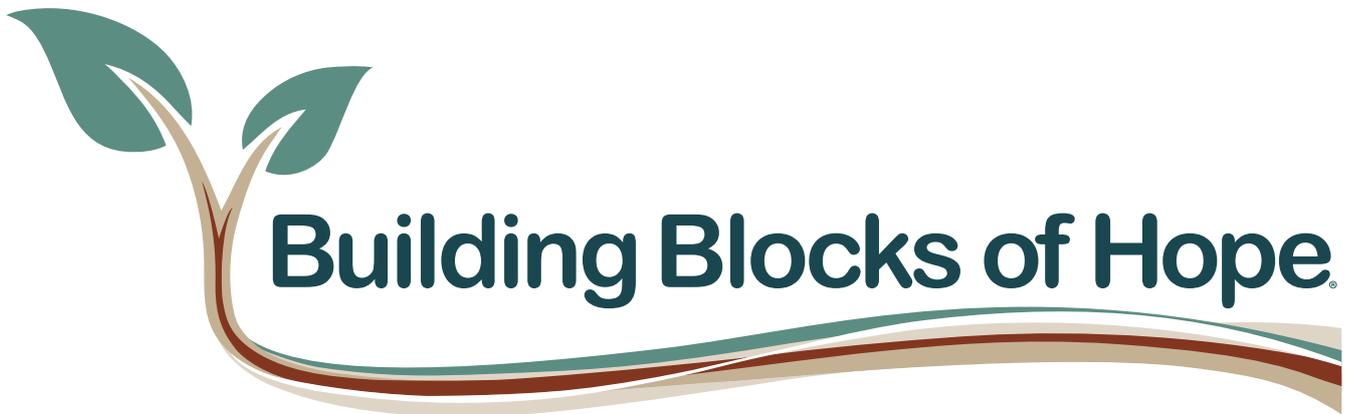


*English Edition (Australia)*



# Building Blocks of Hope<sup>®</sup>

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

by Sandra Kurtin

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



Published by 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 booklet. It is designed to help you get the information that you are looking for and take an active part in your MDS journey.

There are individual chapters, or tabs, 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 – Quick Tips:** The quick tips offered in this section include guidelines for monitoring and managing your symptoms.
- **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 – My MDS Plan:** Understanding the diagnosis of MDS will help you and your caregiver take an active part in your individual treatment plan. My MDS plan provides several tools to allow you to track and manage your journey. You may want to make extra copies of some of these tools before writing on them so that you can continue to track your progress.
- **Chapter 6 – The MDS Foundation:** The MDS Foundation is an international publicly supported organisation 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.

The original Building Blocks of Hope, developed in the United States, has been adapted for regions throughout the world, including Australia. You have received the Australian adaptation. You may also visit the original version of the Building Blocks of Hope online at <http://buildingblocksofhope.com>.

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

## The MDS Foundation

1-800-MDS-0839 (*within US only*)

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

1-609-298-0590 *fax*

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

Email: [patientliaison@mds-foundation.org](mailto:patientliaison@mds-foundation.org)

## Authors of the American Edition:

Karen Abbas  
Nikki Barkett  
John Bennett  
Karen Campbell  
Rochelle Chiffelle  
Nicole Crisp  
Erin Demakos  
Lenn Fechter  
Angela Flowers  
Christopher Flowers  
Denice Gibson  
Peter Greenberg  
Carol Guarnieri  
Lea Harrison  
Audrey Hassan  
Susan Hogan

Tracey Iraca  
Emily Knight  
Rami Komrokji  
Sandra Kurtin  
Alan List  
Cindy Murray  
Deborah Murray  
Eric Padron  
Cynthia G. Paul  
Jean Ridgeway  
Jayshree Shaw  
David Steensma  
Mary Thomas  
Sara Tinsley  
Bob Weinberg  
Patrice Welsh-Benjamin

## Australian Authors

**Rebecca Dring, RN Post Grad Dip in Cancer Nursing**  
Leukaemia Foundation  
National MDS Coordinator  
Royal Melbourne Hospital  
Clinical Nurse Specialist  
Melbourne, Australia

**Jacqueline Jagger, RN, BA(Hons), MN**  
Haematology Nurse Practitioner  
Cancer Services  
Gosford Hospital, NSW  
Australia

**Samantha Soggee, RN, MN**  
Nurse Unit Manager  
Oncology/ Haematology  
Epworth Freemasons  
Victoria, Australia

**Catherine Vassili, RN**  
Haematology – Leukaemia Nurse Practitioner  
(Candidate)  
The Alfred Hospital  
Melbourne, Victoria, Australia

# Understanding MDS

---

*The Myelodysplastic Syndromes (MDS) are a group of bone marrow failure disorders. There are several types of MDS.*

*Each type of MDS has a variable onset, prognosis, treatment options, and risk of developing leukemia.*

*Understanding MDS, the first chapter in the Building Blocks of Hope, provides a description of what happens to the normal bone marrow when MDS develops and what symptoms you may have as a result. Details about how MDS is diagnosed, and how the type is determined are included. Understanding your MDS diagnosis will help you and your caregiver take an active part in your individual treatment plan.*

*contributing authors*

John Bennett  
Peter Greenberg  
Rami Komrokji  
Sandra Kurtin  
Alan List

# Understanding MDS

---

|  |    |
|--|----|
| What Is MDS?   | 3  |
| Is MDS Cancer?   | 3  |
| What Causes MDS?   | 4  |
| What Does Bone Marrow Do?                                    | 5  |
| What Are the Symptoms of MDS?                                | 6  |
| The Bone Marrow Biopsy & Aspirate                            | 7  |
| What Happens to Bone Marrow in MDS?                          | 9  |
| Cytogenetic and Molecular Testing in MDS                     | 11 |
| How Is MDS Classified?                                       | 13 |
| How Severe Is My MDS?  | 15 |
| The Revised International Prognostic Scoring System (IPSS-R) | 16 |

# What is MDS? Is MDS Cancer?

## What is MDS?

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

## What happens?

The bone marrow is the factory for the production of blood cells including red blood cells, white blood cells, and platelets. The 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:

**Anaemia:** low red blood cells (oxygen carrying cells)

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

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

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

## Is MDS cancer?

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

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

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



normal bone marrow



Abnormal bone marrow with dysplastic blood cells and abnormal chromosomes

What is MDS?



### References:

Bejar, R., Levine, R., & Ebert, B.L. (2011) *Unraveling the molecular pathophysiology of Myelodysplastic Syndromes*. *Journal of Clinical Oncology*, 29, 504–515

Kurtin, S. E., Demakos, E., Hayden, J., & Bognione, C. (2012) Initial treatment of Myelodysplastic Syndromes: Practical tools and effective management. *Clinical Journal of Oncology Nursing*, 16 (3, Suppl.1), 23–35

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

**1. It is more common in men (male to female ratio is 4.5:2 per 100,000).**

- a. As with many types of cancer, older age is a predisposing factor. The average age of patients with MDS is 73, and 86% of patients with MDS are older than age 60.

**2. Exposure to chemicals and other toxins are known to increase the risk of developing MDS**

- a. Chronic and high exposure to benzene, other solvents, insecticides or herbicides. Whereas in the past, over 25 years ago, reports of benzene induced MDS/AML in the petrochemical industry were reported, no such series have been published in the recent literature.
- b. There are no known foods that cause MDS.
- c. While alcohol consumed on a daily basis may lower red blood cell and platelet counts, alcohol is not known to cause MDS.
- d. Tobacco smoke/use has been linked to the development of MDS. One of the primary components of tobacco is benzene.

Benzene is highly regulated by federal agencies. There are published guidelines for exposure limits.

**3. Patients who receive certain types of chemotherapy or radiation treatment for other cancers may be at increased risk of developing treatment-related MDS.**

- a. Patients who take chemotherapy drugs or who receive radiation therapy for potentially curable cancers, such as breast or testicular cancers, Hodgkin disease and non-Hodgkin lymphoma, are at risk of developing MDS for up to 10 years following treatment. MDS that develops after use of cancer chemotherapy or radiation is called “secondary MDS” and is usually associated with multiple chromosome abnormalities in cells in the bone marrow. This type of MDS often is more difficult to treat and more often develops into AML.

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

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

# What does bone marrow do?

## What does bone marrow do?

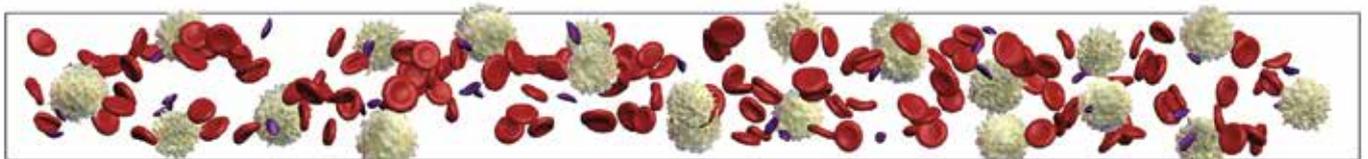
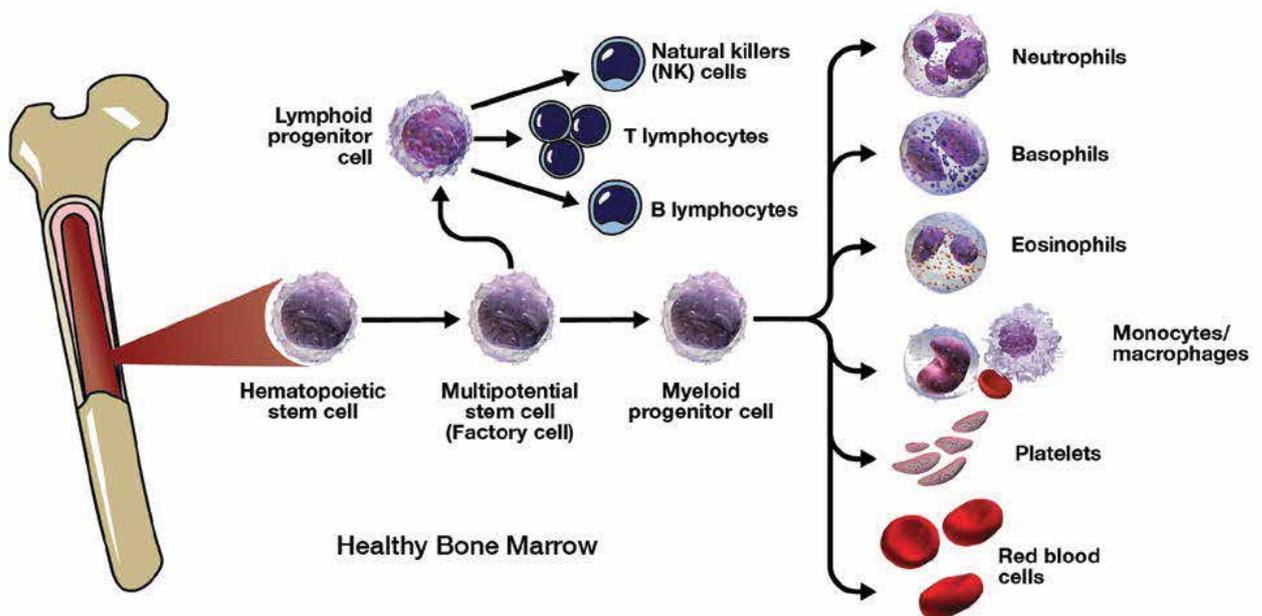
- All blood cells begin as haematopoietic (*hee-muh-toh-poi-et-ik*) stem cells. These cells are often referred to as factory cells. In healthy people, haematopoietic stem cells (the factory cells) develop and mature (differentiate) in the bone marrow to form the different blood cells.
- In the initial stage, the haematopoietic 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 par 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

## What are the symptoms of MDS?

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

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 (anaemia):** 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?  |
|---|---|
| Full blood examination, differential, and platelet count, reticulocyte count  | The presence of cytopenias, peripheral blasts, morphological abnormalities, and bone marrow response to anaemia.  |
| Serum iron, ferritin, transferrin saturation, folic acid, B12                 | Iron deficiency, B12 deficiency, Folic acid deficiency; may also cause anaemia and in some cases thrombocytopenia.  |
| LDH, haptoglobin, reticulocyte count, coombs [Direct Antiglobulin Test (DAT)] | Red blood cells can be destroyed by an overactive immune system. These blood tests are used to look for haemolysis (immune destruction of red blood cells). |
| Serum erythropoietin (EPO)  | Erythropoietin (EPO) is a hormone produced in the kidneys that is necessary to make normal red blood cells. Some patients with MDS do not have enough EPO.  |

## Bone marrow examination

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

## The bone marrow aspirate

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

## The bone marrow biopsy

The bone marrow biopsy is a small core (the shape and size of a medium pencil lead) of the spongy centre 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.

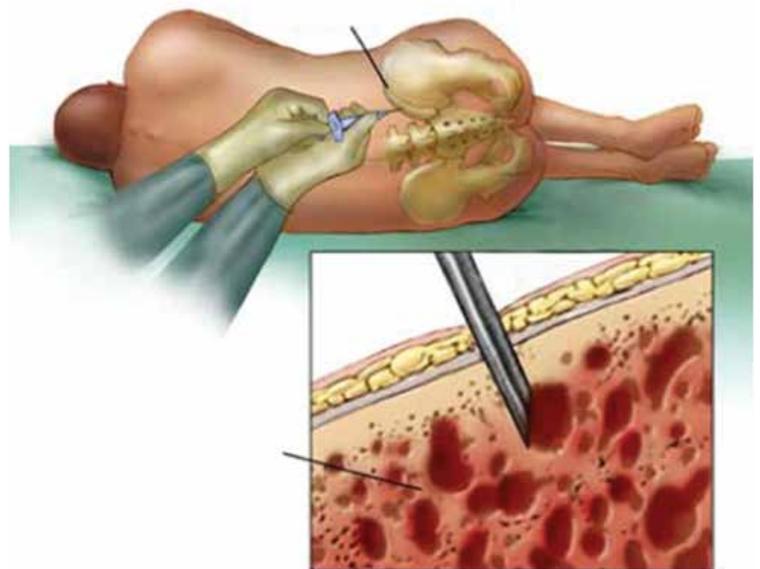
## Processing the sample

The bone marrow biopsy and aspirate samples are placed on glass slides and in various laboratory tubes. These are sent to a haematopathologist—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 one month.

## 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 anaesthesia 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 clinician 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 anaesthetised (numbing the skin) using a form of lignocaine (numbing medicine). You may feel a pin prick from the needle and a very brief sting from the lignocaine.



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 anaesthetised, 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 the clinician 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 doctor.
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. The clinician will twist and shake the needle gently to loosen the bone core to help remove it in one piece. You will feel pressure and some shaking very briefly. There is sometimes a quick sting when the bone is removed.
9. After the procedure, the provider will apply pressure to the site to prevent any bleeding. A pressure dressing is generally applied.
10. You should not shower for 24 hours. No soaking in water (bath, swimming, hot tubs) for 48-72 hours. Ask your provider for instructions on how to care for the biopsy site.
11. Some patients may develop a bruise or swelling under the skin, particularly patients with a low platelet count or patients taking medication to thin the blood. Be sure to let your health care provider know if you are taking aspirin or other medications that thin the blood.
12. Mild pain or discomfort may be experienced at the procedure site for two to three days after the bone marrow exam.
13. For safety reasons, the patient should have a friend, family member, or 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 (haematopoietic 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.

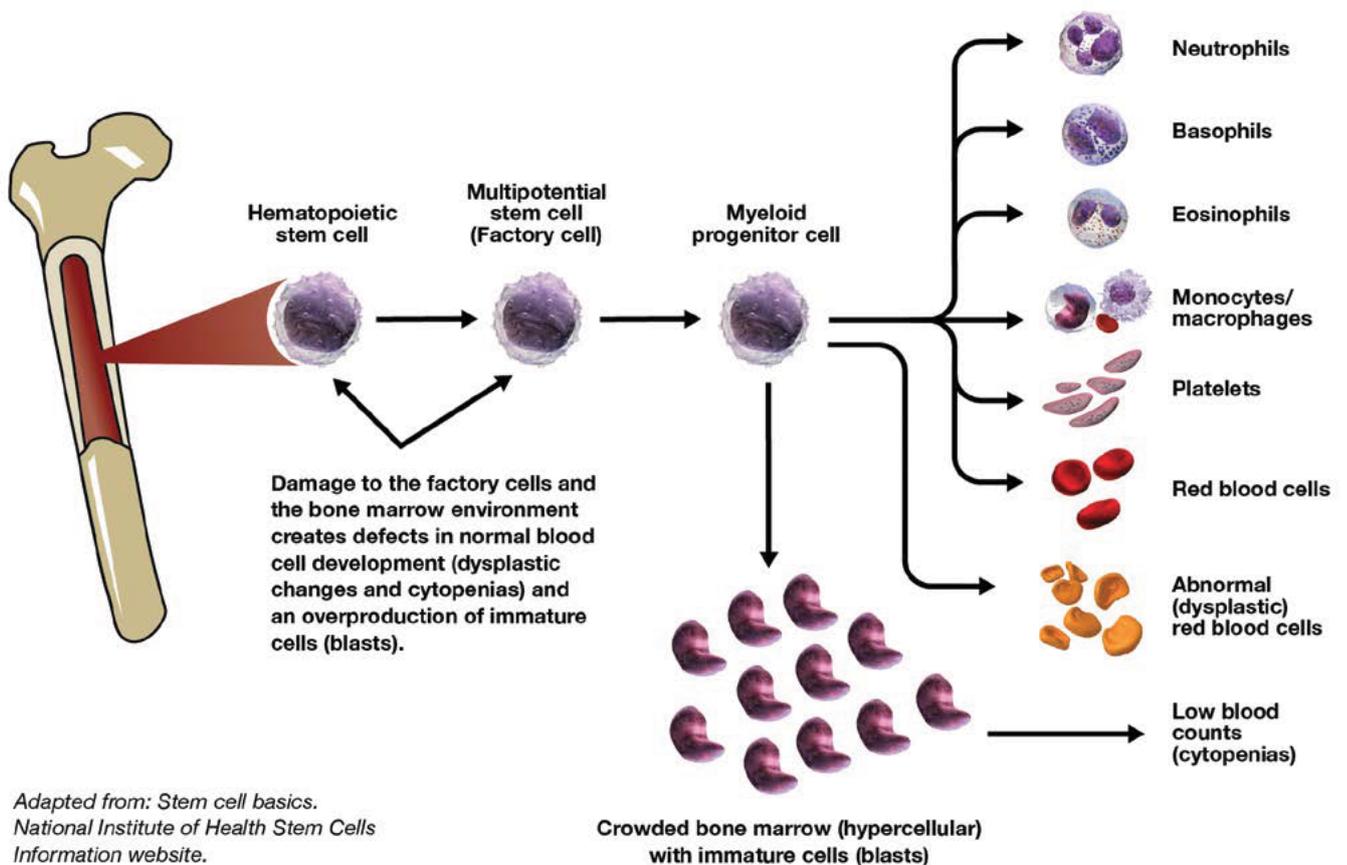
Red blood cells, white blood cells, and platelets all come from the same myeloid factory cell (progenitor cell). These are the cells that we can measure in the peripheral blood. In MDS, these cells are often low in number (cytopenias) and do not function normally.

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.

# What happens to bone marrow in MDS?

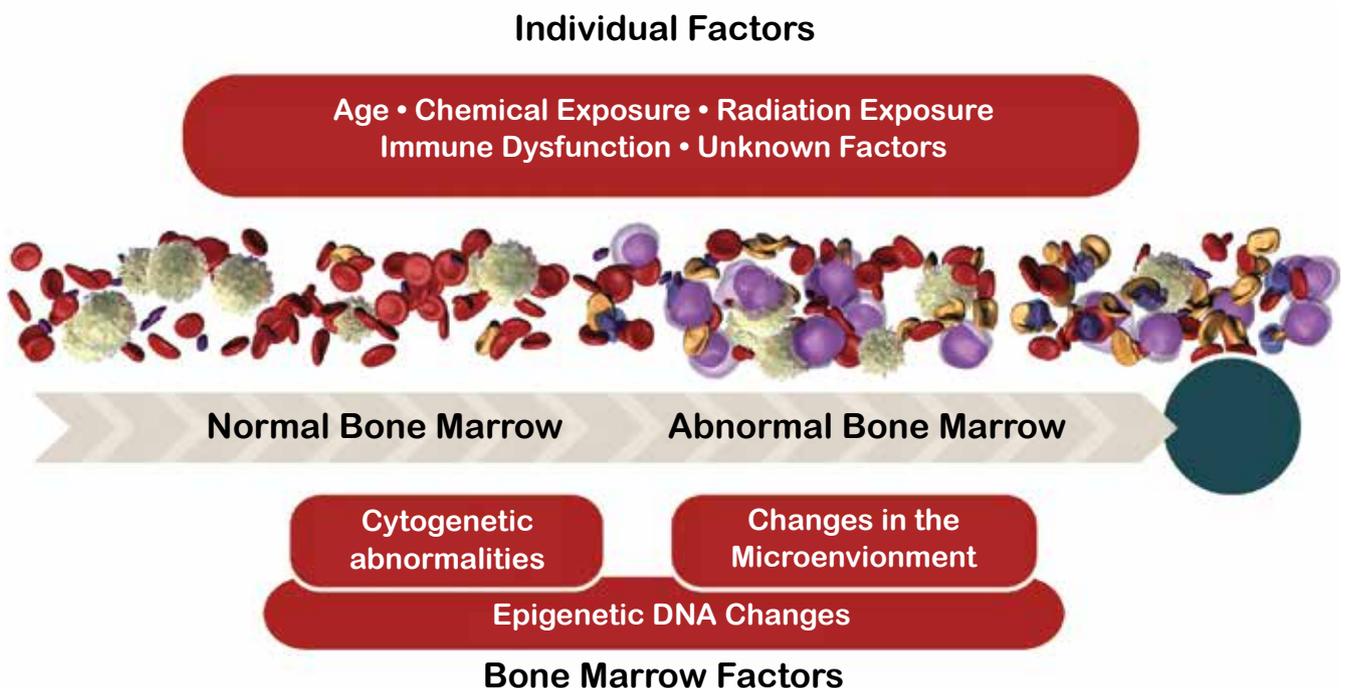
## Epigenetic changes

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

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

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

In MDS, methyl compounds (chemical complexes) may attach to the genes needed for normal haematopoiesis (the development of the components of blood). When too many of these compounds attach to the gene it is known as hypermethylation. Hypermethylation turns off the genes that are needed for normal blood cell development. Hypermethylation is common in MDS. It is a constant process and is associated with disease progression, including the development of acute myeloid leukaemia. 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.



*What happens to the bone marrow in MDS?*

## What is cytogenetics?

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

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

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

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

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

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

Each chromosome has a narrow central point called the centromere, which divides the chromosome into two sections, or "arms." The short arm of the chromosome is labeled the "p arm." The long arm of the chromosome is labeled the "q arm."

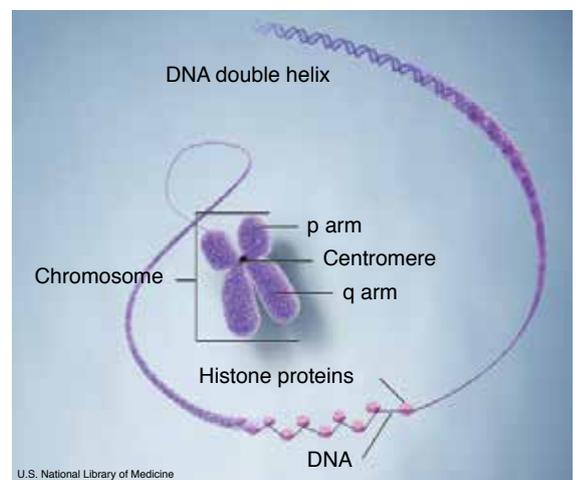
## Gene mutations in MDS: what is molecular study?

Chromosomes contain several thousand genes. Genes are shorter sections of DNA. Each gene acts as a code or set of instructions for making a particular protein. These proteins control the cell's activity - telling the cell what to do, giving the organism particular characteristics (such as male or female), and determining the way the body functions. Many diseases, including MDS, have abnormal proteins as a result of gene changes called mutations. Some of these genes are thought to play a part in the development of MDS and, in some cases, the response to treatments for MDS. Gene mutations can be detected by molecular analysis, which can complement cytogenetic analysis in MDS.

## How are cytogenetic and molecular study results used in MDS?

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

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



### References:

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

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

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

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

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

---

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

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

Molecular study is gaining importance in MDS, but it is currently not as important as cytogenetic analysis (and it is therefore not systematically performed). It can detect mutations in MDS cells in most MDS patients, including gene mutations leading to abnormal epigenetic mechanisms (including TET2 and ASXL1 genes) or other genes (like SF3B1, SRSF2 and TP53 genes, etc.). However, finding a gene mutation currently has limited impact for patient management in most cases, although preliminary results suggest that, for example, the TET2 mutation may be associated with improved response to Azacitidine (Vidaza®).

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

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

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

## French-American-British (FAB) classification system

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

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

## The World Health Organization (WHO) classification system

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

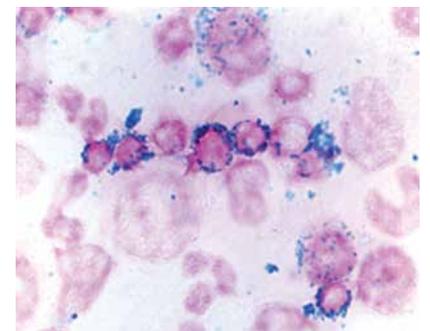
### Refractory anaemia (RA) and refractory anaemia ringed sideroblasts (RARS)

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

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

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

ringed sideroblasts



### Refractory anaemia with excess blasts (RAEB)

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

### 5q- (5q minus) syndrome

Is defined by a cluster of findings including:

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

What stage  
is my MDS?



### Unclassified MDS

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

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

## International Prognostic Scoring System (IPSS)

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

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

## Determining the IPSS score

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

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



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



The IPSS-R has been developed by a group of International MDS experts representing 11 countries and 7,012 patients. These data have been used to estimate life expectancy (survival) for a patient newly diagnosed with MDS without treatment and the risk of developing acute myeloid leukaemia (AML). The risk category (measure of severity) is estimated using results from the bone marrow biopsy and aspirate, the cytogenetics and the peripheral blood test (full blood examination, differential and platelet count).

## IPSS-R for MDS: Prognostic Score Values/Risk

| Score/Attribute    | 0                | 0,5         | 1           | 1,5 | 2                   | 3           | 4                |
|--------------------|------------------|-------------|-------------|-----|---------------------|-------------|------------------|
| Cytogenetics       | <b>Very Good</b> |             | <b>Good</b> |     | <b>Intermediate</b> | <b>Poor</b> | <b>Very Poor</b> |
| Blasts (%)         | <%2              |             | >%2-<%5     |     | %5-10               | >%10        |                  |
| Haemoglobin (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](http://www.mds-foundation.org/ipss-r-calculator)).

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

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

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

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

**Acute**

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

**Acute Myeloid Leukemia (AML)**

A cancer of the 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

**Aetiology**

The cause or origin of a disease.

**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 infection. They are part of the body's normal defence mechanism.

**Antibodies**

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

**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. The term aplastic is a Greek word meaning not to form. Anemia is a condition that happens when the red blood cell count is low. Most scientists believe that aplastic anaemia happens when the immune system attacks the bone marrow stem cells. Aplastic anaemia can be acquired (begin any time in life) or can be hereditary (less common, passed down from parent to child).

Synonyms: acquired aplastic anaemia, hereditary aplastic anaemia

**Apoptosis**

Death of a cell as a part of the normal lifecycle.

**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. Patients with autoimmune diseases frequently have unusual antibodies circulating in their blood that target their own body tissues.

Synonym: Immune deficiency

**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.

**Benzene**

A chemical that is widely used by the chemical industry to make plastics, resins, nylon and synthetic fibres. 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.

**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.

Synonyms: biologic, biological drug

**Blast Cells**

Immature blood cells that normally would 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 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 or blood thinners. 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 relief for some patients with low blood counts.

### Bone Marrow

The soft, sponge-like tissue in the centre 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 centre 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 anaemia, 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).

### 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, idarubicin and mitoxantrone.

### 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.

### 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.

### 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 haemoglobin, and the fraction of the blood made up of red blood cells.

### Cytogenetics

Testing that is performed on bone marrow 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.

Synonym: cytogenetic response

## 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.

## 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.

## 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.

## 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.

## Erythropoietin (EPO)

A protein substance 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 erythropoietin-stimulating agents that can help boost the red blood cell count of some bone marrow failure patients.

## 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 anaemia is diagnosed early in life. People with Fanconi anaemia have a high likelihood of developing cancer. Genetic testing is used to diagnose Fanconi anaemia.

## 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 coloured 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 hemaglobinuria (PNH) take a man-made form of folate called folic acid.

## Haematocrit (HCT)

Percent of the total blood volume that is made up of red blood cells. In men a normal haematocrit is 40-52% while in women the normal is 36-46%. Haematocrit is part of a complete blood count.

Synonyms: packed cell volume, PCV

## Haematologist

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

## Haematopoiesis

The formation and development of blood cells.

## Haemolysis

The destruction of red blood cells.

## 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.

## 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 anaemia 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 tumour 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 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 anaemia. 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.

Synonym: IV infusion

## IPSS / IPSS-R

An International Prognostic Scoring System – system for grading the severity of MDS. The system turns patient data into a score. The score tells how quickly a myelodysplastic syndrome (MDS) case is progressing and 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) have approved two iron chelators to treat iron overload in the U.S. The two types of iron chelators are 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 accumulates in the body. Bone marrow failure disease 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 specific organ or part of the body is cut off, causing a localized lack of oxygen.

## 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.

## 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.

## Mutation

Any change or alteration in a gene. A mutation may cause disease or may be a normal variation.

## Morphology

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

## 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 growth or development. 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 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)

Synonyms: preleukemia, smoldering leukemia

## 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 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.

## 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.

Synonym: 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.

## Paediatric MDS

MDS is rare in children; but it does happen. Most patients are 60 years old or older.

## Pancytopenia

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

## 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 haemoglobin in the urine. Haemoglobin 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.

## 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.

## Petechiae

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

## Pharmacist

A highly trained and licensed professional whose job concerns the preparation, distribution, and use of prescription drugs. A pharmacist also advises 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, colourless cells that are present in blood. Their sticky surface lets them, along with other substances, form clots to stop bleeding.

Synonym: thrombocytes

## Platelet Transfusion

A procedure in which platelets are given to a person through an intravenous (IV) line into the bloodstream. 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.

## 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.

Synonym: PRCA

## 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 anaemia. Before transfused blood is given, donated blood is typed and cross matched to the recipient's blood.

## Refractory

Not responsive to treatment or cure. For example, refractory anaemia 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 the 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).

## Ring Sideroblast

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 disorder or disease. Treatments typically associated with secondary MDS include radiation therapy and chemotherapy used to treat cancer.

Synonyms: T-MDS, therapy-related MDS

## Serum Erythropoietin

Amount of erythropoietin that is present normally in an individual's 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 anaemia, causing fever, rash, joint pain, and muscle aches.

## 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 (haemopoietic) stem cells are found in the bone marrow. These cells make copies of themselves and develop into red cells, white cells, and platelets. Embryonic stem cells come from human embryos and may be used in medical research.

## 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.

Synonyms: palliative care, symptom management

## 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.

## 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 Organisation (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.

## Red Blood Cells

### Erythrocyte

A red blood cell. It carries oxygen to body cells and carbon dioxide away from the cells. (see red blood cells).

### Red Blood Cells (RBC)

These are cells that carry oxygen to your tissues. (see erythrocyte).

## White Blood Cells

### Absolute Neutrophil Count (ANC)

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.

### 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.

### 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.

Synonyms: 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.

Synonym: nonmyeloablative transplant

## Unrelated Donor

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

## Drug Treatment

### Adverse Event (AE)

Any undesired actions or effects of a drug or treatment.

Synonyms: side effect, toxicity

### Antibiotic (AB) Therapy

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<sup>®</sup>, Lymoglobulin<sup>®</sup>, and Atgam<sup>®</sup>.

### 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

## 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).

## Desferal® (deferoxamine)

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 subcutaneously (under the skin).

## Erythropoietin (EPO)

A “recombinant” form of a natural growth factor used to treat symptoms associated with anaemia. It stimulates the bone marrow to produce red blood cells. The three brand-name drugs are Aranesp<sup>®</sup>, Epogen<sup>®</sup>, and Procrit<sup>®</sup>. 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 (GM-CSF).

Synonym: cytokine

## Hycamtin® (topotecan hydrochloride)

Is a chemotherapy agent that may result in remission of MDS. It is administered intravenously.

## 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 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.

**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 anaemia by increasing the red blood cell production.

**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.

**Telintra™ (TLK199)**

A medication that inhibits a key enzyme (glutathione S-transferase P1-1 or GST P1-1) involved in cell growth and proliferation; this results in normal blood cell production. It is given intravenously (IV).

**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 interfere with other proteins (cytokines) that promote premature death of cells in the bone marrow. It is taken orally.

**Trisenox® (arsenic trioxide)**

A medication that inhibits new blood vessel growth and stimulates cell death of abnormal cells. It may increase transfusion independence. It is administered as an intravenous infusion (IV).

**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, haemoglobin, 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).

# Seeking Treatment

---

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

## *contributing authors*

|                 |               |
|-----------------|---------------|
| John Bennett    | Rami Komrokji |
| Karen Campbell  | Sandra Kurtin |
| Nicole Crisp    | Alan List     |
| Lenn Fechter    | Cindy Murray  |
| Peter Greenberg | Eric Padron   |
| Emily Knight    | Jean Ridgeway |
|                 | Jayshree Shaw |

# Seeking Treatment

---

|  |    |
|--|----|
| Preparing for the Initial Visit                            | 3  |
| General Principles of Treatment of MDS                     | 4  |
| Red Blood Cell Transfusion                                 | 7  |
| Platelet Transfusion                                       | 9  |
| Growth Factors   | 11 |
| Disease Modifying Agents                                   | 13 |
| What Is Palliative Care?                                   | 16 |
| Bone Marrow Transplant                                     | 17 |
| The Bone Marrow Transplant Process                         | 18 |
| Bone Marrow Transplant Evaluation                          | 19 |
| What Are Clinical Trials                                   | 20 |
| Participating in a Clinical Trial                          | 21 |
| Clinical Trials in MDS                                     | 23 |
| MDS in Children  | 24 |
| Paediatric Information Resources–MDS and Childhood Cancers | 27 |

# Preparing for the Initial Visit

## What will happen after the diagnosis of MDS is made?

Once the diagnosis of MDS has been established, you will meet with your haematologist or oncologist 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 organise your thoughts, your questions, and your concerns so that you can discuss them with your health care providers. Understanding the goals of treatment, how treatment is selected, and what the effects of the treatment might be for you will help you to make decisions about your treatment plan, prepare for the treatment, and plan your daily activities. Being prepared will allow you to ask for help when needed.

## Preparing for the initial visit

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

Preparing for your doctor's visit



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

If you have questions about MDS or treatment options, you may wish to contact the MDS Foundation or the Leukaemia Foundation of Australia for more information. (see: *About the MDS Foundation*). To be recognised as a Center of Excellence, an institution must have:

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

### References:

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

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

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

## How is treatment selected?

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

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

How is MDS treated?



## What are the goals of treatment?

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

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

### Observation (Watch and Wait)

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

## Supportive care

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

| <b>Common forms of supportive care aimed at improving blood counts include:</b>  |   |
|--|---|
| Blood transfusion  | Packed red blood cells, platelets                     |
| Red blood cell growth factors  | Not available in Australia                            |
| White blood cell growth factors  | Available in Australia                                |
| <b>Common forms of supportive care for transfusion-related iron overload include:</b><br>(see: <i>What Is Iron Overload? and Is Iron Overload Treatable?</i> ) |   |
| Deferasirox (Exjade®)  | Approved for patients with iron overload in Australia |
| Deferoxamine (Desferal®)   | Approved for iron overload in Australia               |

## Disease modifying treatment

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

### Common disease modifying treatments for MDS

|                                      |  |
|--------------------------------------|--|
| Antithymocyte globulin, cyclosporine | Used for low-risk and hypocellular MDS   |
| Azacitidine (Vidaza®)                | Approved for treatment of higher-risk MDS In Australia   |
| Decitabine (Dacogen®)                | Not approved in Australia  |
| Lenalidomide (Revlimid®)             | Approved for treatment of low-risk MDS with del(5q) in Australia who are transfusion dependent |

## Low-risk MDS

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

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

Treatment of low-risk MDS



### Goals of treatment for low-risk MDS:

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

## High-risk MDS

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

|               |                     |                     |
|---------------|---------------------|---------------------|
| <b>IPSS</b>   | Intermediate-2 Risk | Score of = >1.5-2.0 |
|               | High Risk           | Score of = >2.0     |
| <b>IPSS-R</b> | High                | Score of = 4.5-6.0  |
|               | Very high           | Score of = >6.0     |

Treatment of high-risk MDS



### Goals of Treatment for high-risk MDS:

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

Red blood cell transfusions are defined as the intravenous (IV, through a vein) infusion of red blood cells. Whole blood is collected from donors and then separated into various blood components. Red blood cells (RBCs) or packed red blood cells (PRBCs) are one component of whole blood.

## Why are red blood cells given?

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

## How are red blood cells administered?

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

## How do I know if I need a blood transfusion?

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

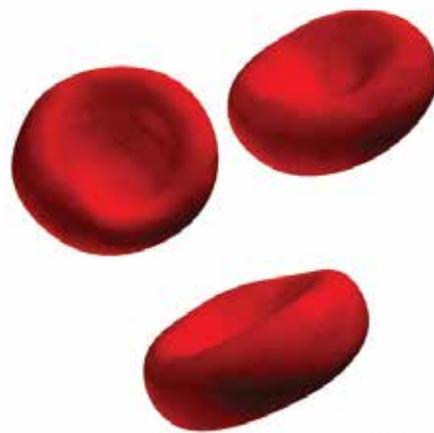


Illustration by Kirk Moldoff

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

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

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

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

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

## How often will I receive red blood cell transfusion?

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

## What are the risks associated with red blood cell transfusion?

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

### Short-term risks

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

### Long-term risks

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

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



# Platelet Transfusion

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

## Why are platelets given?

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

## How are platelets administered?

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

## How do I know if I need a platelet transfusion?

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

## What is the process for receiving a platelet transfusion?

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

You will have a wrist band 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.

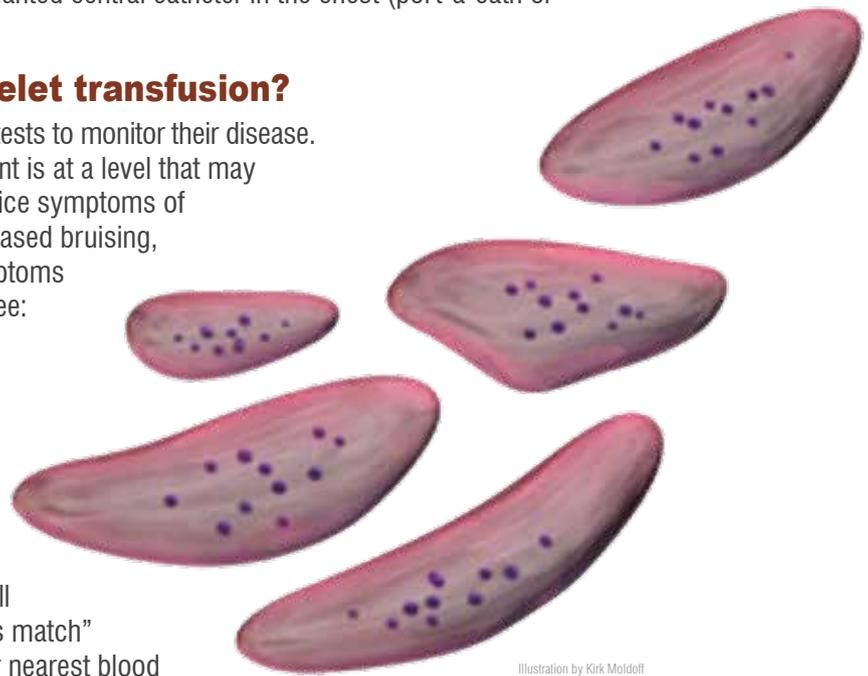


Illustration by Kirk Moldoff

## 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 random donor or single donor platelets are administered based on the patient's symptoms and platelet count. Platelets are infused over 15-30 minutes depending on the volume of each unit. You will need to have an IV catheter placed for the transfusion unless you have an existing intravenous access device. Transfused platelets do not last long (hours to a couple days). The frequency of transfusions will be determined on how well your bone marrow is able to produce platelets, your symptoms and your platelet count.

## What are the risks associated with platelet transfusion?

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

### Short-term risks

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

### Long-term risks

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

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

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

Red blood cell growth factors may improve anaemia by improving red blood cell production. Red blood cell growth factors contain the protein erythropoietin. Erythropoietin (EPO) is a natural hormone produced by the kidneys to help red blood cells develop fully so that they can carry oxygen. The level of erythropoietin in the blood can be measured. Patients with a serum erythropoietin level <500 IU/L who require fewer than two units of packed red blood cells (PRBCs) every 4 weeks have been shown to benefit most from the administration of synthetic erythropoietin stimulating proteins. Red blood cell growth factors are not routinely administered in Australia.

### Available agents:

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

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

## White blood cell growth factors

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

### Available agents:

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

**Pegfilgrastim (Neulasta®)** PEGylated (long-acting) synthetic form of G-CSF.

## Platelet growth factors

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

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

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

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

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

## Australian (PBS) Approved Agents for Treatment of Myelodysplastic Syndromes

|                                       | <b>Azacitidine</b>   | <b>Decitabine</b> <small>Not approved for use in Australia</small>  | <b>Lenalidomide</b>  |
|---------------------------------------|--|---|--|
| <b>Indication</b>                     | All 5 FAB subtypes (RAa, RARSA, RAEB, CMML, RAEB-t)  | Int-1/Int-2/high risk per IPSS, as well as MDS  | Transfusion-dependent MDS low-int-1 MDS with del(5q) with or without additional chromosomal abnormalities  |
| <b>Drug class</b>                     | Hypomethylating agent  | Hypomethylating agent   | Immunomodulatory agent (IMiD)  |
| <b>Key clinical trials in the USA</b> | CALGB 9221, phase I /II CALGB 8421 phase II continuation (2000)<br>Established efficacy and safety<br>AZA-001, phase III international, multicentre<br>Int-2, high-risk MDS<br>First survival data for active therapies in MDS | D-0007, phase I /II (2003)<br>Established efficacy and safety<br>ADOPT trial (2007) phase III randomized, multicentre trial<br>Established new dosing guidelines<br>Decitabine 20 mg/m <sup>2</sup> IV given over 1 h days 1–5<br>Outpatient treatment feasible | MDS-001, phase I /II (2002)<br>Established efficacy and safety<br>MDS-003, phase II multicentre trial, lenalidomide in del(5q) led to FDA approval based on efficacy and safety<br>MDS-002, phase II multicentre trial, lenalidomide in non-del (5q) low-int-1 MDS. Confirmed activity in non-(del)5q MDS; confirmed safety and efficacy |
| <b>Primary end points met (IWG)</b>   | Improved overall survival<br>Hematologic improvement<br>Transfusion independence<br>Cytogenetic response<br>Safety and efficacy  | Hematologic improvement<br>Transfusion independence<br>Cytogenetic response<br>Safety and efficacy  | Hematologic improvement<br>Transfusion independence<br>Cytogenetic response<br>Safety and efficacy   |
| <b>Common side effects</b>            | Myelosuppression is most common<br>Injection site reactions<br>Nausea and vomiting<br>Constipation<br>Contraindicated in patients with hepatic tumours<br>Use with caution in renal impairment<br>May cause foetal harm        | Myelosuppression is most common<br>Nausea and vomiting<br>Constipation<br>Hyperbilirubinemia<br>Use with caution in renal impairment<br>May cause foetal harm   | Myelosuppression is most common<br>Rash<br>Diarrhoea<br>Requires renal dose adjustment<br>Nonteratogenic in animal studies<br>Analog of thalidomide<br>Must be prescribed through RevAid program for safety<br>May cause foetal harm   |
| <b>Mode of use</b>                    | SC or IV x 7 days<br>Every 28 days<br>Outpatient regimen<br>Treat until unacceptable toxicity or disease progression   | IV daily for 5 days over 1 hour<br>Every 28 days<br>Outpatient regimen<br>Treat until unacceptable toxicity of disease progression  | 10 mg orally days 1–21<br>Every 28 days<br>Treat until unacceptable toxicity of disease progression  |

### Hypomethylating agents

Hypermethylation, the accumulation of compounds called methyl groups on portions of DNA, has been identified as one of the contributing factors in the development of MDS and leukaemia. These compounds silence or turn off genes that are necessary for the normal development and maturation of blood cells. Hypermethylation is a constant process. Hypomethylating agents, drugs that block the methyl compounds, have been shown to improve normal blood cell development (haematopoiesis) 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). Decitabine is not PBS listed in Australia.

#### Azacitidine (Vidaza) [www.vidaza.com](http://www.vidaza.com)

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

#### Decitabine (Dacogen®) [www.dacogen.com](http://www.dacogen.com)

Decitabine, (also called 5-deoxyazacytidine), is a DNA hypomethylating agent like azacitidine and works like azacitidine. In other words, decitabine reduces DNA methylation, and restores the normal functioning of tumour suppressor genes in MDS. Positive findings from a major phase III clinical trial that compared decitabine with supportive care in MDS patients revealed that of 170 patients with intermediate to high-risk MDS who participated in the trial, a significantly higher overall response rate was seen in patients receiving decitabine with the responses lasting for about 10 months: 17% response for decitabine-treated patients versus 0% for patients receiving standard of care. Patients who responded to decitabine became or remained transfusion independent. In addition, patients who had a response (complete or partial) to decitabine had a longer time to progression to AML and extended survival compared with patients receiving supportive care alone. The most common side effects seen with decitabine are myelosuppression, nausea, and constipation. Decitabine is not available in Australia.

### Immunomodulatory agents [www.revlimed.com](http://www.revlimed.com)

Immunomodulatory agents are a form of disease modifying treatment targeted at the bone marrow microenvironment and elements of the abnormal MDS cells (malignant clone). Revlimid® (lenalidomide) is approved in Australia for anaemic MDS patients with Low- or Intermediate-1 risk MDS, particularly those with 5q- who are transfusion-dependent. Lenalidomide is taken orally and is available in capsule form. The findings of a landmark study in MDS patients with symptomatic anaemia and chromosome 5q deletion treated with lenalidomide showed that 67% of patients who were initially red blood cell transfusion-dependent achieved transfusion independence, and another 9% had their transfusion requirement decreased by 50% or more. Also, a complete cytogenetic response (i.e., chromosome abnormalities were no longer detectable) was achieved in 45% of patients.

## Disease Modifying Agents

In this study, the response to lenalidomide was rapid, with an average time to response of 4.6 weeks and durable. Most of the patients received continuous daily dosing with 10 mg of lenalidomide. Some patients experienced side effects, such as rash, itching, fatigue, diarrhoea, and nausea. Because lenalidomide is an analogue (chemical look-alike) of thalidomide, there is a potential for birth defects with its use. Because of this potential, the manufacturer of lenalidomide, Celgene, has set up a restricted distribution program called the Celgene i-access Program. Only patients that enrol in and meet all of the conditions of the program are able to receive the drug. In a study of MDS patients without chromosome 5q-, lenalidomide was shown to reduce the red blood cell transfusion need in 43% of patients and eliminate the transfusion need in 26% of patients. The majority of patients had a heavy transfusion burden (two or more red blood cell units/month).

### Immunosuppressive agents

**Immunosuppressive agents**, although not currently PBS 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 anaemia (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 are being used primarily in the clinical trials setting.

### Induction chemotherapy

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

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

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

#### References:

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

Palliative care focuses on relieving the pain and suffering of individuals with illness.

## What is palliative care for MDS?

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

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

## The palliative care team

The palliative care team will work with the patient and their caregivers to identify his or her needs, goals and fears. Palliative medicine utilises 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 centres or clinics have designated palliative care teams; other centres may have access to trained individuals upon request. A palliative care team may include one or more of the following:

- Physician(s)
- Nurse practitioners (NP)
- Haematology/Oncology nurse specialist
- Social worker
- Pain service
- Pastoral care or other spiritual support services
- Nutritionist
- Physical therapist
- Financial counsellor

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

# Bone Marrow Transplant

## What is a bone marrow transplant?

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

## Bone marrow transplant

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

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

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

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

## Am I a candidate for a bone marrow transplant?

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

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

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

- Australian Bone Marrow Donor Registry [www.abmdr.org.au](http://www.abmdr.org.au)
- National Marrow Donor Program (NMDP) [www.marrow.org](http://www.marrow.org)
- Australian Organisation for Young People Living with Cancer [www.canteen.org.au](http://www.canteen.org.au)
- Bone & Marrow Transplant Information Network [www.bmtinphonet.org](http://www.bmtinphonet.org)
- Bone Marrow Transplant Network NSW [www.bmtnsw.com.au](http://www.bmtnsw.com.au)
- Cancer Council of Australia [www.cancer.org.au](http://www.cancer.org.au)
- Centre for Grief and Loss [www.grief.org.au](http://www.grief.org.au)
- Leukaemia Foundation’s online discussion forum [www.talkbloodcancer.com](http://www.talkbloodcancer.com)
- Leukemia & Lymphoma Society of America [www.leukemia-lymphoma.org](http://www.leukemia-lymphoma.org)
- Leukaemia Research Fund (UK) [www.lrf.org.uk](http://www.lrf.org.uk)
- Look Good... Feel Better program <http://lgfb.org.au/>

Am I a BMT candidate?



Blood or bone marrow transplantation is a complex multi-step process. It is important for you and your caregiver(s) to familiarise 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 centre with your designated caregiver(s) for a pre-hospitalisation 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 hospitalised 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 hospitalisation at the bone marrow transplant centre 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  $>0.5 \times 10^9/L$  for three consecutive days or  $>1.0 \times 10^9/L$  for one day, and platelets remain  $>20.0 \times 10^9/L$  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.

In Australia the cost of transplantation is covered by Medicare. You may have to travel to a large tertiary hospital for a bone marrow transplant.

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

- Australian Bone Marrow Donor Registry [www.abmdr.org.au](http://www.abmdr.org.au)
- Leukaemia Foundation [www.leukaemia.org.au](http://www.leukaemia.org.au)
- Leukaemia Research Fund (UK) [www.lrf.org.uk](http://www.lrf.org.uk)
- National Cancer Institute (USA) [www.cancer.gov/cancerinfo](http://www.cancer.gov/cancerinfo)
- Be the Match <http://bethematch.org/>

## The bone marrow transplant evaluation

Once you have identified the transplant centre, 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 consultant, nurses, social workers, and dieticians. 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 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.)
2. What tests will I need before the transplant?
3. Is housing available in the area for post-transplant care and what is the recommended/required duration to reside locally?
4. What is the experience of the transplant team in treating patients with MDS?
5. What is the usual length of hospital stay during transplant?
6. How often will I need to be seen in the clinic after discharge?
7. 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?
8. Are there emotional support services for me, my donor, my caregiver and my family?
9. What is the centre's success rate with stem cell transplants?
10. What are the expectations for the caregiver(s)?

## What Are Clinical Trials

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

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

About clinical trials



### A clinical trial falls into one of four phases:

|                  |   |
|------------------|---|
| <b>Phase I</b>   | 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). |
| <b>Phase II</b>  | 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.   |
| <b>Phase III</b> | 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.  |
| <b>Phase IV</b>  | In Phase IV, the drug, already approved by the PBS and available to the public, undergoes continued evaluation in a large number of patients (several 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 behavioural change, is compared to a control group.

# Participating in a Clinical Trial

## How is a clinical trial conducted?

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

## Members of the research team

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

## 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 enrolment.

- **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](http://www.clinicaltrials.gov)

## Key elements of a clinical trial

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

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

## Am I a candidate for a clinical trial?

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

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

These are most often answered during the informed consent process.

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

## Clinical trials and drug approval information

### European Medicines Agency

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

[www.ema.europa.eu](http://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](http://www.hc-sc.gc.ca)

### National Cancer Institute, National Institutes of Health

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

[www.clinicaltrials.gov](http://www.clinicaltrials.gov)

### National Institute of Health and Clinical Excellence

Guidance for cost effectiveness of treatments for England and Wales

[www.nice.org.uk](http://www.nice.org.uk)

### Nordic MDS Group

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

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

### Pharmaceuticals and Medical Devices Agency

Regulation of drug availability in Japan

[www.pmda.go.jp](http://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](http://www.tga.gov.au)

### U.S. Food and Drug Administration

Approval required for commercial availability of therapy in the United States

[www.fda.gov](http://www.fda.gov)

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

Referenslar:

Kurtin, S. ve d. (2012) *Clin J Oncol Nurs*, 16S, 3, 58-64  
National Institutes of Health @ [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

## How common is MDS in children?

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

## What causes MDS in children?

MDS can appear in an otherwise healthy child. Some evidence suggests that certain children are born with a tendency to develop MDS. This tendency or pre-existing factor can be thought of as a switch that can be triggered by external factors. The most common pre-existing factors in MDS are congenital (present at birth) and genetic (programmed in the cells) syndromes. These are present in about 50% of paediatric 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 anaemia or Diamond-Blackfan anaemia, with acquired aplastic anaemia, 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 anaemia
- Kostmann syndrome
- Diamond-Blackfan syndrome
- Shwachman syndrome
- Down syndrome (trisomy 21)
- 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 leukaemia

There are no known foods 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 haematocrit remains normal. Children with MDS may present with nonspecific symptoms such as a pale complexion, fatigue, petechiae (tiny red or purple spots on the skin), or recurrent infections. In some cases, more severe symptoms such as shortness of breath, weakness, or bleeding may be present.

## Is MDS fatal?

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

Paediatric 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 haematologist in selecting the best treatment. Because the disease course of MDS can vary widely from patient to patient, classification systems for grouping various "subtypes" of the myelodysplastic "syndromes" have been developed, and several classification systems are available that have been developed from those used for the adult forms of MDS (see: *How Severe is My MDS?*).

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

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

#### Myelodysplastic Syndromes

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

#### Myelodysplastic/Myeloproliferative Neoplasm

- Juvenile myelomonocytic leukaemia

#### (JMML) Down Syndrome Disease

- Transient abnormal myelopoiesis
- Myeloid leukaemia of Down syndrome

## Down syndrome disease

Approximately 10% of newborns with Down syndrome develop transient myeloproliferative disorder (TMD). In TMD there are 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 leukaemia (AML) called M7-AML. Myeloid leukaemia in children with Down syndrome is related to MDS, but has its own distinct features.

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

## Juvenile myelomonocytic leukaemia (JMML)

The term JMML includes other childhood leukaemias that were previously known as juvenile chronic myeloid leukaemia, chronic myelomonocytic leukaemia, 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 paediatric 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 anaemia and infection.

Patients with JMML can have varying outcomes based on factors such as, age at diagnosis, number of blood platelets, level of foetal haemoglobin, 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 paediatric 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 anaemia 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 |

Referenstar:

Rau, A.K., ve d. (2012) *The Ochsner Journal* 12:216–220

Vardiman, J.W., ve d. (2009) *Blood*. 114(5):937-951

# Paediatric Information Resources – MDS and Childhood Cancers

## **Alex's Lemonade Stand**

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

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

## **American Cancer Society**

250 Williams Street, NW  
Atlanta, GA 30303  
800-ACS-2345

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

## **American Society of Paediatric Haematology/Oncology (ASPHO)**

4700 W. Lake Avenue  
Glenview, IL 60025  
847-375-4716  
847-375-6475 fax

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

## **Aplastic Anaemia & MDS International Foundation**

100 Parl Avenue, Suite 108  
Rockville, MD 20850  
301-279-7202  
800-747-2820

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

## **Candlelighters Childhood Cancer Foundation**

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

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

## **Childhood Leukaemia Foundation**

Supports children with cancer and their families

[www.clf4kids.com](http://www.clf4kids.com)

## **EWOG (European Working Oncology Group)**

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

## **JMML Foundation**

9921 Carmel Mountain Road #170  
San Diego, CA 92129  
858-243-4651

[www.jmmlfoundation.org](http://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](http://www.marrow.org)

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

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

[www.cancer.gov/cancertopics/pdq/cancerdatabase](http://www.cancer.gov/cancertopics/pdq/cancerdatabase)

## **National Cancer Institute's Clinical Trials Database**

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

[www.cancer.gov/clinicaltrials](http://www.cancer.gov/clinicaltrials)

## **Paediatric Myelodysplastic and Bone Marrow Failure Registry**

Children's Hospital Boston  
Department of Haematology Fegan 7  
300 Longwood Avenue  
Boston, MA 02115 USA  
Phone: 888-5-PediMDS  
Email: [MDS@childrens.harvard.edu](mailto:MDS@childrens.harvard.edu)

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

## **Paediatric Oncology Resource Centre**

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

[www.acor.org/ped-onc](http://www.acor.org/ped-onc)

## **The Leukaemia & Lymphoma Society**

1311 Mamaroneck Avenue, Suite 130  
White Plains, NY 10605  
800-955-4572

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

## **The MDS Foundation, Inc.**

4573 South Broad Street, Suite 150  
Yardville, NJ 08620  
800-MDS-0839 (*within US only*)  
609-298-1035 (*outside US*)  
609-298-0590 fax

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



# Quick Tips

---

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

## **MENTORS**

### ***MDS Foundation International Nurse Leadership Board***

Sandra Kurtin  
Jean Ridgeway  
Jayshree Shah  
Mary Thomas  
Sara Tinsley

### ***The Meniscus Educational Institute***

Karen Abbas

## ***contributing authors***

### **MENTEES**

Nikki Barkett  
Rochelle Chiffelle  
Angela Flowers  
Christopher Flowers  
Denice Gibson  
Carol Guarnieri  
Cynthia G. Paul  
Patrice Welsh-Benjamin

## Quick Tips

---

|   |    |
|---|----|
| Anaemia in MDS                          | 3  |
| Neutropenia in MDS                      | 5  |
| Thrombocytopenia in MDS                 | 7  |
| Fever                                   | 9  |
| Tracking My Blood Counts                | 10 |
| Diarrhoea                               | 11 |
| Constipation                            | 12 |
| Nausea and Vomiting                     | 13 |
| Injection Site Reactions                | 15 |
| Skin Rashes                             | 17 |
| Fatigue                                 | 18 |
| Anxiety                                 | 19 |
| Depression                              | 20 |
| When Should I Call My Health Care Team? | 21 |
| References                              | 22 |



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

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

### Symptoms of anaemia:

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

### How is anaemia measured?

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

Haemoglobin is measured from a blood sample and the amount present is expressed in units of grams per liter, abbreviated g/L. The normal value for haemoglobin varies by age and gender. Anaemia occurs when haemoglobin concentrations fall below 120 g/L for women and 130 g/L for men. The severity of anaemia is categorized by the following haemoglobin concentration ranges:

- **Mild anaemia:** haemoglobin between 95–130 g/L
- **Moderate anaemia:** haemoglobin between 80–95 g/L
- **Severe anaemia:** haemoglobin below 80 g/L

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

### **Things your health care team may recommend:**

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

### **Things you can do:**

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

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

# Neutropenia in MDS

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

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

## How is neutropenia measured?

Neutrophils are the most common type of white blood cell, normally 60-70% of the WBC. The severity of neutropenia is estimated based on the absolute neutrophil count (ANC). The normal WBC is  $3.5-10 \times 10^9 / L$ . The normal ANC is  $1.5-8.0 \times 10^9 / L$ . The ANC is calculated using the following formula:

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

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

- **Mild neutropenia:** ANC  $1.0-1.5 \times 10^9 / L$
- **Moderate neutropenia:** ANC  $0.5-1.0 \times 10^9 / L$
- **Severe neutropenia:** ANC less than  $0.5 \times 10^9 / L$

Febrile neutropenia is considered a medical emergency and should be reported to your health care provider immediately. Febrile neutropenia is present when the ANC is  $<1.0 \times 10^9 / L$  and you have a body temperature  $>38.5^\circ\text{C}$  ( $101.4^\circ\text{F}$ ) or a sustained temperature  $>38.0^\circ\text{C}$  ( $100.4^\circ\text{F}$ ) for more than one hour. Ask your health care team who to contact, how to contact them, and when you should seek urgent or emergency care.

## Symptoms of febrile neutropenia:

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

## Things your health care team may recommend:

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

## Things you can do:

1. Let your doctor know if you develop a fever when your ANC is  $<1.0 \times 10^9 / L$ . If you are not sure what your ANC is, ask your health care team for guidelines on when you should report a fever.
2. Keep all your appointments as scheduled.
3. Have a working thermometer at home.
4. Record and track your blood counts, including the WBC and ANC, any symptoms including fevers, chills, or infections.

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

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

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

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

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

## How is thrombocytopenia measured?

Thrombocytopenia is characterized by a platelet count below normal. Normal platelet levels are between  $150\text{--}450 \times 10^9 / \text{L}$ . The severity of thrombocytopenia is measured by following platelet counts obtained from peripheral blood:

- **Mild thrombocytopenia:** platelet count of  $50\text{--}100 \times 10^9 / \text{L}$
- **Moderate thrombocytopenia:** platelet count of  $25\text{--}50 \times 10^9 / \text{L}$
- **Severe thrombocytopenia:** platelet count less than  $25 \times 10^9 / \text{L}$

## Symptoms of thrombocytopenia:

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

## Things your health care team may recommend:

- Your health care team may recommend platelet transfusions when the platelets are below  $10 \times 10^9 / \text{L}$  or at higher levels for patients with additional risk factors, such as a recent surgery. Platelet transfusions may be given to reduce the risk of bleeding. Platelet transfusions are considered a form of supportive care. They do not change the characteristics of the MDS. The benefits of platelet transfusions are temporary (hours) so that repeated transfusions may be needed. The number and frequency of platelet transfusions will vary for each person based on the severity of symptoms, the characteristics of the MDS, and what other treatments are being used.
- Your doctor will recommend that you stop taking any medications that interfere with platelet function (aspirin) or prevent clotting through other mechanisms (blood thinners such as Warfarin, Plavix, and Heparin). These medications are generally held when the platelet count is below  $50 \times 10^9 / \text{L}$ .
- There are currently no FDA approved growth factors for the treatment of thrombocytopenia in patients with MDS. There are medications used for thrombocytopenia resulting from other causes that are being studied in clinical trials for patients with MDS and thrombocytopenia.
- If thrombocytopenia is severe, it may be necessary to modify your MDS treatment by changing the dose or holding the medication temporarily until the platelet count recovers.

**Things you can do:**

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

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

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

## Signs and symptoms of a fever

The most common recommendations for checking a temperature:

- Feeling warmer than normal
- Flushing (red in the face)
- Low blood pressure
- Shaking chills (can't get warm even with blankets, chattering teeth)
- Feeling lightheaded or dizzy
- Temperature higher than normal (normal = 37°C)

## Things your health care team may recommend:

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

## Things you can do:

1. Have a working thermometer at home. Discuss which type of thermometer is best for you to use with your health care team.
2. Stay hydrated.
3. Record and track your blood counts, including the WBC and ANC, any symptoms including fevers, chills, or infections (see: *My MDS Plan*).
4. Let your doctor know if you develop a fever when your WBC or ANC are  $<1.0 \times 10^9$  /L. If you are not sure what your ANC is, ask your health care team for guidelines on when you should report a fever.
5. Notify your health care team for any fever greater than 38.0°C
6. Shaking chills at any body temperature in patients with neutropenia (see: *Quick Tips: Neutropenia*) should be reported immediately.
7. Keep all of your appointments as scheduled.
8. Ask for help from family and friends.

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

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

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

### The Full Blood Examination (FBE), Differential and Platelet Count

| Blood Count  | Normal Range                  |                    |
|--|-------------------------------|--------------------|
| White Blood Cells (WBC)                                | 4.5-11.0 x 10 <sup>9</sup> /L |                    |
| Absolute Neutrophil Count (ANC) (WBC x % Segs + Bands) | ≥1.5 x 10 <sup>9</sup> /L     |                    |
| Haemoglobin (Hb)                                       | Men: 135-175 g/L              | Women: 120-160 g/L |
| Haematocrit (Hct)                                      | Men: 41-53%                   | Women: 36-46%      |
| Platelets (Plt)  | 150-350 x 10 <sup>9</sup> /L  |                    |

### Things you can do:

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

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

## Symptoms of diarrhoea:

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

## Things your health care team may recommend:

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

## Things you can do:

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

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

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

### Symptoms of constipation:

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

### Things your health care team may recommend:

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

### Things you can do:

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

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

Nausea is a symptom that is often described as an unpleasant feeling associated with flushing, tachycardia (rapid heart rate), and the urge to vomit.

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

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

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

## Symptoms often associated with nausea or vomiting:

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

## Things your health care team may recommend:

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

## Things you can do:

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

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

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

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.

#### Injecton Technique: The Air Sandwich



**Things your health care team may recommend:**

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

**Things you can do:**

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

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

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

## Signs and Symptoms

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

## Things your health care team may recommend:

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

## Things you can do:

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



*Skin rash from Revlimid (Lenalidomide)*

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 anaemia. Insomnia (difficulty sleeping) is common in older adults and may contribute to fatigue. Other things that can contribute to fatigue include: inactivity, pain, emotional distress, poor nutrition, and other illnesses that are not well controlled such as diabetes or thyroid disorders.

## Symptoms of fatigue:

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

## Things your health care team may recommend:

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

## Things you can do:

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

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

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

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

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

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

## Things you can do:

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

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

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

## Things you can do:

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

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

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

- Fevers greater than 38.0 Celsius that lasts longer than one hour, or a single temperature >38.3 Celsius
- Shaking chills at any temperature
- Sudden onset of shortness of breath or chest pain (call 000)
- 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 colour of the urine
  - Uncontrolled diarrhoea or constipation
  - Black or bloody stools
- Uncontrolled nausea or vomiting

- Bisanz, A. ve d (2010)** *Summary of the causative and treatment factors of diarrhoea and the use of a diarrhoea assessment and treatment tool to improve patient outcomes.* *Gastroenterology Nursing*, 33(4) 268-281. doi:10.1097/SGA.0b013e3181394307
- Bohnenkamp, S. & LeBaron, V. (2010)** *Management of Constipation in Patients with Cancer.* *Journal of the Advanced Practitioner in Oncology*, 1,3,211-217
- Hesketh, P.** *Chemotherapy-Induced Nausea and Vomiting.* *NEJM* 2008;358:2482-2494
- Kurtin, S. (2011)** *Current Approaches to the Diagnosis and Management of Myelodysplastic Syndromes.* *Journal of the Advanced Practitioner in Oncology*, Volume 2, Supplement 2
- Kurtin, S.E., & Demakos, E.P. (2010)** *An update on the treatment of Myelodysplastic Syndromes [Online exclusive].* *Clinical Journal of Oncology Nursing*, 14, E24–E39. doi:10.1188/10
- Kurtin, S.E., Demakos, E., Hayden, J., & Boglione, C. (2012)** *Treatment of Myelodysplastic Syndromes: Practical tools and effective management.* *Clinical Journal of Oncology Nursing*, 16(3, Suppl. 1), 23–35. doi:10.1188/12. CJON.S1.23-35
- Muehlbauer, P.M. ve d (2009).** *Putting evidence into practice: evidence-based interventions to prevent, manage, and treat chemotherapy- and radiotherapy-induced diarrhoea.* *Clinical Journal of Oncology Nursing*, 13(3) 336-341. doi:10.1188/09.CJON.336-341
- NCCN Clinical Practice Guidelines in Oncology; Myelodysplastic Syndromes V1.2012*
- Rangwala, F., Zafar, S.Y., & Abernethy, A.P. (2012)** *Gastrointestinal symptoms in cancer patients with advanced disease: new methodologies, insights, and a proposed approach.* *Current Opinion in Supportive and Palliative Care*, 6(1):69-76. doi:10.1097/SPC.0b013e32834f689d
- Smith, L, Bertolotti, P., Curran K., Jenkins B.** *Gastrointestinal Side-Effects Associated with Novel Therapies in Patients with Multiple Myeloma: Consensus statement of the IMF Nurse Leadership Board.* *CJON* 2008;12(3):37-52
- Thomas, M.L., Crisp, N., Campbell, K.** *The Importance of Quality of Life for Patients Living with Myelodysplastic Syndromes.* *Clinical Journal of Oncology Nursing* 2012;16 (0), 47-57

# 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?*

*contributing authors*

Sandra Kurtin  
Alan List  
Jayshree Shah  
David Steensma  
Bob Weinberg

# Iron Overload

---

|  |    |
|--|----|
| Blood Transfusions and MDS                     | 3  |
| What Is Iron Overload                          | 5  |
| How Serious Is Iron Overload?                  | 6  |
| Is Iron Overload Treatable?                    | 6  |
| Chelating Agents Used to Treat Iron Overload   | 9  |
| What Can I Do to Avoid Iron Overload?          | 11 |
| Glossary                                       | 12 |
| Resources                                      | 13 |
| References                                     | 14 |
| Living With Iron Overload: Patient Testimonial | 15 |

# Blood Transfusions and MDS

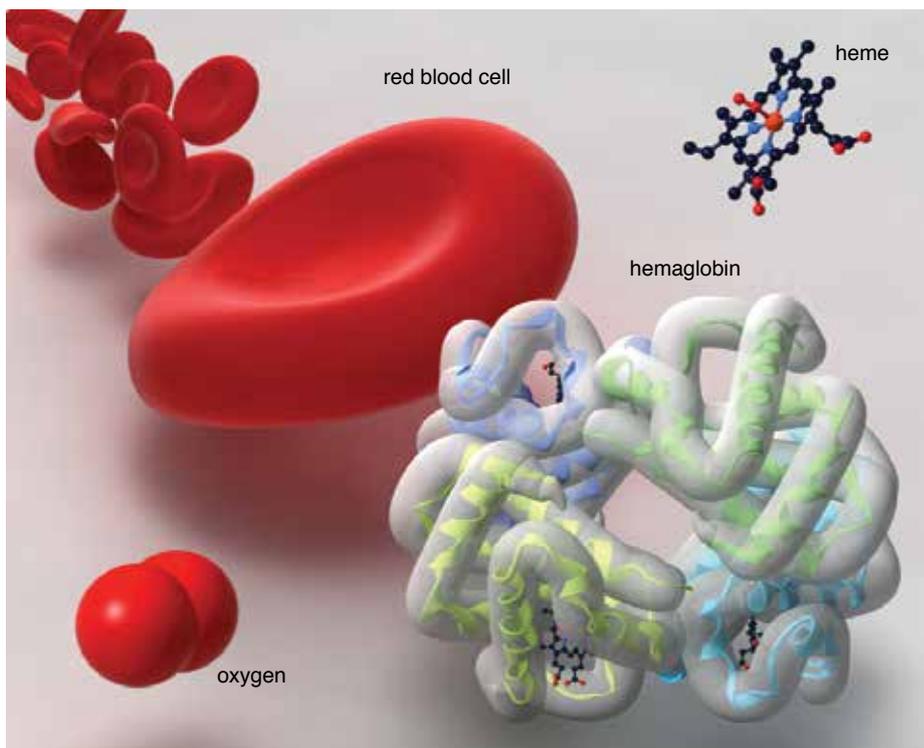
## Why are blood transfusions necessary for patients with MDS?

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

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

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

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



## General Guidelines for Transfusion of PRBCs

- Requires informed consent
- Asymptomatic patients: transfuse to maintain Hb 70-90 g/L
- Symptomatic with haemorrhage: transfuse to maintain hemodynamic stability
- Symptomatic with Hb < 10 Og/L: transfuse to maintain Hb 80-100 g/L
- Acute coronary syndromes with anaemia: transfuse to maintain Hb > 10 Og/L

## BENEFITS

- Rapid increase in haemoglobin (Hb), may reduce fatigue in some patients

## RISKS

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

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

Transfusions and iron overload



### Related Pages:

[What Happens to the Bone Marrow in MDS Quick Tips: Anaemia](#)

### References:

Kurtin, S. (2012) Myeloid Toxicity of Cancer Treatment, *J Adv Pract Oncol*, 3,209-224

Red blood cell transfusions may provide temporary relief from the symptoms of anaemia, 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 anaemia. 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 anaemia 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 haemoglobin. 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.

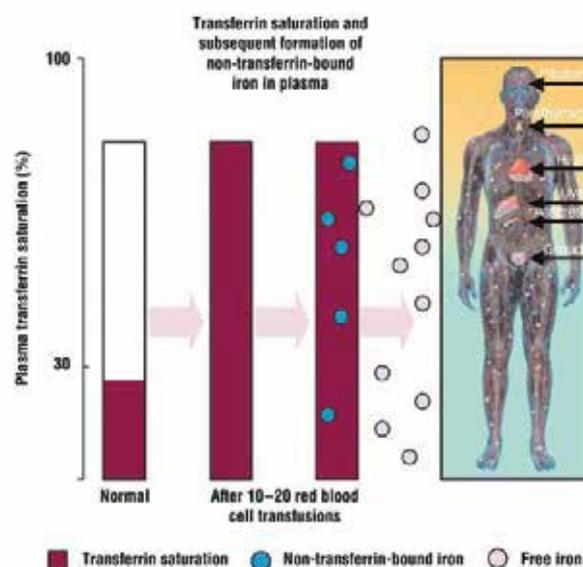
## Red blood cell transfusion and iron overload

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 anaemia 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 ug/L, and those with an IPSS risk of “Low-Intermediate-1” who require continued transfusions.



### References:

Shah, ve d. (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?

## Is Iron Overload Treatable?

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

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 leukaemia. This negative effect on survival depends on the number of red blood cell transfusions received per month. The negative effect on survival is also related to the severity of MDS (see: *How Severe is My MDS?*). Management of iron overload and treatment of iron toxicity by iron chelation (key ·LAY·shun) therapy in patients with MDS and transfusion-dependent anaemia 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 haemoglobin levels can help you understand your risk of iron overload (see: *My MDS Plan*).

In MDS patients, serum ferritin levels have been shown to be related to the number of red blood cell units received. A serum ferritin value of 10  $\mu\text{g/L}$  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<br>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 anaemia. | May indicate haemolytic anaemia, megaloblastic anaemia, or iron overload. | Serum ferritin levels greater than 1,000–2,500 ng/L indicate iron overload in patients with transfusion-dependent anaemia. |

# How Serious Is Iron Overload? Is Iron Overload Treatable?

## Is iron overload treatable?

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

## Phlebotomy

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

## Tests for Iron Overload

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

## How Serious Is Iron Overload? Is Iron Overload Treatable?

### Chelating agents

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

| 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/faeces   | Faeces                      | Urine                    | Faeces                    |

### How long will I receive iron chelation therapy?

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

### What are the side effects of iron chelating drugs?

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

### Iron Chelating Drugs: Common Side Effects

| Desferal® (deferoxamine)         | Exjade® (deferasirox)         | Ferriprox® (deferiprone)                                    | 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                                      |                               |

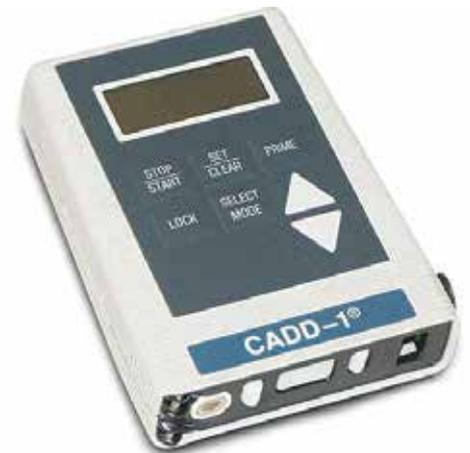
Discuss any symptoms you have after starting chelation therapy with your health care team. Ask about when you should notify them, how to call, what phone number to call, and who you should talk to if you are having symptoms. Find out what symptoms need to be reported immediately so that they can be managed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

# Chelating Agents Used to Treat Iron Overload

## Desferal® (deferroxamine)

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

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



## Exjade® (deferasirox)

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

The most common side effects associated with Exjade® use include diarrhoea, nausea, vomiting, headache, abdominal pain, fever, cough, and mild nonprogressive increases in serum creatinine. Potential long-term adverse reactions to Exjade® include kidney or liver damage, loss of hearing, or cataracts. Keep all appointments with your doctor and the laboratory. Your doctor will order certain laboratory tests to monitor the effects of your chelation therapy. Keep this medication in the container it came in, tightly closed, and out of reach of children. Store it at room temperature and away from excess heat and moisture (not in the bathroom). Throw away any medication that is outdated or no longer needed.



## Chelating Agents Used to Treat Iron Overload

### How to take Exjade®

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

### Ferriprox® (deferiprone)

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

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

### Jadenu™ (deferasirox)

Jadenu™ is an oral treatment for iron overload that is taken once daily at a dose of 14 milligrams per kilogram of body weight (14mg/kg/day). It is a new oral formulation of the Exjade tablets. Whereas the Exjade tablets must be mixed in liquid and taken on an empty stomach, Jadenu tablets can be taken once daily with water or other beverages on an empty stomach or with a light meal. You should avoid taking this medication with a meal high in calories and fat as it may increase your risk of side effects. Ask your doctor or pharmacist for more details. If you have trouble swallowing the tablets, you may crush the tablets and mix it with soft foods (such as applesauce, yogurt). Swallow all of the drug/ food mixture right away. Do not prepare a supply in advance. Take the medication as prescribed by your health care provider. Do not increase your dose or use this drug more often or for longer than prescribed. The dosage is based on your medical condition, weight, laboratory tests, and response to treatment. Your dosage may need to be lowered or your treatment may need to be stopped if you get certain side effects. Follow your doctor's instructions carefully.

The most common side effects associated with Jadenu™ use include diarrhea, nausea, vomiting, abdominal pain, rash and mild increases in serum creatinine. Keep this medication in the container it came in, tightly closed, and out of reach of children. Store it at room temperature and away from excess heat and moisture (not in the bathroom). Throw away any medication that is outdated or no longer needed.

# What Can I Do to Avoid Iron Overload?

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

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

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

## Avoiding iron overload: diet and medications

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

### To decrease the absorption of iron:

- Consume milk products, eggs, certain high fibre 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](http://www.mds-foundation.org)

The MDS Alliance [www.mds-alliance.org](http://www.mds-alliance.org)

## Foundations or Organizations Specific to Iron Overload

Iron Disorders Institute [www.irondisorders.org](http://www.irondisorders.org)

Iron Overload Diseases Association, Inc. [www.ironoverload.org](http://www.ironoverload.org)

## Other Foundations or Organizations

Leukaemia Foundation of Australia [www.leukemia.org.au](http://www.leukemia.org.au)

Aplastic Anemia & MDS International Foundation [www.aamds.org](http://www.aamds.org)

American Cancer Society [www.cancer.org](http://www.cancer.org)

American Society of Haematology [www.hematology.org](http://www.hematology.org)

Caring Bridge [www.caringbridge.org](http://www.caringbridge.org)

National Anemia Action Council [www.anemia.org](http://www.anemia.org)

National Heart, Lung and Blood Institute [www.nhlbi.nih.gov](http://www.nhlbi.nih.gov)

The Leukemia & Lymphoma Society [www.lls.org](http://www.lls.org)

## Drug Specific Resources

Desferal® (deferoxamine) [www.desferal.com](http://www.desferal.com)

Exjade® (deferasirox) [www.exjade.com](http://www.exjade.com)

Ferriprox® (deferiprone) [www.ferriprox.com](http://www.ferriprox.com)

Jadenu™ (deferasirox) [www.jadenu.com](http://www.jadenu.com)

## General Information

Medline Plus [www.nlm.nih.gov/medlineplus/medlineplus.html](http://www.nlm.nih.gov/medlineplus/medlineplus.html)

The Merck Manual Home Edition for Patients and Caregivers [www.merckmanuals.com/home/index.html](http://www.merckmanuals.com/home/index.html)

## Additional reading from the medical literature

- Bennett, J.M. (ed)** *The Myelodysplastic Syndromes: Pathobiology and Clinical Management* New York: Marcel Dekker, Inc. 2002
- Fausel, C.A.** *Iron chelation therapy in Myelodysplastic Syndromes.* Am J Health-Syst Pharm. 2010; 67(suppl 2): S10–15
- Giagounidis, A., Leto di Priolo, S., Ille, S., & Fenaux, P. A** *European survey on the detection and management of iron overload in transfusion-dependent patients with MDS.* Ann Hematol. 2011; 90:667–673
- Kwiatkowski, J.L.** *Oral iron chelators.* Hematol Oncol Clin N Amer. 2010;24:229–248
- Malcovatti, L.** *Red blood cell transfusion therapy and iron chelation in patients with Myelodysplastic Syndromes.* Clin Lymphoma Myeloma. 2009;9:S305–S311
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Myelodysplastic Syndromes. Version 2. 2012** Available online at [www.nccn.org/professionals/physician\\_gls/f\\_guidelines.asp](http://www.nccn.org/professionals/physician_gls/f_guidelines.asp)
- Shander, A., & Sweeney, J.D.** *Overview of current treatment regimens in iron chelation therapy.* US Hematol. 2009;2:59–62
- Steensma, D.** *The role of iron chelation therapy for patients with Myelodysplastic Syndromes.* J Natl Compr Canc Netw. 2011;9:65–75

## How to contact the Myelodysplastic Syndromes Foundation

**The MDS Foundation, Inc.**  
4573 South Broad Street, Suite 150  
Yardville, NJ 08620  
800-MDS-0839 (*within US only*)  
609-298-1035 (*outside US*)

# Living with Iron Overload



*video testimonial*

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

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

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

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

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

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

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

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

**Bob Weinberg**





# MY MDS PLAN

---

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

*contributing authors*

Erin Demakos  
Sandra Kurtin  
Sarah Tinsley

# MY MDS PLAN

---

|   |    |
|---|----|
| Taking an Active Part in Your Care          | 3  |
| Tracking Your Treatment                     | 4  |
| <i>Initial Laboratory Results</i>           |    |
| <i>MDS Treatments</i>                       |    |
| <i>Bone Marrow Results</i>                  |    |
| <i>Blood Counts and Transfusions</i>        |    |
| <i>Appointments and Questions</i>           |    |
| My Health Profile                           | 9  |
| <i>Medical History</i>                      |    |
| <i>Prescription Medications</i>             |    |
| <i>Over The Counter Medications</i>         |    |
| <i>My Health Care Team</i>                  |    |
| <i>Employment and Insurance Information</i> |    |
| Frequently Asked Questions                  | 15 |
| Suggested References                        | 18 |
| Staying Well                                | 19 |
| Selected References                         | 24 |
| Additional Resources                        | 25 |
| Living with MDS: Patient Testimonials       | 32 |

## The diagnosis of MDS

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

## Explore the Building Blocks of Hope

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

## Daily activities

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

# Tracking Your Treatment

## Initial Laboratory Results

| Diagnostic Test             | Normal Result        | My Result        | Date        | Notes        |
|-----------------------------|----------------------|------------------|-------------|--------------|
| Haemoglobin                 | Women: 125-165 g/L   |                  |             |              |
|                             | Men: 135-175 g/L     |                  |             |              |
| White Blood Cell Count      |                      |                  |             |              |
| Absolute Neutrophil Count   |                      |                  |             |              |
| Platelet Count              |                      |                  |             |              |
| Serum Erythropoietin        |                      |                  |             |              |
| Serum Iron                  |                      |                  |             |              |
| Serum Folate                |                      |                  |             |              |
| Serum B12                   |                      |                  |             |              |
| Thyroid Stimulating Hormone |                      |                  |             |              |
| <b>Diagnostic Test</b>      | <b>Normal Result</b> | <b>My Result</b> | <b>Date</b> | <b>Notes</b> |
| WHO Classification          |                      |                  |             |              |
| FAB Classification          |                      |                  |             |              |
| Blast %                     |                      |                  |             |              |
| Cytogenetics                |                      |                  |             |              |
| IPSS/IPSS-R Score           |                      |                  |             |              |

Normal ranges may vary amongst different laboratories.

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









# My Health Profile



| MY HEALTH PROFILE                 |                 |             |
|-----------------------------------|-----------------|-------------|
| Name                              |                 |             |
| Date of Birth                     | Medicare Number |             |
| Address                           |                 |             |
| City                              | State           | Postal Code |
| Home Phone                        | Mobile Phone    |             |
| Work Phone                        | Email           |             |
| Caregivers                        |                 |             |
| Name/ Relationship                |                 | Phone       |
|                                   |                 |             |
|                                   |                 |             |
|                                   |                 |             |
|                                   |                 |             |
|                                   |                 |             |
| Emergency contacts                |                 |             |
|                                   |                 |             |
|                                   |                 |             |
| Marital status / Living situation |                 |             |
|                                   |                 |             |









| EMPLOYMENT INFORMATION |            |             |
|------------------------|------------|-------------|
| Employer               | Job Title  |             |
| Address                | Supervisor |             |
| City                   | State      | Postal Code |
| Phone                  |            |             |

| INSURANCE INFORMATION   |                 |             |
|---|-----------------|-------------|
| Insured or Guarantor <input type="radio"/> self <input type="radio"/> spouse <input type="radio"/> parent |                 |             |
| Date of Birth   | Medicare Number |             |
| Employer  | Phone           |             |
| Address   |                 |             |
| City  | State           | Postal Code |
| Insurance Name  |                 | ID Number   |
| Contact   |                 |             |

|   |                 |             |
|---|-----------------|-------------|
| Insured or Guarantor <input type="radio"/> self <input type="radio"/> spouse <input type="radio"/> parent |                 |             |
| Date of Birth   | Medicare Number |             |
| Employer  | Phone           |             |
| Address   |                 |             |
| City  | State           | Postal Code |
| Insurance Name  |                 | ID Number   |
| Contact   |                 |             |

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

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

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

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

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

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

## **Is MDS inheritable?** *(Sekeres, 2011)*

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

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

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

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

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

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

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

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

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

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

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

**heart** - congestive heart failure

**endocrine glands** - diabetes

**liver** - elevated liver function tests, hepatomegaly, pain

**bone marrow** - dysfunctional haematopoiesis

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

## How likely am I to get better with the treatment?

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

## How long will the treatment take to work?

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

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

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

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

*(Kurtin, 2011; Kurtin & Demakos, 2010)*

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

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

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

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

### **What can I do to keep myself healthy?**

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

# Suggested References

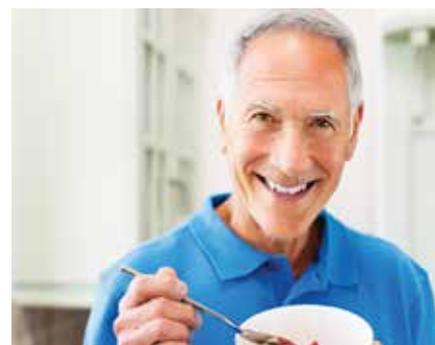


- Bejar, R., Levine, R., & Ebert, B.L. (2011)** *Journal of Clinical Oncology*, 29, 504–515. doi:10.1200/JCO.2010.31.1175
- ClinicalTrials.gov (2012)** *Search for clinical trials*. Retrieved from [www.clinicaltrials.gov/ct2/search](http://www.clinicaltrials.gov/ct2/search)
- Demakos, W., Kurtin, S. (2011)** *Disease burden and treatment impact associated with Myelodysplastic Syndromes: Initial estimates [Abstract 354]*. *Leukemia Research*, 35 (suppl. 1), S142
- Garcia-Manero, G. (2011)** *American Journal of Hematology*, 86, 490–498. doi:10.1002/ajh.22047/10.1002/ajh.22047
- Greenberg, P. ve d. (2011)** *Journal of the National Comprehensive Cancer Network*, 9, 30–56
- Kurtin, S. ve d. (2012)** *Clinical Journal of Oncology Nursing*, 16,3(S), 58-64 doi:10.1188/12.CJON.S1.58-64
- Kurtin, S. (2011)** *Journal of the Advanced Practitioner in Oncology*, 2(suppl. 2), 7–18
- Kurtin, S.E., & Demakos, E.P. (2010)** *Clinical Journal of Oncology Nursing*, 14, E29–E44. doi:10.1188/10.CJON.E24-E39
- Life Beyond Limits (2011)** *MDS treatment matters*. Retrieved from [www.mdslifebeyondlimits.org](http://www.mdslifebeyondlimits.org)
- MDS Foundation (2012)** *Home page*. Retrieved from [www.mds-foundation.org](http://www.mds-foundation.org)
- National Comprehensive Cancer Network Treatment Guidelines: Myelodysplastic Syndromes (2012)** Retrieved from [www.nccn.org/professionals/physician\\_gls/PDF/mds.pdf](http://www.nccn.org/professionals/physician_gls/PDF/mds.pdf)
- National Marrow Donor Program (2011)** *Be the match*. Retrieved from <http://marrow.org/Home.aspx>
- Sekeres, M.A. (2011)** *Journal of the National Comprehensive Cancer Network*, 9, 57–63
- Sekeres, M.A., ve d. (2011)** *Oncologist*, 16, 904–911. doi:10.1634/theoncologist.2010-0199

## Eating healthy

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

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



Another good place to start is with the Australian Dietary Guidelines at <https://www.eatforhealth.gov.au/guidelines>.

## Do I need to follow a special diet with MDS?

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

## General dietary guidelines

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

## Guidelines for healthy eating

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



- Avoid salad bars and deli counters. Buy vacuum-packed lunch meats instead of freshly sliced meats.
- Consume only pasteurized milk, yogurt, cheese, and other dairy products.
- Avoid soft mould ripened and blue-veined cheeses such as Brie, Camembert, Roquefort, Stilton, Gorgonzola, and Bleu.
- At home, it's okay to drink tap water or bottled water, avoid other water sources that may be untreated and carry potential forms of bacteria such as water from a well.

### Hydration

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

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



### Exercise

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

Prior to starting a new exercise program, it is a good idea to discuss your plans with a health care provider to make sure that it is safe for your condition. Individual exercise programs can be designed to fit most needs. An exercise program can be modified to fit each person based on their age, sex, type of MDS and treatment, and physical fitness level.



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

### Sleep

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



### How much sleep is enough?

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

### Make sleeping well a priority.

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

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

### Going out

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

### What can I safely do when I am neutropenic?

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

Guidelines for activities while neutropenic are related to the risk of being exposed to people or things that would increase the chance of developing an infection. As expected, crowded places with close personal contact creates the opportunity for catching an illness. However, whether an infection occurs depends on many factors. The majority of infections that neutropenic patients experience are not related to exposure to other people or places. Instead, most infections are from

bacteria that already live inside the body that turn into problems when the neutrophils are low. Most cancer centres have neutropenic precautions, which vary.

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

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

### Being around children

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

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

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

### Medications

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

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

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

- Anti-inflammatory medications are commonly used to alleviate pain from arthritis, headache, and fever. Examples include ibuprofen, aspirin, Naproxin.
  - This class of drug can cause problems by masking fevers during periods of neutropenia, and interfere with platelet function.
  - When the platelet count is less than 50,000, medications in this class should not be taken. This can increase the risk of bleeding. Check with your treating team about the safe use of these medications in relation to your individual circumstance.
- Antihistamines: Are sometimes used prior to transfusion of packed red blood cells and platelets to help prevent transfusion reactions. Some antihistamines may cause sedation. They may also cause problems with restless legs and agitation with higher doses of the medication. If you experience unpleasant side effects, discuss alternative medications or dose adjustments with your health care team.

### Complementary therapies

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

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

### Other alternative treatments

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

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

*A healthy diet and physical activity help reduce your cancer risk (2012)* CA: A Cancer Journal for Clinicians, 62(1), 68-69. doi: 10.3322/caac.20139

Centers for Disease Control and Prevention. *General recommendations on immunization: Recommendations of the Advisory Committee on immunization practices (ACIP)* Morbidity Mortality Weekly Rep. 2006;55,1–48. Accessed at [www.cdc.gov/mmwr/preview/mmwrhtml/rr5515a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5515a1.htm) on June 21, 2012.

**Finberg, R. (2012)** *Book 86. Infections in Patients with Cancer.* In D.L. Longo, A.S. Fauci

**Kamboj, M., Sepkowitz, K.A. (2007)** *Risk of transmission associated with live attenuated vaccines given to healthy persons caring for or residing with an immunocompromised.* Infection Control Hospital Epidemiology. Jun; 28(6):702-7

**Keogh, J. W. L. & MacLeod, R. D. (2012)** *Body Composition, Physical Fitness, Functional Performance, Quality of Life, and Fatigue Benefits of Exercise for Prostate Cancer Patients: A Systematic Review* Journal of Pain and Symptom Management 43(1): 96-110

**Kushi, L. H., Doyle, C., McCullough, M., Rock, C. L., Demark-Wahnefried, W., & Bandera, E. V., ve d. (2012)** *American Cancer Society guidelines on nutrition and physical activity for cancer prevention.* CA: A Cancer Journal for Clinicians, 62(1), 30-67. doi: 10.3322/caac.20140

**Luthy, K.E., Tiedeman, M.E., Beckstrand, R.L., & Mills, D.A. (2006)** *Safety of live-virus vaccines for children with immune deficiency.* Journal of American Academy of Nurse Practitioners. Oct 18(10):494-503

**Miller, J., & Starks, B. (2010)** *Deciphering Clues in the CBC count.* Nursing July; 40 (7): 52-5

**Mukhopadhyay, S., Mukhopadhyay, A., Gupta, P. R., Kar, M., & Ghosh, A. (2007)** *The Role of Iron Chelation Activity of Wheat Grass Juice in Blood Transfusion Requirement of Intermediate Thalassaemia.* ASH Annual Meeting Abstracts, 110(11), 3829

**Palesh, O.G., Roscoe, J.A., & Mustian, K.M., ve d. Prevalence, demographics, and psychological associations of sleep disruption in patients with cancer: University of Rochester Cancer Center-Community Clinical Oncology Program.** Journal of Clinical Oncology 28 (2): 292-8, 2010

**Platzbecker, U., Aul, C., Ehninger, G., & Giagounidis, A. (2010)** *Reduction of 5-azacitidine induced skin reactions in MDS patients with evening primrose oil.* Annals of Hematology, 89(4), 427-428. doi: 10.1007/s00277-009-0824-5

**Sudano, I., Flammer, A., Roas, S., Enseleit, F., Noll, G., & Ruschitzka, F. Nonsteroidal Antiinflammatory Drugs, Acetaminophen, and Hypertension.** Current Hypertension Reports, 1-6. doi: 10.1007/s11906-012-0274-7

**Wolf, M., King, J., Jacobson, K., Di Francesco, L., Bailey, S., & Mullen, R., ve d. Risk of Unintentional Overdose with Non-Prescription Acetaminophen Products.** Journal of General Internal Medicine, 1-7. doi: 10.1007/s11606-012-2096

# Additional Resources

---

## Pharmaceutical company assistance



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

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

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

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

So the family flew to Seattle in early 2006. We visited the Fred Hutchinson Cancer Centre, which I was told was the place for MUD (matched unrelated donor) transplants. The doctor sat my wife, my 23-year-old daughter, and me

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

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

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

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

Bob Weinberg





## video testimonial

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

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

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

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

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

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

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

### How is my quality of life?

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

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

### What are my fears?

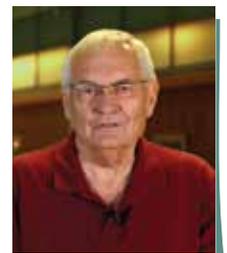
I am apprehensive about my life with MDS. I don't dwell on it and, for the most part, have little fear. The only time I get a bit edgy is after blood tests while I am waiting for results.

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

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

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

William Pearson



# Living with MDS



## video testimonial

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

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

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

The doctor put William on a drug which maintained his haemoglobin counts, and sustained his and my quality of life for about 4 ½ years.

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

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

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

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

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

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

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

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

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

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

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

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

Janet Pearson



# Living with MDS



## video testimonial

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Ryan Szanto



# The MDS Foundation

---

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

*contributing authors*

Lea Harrison  
Audrey Hassan  
Sue Hogan  
Tracey Iraca  
Sandra Kurtin  
Deborah Murray  
Bob Weinberg

# MDS Foundation

---

|   |    |
|---|----|
| About the MDS Foundation                            | 3  |
| The MDS Foundation Staff                            | 4  |
| The MDS Foundation Board of Directors               | 5  |
| International MDS Foundation Nurse Leadership Board | 6  |
| The MDS Foundation Patient Services                 | 7  |
| MDS Centres of Excellence                           | 8  |
| Patients Information Resources                      | 13 |
| Create Your Own Support Group                       | 14 |
| Planned Giving                                      | 17 |



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

Until the Foundation was set up, no formal working group had been devoted to MDS. Since its inception, we have conducted 14 international symposia in Austria, England, the United States (Chicago, Washington, DC), Spain (Barcelona, Valencia), Czech Republic, Sweden, France, Japan, Italy, Greece, Scotland, and Germany. The 15th International Symposium will be held in Copenhagen, Denmark on May 8-11, 2019.

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

In response to the needs expressed by patients, families, and healthcare professionals, we have established patient advocacy groups, research funding, and professional educational initiatives.

The MDS Foundation is a publicly supported organization, exempt from federal income tax under section 501(C)(3) of the IRS code.



## **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 staff projects. 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 and new business development. She serves as liaison to the Foundation's International Nurse Leadership Board, International Working Group for Prognosis in MDS (IWG-PM), and MDS/MPN International Working Group (MDS/MPN IWG).

## **Tami Gilbertson**

### **Director of Development**

Tami joined the Foundation in December 2016 as our first Director of Development. Tami has 25 years of non-profit experience, helping rare disease organizations build a solid strategic development plan in order to engage the community for support. Her passion is creating valuable partnerships while building sustainable programs that will impact the future of rare diseases. Tami is excited to now direct this passion towards MDS.

## **Audrey Hassan**

### **Patient Liaison**

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

## **Lea Harrison**

### **Senior Project Manager**

Lea joined the Foundation in 2001. Lea manages all aspects of various CME programs, live symposia and educational meetings for healthcare professionals. She is also responsible for patient educational projects such as the coordination and translation of our Building Blocks of Hope® patient and caregiver resource. Lea is also leading our new pediatric MDS initiative.

## **Janice Butchko**

### **Project Manager**

Janice joined the Foundation in 2008. Janice manages our database of patients and healthcare professionals. She is responsible for the coordination, quality control, and production of printed and electronic Foundation materials. Janice is also responsible for patient correspondence and registration for our live patient events.

## **Deborah (Dee) Murray**

### **Administrative Support**

Dee joined the Foundation in 2005. Dee manages the Foundation's exhibit shipment needs, coordinates mailings, and is responsible for patient information inquiries, ensuring the fulfillment of requests in a timely manner. Dee is also responsible for administrative bookkeeping services.

## BOARD OF DIRECTORS

**Pierre Fenaux, MD**

Hôpital St Louis, Université Paris 7

**Peter L. Greenberg, MD**

Stanford University School of Medicine

**Sandra E. Kurtin, PhDc, ANP-C, AOCN**

The University of Arizona Cancer Center

**Alan F. List, MD**

Moffitt Cancer Center

**Luca Malcovati, MD**

University of Pavia School of Medicine

**Stephen D. Nimer, MD, Chair**

Sylvester Comprehensive Cancer Center

## MEMBERS EMERITUS

**John M. Bennett, MD**

Rochester, New York, USA

**Charlotte M. Niemeyer, MD**

Freiburg, Germany

**Franz Schmalzl, MD**

Innsbruck, Austria

## OFFICERS

**Tracey Iraca**, Executive Director

**Janice Butchko**, Secretary

**Sandra E. Kurtin, PhDc, ANP-C, AOCN**, Treasurer

## MEDICAL AND SCIENTIFIC ADVISORY BOARD

**Rafael Bejar, MD, PhD**

Moore's Cancer Center at the University of California, San Diego

**Rena Buckstein, MD, FRCPC**

Sunnybrook Health Sciences Centre

**Mario Cazzola, MD, Chair**

University of Pavia School of Medicine

Fondazione IRCCS Policlinico San Matteo

**Theo J.M. de Witte, MD, PhD**

Radboud University Nijmegen Medical Centre  
Nijmegen Centre of Molecular Life Sciences

**Erin P. Demakos, RN, CCRN**

Icahn School of Medicine at Mount Sinai

**Benjamin Ebert, MD, PhD**

Dana-Farber Cancer Institute

**Silvia M. M. Magalhães, MD, PhD**

Federal University of Ceará Hospital  
Universitário Walter Cantídio

**Yasushi Miyazaki, MD**

Nagasaki University

**Ghulam J. Mufti, DM, FRCP, FRCPath**

King's College London & King's College  
Hospital

**Uwe Platzbecker, MD**

Universitätsklinikum Carl Gustav Carus

**Akiko Shimamura, MD, PhD**

Dana-Farber Cancer Institute

**Lewis R. Silverman, MD**

Icahn School of Medicine at Mount Sinai

## DEVELOPMENT BOARD

**Stuart Goldberg, MD**

**Jennifer Keam, MD**

**Deborah Peirce, Chair**

**Julia McGuire, Advisor**

# International MDS Foundation Nurse Leadership Board (NLB)

**Erik Aerts, RN**

Nurse Manager  
University Hospital Zürich  
Internal Medicine-Oncology  
Stem Cell Transplantation Ward and Polyclinic  
Hematology/Apheresis/Stem Cell Transplantation  
Zürich, Switzerland

**Angelika Bitter**

Study Coordinator/Nurse  
University Hospital Dresden  
Dresden, Germany

**Claudia Boglione, RN**

Stem Cell Transplantation Nurse Mentor  
University Hospital Careggi  
Florence, Italy

**Núria Borràs, RN**

Hemato-Oncology Nurse  
ICMHO Hospital Clinic  
Barcelona, Spain

**Karen Campbell, RN**

Macmillan Senior Lecturer  
Programme Leader for MSc in Advanced Practice  
and Flexibility Manged Programme  
Senior Teaching Fellow  
Edinburgh Napier University  
Edinburgh, Scotland, United Kingdom

**Hwang Chung Cheng, RN, MN, Adv. Dip  
(Oncology Nursing)**

Advanced Practice Nurse Intern-Haematology  
Singapore General Hospital  
Singapore

**Nicole Crisp, RN, BScN, MN, NP-adult**

Nurse Practitioner, Hematology  
University of Alberta Hospital  
Edmonton, Alberta, Canada

**Lucy Cussans, RN**

MDS Case Manager  
Royal Adelaide Hospital  
Adelaide, Australia

**Erin Demakos, RN, CCRN**

Administrative Director  
Myelodysplastic Disease Center  
Icahn School of Medicine at Mount Sinai  
New York, New York, United States

**Rebecca Dring, RN Post Grad Dip in  
Cancer Nursing**

Leukaemia Foundation  
National MDS Coordinator  
Royal Melbourne Hospital  
Clinical Nurse Specialist  
Melbourne, Australia

**Corien Eeltink, RN, MA ANP**

Verpleegkundig specialist  
Afdeling hematologie VU  
Universitair Medisch Centrum  
Amsterdam, Nederland

**Lenn Fechter, RN**

Nurse Coordinator, Department of Hematology  
Stanford Hospital and Clinics  
Stanford, California, United States

**Janet Hayden, RN, BSc(hons), MPH**

Myeloid Clinical Nurse Specialist  
Haematological Medicine  
Kings College NHS Foundation Trust  
London, United Kingdom

**Miki Iizuka, RN**

Shinyurigaoka General Hospital  
Kanagawa, Japan

**Jacqueline Jagger, RN, BA(Hons), MN**

Haematology Nurse Practitioner  
Cancer Services  
Gosford Hospital, NSW  
Australia

**Christiane Kahle**

Lead Study Coordinator/Nurse  
University Hospital Dresden  
Dresden, Germany

**Emily A. Knight, RN, BSN, OCN**

Hematology Registered Nurse Coordinator  
Mayo Clinic  
Scottsdale, Arizona, United States

**Sandra E. Kurtin, PhD, ANP-C, AOCN**

Hematology/Oncology Nurse Practitioner  
The University of Arizona Cancer Center  
Adjunct Clinical Assistant Professor of Nursing  
University of Arizona  
Tucson, Arizona, United States

**Petra Lindroos Kolqvist, RN**

Teamleader, Anemia Leukemia Team  
Department of Hematology and Coagulation  
Sahlgrenska University Hospital  
Goteborg, Sweden

**Arno Mank, RN, PhD**

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

**R. Denise McAllister, MS, ARNP, AOCNP**

Florida Cancer Specialists & Research Institute  
Clearwater, Florida, United States

**Cindy Murray, RN, MN, NP-adult**

Malignant Hematology, Princess Margaret Hospital  
Clinical Appointee University of Toronto,  
Lawrence S. Bloomberg Faculty of Nursing  
Toronto, Ontario, Canada

**Geke Ong, RN**

Network Services  
Kings College NHS Foundation Trust  
London, United Kingdom

**Phyllis Paterson, RN, RSCN, Dip Onc**

MDS Clinical Nurse Specialist  
Cambridge University Hospitals NHS Foundation  
Trust  
Addenbrooke's Hospital  
Cambridge, United Kingdom

**Jean A. Ridgeway, MSN, APN, NP-C, AOCN**

Leukemia/Stem Cell Transplant Nurse Practitioner  
University of Chicago Medical Center  
Department of Hematology Oncology  
Chicago, Illinois, United States

**Natalie Singer, MSc, RN, BSc(hons)**

Macmillan Haemato/Oncology CNS  
The Beatson West of Scotland Cancer Centre  
Glasgow, Scotland, United Kingdom

**Samantha Soggee, RN, MN**

Samantha Soggee, RN, MN  
Nurse Unit Manager  
Oncology/ Haematology  
Epworth Freemasons  
Victoria, Australia

**Mary L. Thomas, RN, MS, AOCN**

Hematology Clinical Nurse Specialist  
VA Palo Alto Health Care System  
Palo Alto, California, United States  
Associate Clinical Professor  
University of California, San Francisco  
San Francisco, California, United States

**Sara M. Tinsley, ARNP, AOCN**

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

**Catherine Vassili, RN**

Haematology – Leukaemia Nurse Practitioner  
(Candidate)  
The Alfred Hospital  
Melbourne, Victoria, Australia

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

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

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

## 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. Complimentary breakfast and lunch.
- Visit the MDS Foundation website for more information at [www.mds-foundation.org/patient-and-family-forums](http://www.mds-foundation.org/patient-and-family-forums)

### **MDS Foundation Patient Liaison**

#### **Audrey Hassan**

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

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

1-609-298-0590 fax

e-mail: [patientliaison@mds-foundation.org](mailto:patientliaison@mds-foundation.org)

[ahassan@mds-foundation.org](mailto:ahassan@mds-foundation.org)

## Online patient and caregiver forums

Free online discussion board featuring information exchanged between patients, caregivers, and family members. Have an MDSF expert answer your questions.

For more information or to access the forum please go to [www.mds-foundation.org/forums/forum/patient-forum](http://www.mds-foundation.org/forums/forum/patient-forum)

## Global patient support groups

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

Would you like your treatment centre to become part of the referral system for MDS patients and be designated as a Center of Excellence? To be recognised as a Center of Excellence, an institution must have:

- An established university (or equivalent) program
- Recognised 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 and an application form for your center at:

## THE MDS FOUNDATION

4573 South Broad St. Suite 150

Yardville, NJ 08620

Contact: Audrey Hassan

Within the US: 1-800-MDS-0839, ext. 210

Outside the US: 1-609-298-1035, ext. 210

FAX: 1-609-298-0590

## MDS Centers of Excellence within the United States

The MDS Foundation currently has 68 Center Of Excellence throughout the US. To see a complete listing of CoEs please visit our website at - <https://www.mds-foundation.org/mds-centers-of-excellence/>.

## MDS Centers of Excellence outside of the United States

The MDS Foundation currently has 107 MDS Centers of Excellence outside the US including the following centers in Australia:

### **Cabrini Health**

Melbourne, Australia  
Melita Kenealy, MD

### **Monash Health**

Monash University  
Clayton Victoria, Australia  
Jake Shortt, BMedSc MBChB FRACP FRCPA PhD

### **Peter MacCallum Cancer Institute**

University of Melbourne  
East Melbourne, Australia  
John F. Seymour, MD

### **The Royal Melbourne Hospital**

Parkville Victoria, Australia  
David Ritchie, MD

### **University of Tasmania**

Royal Hobart Hospital  
Hobart, Tasmania, Australia

To see a complete listing of CoEs, please visit our website at <https://www.mds-foundation.org/mds-centers-of-excellence/>.

## MDS – specific organizations

### MDS Alliance

A global health initiative that aims to provide patients, caregivers and health care professionals with training tools and information about MDS, including current treatment options.

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

### MDS Foundation, Inc.

Multidisciplinary, international, non profit organisation 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](http://www.mds-foundation.org)

### United Kingdom MDS Patient Support Group

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

[www.mdspatientsupport.org.uk](http://www.mdspatientsupport.org.uk)

## Organizations that include MDS within the scope of hematologic malignancies

### Aplastic Anemia and MDS Foundation

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

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

### Leukaemia and Lymphoma Research Foundation

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

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

### Leukaemia Care

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

[www.leukaemiacare.org.uk](http://www.leukaemiacare.org.uk)

### Leukaemia Foundation

The Leukaemia Foundation is Australia's leading body for providing free services to support people and their families affected by leukaemia, lymphoma, myeloma and related blood disorders, including MDS.

[www.leukaemia.org.au](http://www.leukaemia.org.au)

### Leukemia and Lymphoma Society

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

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

## General resources

### American Cancer Society

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

### American Society of Clinical Oncology

[www.asco.org](http://www.asco.org) [www.cancer.net](http://www.cancer.net)

### American Society of Hematology

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

### CancerCare

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

### Medline Plus®

[www.nlm.nih.gov/medlineplus/medlineplus.html](http://www.nlm.nih.gov/medlineplus/medlineplus.html)

### Merck Manual Home Edition for Patients and Caregivers

[www.merckmanuals.com/home/index.html](http://www.merckmanuals.com/home/index.html)

### National Anemia Action Council

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

### National Heart, Lung and Blood Institute

[www.nhlbi.nih.gov](http://www.nhlbi.nih.gov)

### National Marrow Donor Registry

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

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

## The MDS Foundation support group guidelines

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

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

### Planning the meeting

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

### How can the MDS Foundation support your group?

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

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

## Suggested format for the meeting

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

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

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

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

## Position description

### Support group facilitator

#### Overview

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

#### Responsibilities

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

#### Suggestion for time required

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

## Suggested meeting activities

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

## Support Group Evaluation

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

## Remember...

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

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

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

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

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

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

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

### Outright lifetime charitable gifts

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

### Outright bequests

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

### Charitable Lead Trusts

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

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

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

### Charitable Remainder Trust

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

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

### Conclusion

By incorporating Planned Giving into our estate and financial plans, each of us may contribute to the fight against MDS in a way that improves our own or our family’s financial circumstances. This allows us, as a group, to create a funding base to finance the research that will eliminate the disease.



**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 colours 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 colours represent welcoming, warmth, stability, healing, passion, and protection. These colours 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 haematological malignancies. The individual pages have been developed in collaboration with members of the International Nurse Leadership Board of the MDS Foundation and members of the MDS Foundation Board of Directors. Creative and technical support was provided by Adam Nichols and his team at Markations. Organizational and communications support was provided by Tracey Iraca, Sue Hogan, 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, health care 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 health care professionals working with MDS patients. Most importantly, we hope the Building Blocks of Hope will empower MDS patients and their caregivers to LIVE with MDS.



The Building Blocks of Hope is a registered trademark of Sandra Kurtin:  
Trademark serial number 85589597 Official USPTO Notice of Allowance published 8/14/12.