewhat outdated, but is still used by some doctors today. The World Health Organization (WHO) Classification System has largely replaced the FAB Classification System.

Fanconi Anemia

A rare inherited disorder that happens when the bone marrow does not make enough blood cells: red cells, white cells, and platelets. Fanconi anemia is diagnosed early in life. People with Fanconi anemia have a high likelihood of developing cancer. Genetic testing is used to diagnose Fanconi anemia.

Fatigue

A feeling of low or no energy, general feeling of tiredness with normal activity. Rest does not necessarily resolve fatigue.

Synonyms: tired, exhaustion, lethargy, malaise

Ferritin

A protein inside of cells that stores iron for later use by your body. Sometimes ferritin is released into the blood. The ferritin level in the blood is called serum ferritin.

Fibrosis

Scarring of tissue. Fibrosis of the bone marrow is a feature seen in some types of unclassified myelodysplastic syndrome (MDS).

Flow Cytometry

A laboratory test that gives information about cells, such as size, shape, and percentage of live cells. Flow cytometry is the test doctors use to assess for specific proteins on the surface of blood cells. It is the standard test for confirming a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH).

Synonyms: Flow, Immunophenotyping, Fluorescence-activated cell sorting (FACS)

Fluorescence In Situ Hybridization (FISH)

An important laboratory test used to help doctors look for chromosomal abnormalities and other genetic mutations. Fluorescence in situ hybridization, also called FISH, directs colored light under a microscope at parts of chromosomes or genes. Missing or rearranged chromosomes are identified using FISH.

Folate

A B-vitamin that is found in fresh or lightly cooked green vegetables. It helps the bone marrow make normal blood cells. Most people get enough folate in their diet. Doctors may have people with paroxysmal nocturnal hema-globinuria (PNH) take a man-made form of folate called folic acid.

Gene Expression

The process that genes use to make their products, such as proteins.

Graft-Versus-Host Disease (GVHD)

Attack by transplanted cells on the recipient's body in which the transplanted cells cause inflammation of some normal tissues.

- **Acute:** within 3 months of transplantation
- **Chronic:** starting more than 3 months after transplantation

Graft-Versus-Leukemia Effect

T cells (part of the immune system) in the donated stem cells can attack the remaining cancer cells.

Granulocyte

Any one of these three types of white blood cells - neutrophils, eosinophils, and basophils. These cells have granules that contain enzymes to help fight infection.

Growth Factor

A substance made by the body that stimulates the bone marrow to produce blood cells. Some growth factors are man-made in the laboratory and used for treating low blood counts. These include red blood cell growth factors called erythropoietin (EPO) and darbepoetin, and white blood cell growth factors called granulocyte colony stimulating factors (GCSF) and granulocyte macrophage colony stimulating factors (GMCSF). Also called cytokines.

Haploidentical Stem Cell Transplantation

The donor's blood markers match half the patient's markers.

Hematocrit (HCT)

Percent of the total blood volume that is made up of red blood cells. In men a normal hematocrit is 40–52% while in women the normal is 36–46%. Hematocrit is part of a complete blood count. Also called HCT, packed cell volume, PCV. (see red blood cells)

Synonyms: packed cell volume, PCV

Hematologist

A doctor who specializes in the diseases and disorders of blood.

Hematopoiesis

The formation and development of blood cells.

Glossary

Hemochromatosis

A condition that occurs when the body absorbs and stores too much iron. This leads to a condition called iron overload. In the United States, hemochromatosis is usually caused by a genetic disorder. Organ damage, particularly to the liver and heart, can occur if iron overload is not treated.

Hemoglobinuria

(hee-muh-gloe-buh-NYOOR-ee-uh) The presence of hemoglobin in the urine.

Hemolytic Anemia

Anemia due primarily to the excessive hemolysis or destruction of red blood cells.

Hemolysis

The destruction of red blood cells.

HLA

See human leukocyte antigen.

Hormone

A part of the body's system that serves as chemical messengers. Hormones move through the bloodstream to transfer information and instruction from one set of cells to another.

Human Leukocyte Antigen

(LEW-kuh-site ANT-i-jun) One of a group of proteins found on the surface of white blood cells and other cells. These antigens differ from person to person and are responsible for balancing the immune system. A human leukocyte antigen test is done before a stem cell transplant to closely match a donor and a recipient. Also called HLA.

Hypercellular

A condition in which there are too many cells within the bone marrow.

Hypocellular

A condition in which there are too few cells, within the bone marrow. Patients with aplastic anemia have hypocellular bone marrow.

Hypomethylating Agent

A hypomethylating agent is a drug that inhibits DNA methylation. Works by preventing certain genes involved in controlling cancer from being silenced, allowing for the normal functioning of the tumor suppressor genes.

Synonym: demethylating agent

Idiopathic

Usually refers to any condition with no known cause.

Immature Blood Cells

May be called stem cells, progenitor cells or blasts.

Immune Deficiency

A decreased ability of the immune system to fight infection.

Immune System

The complex group of organs and cells that defend the body against infection and disease.

Immunocompromised

Occurs when the immune system is not functioning properly, leaving the patient open to infection. A person can be immunocompromised due to low white blood cell count or due to some medicines.

Synonym: immune compromised

Immunosuppressive Drug

Drugs that lower the body's immune response in autoimmune diseases. These drugs may be used to allow the bone marrow stem cells to grow and make new blood cells. ATG (antithymocyte globulin) or ALG (antilymphocyte globulin) with cyclosporine are used to treat bone marrow failure in aplastic anemia. Immunosuppressive drugs may help some patients with myelodysplastic syndromes (MDS) and paroxysmal nocturnal hemoglobinuria (PNH).

Intravenous Infusion

A method of getting fluids or medicines directly into the bloodstream over a period of time. Also called IV infusion.

Synonym: IV infusion

Investigational New Drug

A new drug, antibiotic drug, or biological drug that is used in a clinical trial. It also includes a biological product used in the laboratory for diagnostic purposes. Also called IND. In the USA these drugs are not approved by the FDA.

IPSS/IPSS-R

International Prognostic Scoring System – system for grading the severity of MDS. The system turns patient information into a score. The score helps predict what may happen with the patient's MDS in the future.

Iron Chelation Therapy

A drug therapy to remove extra iron from the body. Patients with high blood iron (ferritin) levels may receive iron chelation therapy. The U.S. Food and Drug Administration (FDA) has approved two iron chelators to treat iron overload in the U.S.: deferasirox, an oral iron chelator, and deferoxamine, a liquid given by injection, these may differ depending on which country you live in.

Iron Overload

A condition that occurs when too much iron which is acquired from blood transfusions accumulate in the body. Patients who need regular red blood cell transfusions are at risk for iron overload. Organ damage can occur if iron overload is not treated.

Ischemia

Occurs when the blood supply to a specific organ or part of the body is cut off, causing a localized lack of oxygen.

Lactate DeHydrogenase

(LAK-tate dee-high-DROJ-uh-nase) An enzyme found in the blood and in many of the body's organs. High levels of LDH in the blood can mean that red blood cells are breaking apart (hemolysis) or that there is tissue damage in the body. It is important for patients with paroxysmal nocturnal hemoglobinuria (PNH) to have their LDH monitored regularly. Also called lactic dehydrogenase, LDH.

Leukocyte

(LEW-kuh-site) See white blood cell.

Lymphatic System

A network of organs, lymph nodes, lymph ducts, and lymph vessels that help keep the body's fluids in balance and help the body fight infection.

Glossary

Lymphocyte

A type of white blood cell. B lymphocytes, or B cells, help make special proteins called antibodies that fight bacteria and viruses (immune response). T lymphocytes, or T cells, help kill tumor cells and help the body's immune response.

Matched Related Donor

A bone marrow/stem cell donor that is a sibling or another family member to the patient.

Mean Corpuscular Volume

A measurement of the average size of a person's red blood cells. If the mean corpuscular volume is high, the red blood cells are larger than normal (macrocytic). If the mean corpuscular volume is low, the red blood cells are smaller than normal (microcytic). Also called MCV.

Megakaryocyte

A large bone marrow cell that makes platelets, necessary for normal blood clotting.

Mini Transplant (aka reduced intensity transplant)

A procedure similar to standard bone marrow transplant. The mini transplant uses a reduced form of chemotherapy pre-treatment. This reduces side effects caused by chemotherapy, making it more tolerable to older adults. It does not reduce the risk of graft-versus-host disease. Also called nonmyeloablative transplant.

Minimal Residual Disease

Small numbers of cancer cells that stay in the body after treatment and can be measured. Also called MRD.

Monosomy 7

Describes the loss of one of the two number 7 chromosomes. "Mono" means one and "somy" comes from the word chromosome. Bone marrow samples are used to detect monosomy 7 and other genetic abnormalities. Monosomy 7 can occur in adult patients with MDS and can occur in childhood bone marrow failure diseases.

Monoclonal Antibody

A type of protein called an antibody that is engineered to look for a specific substance in the body. There are many kinds of monoclonal antibodies. Each one looks for only one substance. Eculizumab (Soliris) is a monoclonal antibody that may be prescribed to treat patients with paroxysmal nocturnal hemoglobinuria (PNH).

Monocyte

A large white blood cell. Monocytes move through the blood to the tissues where they become macrophages. Macrophages are immune cells that surround and kill germs such as bacteria and viruses.

Morphology

The study of the structure and form of an organism or one of its parts.

Multilineage Dysplasia

Abnormalities in more than one type of blood cell

Mutation

Any change or alteration in a normal gene. A mutation may cause disease or may be a normal variation. Examples of mutations are deletions or additions of genetic material.

Myelo

A Greek word meaning marrow.

Myelodysplastic Syndromes (MDS)

The Myelodysplastic Syndromes (MDS) are a group of bone marrow failure disorders. Myelo refers to the bone marrow. Dysplastic means abnormal looking cells. In MDS, the bone marrow does not make blood cells normally. The result is too few cells or low blood counts (cytopenias) and cells that have an abnormal form and 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)

Natural Killer Cells

A type of cell that lacks B-cell and T-cell receptors and attacks mutant and virus-infected cells.

Neutropenia

A deficiency (below-normal number) of mature white blood cells called neutrophils that assist in fighting bacterial infections.

Neutropenic Diet

A diet that can be recommended for a patient with very low white blood cell count. A neutropenic diet avoids the use of certain foods that can contain bacteria or fungus, such as raw meats, unpasteurized dairy products, aged cheeses, fermented drinks, and unwashed fruits and vegetables. The concern is the food be "safe" for a patient with low WBC count.

Occlusion

Obstruction; blockage.

Off Label Drug

An approved medicine that is prescribed by a licensed healthcare professional for a purpose other than that for which it was approved by the U.S. Food and Drug Administration (FDA).

Oncologist

A doctor who specializes in the treatment and prevention of cancer.

Over-the-Counter (OTC) Medicine

A medicine that is available without a prescription from the doctor. Also called OTC medicine.

Packed RBCs

A concentrated blood product in which most of the plasma, the fluid part of blood, is removed to make red blood cell transfusions easier and faster.

Pancytopenia

A reduced number of all types of blood cells – red blood cells, white blood cells, and platelets.

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Paroxysmal Nocturnal Hemoglobinuria (PNH)

A rare and serious blood disease that causes red blood cells to break apart. Paroxysmal means sudden and irregular. Nocturnal means at night. Hemoglobinuria means hemoglobin in the urine. Hemoglobin is the red part of red blood cells. A person with PNH may have episodes of dark urine in the morning, but this symptom is not present in all PNH patients.

Pathophysiology

Abnormal function or processes that cause or are associated with disease or injury.

Pediatric MDS

MDS is rare in children; but it does happen.

Peripheral Blood Stem Cell (PBSC) Transplant

A procedure where stem cells are collected from the donor's circulating (peripheral) blood. These stem cells are then given to the patient through an intravenous (IV) line. In time, donated stem cells start making new, healthy blood cells. Also called PBSC transplant. This is the most common type of stem cell transplantation that occurs.

Petechiae

Small, flat red or purplish spots caused by pinpoint bleeding into the skin. It is often a sign of a low platelet count.

Phagocyte

A type of white blood cell that surrounds and kills microorganisms, such as bacteria and fungi. They also remove dead cells. Monocytes, macrophages, and neutrophils are phagocytes.

Pharmacist

A highly trained and licensed professional whose job concerns the preparation, distribution, and use of prescription drugs. A pharmacist also can advise patients, as well as physicians and other health practitioners, on the selection, dosages, interactions, and side effects of medications.

Placebo

A placebo is an inactive pill, liquid, or powder that has no treatment value. Placebo use in clinical trials is extremely uncommon today.

Platelets

Irregularly shaped, colorless cells that are present in blood. Their sticky surface lets them, along with other substances, form clots to stop bleeding. Also called thrombocytes.

Platelet Transfusion

A procedure in which platelets are given to a person through an intravenous (IV) line into the blood-stream. Platelets are more likely than red blood cells to cause an immune response, such as chills and fever. The use of platelets from one donor (apheresis) reduces the chance of reaction to transfused platelets. Transfused platelets increase the blood platelet count and help control bruising and bleeding.

Prophylactic

Something that prevents or protects. For example, blood thinners may be given as a prophylactic measure to prevent blood clots in high risk patients.

Protocol

An action plan that describes what will be done in a clinical trial and how it will be carried out. This plan is reviewed and approved by a committee at each place doing the clinical trial. This committee is known as the Institutional Review Board.

Pulmonary Embolism

A blockage of an artery that carries blood to the lungs. See Embolus.

Pure Red Cell Aplasia (PRCA)

A condition that occurs when the bone marrow stem cells do not make red blood cells. Red blood cell counts are low. White blood cell and platelet counts are normal.

Red Blood Cell

The most numerous type of blood cell in healthy people. Red blood cells contain hemoglobin, a protein that picks up oxygen in the lungs and brings it to cells in all parts of the body. Also called erythrocyte, RBC.

Red Blood Cell Growth Factor

See erythropoietin-stimulating agent.

Red Blood Cell (RBC) Transfusion

A procedure in which packed red blood cells are given to a person through an intravenous (IV) line into the bloodstream. Transfused red blood cells increase the blood count and help improve symptoms of anemia. Before transfused blood is given, donated blood is typed and cross matched to the recipient's blood. Also called RBC transfusion.

Reduced Intensity Transplant

Also called "mini-transplant". A procedure similar to standard stem cell transplant. The mini transplant uses a reduced form of chemotherapy pre-treatment. This reduces side effects caused by chemotherapy, making it more tolerable to older adults. It does not reduce the risk of graft-versus-host disease. Also called nonmyeloablative transplant.

Refractory

Not responsive to treatment or cure. For example, refractory anemia is a low red blood cell count that doesn't respond to standard treatments.

Reticulocyte

An immature red blood cell. Reticulocytes are normally found in bone marrow. They are present in the bloodstream only in very low numbers.

Remission

Disappearance of the signs and symptoms of cancer. A remission may be complete (CR) or partial (PR).

Revised IPSS (IPSS-R)

More recent MDS scoring system. It uses additional information than the IPSS and categorizes patients into five risk groups instead of four.

Ring Sideroblast

(SID-uh-ruh-blast) A red blood cell that has too much iron. The iron typically forms a ring around the cell's nucleus.

Secondary MDS

A type of MDS that is caused by a previous treatment for another

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disorder or disease. Treatments typically associated with secondary MDS include radiation therapy and chemotherapy used to treat cancer. Also called therapy-related MDS, T-MDS.

Synonyms: T-MDS, therapy-related MDS

Serum Erythropoietin

Amount of erythropoietin that is present normally in an individual's blood. It can be measured in the blood.

Serum Sickness

An immune system reaction to foreign proteins in certain medicines. Serum sickness can be a side effect of ATG, a medication used in the treatment of aplastic anemia, causing fever, rash, joint pain, and muscle aches.

Single Lineage Dysplasia

Abnormalities in only one type of blood cell.

Social Worker

A licensed professional trained to help people manage their daily lives, understand and adapt to changes in health and lifestyle. A social worker also will help people find appropriate community resources, healthcare, legal resources, and government assistance.

Somatic Mutation

Change in a DNA that happens after conception in a patient's cells, is not inherited, and is not passed on to the patient's children.

Stem Cells

Cells in the body that develop into other cells. Adult stem cells in the body repair and maintain the organ or tissue in which they are found. Blood forming (hematopoietic) stem cells are found in the bone marrow. These cells make copies of themselves and can also develop into red cells, white cells, and platelets. These are the cells used in stem cell transplantation. Embryonic stem cells come from human embryos and may be used in medical research. Embryonic stem cells are not approved for treatment.

Stem Cell Transplant (SCT)

A procedure where blood-forming (hematopoietic) stem cells are taken from a healthy donor. They enter the patient's bloodstream through an intravenous (IV) needle and make their way into the bone marrow. The donor cells are called a graft. There are three sources of stem cells – bone marrow, cord blood, and circulating (peripheral) blood. The most common source for MDS is peripheral blood stem cells.

Subcutaneous Injection

A method of giving medicine in the fatty tissue area under the skin using a short needle.

Synonyms: shot, injection

Supportive Care

Care given to improve the quality of life, or comfort, of a person with a chronic illness. Supportive care treats the symptoms rather than the underlying cause of a disease. The goal is to help the patient feel better. Patients with low blood counts may be given blood transfusions as supportive care to help manage the symptoms of their disease. Also called palliative care, symptom management.

Synonyms: palliative care, symptom management

T cell

See lymphocyte

T lymphocyte

See lymphocyte

Therapy-Related MDS

See Secondary MDS

Thrombus

A blood clot that develops and attaches to a blood vessel.

Thrombosis

The process of forming a blood clot.

Thrombocytopenia

A condition in which the number of mature platelets, or thrombocytes, is below normal. When severe, the tendency to bruise and bleed more easily can occur.

Transfusion

Process by which blood or one of its components (e.g., red blood cells, plasma, platelets) is delivered directly into the bloodstream by vein (intravenous or IV), similar to other IV medications.

Transfusion Independence

No longer needing any type of blood transfusion.

Treatment Failure

Occurs when a patient does not respond to the treatment, responds only temporarily, or has to stop the treatment because of side effects.

Unrelated Donor

A donor that is not a sibling or other familial relation of the patient (recipient).

Venous thrombosis

Blood clot in a vein.

Vitamin B12

A complex vitamin found in animal products. Vitamin B12 helps maintain healthy red blood cells and nerve cells. A shortage of Vitamin B12 and folate can reduce blood cell production in the bone marrow. Also called B complex vitamins. Levels of B12 can be measured in the blood.

White Blood Cells (WBC)

Cells produced in the bone marrow and lymph nodes. White cells are key cells in the immune system that prevent or fight infection.

World Health Organization (WHO) Classification

The most current system for classifying leukemia and myelodysplastic syndromes (MDS), it was developed by the World Health Organization (WHO). This system is based on patient data from around the world and on the most up-to-date knowledge of MDS. WHO Classification of MDS consists of many subtypes based on tests of the blood and bone marrow.

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WHITE BLOOD CELLS

ANC (absolute neutrophil count)

A measure of the actual number of mature neutrophils in a given volume of blood.

Basophil

Type of white blood cell that plays a role in allergic reactions and asthma.

Eosinophil

Type of white blood cell that kills parasites and plays a role in allergic reactions.

Granulocyte

A term for any of the white blood cell types that have granules containing enzymes to help fight infection: neutrophils, eosinophils and basophils.

Lymphocytes

Small white blood cells produced in the lymphoid organs (the lymph nodes, spleen, thymus, and tonsils) or bone marrow that are essential for normal function of the immune system.

Monocyte

A white blood cell that helps the body fight infections from some bacteria such as tuberculosis.

Neutrophil

A type of white blood cell that functions to destroy bacteria. When the number of neutrophils is too low, the body is at greater risk for developing an infection.

BONE MARROW BIOPSY

Biopsy

A medical procedure to remove a small piece of solid bone marrow using a needle that goes into the marrow of the hip bone. The solid bone marrow is examined for cell abnormalities, the number of different cells, and checked for scarring of the bone marrow.

Iliac Crest

The hip bone area from which bone marrow samples are most commonly taken.

BONE MARROW TRANSPLANT

Allogeneic Stem Cell Transplantation

A procedure in which matched bone marrow or peripheral blood stem cells from a donor (usually related) are collected, stored, and infused into a patient (recipient) following high dose chemotherapy with or without radiation therapy. In time, donated stem cells given to the patient begin making new, healthy blood cells (known as engraftment).

Allograft

An allogeneic stem cell collection used for transplant.

Autograft

An autologous stem cell collection used for transplant.

Autologous Stem Cell Transplantation

A procedure in which a patient's own stem cells from bone marrow or peripheral blood are collected, stored, and reinfused following high dose chemotherapy or radiation therapy. In time, donated stem cells given to the patient begin making new, healthy blood cells (known as engraftment).

Bone Marrow Transplant

A procedure in which high doses of chemotherapy or radiation therapy are used to eradicate disease in the bone marrow and lymphatic system and then are replaced with healthy bone marrow from a donor or the patient.

Cord Blood Transplant

A procedure where umbilical cord stem cells are given to the patient through an intravenous (IV) line. Stem cells are collected from an umbilical cord right after the birth of a baby. They are kept frozen until needed. In time, donated stem cells given to the patient begin making new, healthy blood cells.

Donor Lymphocyte Infusion

Donor lymphocytes infusions (DLI) with or without Azacitidine may be used as a salvage treatment for acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) relapsing after allogeneic hematopoietic stem cell transplantation (HSCT).

Engraftment

Refers to how well the donor cells (graft) are accepted by the patient's immune system (host) after a bone marrow or stem cell transplant. Several factors contribute to better engraftment: physical condition of the patient, how severe the disease is, type of donor available, age of patient. Successful engraftment results in new bone marrow that produces healthy blood cells (new white blood cells, red blood cells, and platelets).

Graft-Versus-Host Disease (GVHD)

GVHD is a common complication of allogeneic bone marrow/stem cell transplantation. It is caused when the donor's immune cells, now in the patient, begin to see the patient's body as foreign and mount an immune response. GVHD most commonly affects the recipient's skin, intestines, or liver. Severity can range from mild to very severe. In some cases, GVHD can be prevented or treated with specific drugs to suppress the body's immune cells (immunosuppressive drug therapy).

Human Leukocyte Antigen (HLA)

One of a group of proteins found on the surface of white blood cells and other cells. These antigens differ from person to person. A human leukocyte antigen test is done before a stem cell transplant to closely match a donor and a recipient.

Matched Related Donor

Bone marrow/stem cell donor that is a sibling or another blood relative to the patient.

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Mini-Transplant

See *Non-Myeloablative Transplant*

Myeloablation

The killing of bone marrow by radiation or chemotherapy. This term usually refers to the complete or near-complete destruction of the bone marrow.

Non-Myeloablative Transplant

Type of allogeneic stem cell or bone marrow transplant that uses lower doses of chemotherapy. This reduces side effects caused by chemotherapy, making it more tolerable for older adults. It does not reduce the risk of graft-versus host disease. Also called *nonmyeloablative transplant* or *reduced intensity transplant*.

Reduced Intensity Transplant

Procedure similar to standard bone marrow transplant. The reduced intensity transplant uses a mild form of chemotherapy pre-treatment. This reduces side effects caused by chemotherapy, making it more tolerable for older adults. It does not reduce the risk of graft-versus-host disease. Also called *nonmyeloablative transplant*.

Unrelated Donor

A donor that is not a sibling or other familial relation of the patient (recipient).

MEDICATIONS

Adverse Event (AE)

Any undesired actions or effects of a drug or treatment.

Synonyms: *side effect*, *toxicity*

Antibiotic Therapy (AB)

Used to treat bacterial infections or prevent recurrence of bacterial infections.

Antithymocyte Globulin (ATG)

An immunosuppressive medication that eliminates abnormally proliferating white blood cells called T lymphocytes which disrupt normal blood cell growth. This may restore normal production of red blood cells which may lead to transfusion independence. The three brand-name drugs are *Thymoglobulin*®, *Lymoglobulin*®, and *Atgam*®.

Azacitidine

Azacitidine is an injectable medicine that can be administered either subcutaneously using a syringe and a small needle inserted under the skin in the stomach or legs, like the technique used to administer insulin, or intravenously. Azacitidine is given for 7 days each month for most patients.

Colony-Stimulating Factor (CSF)

Protein that stimulates the development and growth of blood cells; sometimes called *growth factor*. *Granulocyte colony-stimulating factor* is a CSF that is used to stimulate stem cells from the bone marrow into the bloodstream prior to apheresis.

Corticosteroids

Also called "steroids," corticosteroids are powerful anti-inflammatory medicines used to treat many diseases and conditions. They are similar to a protein called cortisol that is made in the adrenal glands. Names of corticosteroids include prednisone and dexamethasone.

Synonym: *steroids*

Cytarabine (Cytosar-U®)

May be used for high intensity or low intensity treatment for newly diagnosed or relapsed AML and in some cases of MDS.

Dacogen™ (decitabine)

A medication used in treating some types of MDS and AML. *Dacogen* works by preventing certain genes involved in controlling cancer from being silenced, allowing for the normal functioning of genes within the body. It is a DNA hypomethylating agent that is administered intravenously (IV) or by mouth (*Inqovi*).

Decitabine + cedazuridine (Inqovi®)

An oral formulation of decitabine with an added agent that allows the drug to be given by mouth. It is approved for the treatment of patients with higher-risk MDS.

Desferal® (deferoxamine)

A medication that binds to iron and promotes its removal from the body for treatment transfusion dependent iron overload. It is an iron-chelating drug that is administered subcutaneously (under the skin).

Erythropoietin (EPO)

A "recombinant" form of a natural growth factor used to treat symptoms associated with anemia. It stimulates the bone marrow to produce red blood cells. The three brand-name drugs are *Aranesp*®, *Epogen*®, and *Procrit*®. These drugs are administered intravenously or subcutaneously.

Exjade® (deferasirox)

A medication that binds to iron and promotes its removal from the body for treatment of transfusion-dependent iron overload. It is an iron-chelating drug that is administered orally.

Growth Factors (hematopoietic)

A substance made by the body that stimulates the bone marrow to produce blood cells. Some growth factors are man-made in the laboratory and used for treating low blood counts. These include red blood cell growth factors called erythropoietin (EPO) and darbepoetin, and white blood cell growth factors called granulocyte colony stimulating factors (GCSF) and granulocyte macrophage colony stimulating factors (GMCSF). Also called *cytokines*.

Synonym: *cytokine*

JADENU™ (deferasirox)

A medication that binds to iron and promotes its removal from the body for treatment of transfusion-dependent iron overload. It is an iron chelating drug that is administered orally. It is a new oral formulation of *Exjade* tablets. Whereas the *Exjade* tablet must be

Glossary

mixed in liquid and taken on an empty stomach, Jadenu can be taken in a single step, with or without a light meal, simplifying administration of treatment for chronic iron overload.

Leukine® (sargramostim)

A growth factor, granulocyte macrophage colony-stimulating factor (GM-CSF), used for the treatment of neutropenia. It increases white cell production, which may help to reduce the likelihood of additional infection. It is administered subcutaneously.

Liposomal Cytarabine + Daunorubicin (Vyxeos®)

A form of high-intensity treatment used to treat certain types of MDS-MR.

Neupogen® (filgrastim)

A growth factor, granulocyte colony-stimulating factor (G-CSF), used for the treatment of neutropenia. It increases white cell production, which may help to reduce the likelihood of additional infection. It is administered subcutaneously.

Prednisone

A corticosteroid that is used for many reasons. It is prescribed when the body is not producing enough of this chemical on its own. It is sometimes prescribed with ATG treatment to reduce the risk of anaphylaxis or serum sickness. It helps by reducing the antibody production of the immune system and in treating various allergic conditions. There are many brand names of prednisone. (See corticosteroid)

Pyridoxine (Vitamin B6)

A vitamin needed to make red blood cells. It can be useful in improving red blood cell counts in sideroblastic anemia by increasing the red blood cell production.

Reblozyl® (luspatercept-aamt)

First erythroid maturation agent (EMA) approved by the FDA for the treatment of anemia in adult patients with myelodysplastic syndromes (MDS) who have been failed an erythropoiesis stimulating agent (ESA) or are unlikely to respond to an ESA, and are requiring transfusions of 2 or more red blood cell (RBC) units over 8 weeks.

In 2023, FDA approval was expanded to include first-line treatment for low- to intermediate risk myelodysplastic syndromes (MDS) patients without previous erythropoiesis stimulating agent (ESA) use who may require regular red blood cell transfusions.

Luspatercept may restore differentiation and maturation of red blood cells (normal development) in the last phase of erythroid cell (red blood cell) development in some patients with lower risk MDS.

Revlimid® (lenalidomide)

A medication that works by stimulating the immune system, preventing new blood vessel growth, and stimulating cell death. It is categorized as an immunomodulatory agent and is taken orally.

Thalomid® (thalidomide)

A medication that reduces the blood supply in the marrow, thereby working to limit the growth of abnormal blood cells. It also acts to interfere with other proteins (cytokines) that promote premature death of cells in the bone marrow. It's taken orally.

Vidaza™ (azacitidine, 5-azacytidine)

A medication that works by preventing a cellular process (methylation) that silences the genes involved in controlling the development of cancer. It may increase red blood cells, transfusion independence, hemoglobin, white blood cells, platelets, and/or decreases the amount of blast cells within the bone marrow. It is categorized as a DNA hypomethylating agent and can be administered intravenously (IV) or subcutaneously (under the skin).

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?

IRON OVERLOAD

Red Blood Cell Transfusions and Iron Overload	3
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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.

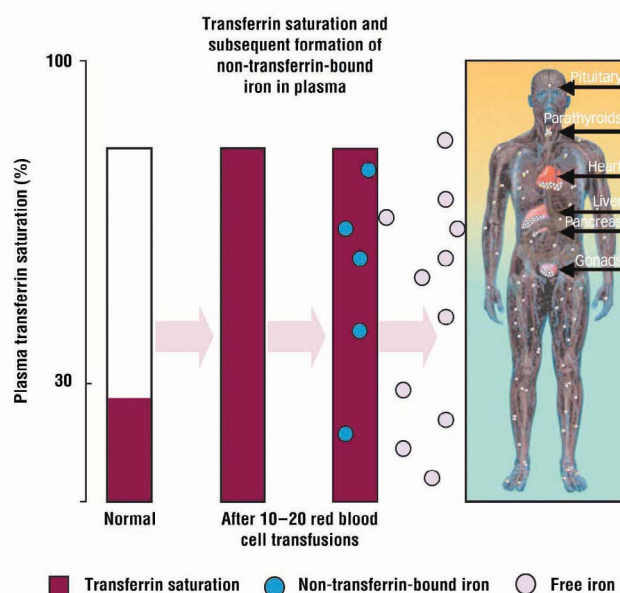
Red blood cell transfusion and iron overload

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.



References:

Shah, et. al. (2012) Management of Transfusion-Related Iron Overload in Patients with Myelodysplastic Syndromes. Clin J Oncol Nurs, 16 (suppl 1), 37–46.

How Serious Is Iron Overload?

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 including heart failure, cirrhosis and fibrosis of the liver, gallbladder disorders, diabetes, arthritis, depression, impotence, infertility, and cancer. In some cases, these conditions are not reversible and may be life-threatening.

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.

Management of iron overload and treatment of iron toxicity by iron chelation 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.

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.

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](#)). Patient with impaired kidney function or those with very low blood counts may not be eligible for chelation therapy.

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 (Most common method)	<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 (Limited use due to risk)	<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 (Used to evaluate abnormal liver enzymes in patients with elevated ferritin)	<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 (Used primarily to evaluate cardiac symptoms in patients with elevated ferritin)	<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 four iron chelating drugs available for MDS patients:

Property	Deferoxamine (Desferal®)	Deferasirox (Exjade®)	Deferiprone (Ferriprox®)	Deferasirox (Jadenu™)
Route of administration	Subcutaneous, intramuscular, or intravenous	Tablets for oral suspension	Oral	Oral tablets
Dose	25–50 mg/kg	Starting dosage: 20 mg/kg	75 mg/kg	Starting dosage: 14 mg/kg
Schedule	Administered over 8–24 hours daily for 3–7 days per week	Once daily	Three times per day	Once daily
Main route of excretion	Urine/feces	Feces	Urine	Feces

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 healthcare 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 healthcare 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 healthcare provider. Discuss any symptoms you have after starting chelation therapy with your healthcare 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.

Iron Chelating Drugs: Common Side Effects

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

What Can I Do to Avoid Iron Overload?

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

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. 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

Foundations and Organizations Specific to MDS

Myelodysplastic Syndromes Foundation, Inc.
www.mds-foundation.org

The MDS Alliance www.mds-alliance.org

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® (deferrioxamine) <https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/desferal.pdf>

Exjade® (deferisirox) www.exjade.com

Ferriprox® (deferiprone) www.ferriprox.com

Jadenu™ (deferisirox) www.jadenu.com

General Information

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

The Merck Manual Home Edition for Patients and Caregivers <https://www.merckmanuals.com/home>

Financial assistance

Novartis Patient Assistance Foundation

<https://www.pharma.us.novartis.com/our-products/patient-assistance/patient-assistance-foundation-enrollment>

<https://www.patientassistanzenow.com/>
800-277-2254

Diplomat Specialty Pharmacy Co-Pay Assistance Navigator Program

<https://www.diplomatpharmacy.com/resources/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)

THE MDS FOUNDATION, INC.

The MDS Foundation, Inc. is a global non-profit advocacy organization dedicated to serving MDS patients, their caregivers, and the professionals that are working to improve the lives of patients living with MDS. The MDS Foundation provides a number of educational materials which support the Building Blocks of Hope resource.

contributing authors

Lea Harrison
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THE MDS FOUNDATION, INC.

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About the MDS Foundation, Inc.

About the MDS Foundation, Inc.

The MDS Foundation is a global non-profit advocacy organization that for over 25 years has supported patients and their families as well as healthcare providers in the fields of MDS and its related diseases.

Our vision is that every MDS patient will benefit from our initiatives and research as early as possible.

Our mission is to support and educate patients, their communities, and healthcare providers, and contributes to innovative research in the fields of MDS and its related continuum of diseases to better diagnose, control and ultimately cure these diseases.

Patient Advocacy & Education

The first focus of the Foundation is patient advocacy, support and education. We provide extensive resources to patients and their families about MDS treatment options, upcoming clinical trials, and recent research so that they can make educated decisions about treatment and how to approach the disease. One such program is our Building Blocks of Hope® Patient and Caregiver Resource, which is an extensive print and online patient advocacy initiative that provides a personalized education program for the patient and caregiver to prepare, participate and LIVE with MDS. We also provide various printed and electronic patient resources and handbooks that are available in multiple languages.

The MDS Foundation partnered with SparkCures, LLC, to offer MDS patients, caregivers and healthcare professionals a custom platform that offers fast and personalized clinical trial screening and matching services, simplifying the complex landscape of clinical trial options for MDS patients. <https://www.mds-foundation.org/clinical-trials/>

In addition to the educational component, the MDS Foundation develops patient support groups, hosts Quality-of-Life Patient and Family Forums, and provides access to a full-time Patient Liaison who is available to advise and refer patients to the appropriate resources, studies, and/or specialists.

The Foundation provides patients with preferential referrals to MDS Centers of Excellence to ensure the best possible treatment.

Professional Education

In an effort to advance medical research and improve the quality of healthcare for MDS patients, we disseminate information to professionals about new treatment options and facilitate an informational exchange between healthcare providers. To do this, we host an MDS symposium preceding the annual American Society of Hematology (ASH) Congress Meeting, which allows us to directly educate more than 600 hematologists, with additional access to 20,000 hematologists throughout the full congress meeting.

We also hold a Biennial MDS International Congress. Since its inception, we have conducted 17 international educational symposia for healthcare professionals in Austria, England, the United States (Chicago, Washington DC), Spain (Barcelona, Valencia), Czech Republic, Sweden, France, Japan, Italy, Greece, Scotland, Germany, Denmark, Canada and France. The 18th International Congress on MDS will be held in Rotterdam, The Netherlands on May 7-10, 2025. For these congresses, we host an average of 800 healthcare professionals containing three workshops and meet-the-expert sessions dedicated to specific MDS-related research developments, scientific plenary sessions, which consist of abstract lectures, roundtables and debates, as well as an abstract poster viewing. We also offer the opportunity to include corporate satellite symposia, pharmacist and nursing sessions, as well as medical pipeline sessions.

During the off year from the International Congress, the Foundation hosts an MDS Regional Symposium. These symposia bring cutting edge MDS information to healthcare professionals around the world. Our first Regional Symposium was held in Brazil in 2018. In 2020 we hosted a Regional Symposium in Israel, in 2022 Uruguay and in 2024 Japan. These symposia allow us to reach MDS healthcare professionals worldwide.

In addition to these programs, the MDS Foundation also maintains an online Clinical Toolbox resource for healthcare professionals and provides educational support for investigators. This clinical toolbox includes a Learning Management System where professionals can earn continuing education credits.

About the Foundation

Global Working Groups

International Working Group for Prognosis in MDS (IWG-PM) – The objective of this group is to continue to refine the currently accepted and utilized prognostic scoring systems based on the current research discoveries. (Responsible for continued revisions to the International Prognostic Scoring System (IPSS) for MDS.)

MDS/MPN International Working Group (MDS/MPN IWG) – Developed to foster collaboration among translational scientists in the area of myeloid malignancy to better define, risk stratify, and treat patients with overlap syndrome. The overarching goal of this group is to identify key knowledge gaps in the area of MDS/MPNs (Myeloproliferative Neoplasms) and facilitate international, collaborative, translational science geared to rapidly improve our understanding of these neoplasms.

International Nurse Leadership Board (NLB) – Composed of more than 30 members worldwide, and includes three subcommittees: Professional Education, Patient Education, and Quality of Life.

Research

From 2012-2023, we have awarded more than \$650,000 in grants through our Young Investigator Grant program. These funds have helped to make great strides in research into areas such as aberrant mRNA splicing induced by ZRSR2 mutation in the pathogenesis of myelodysplastic syndromes, unraveling the role of alternative splicing in normal and MDS hematopoietic stem and progenitor cells, HIF-1a as a central pathobiologic mediator of myelodysplastic syndromes, and targeting TP53 gene mutations in myelodysplastic syndromes through functional reconstitution and immune activation. Providing the resources for these research projects directly improves the quality of life of MDS patients and their caregivers.

The Foundation also assists our industry partners through the clinical trial process by raising awareness of these vital trials and incorporating the patient voice into these trials in an effort to increase enrollment of MDS patients. These research related efforts each year bring us closer to a cure for MDS.

The MDS Foundation, Inc. is a 501c3 tax exempt organization.



Contact us

1-800-MDS-0839 (within the US and Canada)

1-609-298-1035 (outside the US)

1-609-298-0590 fax

or write

The MDS Foundation, Inc.
4573 South Broad St., Suite 150
Yardville, NJ 08620

Tracey Iraca

Executive Director

Tracey joined the MDS Foundation in 2004 as a part-time Patient Coordinator, assisting with patient education programs. As Executive Director, Tracey now oversees all daily business activities, including finances, staffing, and projects to support the mission of MDSF. She works with the MDSF Board of Directors on strategic planning for meeting the ongoing needs of MDS patients and healthcare professionals. Tracey manages the corporate grants program and is responsible for all corporate relations, organizational partnerships, and new business development.

Lea Harrison

Senior Project Manager

Lea joined the Foundation in 2001. Lea manages all aspects of professional education including our biennial International MDS Congress and Regional MDS Symposium as well as our podcast initiative, educational meetings and partnerships. She also coordinates our Young Investigator Grant program. Lea is also the Secretary of our Board of Directors.

Janice Butchko

Senior Project Manager

Janice joined the Foundation in 2008 and is primarily responsible for enhancing communications with our patient community regarding registration for patient events and coordination of philanthropic support through her organization and management of our contact database. Janice is responsible for the coordination, quality control, and production of printed and electronic Foundation materials; she manages the patient educational initiatives.

Madelyn Geltch

Development and Community Manager

Madelyn joined the MDS Foundation in 2020 to assist with enhancing our community outreach initiatives. Madelyn oversees the planning and implementation of outreach strategies through a variety of programs including grassroots fundraising, direct mail, social media, events and workplace giving. She is primarily responsible for connecting people in the broader community by cultivating relationships with individuals, businesses, and other relevant organizations. Madelyn focuses on public relations, volunteer relations, and fundraising and is responsible for a variety of tasks, from data collection and analysis to organizing media events. Madelyn holds a bachelors degree from Syracuse University, College of Visual and Performing Arts.

Tanya Rhodes

Director of Development

Tanya joined the MDS Foundation in 2022 to oversee the development and fundraising needs of the organization. She develops and implements effective fundraising initiatives to increase overall short and long-term donations to the MDS Foundation, including major and planned gifts. Tanya works in conjunction with the organization's Development Board, Board of Directors, Medical and Scientific Advisory Board, internal MDSF team, and external patient and family volunteers to identify and cultivate relationships with prospects and donors, identify potential grant opportunities, and secure donations to carry out the mission and vision of the foundation to make potentially curative therapies available for all patients with MDS. Tanya also assists the marketing team with the organization's branding and public relations strategies.

Ashley Moncrief

Director of Patient Care

Ashley graduated from Austin Peay State University in May 2012 with a Bachelor of Science in Nursing and a minor in leadership studies. Her dedication has been to oncology from the start. She began her career as an infusion nurse at a local outpatient oncology clinic. She made the transition from outpatient to inpatient nursing at Centennial Medical Center in 2013 where she worked on the hematology/BMT floor. Ashley then accepted a position on Vanderbilt's inpatient myelosuppression unit in 2015. In 2017 she joined the hematology research team where she mainly focused on Phase II/III trials. Ashley's love of details led her to transition to Phase I hematology trials after about a year in the research department. After five years, she transitioned to her most recent position as the Manager of Research Projects for Malignant Hematology, Cellular Therapy and Toxicity, and Plasma-Cell Lymphoma.

Outside of work, Ashley serves as the Secretary for the Middle TN chapter of the Oncology Nursing Society (ONS). During her tenure with the society, she has published abstracts to include The Need for Paper in an EMR Based System in 2020. In addition to the collaboration with pharmaceutical companies in the realm of research, she has done consultant work for Celgene, the Cancer Support Community, and Taiho with a focus on improving the patient experience. Ashley first became affiliated with the MDS Foundation in 2019 when she spoke at their patient forum in Nashville. She knew immediately that she wanted to be part of this team. Ashley was honored to be selected to be on the MDS Foundation Nurse Leadership Board in 2020. In October of 2022, she was selected as the recipient for the foundation's Compassionate Care Award which she considers one of the highlights of her career. Ashley is very excited to start this new journey and looks forward to being able to contribute the MDS population at large to include patients, caregivers, and healthcare providers in this new role.

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International Nurse Leadership Board (NLB)

The International Nurse Leadership Board (NLB)

The International Nurse Leadership Board (NLB) is composed of more than 30 members worldwide and includes three subcommittees: Professional Education, Patient Education, and Quality of Life. It is important to note that all nurse members of this Leadership Board participate on a volunteer basis.

To see a complete list of members, please visit our website at www.mds-foundation.org/nursing-leadership-board-nlb/

Mission

The mission of the NLB is to provide an international nursing forum for the development of patient, caregiver and nursing focused initiatives that promote excellence in the comprehensive care of patients with bone marrow disorders. Members are invited to participate based on demonstrated excellence in nursing practice and research related to patients with bone marrow disorders, including MDS. The NLB represents various regions and practice settings throughout the world.

Accomplishments to date:

- Formalization of the NLB with international representation.
- Facilitation of patient forums in the US and Europe.
- Development of an MDS Nurse Mentorship Program including facilitation/presentation at six regional meetings.
- Nursing sessions at MDSF international symposia.
- Poster presentations for QOL data on behalf of the Foundation (at ASH and MDSF symposia).
- Development of Nursing Education Slide Modules for Europe.
- MDS Foundation Newsletter contributions.
- Development and updates of patient and caregiver guides, including our Building Blocks of Hope: Strategies for Patients and Caregivers LIVING with MDS (BBoH).
- Modification of the content for Patient Forums with incorporation of Building Blocks of Hope program information for patients and caregivers – including a mobile application for patients to track and manage their treatments – MDS Manager.
- ONS Symposia with release of the CJON supplement dedicated to MDS, developed by the NLB.
- MDS Glossary pocket guide

Goals:

- Expand membership into areas/regions in need.
- Continued translations and cultural adaptations of the Building Blocks of Hope and other patient/caregiver resources
- Updates to the Nursing Education Slide Modules – translations and cultural adaptations for various regions.
- Identify new initiatives for nursing education.
- Identify areas that would benefit from development of new materials for patients and caregivers – online and in print.
- Efforts specifically related to quality-of-life:
 - Age, Comorbidities, Frailty, and Resilience: Strategies to Improve Options for Treatment in MDS – A wellness and awareness campaign
 - Transfusions in MDS: When to transfuse and when to initiate disease modifying therapies – An awareness campaign for providers and patients integrating the most recent transfusion guidelines from ASH
 - General QOL in MDS: Continued analysis of the patient survey results.

Patient Services

The MDS Foundation provides a number of patient and caregiver services globally. These include referrals to an MDS Foundation Center of Excellence, referrals 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 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 patients and those seeking a second opinion 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 patients in need of support and guidance.

In-Person patient and caregiver 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 and meet patients and caregivers just like you. Complimentary breakfast and lunch.
- Visit the MDS Foundation website for more information at www.mds-foundation.org/patient-and-family-forums

MDS Foundation Patient Liaison Ashley Moncrief

1-800-MDS-0839 x210 (within the US)

1-609-298-1035 x210 (outside the US)

1-609-298-0590 fax

email: patientliaison@mds-foundation.org

amoncrief@mds-foundation.org

Online patient and caregiver message board

Free online discussion board featuring information exchanged between patients, caregivers, and family members. For more information or to access the forum please go to <https://www.mds-foundation.org/forums/forum/patient-message-board/>

Global patient support groups

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

The MDS Foundation has assisted in establishing over 25 MDS global patient support groups. To view a current listing of support groups, please visit our website at www.mds-foundation.org/global-patient-support-groups.

With your help we can create additional support groups. If you are interested in starting an MDS support group in your area, please contact our Patient Liaison at 609-298-1035 or via email at patientliaison@mds-foundation.org.

MDS Centers of Excellence

MDS Foundation's MDS Centers of Excellence

The MDS Foundation designates MDS Centers of Excellence if the center meets specific criteria in the diagnosis and treatment of MDS. These criteria include:

- 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.

The MDS Foundation currently has 76 MDS Centers of Excellence throughout the US and 118 MDS Centers of Excellence in 36 countries outside the US. These numbers are continually increasing as more centers are approved.

To see a complete listing, please visit our website at www.mds-foundation.org/mds-centers-of-excellence-map-new/



US-Based Resources

MDS Foundation, Inc.

A multidisciplinary, international, non-profit 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

Aplastic Anemia and MDS International Foundation

A non-profit health organization dedicated to supporting patients and families living with aplastic anemia, MDS, paroxysmal nocturnal hemoglobinuria, and related bone marrow failure diseases.

www.aamds.org

Be The Match

A non-profit organization that's dedicated to helping every patient get the life-saving transplant they need. As trusted leaders in advancing treatments for those facing life-threatening blood cancers, we provide the ground-breaking research, innovative technologies, patient support and education that save lives.

www.bethematch.org

Leukemia and Lymphoma Society

A non-profit organization whose mission is to cure leukemia, lymphoma, Hodgkin disease, and myeloma and improve the quality of life of patients and their families.

www.lls.org

NCCN Patient and Caregiver Resources

An alliance of leading cancer centers devoted to patient care, research, and education. Their mission is to improve the quality, effectiveness, and efficiency of cancer care so that patients can live better lives. Their vision is to be the world's leader in defining and advancing high-quality, high-value cancer care.

www.nccn.org/patients

Patient Worth

An online publication that provides relevant information to rare disease patients, caregivers and advocates alike.

www.patientworthy.com

Internationally-Based Resources

AAMAC (Canada)

A leading funder of research into bone marrow failure diseases in Canada. This volunteer-run organization supports patients and caregivers across the country who are living with aplastic anemia, myelodysplastic syndrome (also called MDS or myelodysplasia) and paroxysmal nocturnal hemoglobinuria (PNH).

www.aamac.ca/e

Leukaemie Hilfe Rhein-Main (Germany)

The Leukemia Aid RHEIN-MAIN is for adult patients with all haematological diseases (concerning the blood and lymphatic system) and their relatives. The LHRM represents its patient interests both regionally and nationally and at European and international level.

www.leukaemihilfe-rhein-main.de

Lyle (Denmark)

A patient association for people affected by lymphoma, leukemia or MDS-directly as patients or indirectly as relatives.

www.lyle.dk

MDS Alliance

A global health coalition of MDS advocacy groups that aim to provide patients, caregivers and healthcare professionals with information about MDS.

www.mds-alliance.org

MDS-Patienten Interessengemeinschaft, Deutschland (MDS-PAT-IG) (Germany)

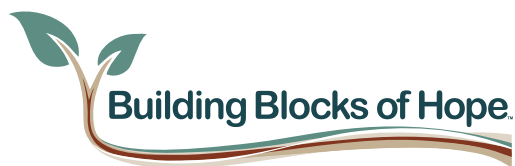
An association that provides education, advocacy, contacts and information.

www.mds-patienten-ig.org

UK MDS Patient Support Group (United Kingdom)

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

www.mdspatientsupport.org.uk



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 and Nursing at the University of Arizona Cancer Center, Executive Committee and 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, Lea Harrison and the MDS Foundation staff. Bone marrow illustrations provided by Kirk Moldoff.

A special thanks to our MDS patients and their caregivers for sharing their life experiences within their MDS journey. Additional thanks to the Executive Committee for the MDS Foundation, Peter Greenberg, M.D., Alan List, M.D., Stephen Nimer, M.D., and Pierre Fenaux, M.D., Ph.D., and to John Bennett, M.D. for ongoing contributions to the MDS Foundation. In memory of Bob Weinberg, who generously donated his time and legal expertise, and shared his own personal journey with MDS. Thanks to the scientists, healthcare professionals, and volunteers who continue to work towards improving the lives of MDS patients and their caregivers. To the countless numbers of patients and their caregivers who have participated and continue to participate in clinical trials that have led to a better understanding of and improved treatment strategies for MDS; we would not be where we are without your continued involvement. Thank you to our International Colleagues for their work in adapting the Building Blocks of Hope incorporating translation and integration of their culture for regions throughout the world.

We are grateful to all of our supporters; your contributions make the work of the MDS Foundation and support of patients and caregivers **LIVING** with MDS possible. A special thanks to my family for understanding my passion for this work.

We hope this project will provide a useful tool for healthcare 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

Thank you to Acceleron Pharma, Bristol-Myers Squibb, Novartis Pharmaceuticals, Syros Pharmaceuticals, and Takeda Oncology for supporting this resource.



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