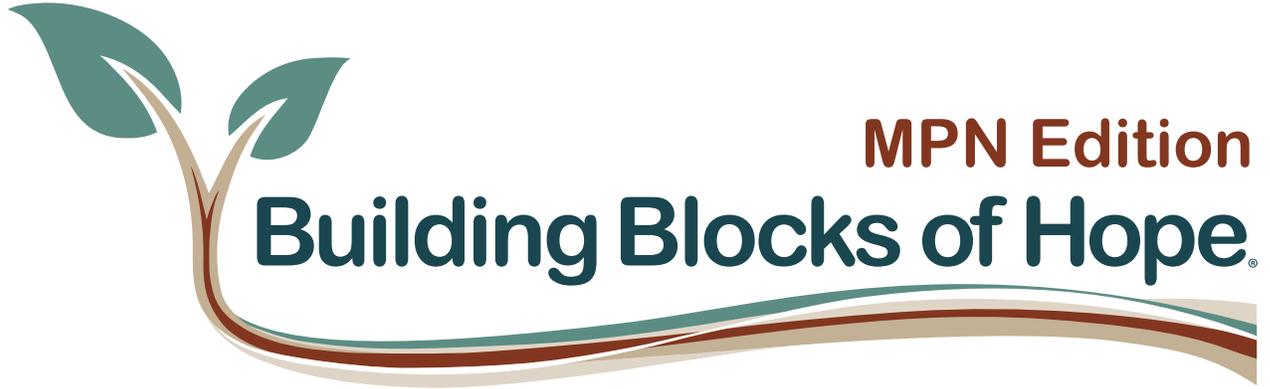


English Edition
(USA)



MPN Edition Building Blocks of Hope®

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

Myeloproliferative Neoplasms (MPNs) Edition

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 MPNs.



Published by the Myelodysplastic Syndromes Foundation, Inc.

You or someone you know has been diagnosed with a Myeloproliferative Neoplasm or MPN. There are several types of MPNs. This project will focus on three types of MPNs, Polycythemia Vera, Essential Thrombocythemia, and Primary Myelofibrosis. Hearing the words Myeloproliferative Neoplasm can be frightening. The diagnosis of a MPN 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 for MPNs. It is designed to help get you the information that you are looking for, connect you to resources, and provide you with tools and strategies to take an active part in your MPN journey.

The Building Blocks of Hope-MPN program includes both a print and digital version of educational materials divided into 6 chapters:

- **Chapter 1 – Understanding Myeloproliferative Neoplasms**
General information about Myeloproliferative Neoplasms (MPNs) including what we currently know about what happens in the bone marrow when MPNs develop is included in Chapter 1.
- **Chapter 2 – Polycythemia Vera (PV)**
Information about PV including how it is diagnosed, what symptoms you might experience, and how PV can be treated is included in Chapter 2.
- **Chapter 3 – Essential Thrombocythemia (ET)**
Information about ET including how it is diagnosed, what symptoms you might experience, and how ET can be treated is included in Chapter 3.
- **Chapter 4 – Primary Myelofibrosis (MF), Post PV-MF and Post ET-MF**
Information about MF, Post-PV MF and Post ET-MF including how MF is diagnosed, what symptoms you might experience, and how MF can be treated is included in Chapter 4.
- **Chapter 5 – General Resources for Living with MPNs**
Chapter 5 will provide you with strategies for staying well, managing your health and your MPN, and includes several Quick-Tips to recognize and manage common symptoms or problems experienced by patients and caregivers living with MPNs. Each Quick-Tip includes links to several digital resources that may help you manage your health. This chapter also includes a glossary of terms that will help you to understand the complex language used to describe these diseases.
- **Chapter 6 – The MDS Foundation (MDSF)**
The MDS Foundation is an international non-profit advocacy organization devoted to the support and education of patients and healthcare providers with innovative research in the fields of MDS, AML and related myeloid neoplasms in order to accelerate progress in the diagnosis, control and cure of these diseases.

Allow yourself time to adjust to the diagnosis of MPNs. Take time to explore the Building Blocks of Hope-MPN. 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 MPNs.

The MDS Foundation, Inc.

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

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

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UNDERSTANDING MYELOPROLIFERATIVE NEOPLASMS

General information about Myeloproliferative Neoplasms (MPNs) including what we currently know about what happens in the bone marrow when MPNs develop is included in Chapter 1.



UNDERSTANDING MYELOPROLIFERATIVE NEOPLASMS

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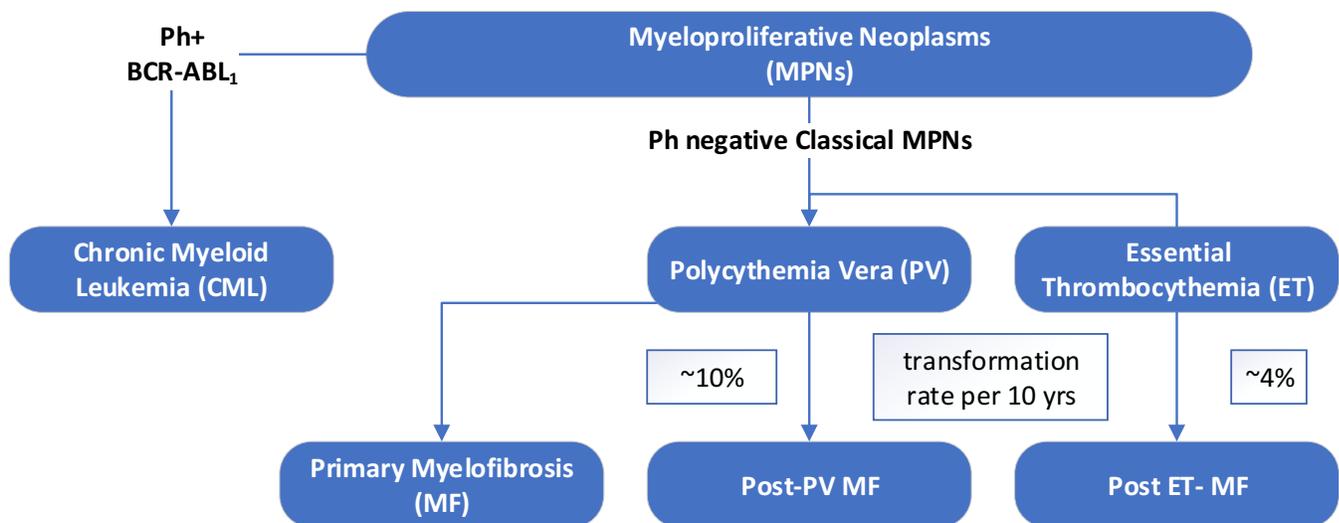
What are Myeloproliferative Neoplasms (MPN)?

The Myeloproliferative Neoplasms (MPN) are a group of bone marrow cancers characterized by the overproduction of myeloid cells, including certain white blood cells (WBC), red blood cells (RBC) and platelets. The myeloid cells originate in the bone marrow, the factory that produces blood cells.

Are MPNs cancer?

In 2002, the World Health Organization (WHO) changed the name of these diseases from Myeloproliferative Disorders to Myeloproliferative Neoplasms, citing the underlying feature of uncontrolled growth of one or more myeloid cells¹. Uncontrolled growth of cells is a common characteristic of cancer. Since 2002, additional underlying features of MPNs have been characterized. The WHO have updated the criteria for the diagnosis of each of these diseases, the most recent version being published in 2016².

There are four common types of MPNs: Polycythemia Vera (PV), Essential thrombocythemia (ET), and Primary Myelofibrosis (MF). Each MPN has very specific criteria for diagnosis². Chronic Myelogenous Leukemia (CML) is included as an MPN, however, CML is distinctly different in that it carries a specific genetic marker known as the Philadelphia Chromosome (Ph) or BCR-ABL1 oncogene. Therefore, PV, ET and MF are described as Ph negative classical MPNs. The criteria for diagnosis of each disease will be discussed in the individual chapters for PV, ET and MF.



As with many forms of cancer, MPNs may behave as an indolent (slow growing) disease or as a more aggressive disease. All MPNs have a risk of transforming (changing over time) to acute leukemia. Both PV and ET are more indolent, however, they can transform to Post-PV myelofibrosis or Post-ET myelofibrosis over the course of the disease. Primary Myelofibrosis tends to behave more aggressively and is associated with a higher risk of leukemic transformation.



Illustration by Kirk Moldoff

Normal Hematopoiesis (formation and development of blood cells)

What causes MPNs?

There are suspected contributing factors that may include:

Aging: Older age is associated with clonal (one cell line) changes that lead to abnormal proliferation and/or function of cells, including cells that originate in the bone marrow³. The average age at diagnosis for MPNs is 67.

Chemical Exposure: Exposure to benzenes, certain solvents or pesticides, and heavy metals, such as mercury or lead have been associated with changes in bone marrow stem cells and or the bone marrow microenvironment⁴.

Acquired (somatic) mutations: In most cases of MPNs, genes that "drive" the changes in bone marrow stem cells become abnormal (mutated) because of secondary events such as age and exposures⁷.

Are MPNs hereditary?

Familial or hereditary traits (germline): Hereditary MPNs are rare, however, germline mutations (changes in genes that are passed on at birth), have been identified in these rare cases⁴⁻⁶.



Illustration by Kirk Moldoff

Abnormal Hematopoiesis (formation and development of blood cells) with MPNs

What Does Bone Marrow Do?

What does bone marrow do?

All blood cells begin as hematopoietic stem cells. These cells are often referred to as factory cells. In healthy persons, hematopoietic stem cells (the factory cells) develop and mature (differentiate) in the bone marrow to produce all types of blood cells.

In the initial stage, the hematopoietic stem cell differentiates into a multipotent stem cell. These cells can form new blood cells. Hematopoietic stem cell transplantation uses these cells to repopulate the bone marrow with cells that can produce all the elements of blood.

The multipotent stem cell further differentiates to form either a lymphoid progenitor cell or a myeloid progenitor cell (progenitor cells).

The myeloid progenitor cell gives rise to granulocytes (myeloid white blood cells), platelets, and red blood cells.

Granulocytes: There are several types of granulocytes including neutrophils, basophils, eosinophils, monocytes, and macrophages. Granulocytes, together with other WBCs, 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. You can learn more about [What Does Bone Marrow Do](#).

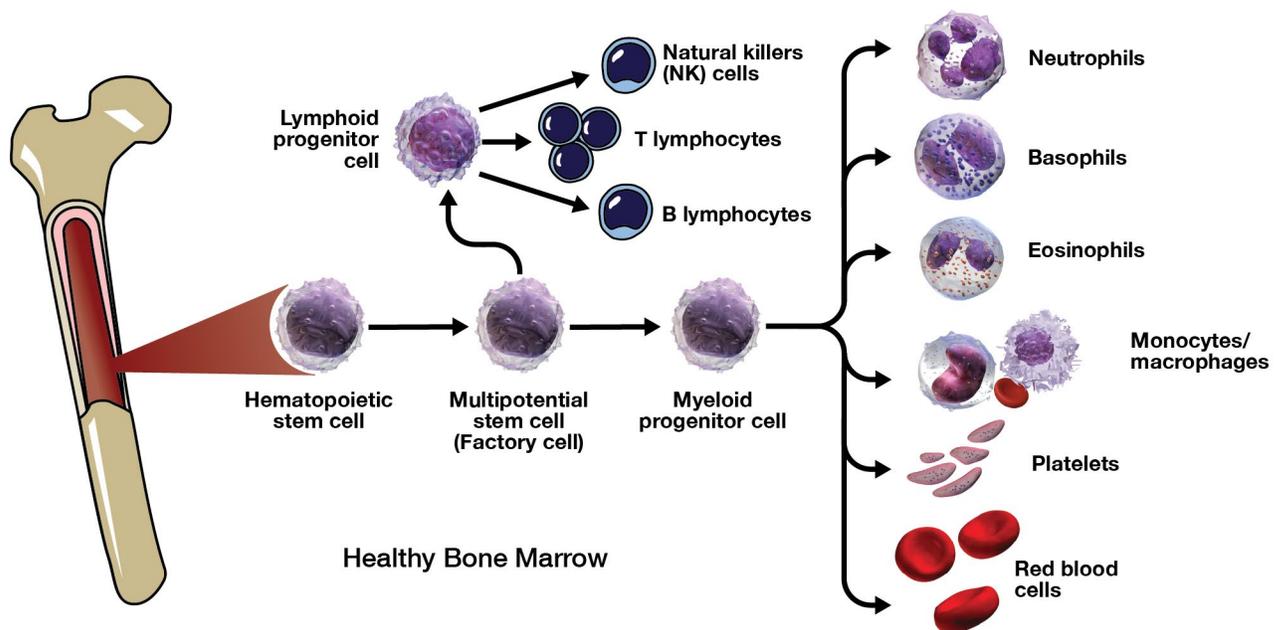


Illustration by Kirk Moldoff

Bone marrow examination

When blood tests indicate the presence of too many blood cells, common in MPNs, your physician may recommend a bone marrow examination. A bone marrow examination can reveal abnormalities in the cells of the bone marrow and the bone marrow microenvironment ([What Does Bone Marrow Do](#)). These tests provide additional information that can help in establishing a diagnosis. There are two parts to a bone marrow examination: the aspirate and the core biopsy. 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. These cells provide 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 prognosis and possible targets for treatment, such as cytogenetic (chromosome) and molecular (genes) changes.

The bone marrow biopsy

The bone marrow biopsy involves taking a small core (the shape and size of a medium pencil lead) of the spongy center of the bone marrow. The bone marrow core is usually 1.5–2.0 cm in length. It provides information about the cellularity of the bone marrow (crowded=hypercellular, empty=hypocellular). It also provides 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. The samples are sent to a hematopathologist, a physician trained to evaluate blood and bone marrow samples to diagnosis diseases. The physician uses a microscope to examine the cells and the bone marrow core sample. The results of a bone marrow biopsy and aspirate generally take 2–4 days. Cytogenetic and molecular studies and other special studies may require up to 2 weeks for processing.



Illustration by Kirk Moldoff

Normal Hematopoiesis (The formation and development of blood cells)

The bone marrow and biopsy procedure⁸

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

1. The patient is placed either on their side or on their abdomen. It is always useful to empty your bladder prior to the procedure. It is important to continue to breathe slowly throughout the procedure to help relax the muscles.
2. The health care provider performing the procedure will prepare a sterile field, including cleaning the skin over the posterior iliac crest, a bony protrusion on the right or left back side of the hip (near where your back pocket might be on a pair of jeans).
3. The skin above the site will be anesthetized (numbing the skin) using a form of lidocaine (numbing medicine). You may feel a pin prick from the needle and a very brief sting from the lidocaine.
4. A second needle is then inserted to numb the surface of the bone (periosteum)—this is where the nerve endings are. You may feel a brief stinging sensation with the first injection, like having the gums numbed for a dental procedure.
5. Once the skin and bone has been anesthetized, a small incision may be made on the surface of the skin to allow insertion of the bone marrow needle. There are a variety of needles being used today. Most allow for both the aspirate and the biopsy to be obtained during the same procedure.
6. The bone marrow needle allows for penetration through the outer layer of the bone (cortical bone). The needle is roughly the size of a meat thermometer with a hollow core. You will feel pressure. Some patients have very hard bones requiring more pressure to be used to penetrate the bone. Be sure to let your provider know if you are experiencing sharp pain at the site or pain that is traveling down your leg.
7. Once the needle reaches the spongy bone marrow (red marrow), the inner portion of the needle is removed, and the aspirate is obtained. You may experience a brief (few seconds) quick pressure sensation, almost like a cramp, with the first draw of the bone marrow. It will help to take a deep breath when the aspirate is being drawn. The number of samples drawn will be determined by the tests being ordered by your physician.
8. Either a new needle or the same needle will be used to obtain the core biopsy. The inner sheath is removed once the cortical bone has been penetrated. The hollow needle is then inserted into the bone marrow. Your provider will twist and shake the needle gently to loosen the bone core to help remove it in one piece. You will feel pressure and some shaking very briefly. There is sometimes a quick sting when the bone is removed.
9. After the procedure, the provider will apply pressure to the site to prevent any bleeding. A pressure dressing is generally applied.
10. You should not shower for 24 hours. No soaking in water (bath, swimming, hot tubs) for 48–72 hours.
11. Ask your provider for instructions on how to care for the biopsy site.
12. 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.
13. Mild pain or discomfort may be experienced at the procedure site for two to three days after the bone marrow exam. If your pain is more severe or persistent, contact your health care provider.
14. For safety reasons, the patient should have a friend, family member, or caregiver travel home with them. The patient should not drive.

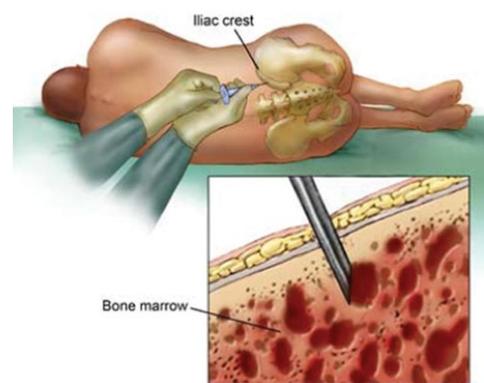


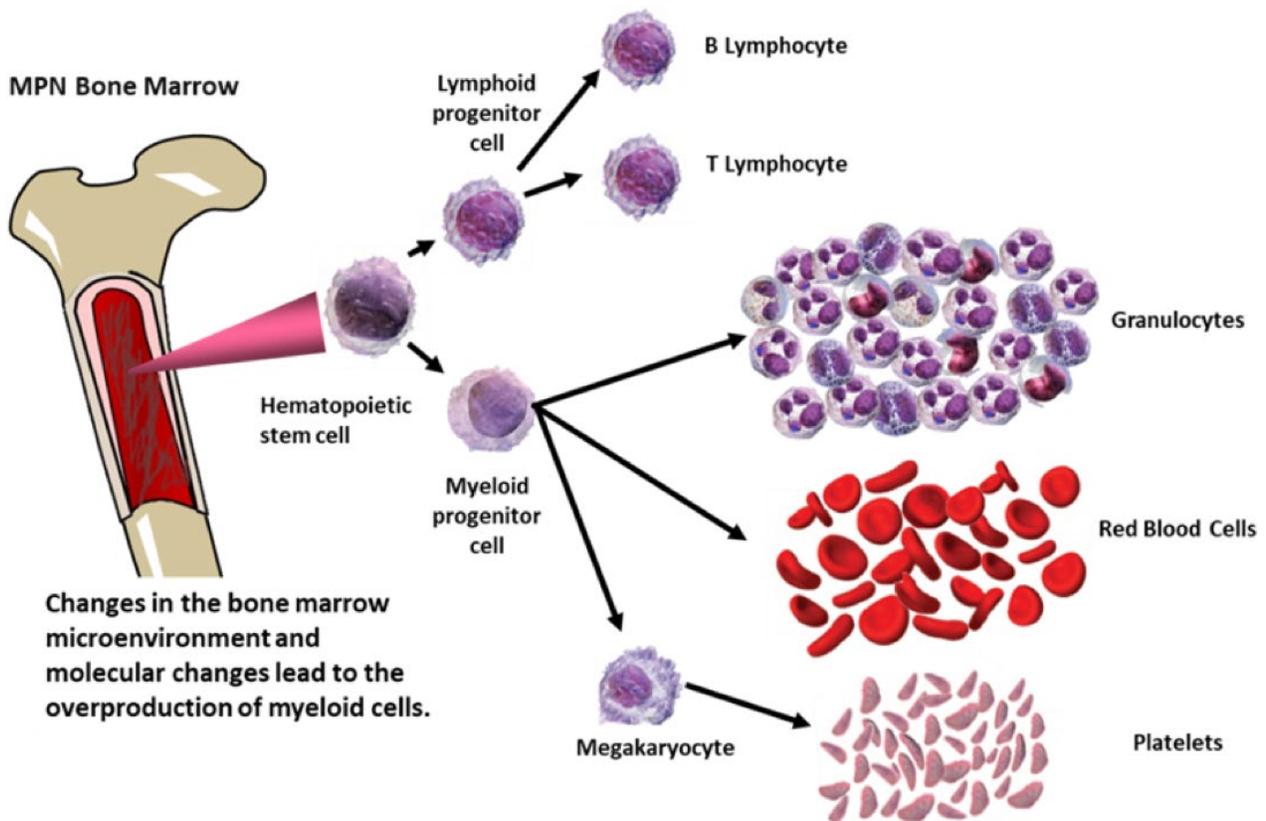
Illustration by Kirk Moldoff

What happens to bone marrow in MPNs?

The bone marrow is a very complicated organ with many working parts and processes ([What Does Bone Marrow Do?](#)). Cancers that originate in the bone marrow, including MPNs, are generally a result of changes in one or more elements of the bone marrow factory including changes in the hematopoietic stem cells, the bone marrow microenvironment, and genes associated with the JAK-STAT pathway.

Bone marrow changes in MPNs

Normally, the human body has a system of checks and balances that regulate how many of each type of cell is produced by the bone marrow. In MPNs the bone marrow makes too many blood cells. The MPNs are associated with the overproduction of one or more of the myeloid cells lines and inflammatory cytokines. Cytokines, are substances, such as interferon, interleukin, and growth factors, that are secreted by certain cells of the immune system and influence other cells. Too many blood cells and an overproduction of cytokines largely explain the signs and symptoms you may be experiencing, and the risk associated with MPNs. The signs and symptoms vary based on which myeloid cell or cells are overproduced.



Definitions

Myelo:

bone marrow

Proliferative:

Producing

Myeloid:

includes all cells belonging to the granulocytic (neutrophil, eosinophil, basophil), monocytic/macrophage, erythroid, megakaryocytic and mast cell lineages

Myeloproliferative:

overproduction of myeloid cells

Cytokines:

substances, usually proteins, such as interferon, interleukin, and growth factors, that are produced by cells of the immune system that effect other cells. In MPNs, cytokines may be overproduced and lead to an inflammatory state.

Hematopoietic stem cell (HSC):

Cells that originate in the bone marrow and have the capacity to produce WBCs, RBCs, and platelets. Changes in the cells themselves or in the bone marrow microenvironment have been associated with bone marrow cancer, including MPNs.

Bone marrow microenvironment:

A complex network of cells that support the growth and development of individual blood cells. These supportive cells include stromal cells, fat cells, blood vessel cells, bone cells, and connective cells. All cells are subject to changes that may contribute to the development of abnormal cells.

Molecular attributes:

All processes in the body are regulated by proteins and signaling pathways. Genes are comprised of proteins. Signaling pathway are a series of messages that are required to develop normal cells. There are many genes and signaling pathways that regulate the normal production of blood cells. All molecular attributes and their associated signaling pathways are subject to changes (mutations). These mutations may contribute to the development of abnormal cells, abnormal signaling pathways and the overproduction of cytokines.

You can find more definitions in the [Glossary of Terms](#) and can learn more about [What Does Bone Marrow Do](#).

In patients with MPNs, the development and maturation (differentiation) of the factory cells in the bone marrow (hematopoietic stem cells) is impaired. This leads to an overproduction of one or more types of myeloid cells.

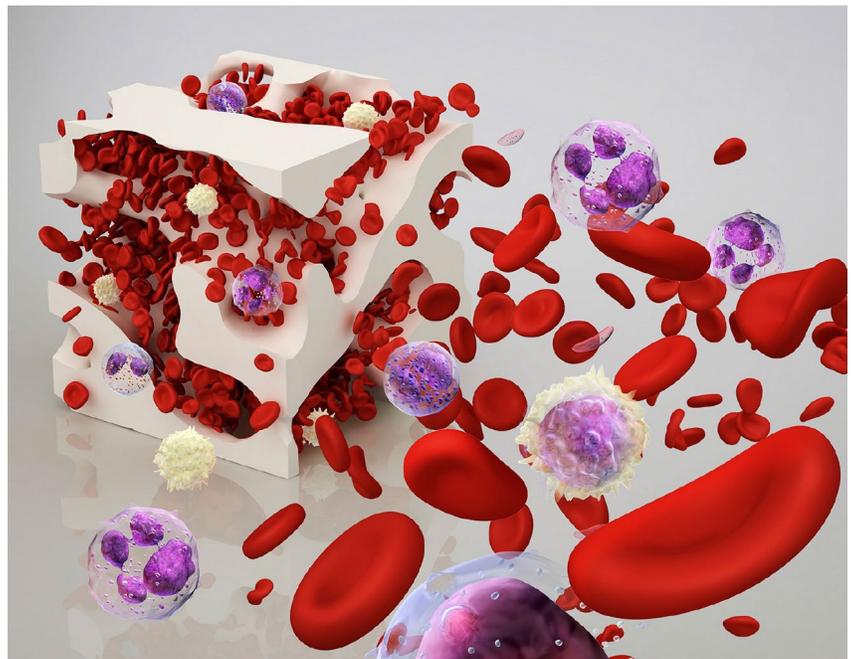


Illustration by Kirk Moldoff

Normal Hematopoiesis (The formation and development of blood cells)

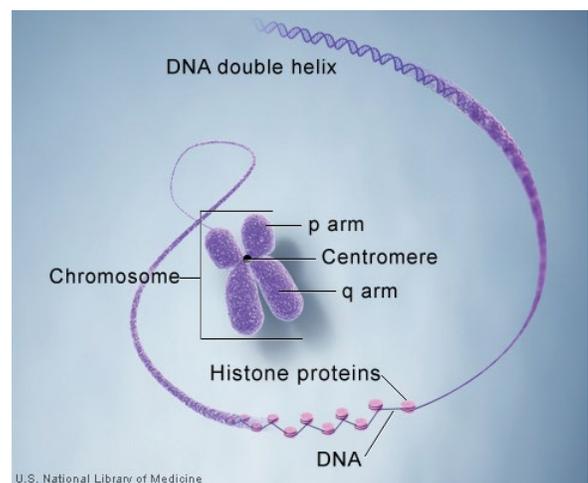
Chromosomes and genes in MPNs

Cells are the fundamental working units of every living system. The instructions needed to direct their development and activities are contained within the DNA and RNA. The DNA, a combination of proteins, provides a blueprint for making each type of cells in the human body. DNA is found in the nucleus of every cell in the body (except red blood cells which have no nucleus). Inside the nucleus of a cell, long strings of DNA are coiled up onto chromosomes.

The number of chromosomes in human cells is 46 with 22 autosomal pairs (one of each type contributed by the mother and one of each type from the father) and 2 sex chromosomes, 2 X chromosomes for females (one from father and one from mother) or an X and a Y chromosome for males (the X from the mother and the Y from the father). Each chromosome has a narrow center called the centromere, which divides the chromosome into two sections, or "arms". The short arm of the chromosome is labeled the "p". The long arm of the chromosome is labeled the "q".

Chromosomes contain several thousand genes. Genes are shorter sections of DNA. Each gene acts as a code or set of instructions for making a specific protein. These proteins control the cell's activity, telling the cell what to do and giving the organism individual characteristics.

Genes can become mutated (altered, faulty). In most cases, the cause of these mutations is not fully understood. Some of these genes, when mutated, are known to cause or promote the development of MPNs. In some cases, the gene can be targeted to interrupt the abnormal production of blood cells and cytokines, both hallmarks of clinical findings in MPNs.



Chromosome testing

Metaphase cytogenetics: Most of what researchers know about chromosomes has been learned by observing chromosomes during cell division (metaphase). A standard metaphase chromosome analysis will study 20 metaphases. In most cases, chromosome testing requires a bone marrow aspirate.

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]

Fluorescent in-situ Hybridization (FISH): Special fluorescent dyes are used to highlight specific parts of certain chromosomes. This increases the visibility of the chromosomes included in the specific probe (preset group of tests to isolate one or more specific chromosome abnormalities).

Molecular testing in MPNs

Molecular studies are very sensitive, specific tests used to isolate specific gene mutations associated with MPNs. These tests can be performed on the bone marrow aspirate and in some cases on peripheral blood.

Polymerase chain reaction (PCR): This type of test is used to determine the presence or absence of a specific gene mutation. PCR testing can be performed on peripheral blood or on bone marrow.

Next Generation Sequencing (NGS): This type of test is used to conduct a detailed analysis of your gene profile, including the genes found to be mutated in MPNs.

Common gene mutations associated with MPNs⁵

BCR-ABL1: A gene that fused part of two different genes to form an oncoprotein that drives the development of and progression of Chronic Myelogenous Leukemia (CML). 100% of all cases of CML are BCR-ABL1 positive. This gene may also be present in approximately 25% of patients with Acute Lymphoblastic/Lymphocytic Leukemia (ALL).

JAK2 V617F: A mutation found in more than 90 percent of cases of PV and approximately 50 percent of cases of ET and PMF. The Janus kinase (JAK)2 V617f mutation was first discovered in 2005.

JAK2 exon 12: A variant of the JAK2 mutation, found in ~ 2% of patients with PV. JAK2 V617F, exon 12 mutations are not seen in ET or MF. Therefore, testing for the JAK2 exon 12 mutation is important in patients who do not have the JAK2 V617F mutation, but are suspected to have PV.

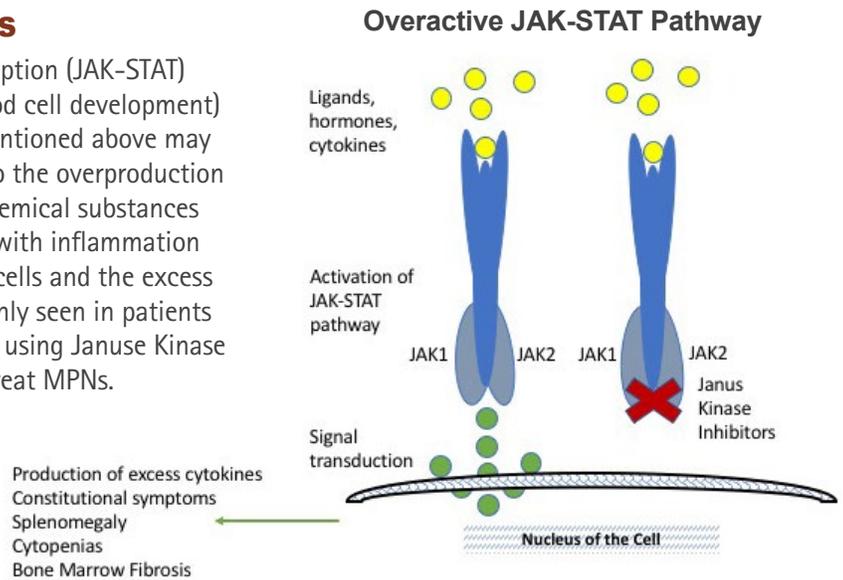
MPL W515I and MPL W515K: MPL mutations are absent in PV and are found in 5–10% of patients with ET and PMF. The MPL mutation was first discovered in 2006.

CALR exon 9: Calreticulin gene (CALR) mutations are present in 20–35% of patients with ET or PMF. The CALR mutation was first discovered in 2013. CALR is not found in PV.

The JAK-STAT Pathway and Splenomegaly in MPNs

The JAK-STAT pathway and MPNs

The JAK signal transducer and activator of transcription (JAK-STAT) pathway is involved in normal hematopoiesis (blood cell development) and immune function. Mutations in the genes mentioned above may cause the pathway to always be "on". This leads to the overproduction of blood cells (clonal expansion) and cytokines (chemical substances that contribute to cell growth and are associated with inflammation and immune function). The increase in the blood cells and the excess of cytokines largely explain the symptoms commonly seen in patients with MPNs. Interruption of the JAK-STAT pathway using Janus Kinase (JAK) inhibitors is a therapeutic strategy used to treat MPNs.



The spleen and other organs in MPNs⁹

The spleen is an organ located in the upper abdomen on the left side, just under the rib cage and stomach. The spleen is a reservoir for blood cells, including the myeloid blood cells. When there are too many cells, such as in MPNs, or when the bone marrow has developed fibrosis (scarring), the spleen can begin to act as a factory for making blood cells. This is known as extramedullary (outside the bone marrow) hematopoiesis.

An enlarged spleen, splenomegaly, is most common in MF, but may be present in some patients with PV. Splenomegaly is uncommon in ET. Patients with an enlarged spleen may also develop an enlarged liver, known as hepatomegaly.

Patients with an enlarged spleen can experience a sense of fullness, discomfort or pain in the abdomen. An enlarged spleen may also cause decreased appetite if it crowds the stomach.

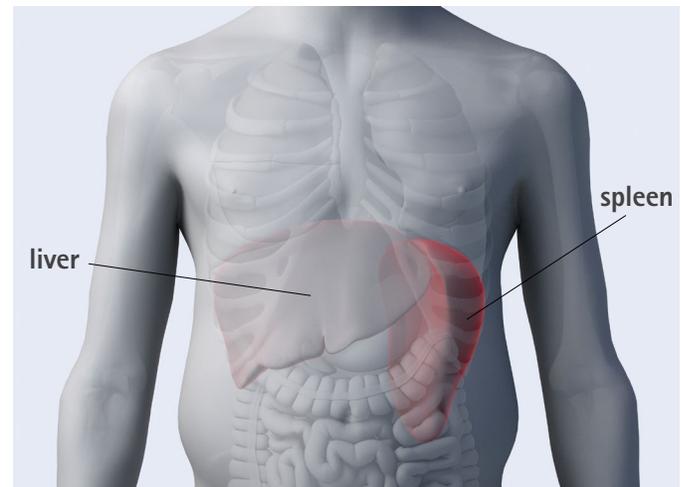


Illustration by Kirk Moldoff

Body depiction and organ system affected by MPNs.

About clinical trials⁸

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

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

A clinical trial falls into one of four phases:

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

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

How is a clinical trial conducted?

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

Members of the research team

1. Lead physician, scientist, or nurse researcher – primary investigator (PI)
2. Other clinicians: physician assistants, pharmacists or laboratory scientists
3. Statisticians
4. Research nurses
5. Data managers

How are clinical trials monitored?

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

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

Key elements of a clinical trial

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

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

Am I a candidate for a clinical trial?

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

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

These are most often answered during the informed consent process.

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

Clinical trials and drug approval information

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

www.cancer.gov/about-cancer/treatment/clinical-trials/search

National Institute of Health and Clinical Excellence

Guidance for cost effectiveness of treatments for England and Wales

www.nice.org.uk

European Medicines Agency

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

www.ema.europa.eu

Health Canada

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

www.hc-sc.gc.ca

Pharmaceuticals and Medical Devices Agency

Regulation of drug availability in Japan

www.pmda.go.jp

Therapeutic Goods Administration

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

www.tga.gov.au

U.S. Food and Drug Administration

Approval required for commercial availability of therapy in the United States

www.fda.gov

POLYCYTHEMIA VERA

Information about PV including how it is diagnosed, what symptoms you might experience, and how PV can be treated is included in Chapter 2.

POLYCYTHEMIA VERA

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Polycythemia Vera

Polycythemia Vera is a type of MPN characterized by the overproduction of one or more myeloid cell lines, most often red blood cells. The overproduction of myeloid blood cells is a result of faulty signals in the [JAK-STAT pathway](#). The abnormalities in this pathway also produce an excess of inflammatory cytokines, substances that interact with blood cells and the immune system. The overproduction of red blood cells is a defining feature of PV.

What are the signs and symptoms of PV?

The symptoms of PV are closely related to the overproduction of myeloid blood cells and inflammatory cytokines. Symptoms can range from none to severe and can be grouped together based on the underlying cause²:

1. Too many blood cells (thickening of the blood) can impair oxygen delivery to vital organs and therefore may lead to:
 - a. Fatigue, headaches, numbness or tingling in the fingers and toes, double/blurred vision, ringing in ears, or difficulty concentrating.
 - b. Blood clots (in the veins or arteries)
 - c. Pain/swelling/redness in the arms or legs
 - d. Redness of the face and hands (plethora)
 - e. Enlarged spleen (~30–40% of patients with PV at presentation)
 - i. Abdominal pain, under the ribs on the left side, getting full quickly when eating, in most cases due to an enlarged spleen (splenomegaly)
2. Symptoms associated with thrombosis (blood clots)
 - a. Chest pain, shortness of breath, nausea that may indicate a heart attack
 - b. Severe headache, impaired thinking or speech, weakness in the arms or legs that may indicate a stroke
3. Overactive signaling pathway (JAK-STAT) with overproduction of inflammatory cytokines
 - a. Itching (especially after getting out of a hot shower)
 - b. Flushing of the face
 - c. Burning feeling in skin
 - d. Bone pain
 - e. Night sweats

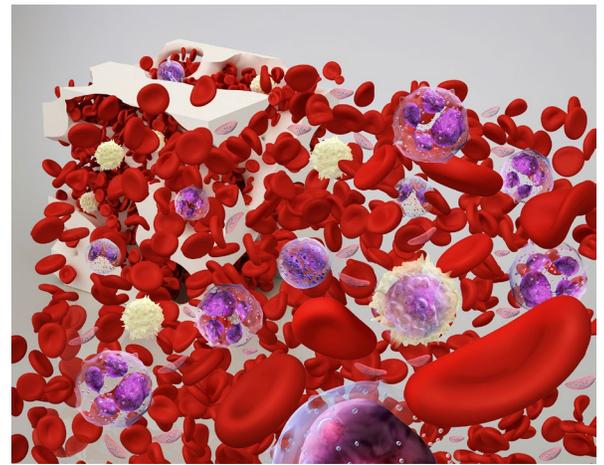


Illustration by Kirk Moldoff

Abnormal Hematopoiesis (The formation and development of blood cells) with Polycythemia Vera

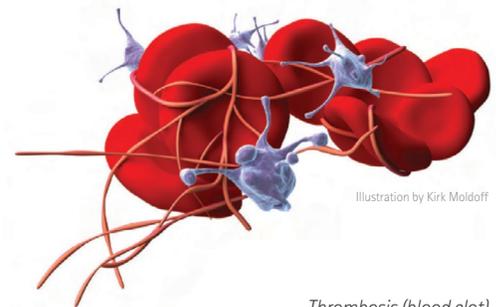


Illustration by Kirk Moldoff

Thrombosis (blood clot)

How is PV diagnosed²?

Many patients present to a health care provider with signs and symptoms they are experiencing due to the overproduction of red blood cells and inflammatory cytokines. Other patients have no symptoms but have routine laboratory testing done as a part of their regular visit with a health care provider that show abnormal findings.

The most common finding in routine laboratory testing is an elevated hematocrit (Hct), a measure of the percentage of red blood cells in whole blood. Some patients with PV also have elevated white blood cell (WBC) counts and/or elevated platelet (Plt) counts. These abnormal counts generally lead to a referral to a Hematologist, a physician that specializes in blood cancers and other blood disorders.

Determining the cause of erythrocytosis (elevated red blood cells) includes:

1. Checking the patient's history for tobacco use
2. Checking for sleep apnea
3. Reviewing medication that may cause an elevation of red blood cells including testosterone and erythropoietin stimulating proteins (red blood cell growth factors).

If these tests are negative. The patient will be evaluated for a possible MPN:

1. Review of symptoms to determine if there are symptoms suspicions for a diagnosis of PV.
2. Physical examination with attention to splenomegaly (enlarged spleen) or hepatomegaly (enlarged liver).
3. Laboratory testing:
 - a. Complete blood cell count (CBC) to measure the hemoglobin and hematocrit, white blood cells and platelets.
 - b. Blood test to evaluate iron stores.
 - c. Blood test for the JAK2 mutation, present in 97% of patients with PV.
 - d. Blood test for erythropoietin (Epo), a hormone produced by the kidneys necessary to produce normal red blood cells. In patients with PV, the Epo level will be lower than normal.

The World Health Organization is a specialized agency of the United Nations that is concerned with International health. It provides classifications of diseases to describe and clearly define them, so they can be diagnosed and treated. The World Health Organization (WHO) criteria for the diagnosis of PV have been recently updated.²

Diagnosis requires meeting either all 3 major criteria or the first 2 major criteria and the minor criterion.

	Major Criteria	Minor Criteria
1.	Elevation in red blood cell count	Decrease in erythropoietin (EPO) levels in blood
	Men: Hgb >16.5 or Hct >49%	
2.	Women: Hgb >16 or Hct 48%	
	Bone marrow biopsy showing too many cells (hypercellular for age)	
3.	Identification of a molecular mutation	
	JAK2 V617F (95%) or JAK2 Exon 12 (2%)	

What are the risks associated with PV^{10,11}?

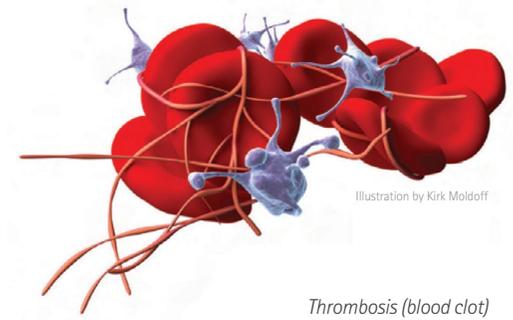
The primary concern for patients with PV is the development of blood clots (thrombosis) in veins (>12%) or in arteries (>17%). Once the diagnosis of PV is confirmed, it is important to determine the risk of thrombosis:

High Risk: Age >60 and/or a history of a blood clot
Low Risk: Age <60 and no history of a blood clot

Classifying patients into these two categories will help to estimate prognosis and will play a role in treatment decisions.

There are several other factors that can increase the risk of clotting:

- Elevated white blood cell count
- Cardiovascular risk factors:
 - Congestive heart failure
 - Arterial hypertension
 - Hypercholesterolemia
- Diabetes mellitus
- Tobacco use
- Obesity
- Immobility



Why do we need to treat PV?

Uncontrolled blood cell production increases risk of a thrombosis (blood clot) in the arteries or veins. These vessels carry blood throughout the body. A blood clot can block the flow of blood to one or more areas of the body.

- Arterial clots: blood clots in the heart or brain resulting in a heart attack or stroke.
- Venous clots: blood clots in one or more veins, often in the legs or arms known as a deep vein thrombosis (DVT), or in the lungs, known as a pulmonary embolism (PE) are the most common.

The goals of treatment for PV are to:

- Reduce the risk for blood clots
- Reduce the risk of cardiovascular and cerebrovascular events
- Reduce the risk of bleeding
- Manage disease-related symptoms
- Reduce the risk of leukemic transformation
- Improve quality of life

How is PV treated?

Treatment of PV is aimed at reducing excess blood volume and reducing the risk of thrombosis or bleeding:

- Strict control of the hematocrit (Hct) to keep it below 45% is recommended for all patients with PV¹². The Hct is a measure of the percentage of red blood cells in whole blood. It is the most common test used to estimate blood volume. Exact hematocrit goals may be determined by your doctor depending on where you live (altitude may affect Hct), gender or other medical conditions.

Therapeutic phlebotomy

Reducing the blood volume using therapeutic phlebotomy is the initial strategy used for patients with PV. This procedure involves placing a needle into a vein in the arm and removing 500 milliliters of blood, like the procedure used for blood donation. Some patients may feel dizzy or lightheaded during or after this procedure. Be sure to eat and drink plenty of fluids before your phlebotomy procedure. Some patients will receive intravenous fluids, usually normal saline, if there are changes in symptoms during the procedure such as a change in blood pressure.

Low-dose aspirin (80-100 mg)

Aspirin will help make the blood less sticky and reduces the risk for blood clots that can cause strokes or heart attacks¹³.

- The exception to aspirin therapy is if the platelets are very high (>1 million) and you have been diagnosed with an acquired bleeding disorder (von Willebrand disorder) or have known bleeding problems^{14,15}

Cytoreductive therapy¹⁶

A group of medications that work to slow down or reduce the amount of blood cells that your bone marrow produces. The need for cytoreductive therapy will be based on risk stratification, response to or tolerance of phlebotomy and quality of life:

- Low Risk: Continued daily low-dose aspirin and phlebotomy as needed to keep the Hct <45%
- High Risk: Requires cytoreductive therapy to control blood cell production to keep the Hct <45%
 - High-risk disease (Age >60 and/or history of a blood clot)
- Poor tolerance to phlebotomy
- Enlarged spleen causing symptoms
- Symptoms of the disease affecting quality of life

Cytoreductive therapy for PV

There are several types of cytoreductive therapy used to treat PV:

Chemotherapy: Drugs that affect DNA, RNA and or proteins in the cells

Biotherapy: Drugs that work by modifying the immune system

Targeted therapy: Drugs that work by modifying a specific molecular mutation or signaling pathway

Hydroxyurea

- A type of chemotherapy
- Decreases production of blood cells in the bone marrow
- While not FDA approved for PV, Hydroxyurea is the most commonly used therapy for PV and is often the first medication prescribed when cytoreductive treatment is indicated
- Hydrea is taken orally by swallowing capsules. The number of capsules taken and the schedule for taking them will vary for each patient based on the ability to control the hematocrit.
- The most common side effects include:
 - Low WBC – increases the risk of infection
 - Low platelets – increases the risk of bleeding
 - Nausea or diarrhea
 - Ulcers in the mouth or on the legs after being on this medication for a long time
 - Increased potential for non-melanoma skin cancers

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

Pegylated (long-acting) Interferon¹⁷

- Pegylated [PEG]-interferon is a biologic agent that can slow down production of blood cells by a variety of different mechanisms
- Although this is not FDA approved for PV, there is good clinical data to support its use as well as ongoing clinical trials in patients with PV
- Interferon is an injectable medicine that can be administered at home using a syringe and a small needle inserted under the skin in the stomach or legs, like the technique used to administer insulin. The long acting nature of this medicine allows for less frequent injections and may only need to be injected once per week.
- The most common side effects include:
 - Fever or chills
 - Fatigue
 - Nausea or diarrhea
 - Depression
 - Headache
 - Musculoskeletal pain
 - Weight loss
 - Potential for hypothyroidism
 - Abnormal liver function tests
 - Pneumonia

You can learn more about interferon at www.gene.com/patients/medicines/pegasys

Jakafi® (Ruxolitinib)^{18,19}

- Jakafi is the first FDA-approved therapy for PV patients who have tried hydroxyurea and who cannot take it due to side effects or lack of disease control. The approval is based on the RESPONSE trial which compared Ruxolitinib to best available therapies, showing that maintaining the Hct <45%, reducing spleen volume by >35%, and reducing MPN related symptoms was superior in the patients taking Ruxolitinib compared to those receiving best available therapies.
- Works by targeting the overactive JAK-STAT signaling pathway, thereby blocking the overproduction of myeloid cells and inflammatory cytokines.
- Jakafi® is a tablet taken orally twice daily
- The most common side effects include:
 - Low WBC – increases the risk of infection
 - Low platelets – increases the risk of bleeding
 - Nausea or diarrhea
 - Headache
 - Less common side effects may include elevated cholesterol levels, non-melanoma skin cancers, atypical infections (such as shingles), reactivation of latent tuberculosis or hepatitis.
- Do not change your dose or stop taking Jakafi® without first talking to your healthcare provider. This may cause a rapid flare of your PV symptoms and increase the risk of thrombosis.
- Do not drink grapefruit juice while on Jakafi®.
- Women should not take Jakafi® while pregnant or planning to become pregnant, or if breast-feeding.
- Find more information and patient education at www.jakafi.com/medication.aspx

About clinical trials⁸

Clinical trials are a very important part of discovering new treatments for MPNs. Without patients participating in clinical trials, we would not have the medicines we have today. Clinical trials are available in many locations throughout the world. You can find out more about currently available clinical trials for MPNs at

Center Watch - Provides the phase of clinical trial and proximity from identified location.

www.centerwatch.com/clinical-trials/listings/condition/856/myelofibrosis/

National Institute of Health (NIH)

<https://clinicaltrials.gov>

Myeloproliferative (MPN) Research Foundation

www.mpnresearchfoundation.org/Clinical-Trials

European Union Clinical Trials Register

www.clinicaltrialsregister.eu/ctr-search/search?query=mpn

National Cancer Institute

www.cancer.gov/about-cancer/treatment/clinical-trials

MPN Advocacy and Education International

<http://mpnadvocacy.com/clinical-trials-myelofibrosis-etpv/>

Palliative or supportive care for PV

Treatment aimed at reducing symptoms and improving quality of life is known as palliative or supportive care. The overactive JAK-STAT pathway increases the production of myeloid blood cells and inflammatory cytokines ([What Happens to Bone Marrow in MPNs?](#)). In addition to the risk of thrombosis or bleeding, many patients with PV will experience symptoms that are a result of the increased inflammation ([What are the symptoms of PV?](#)).

Ensuring that other medical conditions are well controlled can help reduce complications that are associated with PV. Specific attention is paid to optimal management of diseases that may increase the risk of blood clots ([What are the risks associated with PV?](#)).

Smoking increases the risk of thrombosis. Patients with MPNs should not smoke tobacco products. Talk with your health care provider about strategies to quit smoking. You can find out more at <https://ashline.org/>

Additional strategies for managing symptoms common with PV or other MPNs can be found in the [Quick-Tips for MPNs](#).

There are a variety of educational and support networks for patients with PV. It is important to use reputable sources for information regarding your disease.

<http://mpnadvocacy.com/clinical-trials-myelofibrosis-etpv>

www.pvreporter.com

www.patientpower.info/myeloproliferative-neoplasms

www.mpnresearchfoundation.org/Polycythemia-Vera-28PV-29

Prognosis-long term outlook

PV is a disease that may stay stable for many years. Many people will have the same or similar life expectancy as they would have without the disease. However, there is a small chance that it will transform over time to Post-PV myelofibrosis or acute myeloid leukemia. Your doctor will see you and do blood tests frequently to monitor your PV.

ESSENTIAL THROMBOCYTHEMIA

Information about ET including how it is diagnosed, what symptoms you might experience, and how ET can be treated is included in Chapter 3.

ESSENTIAL THROMBOCYTHEMIA

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Essential Thrombocythemia

Essential Thrombocythemia (ET) is a type of MPN characterized by the overproduction of platelets. The overproduction of platelets is a result of faulty signals in the [JAK-STAT pathway](#). The abnormalities in this pathway also produce an excess of inflammatory cytokines, substances that interact with blood cells and the immune system. About half of the patients with ET have a mutation in the JAK2 protein (referred to as JAK2 V617F), resulting in an overproduction of blood platelets. Most people are over the age of 50 at diagnosis and slightly more women than men have ET.

Platelets are a component of blood that are involved in blood clotting and help stop bleeding. When there are too many platelets, the blood may become thick and blood clots can form. These blood clots can block the flow of blood causing pain and swelling and disruption of circulation in veins (deep vein thrombosis or pulmonary embolism) or in the arteries (heart attack or stroke). Blood clots can cause serious complications or death.

Many people don't know they have ET until they are found to have a high platelet count on a routine blood test. Others are diagnosed after having a blood clot, miscarriage of a pregnancy, or during a work up of other symptoms of ET.

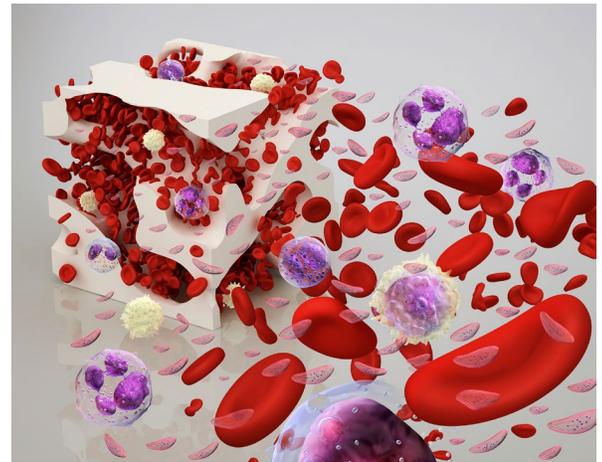


Illustration by Kirk Moldoff
Abnormal Hematopoiesis (The formation and development of blood cells) with Essential Thrombocythemia

What are the signs and symptoms of ET?

- 1. Blood Clots:** Too many platelets (thrombocythemia) can may lead to blood clots (in the veins or arteries). Thrombosis is another word for blood clot. Blood clots in the veins or arteries are a potential complication of ET and come with their own set of symptoms:
 - a. Pain/swelling/redness in the arms or legs may be symptoms of a Deep Vein Thrombosis (DVT)
 - b. Chest pain, shortness of breath, and nausea, may indicate a heart attack or a pulmonary embolism. A pulmonary embolism (PE) is a blood clot in the lungs. Seek medical attention immediately if you suspect a pulmonary embolism.
 - c. Severe headache, visual changes, balance issues, slurred speech, weakness, facial droop, and difficulty speaking may all be symptoms of blood clots in the head (stroke). Seek medical attention immediately if you suspect a stroke.
- 2. Bleeding:** Increased bleeding and bruising can also be a symptom of ET if the platelet count is very high, usually over 1 to 1.5 million per microliter of blood, which can cause a decrease in an important blood clotting factor called von Willebrand factor. This can cause secondary von Willebrand disease leading to bruising, bleeding, including nose bleeds, heavy menstrual flow, or gastrointestinal bleeding.
- 3. Inflammatory symptoms** due to an overactive signaling pathway (JAK-STAT) with overproduction of inflammatory cytokines can cause several symptoms in patients with MPNs including:
 - a. Itching (especially after getting out of a hot shower)
 - b. Flushing of the face
 - c. Burning feeling in skin
 - d. Bone pain
 - e. Night sweats

How is ET diagnosed?

Many patients present to a health care provider with signs and symptoms they are experiencing due to the overproduction of platelets and inflammatory cytokines. Other patients have no symptoms but have routine laboratory testing done as a part of their regular visit with a health care provider that show abnormal findings.

The most common finding in routine laboratory testing is an elevated platelet count. These abnormal counts generally lead to a referral to a Hematologist, a physician that specializes in blood cancers and other blood disorders.

Determining the cause of thrombocythemia (elevated platelet count) includes:

1. Iron deficiency
2. Infection
3. Inflammation

If these tests are negative. The patient will be evaluated for a possible MPN:

1. Review of symptoms to determine if there are symptoms suspicions for a diagnosis of ET.
2. Physical examination with attention to splenomegaly (enlarged spleen) or hepatomegaly (enlarged liver). An enlarged spleen is uncommon in ET and may lead to consideration of Polycythemia Vera or Myelofibrosis.
3. Laboratory testing:
 - a. Complete blood cell count (CBC) to measure the WBC, hemoglobin and hematocrit, and platelet count.
 - b. Blood test to evaluate iron stores.
 - c. Blood test for the JAK2 mutation, present in 50% of patients with ET.
 - d. Blood test for the CALR mutation, present in 20–30% of patients with ET.
 - e. Blood test for the MPL mutation, present in ~5% of patients with ET.

World Health Organization (WHO) Classification for ET²

The World Health Organization is a specialized agency of the United Nations that is concerned with International health. It provides classifications of diseases to describe and clearly define them, so they can be diagnosed and treated.

For a diagnosis of ET to be met according to 2016 WHO diagnostic criteria, either all four major criteria are met, or the first three major criteria and the minor criteria are met.

MAJOR CRITERIA	
1	Platelet count >450 X 10 ⁹ /L
2	BM biopsy showing proliferation mainly of the megakaryocyte lineage with increased numbers of enlarged, mature megakaryocytes with hyperlobulated nuclei. No significant increase or left shift in neutrophil granulopoiesis or erythropoiesis and very rarely minor (grade 1) increase in reticulin fibers
3	Not meeting WHO criteria for BCR-ABL ₁ , CML, PV, PMF, myelodysplastic syndromes, or other myeloid neoplasms
4	Presence of JAK2, CALR, or MPL mutation
MINOR CRITERIA	
1	Presence of a clonal marker or absence of evidence for reactive thrombocytosis

The goals of treatment for ET are to:

- Reduce the risk for blood clots
- Reduce the risk of cardiovascular and cerebrovascular events
- Reduce the risk of bleeding
- Manage disease-related symptoms
- Reduce the risk of leukemic transformation
- Improve quality of life

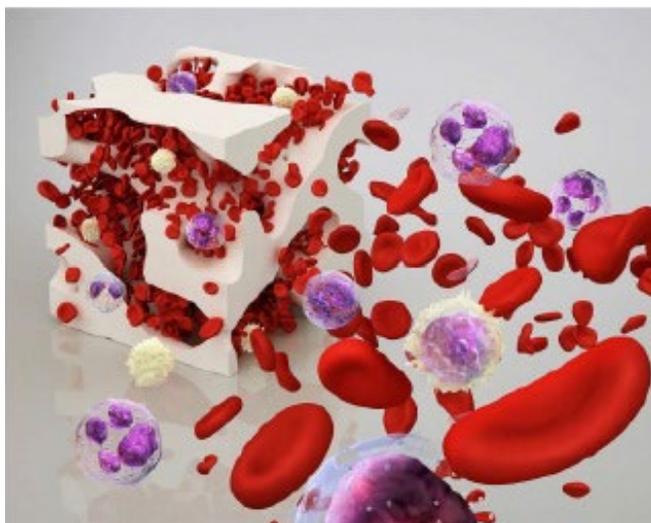


Illustration by Kirk Moldoff

Normal Hematopoiesis (The formation and development of blood cells)

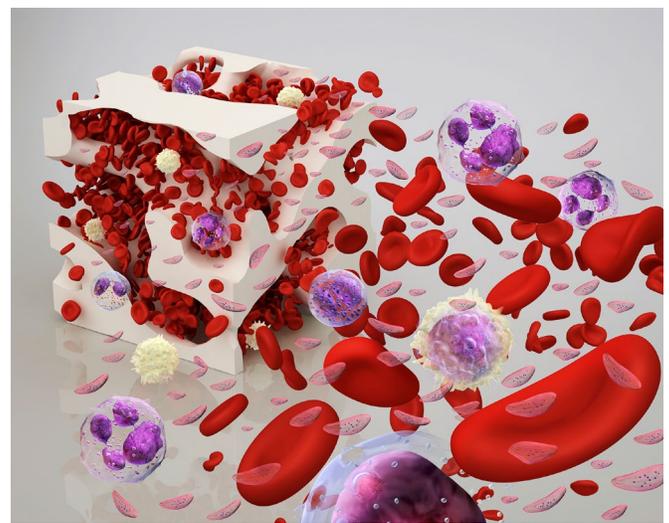


Illustration by Kirk Moldoff

Abnormal Hematopoiesis (The formation and development of blood cells) with ET

How is ET treated?

Decreasing the number of platelets as well as controlling other risk factors for blood clots, heart attack, and stroke are the primary goals of treatment for ET. Secondary health problems may increase the risk of thrombosis (blood clots). Treatment of these conditions and lifestyle modifications are recommended for all patients with ET including:

1. Effective medical management of high blood pressure, diabetes, cardiovascular disease
2. Smoking cessation
3. Increased activity for those that are sedentary
4. Management of obesity through diet and exercise

Patient will then be evaluated for the risk of thrombosis based specific risk categories:

Risk Category	Characteristics
Very low risk	No thrombosis history, age 60 yrs. or younger, and JAK2 wild type
Low risk	No thrombosis history, age 60 yrs. or younger, with JAK2 mutation
Intermediate risk	No thrombosis history, age older than 60 yrs., and JAK2 wild type
High risk	Thrombosis history or age older than 60 yrs., with JAK2 mutation

Low-dose aspirin (80-100 mg)

Aspirin will help make the blood less sticky and reduces the risk for blood clots that can cause strokes or heart attacks¹³. Low-dose aspirin is used for all patients with ET except:

- Patients with platelets that are very high (>1 million) and you have been diagnosed with an acquired bleeding disorder (von Willebrand disorder) or have known bleeding problems^{14,15}

Cytoreductive therapy¹⁶:

A group of medications that work to slow down or reduce the amount of blood cells that your bone marrow produces. The need for cytoreductive therapy will be based on risk stratification:

- Very low risk: observation with or without daily low dose aspirin and monitoring of blood counts.
- Low risk: Daily low dose aspirin and monitoring of blood counts.
- Intermediate risk: Daily low dose aspirin and monitoring of blood counts.
- High risk: Low dose aspirin plus cytoreductive therapy with the goal of keeping the platelet count less than 450.
- Symptoms of disease affecting quality of life: consider cytoreductive therapy.
- Enlarged spleen affecting quality of life: rule out myelofibrosis, then consider cytoreductive therapy.

Hydroxyurea

- A type of chemotherapy
- Decreases production of blood cells in the bone marrow
- While not FDA approved for ET, Hydroxyurea is commonly used for the treatment of ET and is often the first medication prescribed when cytoreductive treatment is indicated
- Hydrea is taken orally by swallowing capsules. The number of capsules taken and the schedule for taking them will vary for each patient based on the ability to control the platelet count.
- The most common side effects include:
 - Low WBC – increases the risk of infection
 - Low platelets – increases the risk of bleeding
 - Nausea or diarrhea
 - Ulcers in the mouth or on the legs after being on this medication for a long time
 - Potential risk of non-melanoma skin cancers

You can learn more about hydroxyurea at

<http://chemocare.com/chemotherapy/drug-info/hydroxyurea.aspx>

Anagrelide

- Anagrelide is an inhibitor of cyclic AMP phosphodiesterase III that reduces platelet production.
- Anagrelide is taken orally by swallowing capsules, usually daily. The dose will be determined by how well the drug controls the platelet count.
- The most common side effects include:
 - Low platelets – increases the risk of bleeding
 - Nausea, vomiting or diarrhea
 - Lower extremity edema
 - Headaches
- It should be avoided if you have an irregular heart beat (arrhythmia).

You can learn more about anagrelide at

http://npra.moh.gov.my/images/reg-and-noti/PI/scheduled-poison/Anagrelide_Capsule.pdf

Pegylated (long-acting) Interferon¹⁷

- Pegylated [PEG]-interferon is a biologic agent that can slow down production of blood cells by a variety of different mechanisms
- Although this is not FDA approved for ET, there is good clinical data to support its use as well as ongoing clinical trials in patients with ET. It is more commonly used in younger patients, in patients where other treatments have failed, or by women with ET who are pregnant or would like to become pregnant since it is felt to be the safest medication in this context.
- Interferon is an injectable medicine that can be administered at home using a syringe and a small needle inserted under the skin in the stomach or legs, like the technique used to administer insulin. The long acting nature of this medicine allows for less frequent injections and may only need to be injected once per week.
- The most common side effects include:
 - Fever or chills
 - Fatigue
 - Nausea or diarrhea
 - Depression
 - Headache
 - Musculoskeletal pain
 - Weight loss

You can learn more about interferon at <https://www.gene.com/patients/medicines/pegasys>

About clinical trials⁸

Clinical trials are a very important part of discovering new treatments for MPNs. Without patients participating in clinical trials, we would not have the medicines we have today. Clinical trials are available in many locations throughout the world. You can find out more about currently available clinical trials for MPNs at

NIH (National Institute of Health): www.clinicaltrials.gov

MPN Research Foundation: www.mpnresearchfoundation.org/Clinical-Trials

National Cancer Institute (NCI): www.cancer.gov/about-cancer/treatment/clinical-trials/search

MPN Advocacy and Education International: <http://mpnadvocacy.com/clinical-trials-myelofibrosis-etpv>

Palliative and Supportive care for ET

Treatment aimed at reducing symptoms and improving quality of life is known as palliative or supportive care. The overactive JAK-STAT pathway increases the production of myeloid blood cells and inflammatory cytokines ([What Happens to Bone Marrow in MPNs?](#)). In addition to the risk of thrombosis or bleeding, many patients with ET will experience symptoms that are a result of the increased inflammation.

Supportive care for ET patients includes leading a healthy life style and decreasing the risk of complications of the disease. Ensuring that other medical conditions are well controlled can help reduce complications that are associated with ET. Specific attention is paid to optimal management of diseases that may increase the risk of blood clots.

Smoking increases the risk of thrombosis. Patients with MPNs should not smoke tobacco products. Talk with your health care provider about strategies to quit smoking. You can find out more at <https://ashline.org/>

Additional strategies for managing symptoms common with ET or other MPNs can be found in the [Quick-Tips for MPNs](#).

There are a variety of educational and support networks for patients with ET. It is important to use reputable sources for information regarding your disease.

www.pvreporter.com

www.patientpower.info/myeloproliferative-neoplasms

www.mpnresearchfoundation.org/Essential-Thrombocythemia

<http://mpnadvocacy.com/understanding-mpns/essential-thrombocythemia>

Prognosis-Long Term Outlook

ET is a disease that may stay stable for many years or for your entire life. Many people will have the same or similar life expectancy as they would have without the disease. However, there is a small chance that it will transform over time to Post-ET myelofibrosis ([Are MPNs cancer? How will I know if I have Post-PV-MF or Post-ET-MF?](#)). Your doctor will see you and do blood tests frequently to monitor your ET. In the presence of symptoms, your physician will perform another bone marrow biopsy. Studies have shown that ET may transform to Post-ET Myelofibrosis in about 10% of cases. Less than 5% of people with ET will progress to Acute Myeloid Leukemia or Myelodysplastic Syndrome (which can be related to previous chemotherapy in a low proportion of patients). If your disease does change, your treatment and prognosis will need to be re-evaluated.

PRIMARY MYELOFIBROSIS (MF) POST PV MYELOFIBROSIS AND POST ET MYELOFIBROSIS

Information about MF, Post-PV MF and Post ET-MF including how MF is diagnosed, what symptoms you might experience, and how MF can be treated is included in Chapter 4.

Primary Myelofibrosis (MF) Post PV Myelofibrosis and Post ET Myelofibrosis

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What is Primary Myelofibrosis?

What is primary myelofibrosis?

Primary Myelofibrosis is a condition characterized by the buildup of scar tissue (fibrosis) of the bone marrow, the blood cell forming tissue found in the center of bones.

What is post polycythemia vera (PV) myelofibrosis and post essential thrombocythemia (ET) myelofibrosis?

Post PV myelofibrosis and post ET myelofibrosis are conditions characterized by the buildup of scar tissue (fibrosis) of the bone marrow following a diagnosis of PV or ET.

What happens?

In primary and secondary myelofibrosis, excessive scar tissue accumulates in the bone marrow and limits its ability to make normal blood cells. There is also increased inflammation.

Bone marrow changes in myelofibrosis

In myelofibrosis and post PV and ET myelofibrosis, the bone marrow does not make blood cells normally because of clonal (arising from one cancer cell) bone marrow stem cells.

Fibrosis: Reticulin or collagen stain of the bone marrow

Chromosome changes: Cytogenetic abnormalities

Molecular mutations: JAK2 V617F, JAK2 EXON12, MPL, CALR, and others.

The most common changes in the complete blood cell count (CBC) are:

Increased or decreased white blood cell count

Decreased hemoglobin - anemia

Increased or decreased platelet count

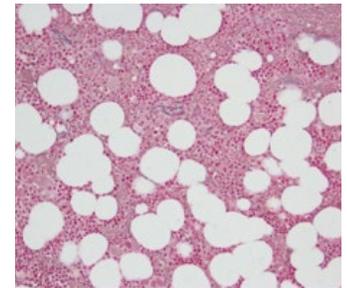


Photo courtesy of Moffitt Cancer Center, Pathology Dept

Normal reticulin stain without fibrosis of the bone marrow.

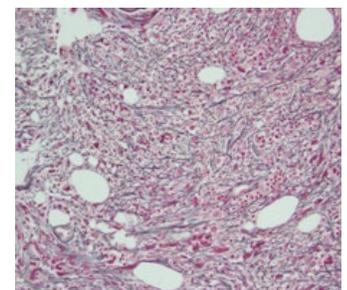


Photo courtesy of Moffitt Cancer Center, Pathology Dept

Reticulin stain demonstrating fibrosis of the bone marrow.

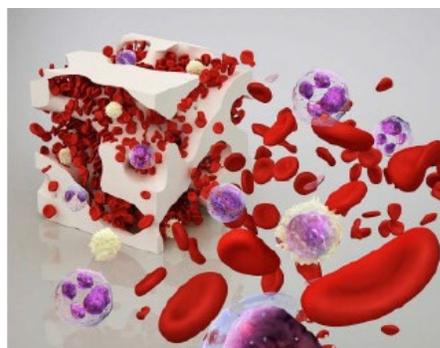


Illustration by Kirk Moldoff

Normal Hematopoiesis (The formation and development of blood cells)

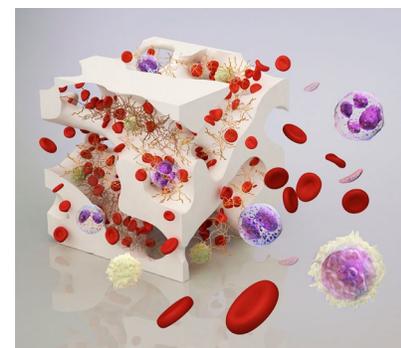
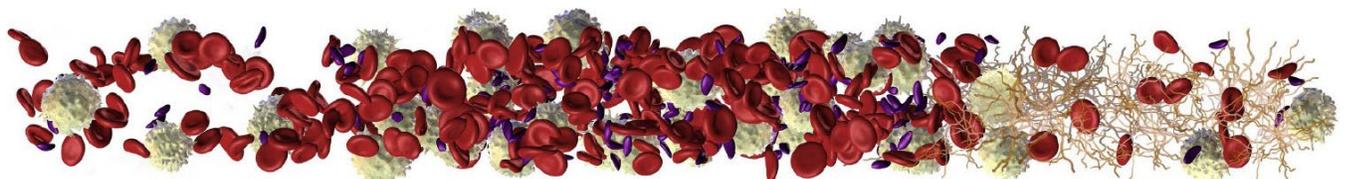


Illustration by Kirk Moldoff

Abnormal Hematopoiesis (The formation and development of blood cells) with Myelofibrosis



Continuum of Myelofibrosis with early increase in myeloid cells and eventual increasing fibrosis

Illustration by Kirk Moldoff

What are the signs and symptoms of MF?

The symptoms of MF are closely related to the overproduction of myeloid blood cells and inflammatory cytokines. Symptoms can range from none to severe and can be grouped together based on the underlying reason²:

1. Too many blood cells (thickening of the blood) can impair oxygen delivery to vital organs and therefore may lead to:
 - a. Fatigue, headaches, numbness or tingling in the fingers and toes, double/blurred vision, ringing in the ears, or difficulty concentrating.
 - b. Blood clots (in the veins or arteries)
 - c. Pain/swelling/redness in the arms or legs
 - d. Redness of the face and hands (plethora)
 - e. Enlarged spleen (~30-40% of patients with MF at presentation)
 - f. Enlarged liver (hepatomegaly)
 - g. Abdominal pain, under the ribs on the left side, getting full quickly when eating, in most cases due to an enlarged spleen (splenomegaly)
2. Symptoms associated with thrombosis (blood clots)
 - a. Chest pain, shortness of breath, nausea that may indicate a heart attack
 - b. Severe headache, impaired thinking or speech, weakness in the arms or legs that may indicate a stroke
3. Overactive signaling pathway (JAK-STAT) with overproduction of inflammatory cytokines
 - a. Itching (pruritus), especially after getting out of a hot shower
 - b. Flushing of the face
 - c. Burning feeling in skin
 - d. Bone pain
 - e. Night sweats

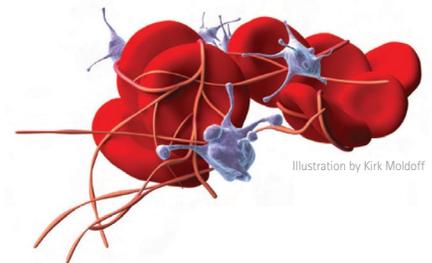


Illustration by Kirk Moldoff

Thrombosis (blood clot)

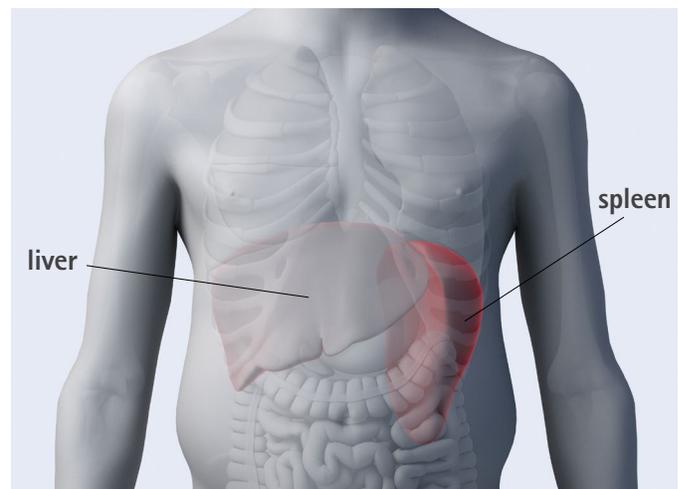


Illustration by Kirk Moldoff

Hepatosplenomegaly (enlarged liver and spleen) in Myelofibrosis

How is MF diagnosed?

Many patients present to a health care provider with signs and symptoms they are experiencing due to the overproduction of red blood cells and inflammatory cytokines (*What are the symptoms of MF?*). Other patients have no symptoms but have routine laboratory testing done as a part of their regular visit with a health care provider that show abnormal findings.

The most common finding in routine laboratory testing may include either elevated or decreased myeloid blood counts. Splenomegaly and hepatomegaly are also common in patients with MF. These abnormal counts or physical findings generally lead to a referral to a Hematologist, a physician that specializes in blood cancers and other blood disorders.

Evaluation for possible MF will include:

1. Review of symptoms to determine if there are symptoms suspicions for a diagnosis of MF.
 - a. Myeloproliferative Symptom Assessment form (MPN-SAF)
2. Physical examination with attention to splenomegaly (enlarged spleen) or hepatomegaly (enlarged liver).
3. Laboratory testing:
 - a. Complete blood cell count (CBC) to measure the hemoglobin and hematocrit.
 - b. Blood test to evaluate iron stores
 - c. Blood test for erythropoietin (Epo)
 - d. A comprehensive metabolic panel (CMP)
 - e. Lactate dehydrogenase (LDH)
 - f. Uric Acid
 - g. Human leukocyte antigen (HLA) testing if hematopoietic stem cell transplant is a consideration
 - h. Molecular testing (Molecular Testing in MPNs)
 - i. *JAK2 V617F*
 - ii. *CALR*
 - iii. *MPL*
 - iv. *JAK2 Exon 12*
 - v. *additional molecular testing may include: ASXL1, EZH2, SRSF2, IDH1, and IDH2*
 - i. Coagulation studies to evaluate for von Willebrand disease and other coagulopathies (bleeding disorders)
 - i. *Prothrombin time*
 - ii. *Partial prothrombin time*
 - iii. *Fibrinogen*
 - iv. *Plasma von Willebrand Factor Antigen*
 - v. *Von Willebrand Cofactor activity and von Willebrand multimers*
4. Bone marrow biopsy with aspiration
 - a. Aspiration is frequently not possible (dry tap) due to scarring
 - b. Trichrome and reticulin stain
 - c. Cytogenetics (on peripheral blood if dry tap)

World Health Organization 2016 diagnostic criteria for overt primary myelofibrosis

Requires meeting all 3 major criteria, and at least 1 minor criterion

MAJOR CRITERIA	
1	Presence of megakaryocytic proliferation and atypia, accompanied by either reticulin and/or collagen fibrosis grades 2 or 3
2	Not meeting WHO criteria for ET, PV, CML, myelodysplastic syndromes, or other myeloid neoplasms
3	Presence of JAK2, CALR, or MPL mutation or in the absence of these mutations, presence of another clonal marker, or absence of reactive myelofibrosis
MINOR CRITERIA	
Presence of at least 1 of the following, confirmed in 2 consecutive determinations	
1	Anemia not attributed to a comorbid condition
2	Leukocytosis $\geq 11 \times 10^9/L$
3	Palpable splenomegaly
4	LDH increased to above upper normal limit of institutional reference range
5	Leukoerythroblastosis

International Working Group for Myelofibrosis Research and Treatment (IWG-MRT) diagnostic criteria for post-polycythemia vera myelofibrosis (Post-PV-MF)

REQUIRED CRITERIA	
1	Documentation of a previous diagnosis of PV as defined by the World Health Organization criteria
2	Bone marrow fibrosis grade 2-3 (on 0-3 scale) or grade 3-4 (on 0-4 scale)
ADDITIONAL CRITERIA	
Presence of at least 2 are required	
1	Anemia or sustained loss of requirement of either phlebotomy (in the absence of cytoreductive therapy) or cytoreductive treatment for erythrocytosis
2	A leukoerythroblastic peripheral blood picture
3	Increasing splenomegaly defined as either an increase in palpable splenomegaly or $> 5\text{cm}$ (distance of the spleen from the left costal margin) or the appearance of newly palpable splenomegaly
4	Development of > 1 of three constitutional symptoms: $>10\%$ weight loss in 6 months, night sweats, unexplained fever ($>37.5^\circ\text{C}$)

International Working Group for Myelofibrosis Research and Treatment (IWG-MRT) diagnostic criteria for post-essential thrombocythemia myelofibrosis (Post-ET-MF)

REQUIRED CRITERIA	
1	Documentation of a previous diagnosis of ET as defined by the World Health Organization criteria
2	Bone marrow fibrosis grade 2-3 (on 0-3 scale) or grade3-4 (on 0-4 scale)
ADDITIONAL CRITERIA Presence of at least 2 are required	
1	Anemia and > 2g/dL decrease from baseline hemoglobin level
2	A leukoerythroblastic peripheral blood picture
3	Increasing splenomegaly defined either as an increase in palpable splenomegaly or > 5cm (distance of the spleen from the left costal margin) or the appearance of newly palpable splenomegaly
4	Development of >1 of three constitutional symptoms: >10% weight loss in 6 months, night sweats, unexplained fever (>37.5°C)

How Will I Know if I Have Post-PV-MF or Post-ET-MF?

How will I know if I have Post-PV-MF or Post-ET-MF?

Polycythemia Vera and essential thrombocythemia can progress to myelofibrosis over time in a small percentage of patients,

- approximately 10% every 10 years for PV
- approximately 4% every 10 years for ET

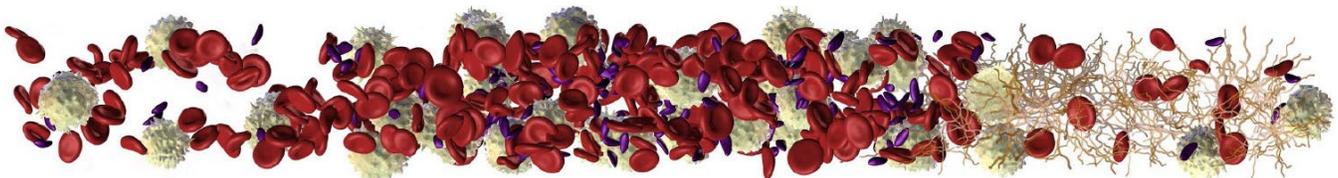
Your doctor will see you and do blood tests frequently to monitor your PV or ET. Some signs that your disease may be changing are:

1. A change in your blood cell counts such as increasing white blood cells, red blood cells or platelets
2. A change in your blood cell counts such as decreasing white blood cells, red blood cells or platelets
3. Night sweats
4. New decreased appetite
5. Enlarging spleen
6. Increasing fatigue
7. Increased of new bleeding
8. A new blood clot

Changes in the hemoglobin, from the complete blood cell count, can be a sign of the development of myelofibrosis.

In PV, phlebotomy or cytoreductive therapy may no longer be needed. Over time, this may progress to anemia.

For ET, a drop in hemoglobin of 2 grams or greater from baseline is a sign that myelofibrosis may be developing.



Continuum of Myelofibrosis with early increase in myeloid cells and eventual increasing fibrosis

Illustration by Kirk Moldoff

How is myelofibrosis staged?

Three prognostic scoring systems commonly used are the International Prognostic Scoring System (IPSS), Dynamic International Prognostic Scoring System (DIPSS), and the DIPSS-Plus²⁰⁻²¹. Each risk factor is scored, then a total risk score is calculated. There are four risk categories: low, intermediate-1, intermediate-2, and high risk as depicted in the table below.

Most recently the MIPSS70-plus has been developed to add molecular and expanded cytogenetic risk factors applicable to patients with primary myelofibrosis of transplant-age (<70 years)²². MIPSS70+ incorporates scores based on the absence of CALR type 1/like mutation and the presence of one or more mutated genes among ASXL1, EZH2, SRSF2, IDH1, and IDH2. You can access the MIPSS70+ calculator at www.mipss70score.it

PROGNOSTIC SCORING SYSTEMS FOR PRIMARY MYELOFIBROSIS			
Risk factor	IPSS	D-IPSS	D-IPSS-Plus
Age > 65	1	1	
Constitutional symptoms	1	1	
Hemoglobin <10	1	2	
Leukocytes >25x10 ⁹ /L	1	1	
Peripheral blood blasts >1%	1	1	
Platelet count <100 x 10 ⁹ /L			1
Transfusion dependence			1
Unfavorable karyotype**			1
DIPSS Low risk			0
DIPSS Intermediate-1			1
DIPSS Intermediate-2			2
DIPSS High risk			3
RISK STRATIFICATION (MEDIAN SURVIVAL)			
Low	0 points (11.2 years)	0 points (Not reached)	0 points (Not reached > 15 years)
Intermediate-1	1 point (7.9 years)	1-2 points (14.2 years)	1 point (6.5 years)
Intermediate-2	2 points (4 years)	3-4 points (4 years)	2-3 points (2.9 years)
High	> 3 points (2.3 years)	5-6 points (1.5 years)	4-6 points (1.3 years)
IPSS = International Prognostic Scoring System; D-IPSS = Dynamic International Prognostic Scoring System ** the presence of complex karyotype or sole or two abnormalities that included +8, -7/7q-, i(17q), inv(3), -5/5q-, 12p- or 11q23 abnormalities			

Myelofibrosis, whether primary or secondary to PV or ET, is treated similarly.

Allogeneic stem cell transplantation remains the only potentially curative treatment for myelofibrosis.

Most myelofibrosis patients receive treatment with the goal of improving their symptoms, reducing spleen size, and improving blood counts.

Treatments match the "stage" of disease, or prognostic risk score. Recent guidelines have been updated to include molecular and cytogenetic risk factors²³⁻²⁵.

Treatment for low-risk myelofibrosis

Low-risk myelofibrosis is defined as a score of 0 on the IPSS, DIPSS and DIPSS-Plus.

The first step in the evaluation of the need for treatment is assessment of symptoms utilizing the Myeloproliferative Symptom Assessment Form- Total Symptom Score (MPN-SAF TSS²²). If there are no symptoms of disease, observation, or enrollment in a clinical trial is recommended, with close monitoring for signs or symptoms of disease progression every 3-6months. For patients who are symptomatic, treatment options include Ruxolitinib, Interferons (Interferon alfa-2b, peg-interferon alfa-2a, or peg-interferon alfa-2b), hydroxyurea, or clinical trial enrollment.

Treatment for intermediate risk-1 myelofibrosis

Intermediate-1 risk myelofibrosis is a score of one on the IPSS and DIPSS, and 1-2 on the DIPSS-Plus.

For intermediate-1 risk, treatment considerations are careful observation every 3-6months, Ruxolitinib if symptomatic, and allogeneic hematopoietic stem cell transplant, or enrollment in a clinical trial if available.

Treatment for intermediate risk-2 and high-risk myelofibrosis

Intermediate risk-2 myelofibrosis is a risk score of two on the IPSS, 2 or 3 on the DIPSS-Plus, and 3 or 4 on the DIPSS.

High-risk myelofibrosis is a risk score of >3 on the IPSS, DIPSS-Plus risk score of 4-6, and a DIPSS score of five or six.

For patients who are transplant candidates, this is the recommended treatment. For non-transplant candidates, with symptomatic anemia only, the focus is on improving the anemia. Patients with platelets less than 50,000 with myelofibrosis related symptoms should pursue clinical trial participation. Patients with platelets greater than 50,000 can be treated with Ruxolitinib or pursue participation in a clinical trial.

Treatment of Symptoms in MF

Because the goals of therapy for MF are largely focused on improvement of symptoms, use of the Myeloproliferative Symptom Assessment Form- Total Symptom Score (MPN-SAF TSS) is recommended to accurately measure improvement or deterioration in symptoms²³.

Symptoms included in the MPN-SAF TSS include fatigue, early satiety (filling up quickly), abdominal discomfort, inactivity, problems with concentration, numbness and tingling in the hands and feet, night sweats, itching (pruritus), diffuse bone pain, fevers >100 F, and unintentional weight loss. Each symptom is scored on a scale of 0-10, where 0=none and 10=worst imaginable.

Management of myelofibrosis-related anemia

Anemia is a frequent problem in patients with myelofibrosis, affecting more than 50% of patients at the time of diagnosis. It is important to investigate other causes of anemia. This begins with obtaining an accurate history and performing a thorough physical examination. A complete blood cell count with differential is essential, including evaluation of the peripheral smear. A bone marrow biopsy with aspiration is necessary when there are changes in the hemoglobin/hematocrit.

Potential co-existing causes of anemia are bleeding, iron deficiency, B12 deficiency, and hemolysis (destruction of blood cells, often because of an overactive immune system). These should be treated prior to other treatments for anemia from myelofibrosis. If the anemia is determined to be primarily from the myelofibrosis, patients should consider clinical trial enrollment.

Erythropoietin-stimulating agents may be beneficial if the serum erythropoietin level is less than 500mU/ml. Available erythropoietin stimulating agents are recombinant human erythropoietin and darbepoetin alfa which are administered subcutaneously to improve hemoglobin levels, with the goal of eliminating or decreasing transfusion requirements of packed red blood cells.

Alternate treatments, including clinical trials, are recommended when the serum erythropoietin level is greater than 500mU/ml, or anemia that is no longer responding to erythropoietin stimulating agents.

Medications for treatment of myelofibrosis

Ruxolitinib (Jakafi®)²⁶⁻²⁸

- Ruxolitinib is the first FDA-approved therapy for treating intermediate-risk and high-risk myelofibrosis²⁶. Results from studies suggest that it can also benefit lower-risk myelofibrosis patients who have symptoms²⁷. In clinical trials, Ruxolitinib decreased spleen size, and improved symptoms associated with myelofibrosis²⁶. It is therefore important to measure spleen size prior to starting treatment.
- Works by targeting the overactive JAK-STAT signaling pathway, thereby blocking the overproduction of myeloid cells and inflammatory cytokines ([What Happens to Bone Marrow in MPNs?](#)).
- Jakafi® is a tablet taken orally twice daily
- The most common side effects include:
 - Low WBC – increases the risk of infection
 - Low platelets – increases the risk of bleeding
 - Nausea or diarrhea
 - Headache
 - Less common side effects may include elevated cholesterol levels, non-melanoma skin cancers, and atypical infections.
- Do not change your dose or stop taking Jakafi® without first talking to your healthcare provider. This may cause a rapid flare of your MF symptoms and increase the risk of thrombosis.
- Do not drink grapefruit juice while on Jakafi®.
- Women should not take Jakafi® while pregnant or planning to become pregnant, or if breast-feeding.
- You can learn more about Jakafi® at www.jakafi.com/medication.aspx

Hydroxyurea

- A type of chemotherapy
- Decreases production of blood cells in the bone marrow
- While not FDA approved for MF, Hydroxyurea is commonly used for the treatment of MF. In a small study, it decreased symptoms associated with myelofibrosis (constitutional symptoms, pruritus, bone pain, splenomegaly, and high white blood cell and platelet counts). The National Comprehensive Cancer Network expert panel lists hydroxyurea as a treatment option for low-risk myelofibrosis.
- Hydrea is taken orally by swallowing capsules. The number of capsules taken and the schedule for taking them will vary for each patient based on the ability to control the platelet count.
- The most common side effects include:
 - Low WBC – increases the risk of infection
 - Low platelets – increases the risk of bleeding
 - Nausea or diarrhea
 - Ulcers in the mouth or on the legs after being on this medication for a long time
 - Non-melanoma skin cancers

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

Pegylated (long-acting) Interferon²⁹⁻³⁰

- Pegylated [PEG]-interferon is a biologic agent that can slow down production of blood cells by a variety of different mechanisms.
- Although this is not FDA approved for MF, interferon may reduce splenomegaly, improve bone marrow findings and may provide a survival benefit for intermediate or high-risk MF^{28,29}. It is most effective in early MF with less benefit seen in later stages of disease.
- Interferon is an injectable medicine that can be administered at home using a syringe and a small needle inserted under the skin in the stomach or legs, like the technique used to administer insulin. The long acting nature of this medicine allows for less frequent injections and may only need to be injected once per week.
- Interferons are the medication of choice in patients who are pregnant and require treatment.
- The most common side effects include:
 - Fever or chills
 - Fatigue
 - Nausea or diarrhea
 - Depression
 - Headache
 - Musculoskeletal pain
 - Weight loss

You can learn more about interferon www.gene.com/patients/medicines/pegasys

Palliative and Supportive Care for Myelofibrosis

Palliative and supportive care for myelofibrosis

Supportive care is a key feature of care for individuals with myelofibrosis. Most patients live with their illness for many years. Close monitoring of disease related symptoms is essential.

Throughout the disease course, counseling is directed to modifying lifestyle factors that influence cardiovascular risk factors. These risk factors include smoking cessation, regular exercise, healthy diet, and thrombotic and hemorrhagic risk factors.

Yoga and regular exercise have been studied and found to help alleviate symptoms, improve fatigue, anxiety, and depression in patients with myeloproliferative neoplasms.

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

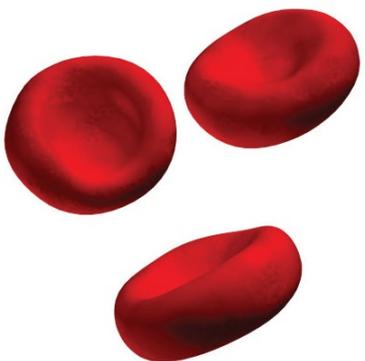
Transfusions

Packed red blood cell transfusions can alleviate symptomatic anemia.

Platelets transfusions are necessary for bleeding or severe thrombocytopenia, a platelet count less than 10,000. For patients with low platelets that do not respond to platelet transfusions, antifibrinolytic medications can prevent bleeding. Examples of antifibrinolytic drugs include aprotinin, tranexamic acid (TXA), epsilon-aminocaproic acid, and aminomethylbenzoic acid.

For transplant eligible candidates, transfusions need to be leukocyte depleted to prevent human leukocyte antigen alloimmunization. This also helps reduce the risk of cytomegalovirus transmission.

For patients with more than 20 units of packed red blood cells transfused, iron chelation, the removal of iron by either phlebotomy or with medications, is a consideration.



Red Blood Cells

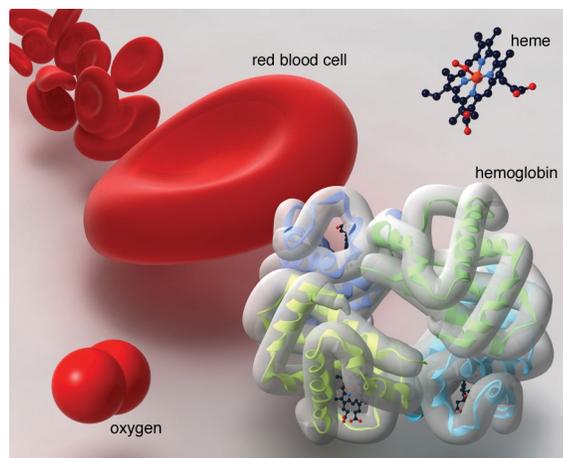
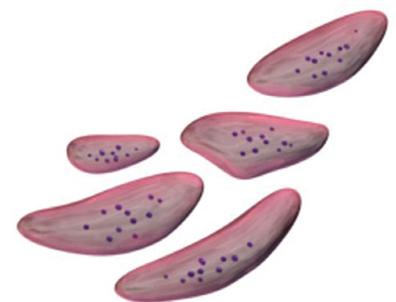


Illustration by Kirk Moldoff



Platelets

Allogeneic hematopoietic stem cell transplant for myelofibrosis

Allogeneic hematopoietic stem cell transplant is the only treatment that is potentially curative for myelofibrosis patients.^{24, 25, 31}

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 ([What does bone marrow do?](#)).

There are significant risks with this procedure. Therefore, although blood or marrow transplantation offers a potential cure for MF, this procedure is available to only a small proportion of adult MF patients.

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

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:

1. Age less than 65 years (some exception may be made at some centers)
2. Availability of a HLA identical matched donor
3. Good heart, lung, liver, and kidney function
4. Physically active and able to perform daily activities independently
5. Consistent availability of a caregiver

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

National Marrow Donor Program (NMDP) Be the Match: www.marrow.org

Blood and Marrow Transplantation Information Network: www.bmtinfonet.org

National Coalitions for Cancer Survivorship: www.canceradvocacy.org/toolbox

Myeloablative and reduced intensity conditioning (chemotherapy) are the two major types of transplants used for myelofibrosis.

The transplant center and healthcare team determine the type of transplant. Myeloablative conditioning, or chemotherapy prior to transplant that cleans out the bone marrow, has been associated with increased mortality.

Long-term survival with an allogeneic transplant is in the range of 40–50%, but factors such as patients age, DIPSS (Plus)-prognostic risk group, and type of donor, may all impact outcomes. Higher treatment-related mortality is observed in myeloablative compared to reduced intensity conditioning transplants; however, higher rates of relapse are observed in reduced intensity conditioning transplants vs. myeloablative transplants. While transplants are not recommended for patients with low-risk disease, it is a consideration for patients with intermediate-2 or high-risk disease because the risk of death from disease may be higher than the treatment-related mortality of transplant.

For patients with intermediate-1 risk disease, this risk benefit ratio becomes less certain and a discussion of risks and benefits of undergoing transplant, current disease status at that time versus waiting needs to be taken into consideration.

Clinical trials for myelofibrosis

Clinical trials are research studies in which people are assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions. Clinical trials also test the safety of a new intervention or medication. The level of testing determines the phase of the clinical trial.

Follow the links for more information on clinical trials recruiting for patients with myelofibrosis.

Center Watch - Provides the phase of clinical trial and proximity from identified location

www.centerwatch.com/clinical-trials/listings/condition/856/myelofibrosis

National Institute of Health (NIH) <https://clinicaltrials.gov>

Myeloproliferative (MPN) Research Foundation www.mpnresearchfoundation.org/Clinical-Trials

European Union Clinical Trials Register www.clinicaltrialsregister.eu/ctr-search/search?query=mpn

National Cancer Institute www.cancer.gov/about-cancer/treatment/clinical-trials

MPN Advocacy and Education International <http://mpnadvocacy.com/mf>

There are a variety of educational and support networks for patients with ET. It is important to use reputable sources for information regarding your disease.

www.pvreporter.com

www.patientpower.info/myeloproliferative-neoplasms

www.mpnresearchfoundation.org/Polycythemia-Vera-28PV-29

<http://mpnadvocacy.com/understanding-mpns/myelofibrosis>

GENERAL RESOURCES FOR LIVING WITH MPNS

Chapter 5 will provide you with strategies for staying well, managing your health and your MPN, and includes several Quick-Tips to recognize and manage common symptoms or problems experienced by patients and caregivers living with MPNs. Each Quick-Tip includes links to several digital resources that may help you manage your health. This chapter also includes a glossary terms that will help you to understand the complex language used to describe these diseases.

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Bleeding and bruising

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

If you have excessive bleeding and bruising and your platelet count is over 1 to 1.5 million per microliter of blood, your physician will do blood tests for acquired von Willebrand Disease. If your test results come back positive, cytoreduction is indicated. Cytoreduction may also be indicated prior to surgery, even if you aren't currently having bleeding or bruising, to help prevent complications during and after surgery.

In some patients with Myelofibrosis or those receiving treatment, the platelets count may be too low (thrombocytopenia). The risk of bleeding is related to the severity of the thrombocytopenia. Certain medications may increase the risk of bleeding, such as blood thinners, aspirin, and other anti-inflammatory medications.

Things you can do:

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

Additional Resources:

Cancer.net: Thrombocytopenia [Thrombocytopenia](#)

Oncolink: [Low Platelet Count](#)

Blood clots (thrombosis)

Uncontrolled blood cell production, the hallmark of MPNs, increases the risk of a thrombosis (blood clot) in the arteries or veins. These vessels carry blood throughout the body. A blood clot can block the flow of blood to one or more areas of the body.

- Arterial clots: to the heart or brain resulting in a heart attack or stroke.
- Venous clots: blood clots in one or more veins, often in the legs or arms known as a deep vein thrombosis (DVT), or in the lungs, known as a pulmonary embolism (PE) are the most common.

There are several other factors that can increase the risk of clotting:

- Elevated white blood cell count
- Cardiovascular risk factors:
 - Congestive heart failure
 - Arterial hypertension
 - Hypercholesterolemia
- Diabetes mellitus
- Tobacco use
- Obesity
- Immobility

Managing blood clots

If you've had a blood clot, your physician will recommend anticoagulation or a "blood thinner". Typically, Low Molecular Weight Heparin (LMWH) is prescribed first because it acts quickly. LMWH is an injection taken once or twice a day. If possible, your physician may transition you to a pill form of anticoagulant such as warfarin, which requires monitoring to ensure the correct amount of anticoagulation is achieved, or oral anticoagulants such as apixaban or rivaroxaban, which do not require blood monitoring. Talk with your health care team to determine which medication is right for you.

Things you can do:

1. Keep track of all your medications.
2. Keep all your appointments as scheduled.
3. Let your health care providers know if you experience unusual bruising, uncontrolled bleeding.
4. Be active, immobility increases the risk of clotting.
5. Keep appointments with other health care providers that help you to manage your other illnesses.
6. Quit smoking.
7. Take your anti-coagulation medication as prescribed. Missing even a single dose may increase the risk of developing another clot.
8. Ask for help from family and friends.
9. If you are scheduled for a surgery, your anticoagulation clinic or physician will give you special instructions regarding whether these medications need to be held in the perioperative setting.

Additional Resources:

Cancer.net: [Preventing and treating blood clots](#)

Caregiving: Resources for managing each day

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

Common roles for a caregiver:

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

Caring for or being around children

The time spent enjoying the company of family, including children, is important. Most patients with MPNs can enjoy their family without restrictions. Discuss any recommendations for limiting contact with children with your health care team. Specific recommendations for contact with children are recommended for patients undergoing a stem cell transplant, leukemia therapy, or who have a very low white blood cell counts (neutropenia).

Things you can do:

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

Additional Resources:

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

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

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

Be the Match: Caregivers and Bone Marrow Transplant

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

Constipation

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

Things you can do for Constipation

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

Additional Resources:

Cancer.net: Constipation www.cancer.net/navigating-cancer-care/side-effects/constipation

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

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

Diarrhea

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

Things you can do for Diarrhea:

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

Additional Resources:

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

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

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

Diet and nutrition

A balanced diet, daily activity and exercise as tolerated, and participation in activities of enjoyment are important to maintain optimal health and well-being. A balanced diet can help combat fatigue and illness. Adequate intake of food and fluids also helps individuals tolerate treatment. Fluids are an essential part of a healthy diet. Your body needs fluids to function properly, like a car needs gas to run.

Patients with splenomegaly may find they get full fast (early satiety) because the spleen is pressing up into the stomach. In some cases, you may experience pain after eating. Eating small frequent meals may reduce the pain associated with eating.

People living with MPNs may need to follow a special diet if they have a very low white blood cell count or are undergoing a stem cell transplant. Ask your health care providers if there are specific restrictions for you.

Things you can do:

1. The Dietary Guidelines for America 2015 (www.dietaryguidelines.gov) provide the basic principles of a healthy diet.
2. Meet with a registered dietician to determine your daily caloric needs and how you might get these in the foods you like to eat.
3. Stay hydrated: Carry fluids with you wherever you go. If drinking a full glass causes bloating, take small sips throughout the day. Drink most of your fluids between meals.
4. Eat a balanced diet:
 - a. Eat fruits and vegetables. Wash all fruits and vegetables well prior to eating. Eat dark green vegetables like leafy greens or broccoli and orange vegetables like carrots and sweet potatoes.
 - b. 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.
 - c. Have three servings of low-fat or fat-free dairy (milk, yogurt or cheese) that are fortified with vitamin D to help keep your bones healthy. Consume only pasteurized milk, yogurt, cheese, and other dairy products.
 - d. Make the fats you eat healthy ones (polyunsaturated and monounsaturated fats).

Additional Resources:

Cancer.net: Nutrition Recommendations During and After Treatment

www.cancer.net/survivorship/healthy-living/nutrition-recommendations-during-and-after-treatment

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

Anxiety

Anxiety is a common reaction to learning that one has a MPN. Anxiety can range from a mild and vague feeling that something may be wrong, to an overwhelming feeling that interferes with a person's ability to function. All people experience periods of anxiety in their lives. Uncertainty about the diagnosis of a MPN, what treatments might be right for you, how they will work, and what side effects you may experience may contribute to your anxiety.

Things you can do:

1. There are several resources to help you understand your diagnosis, treatment options, and strategies to take an active part in your journey. Explore the Building Blocks of Hope® www.buildingblocksofhope.com, the MDS Foundation website www.mds-foundation.org, and the MPN Research Foundation website www.mpnresearchfoundation.org
2. Evaluate other parts of your life where you have been successful in mastering control—use those techniques to help you meet the challenges you face while living with MPNs.
3. Try to simplify your life. Eliminate or reduce the activities that are not essential to your physical and emotional well-being.
4. Ask for help. This can be from family, friends, or professionals. Counseling from a psychologist or social worker can also be useful.
5. Consider joining a support group—in person, or by computer. Others living with MPNs 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.
6. Explore resources that will help you with relaxation such as meditation, massage, yoga, or listening to relaxing music.
7. Try to eat well and maintain some sort of activity.
8. Avoid excess amounts of alcohol or caffeine.
9. You may find it difficult to remember instructions, or to concentrate when hearing information, so write them down or bring a caregiver or advocate with you to appointments.
10. Talk to your health care team about other options for managing your anxiety. Ask if an anti-anxiety medication might be helpful.

Additional resources:

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

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

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

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

Depression

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

Things you can do:

1. Recognize some of the common signs of depression:

- A lack of interest or pleasure in doing things
- Feeling down, depressed, or hopeless
- Difficulty sleeping
- Decreased appetite
- Tearfulness

If you are having any of these symptoms, you may have clinical depression. It may also be helpful to ask someone who knows you well if they think that you may be depressed.

2. Give yourself time to adjust to the diagnosis and changes in your daily routines. While you may not be able to return to as active a lifestyle as you once had, you may be able to substitute those activities with less strenuous ones that are still enjoyable.
3. Set priorities for activities that are necessary to maintain your physical and emotional health.
4. Try to find some activity that you can still enjoy—such as listening to music or watching a ball game. These activities can help you keep a positive outlook.
5. Continue with a diet and exercise routine that will help you to stay healthy. Get enough rest.
6. Avoid alcohol—it can make depression worse.
7. Talk with your health care team about resources available to help you.
8. Prayer or meditation may be useful to provide peace.
9. Consider joining a support group—in person, or by computer. Others living with MPNs 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.

Additional resources:

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

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

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

Employment

Many patients or caregivers LIVING with MPN continue to work.

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

It is important to ask about your employers' options for sick-leave and family medical leave.

The [Family and Medical Leave Act \(FMLA\)](#) provides certain employees with up to 12 weeks of unpaid, job-protected leave per year. It also requires that their group health benefits be maintained during the leave.

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

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

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

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

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

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

Additional resources:

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

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

Fatigue

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

Things you can do:

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

Additional resources:

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

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

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

Fever and infections

Fever may be a result of infections or may be a side effect of certain chemotherapy agents used to treat MPNs. The Absolute Neutrophil Count (ANC) is used to determine your risk of infection. Guidelines for activities while neutropenic are related to the risk of being exposed to people or things that would increase the chance of developing an infection. Ask your health care providers when you should report a fever, who to call and when you might need emergent treatment. It is essential to treat MPN patients with fevers quickly to avoid the possibility of developing more serious infections.

Things you can do:

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

Additional resources:

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

Cancer Care: Infections: www.cancercare.org/publications/216-neutropenia-and-infections-what-you-need-to-know

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

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

Finances and insurance

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

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

Drug Assistance Programs

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

General Finances

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

Additional Financial Resources:

Chronic Disease Fund

877-968-7233 www.cdfund.org

of more than 475 public and private patient assistance programs including nearly 200 programs offered by pharmaceutical companies.

Health Well Foundation

800-675-8416 www.healthwellfoundation.org
Provides aid to underinsured patients who are diagnosed with chronic or life-altering diseases.

Patient Access Network Foundation

866-316-PANF (866-316-7263)
www.panfoundation.org
This foundation assists patients with their coinsurance associated with MPN treatments/medications.

National Organization for Rare Diseases Medication Assistance Program

800-999-6673 or 203-744-0100
<https://rarediseases.org/for-patients-and-families/help-access-medications/patient-assistance-programs-2>
This charitable organization offers co-pay assistance for MPN medications.

Patient Advocate Foundation

800-532-5274 www.patientadvocate.org
This program provides direct copayment assistance for pharmaceutical products to insured Americans who financially and medically qualify.

Partnership for Prescription Assistance

888-4PPA-NOW (888-477-2669) www.pparx.org
Prescription assistance programs, often sponsored by drug makers, to help patients who qualify based on financial need. Search this website for a comprehensive listing

Patient Services, Inc.

800-366-7741 www.patientservicesinc.org
A nonprofit charitable organization primarily dedicated to subsidizing the high cost of health insurance premiums and pharmacy copayments for persons with specific chronic illnesses and rare disorders.

Additional Resources:

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

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

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

Home management

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

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

Additional resources:

Cancer.net: Coping with Cancer

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

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

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

MPN Resources

The diagnosis of MPN is often unexpected and filled with both immediate and long-term challenges. Assisting patients and their caregivers to live with the highest quality of life possible despite the diagnosis of a MPN and other myeloid malignancies, including MPNs is the primary mission of The Myelodysplastic Syndromes Foundation. Cancer patients need both specialized medical care and support services to address a range of issues that can affect their health and well-being.

There are many excellent resources to aid in managing day to day challenges. Organizing your resources and asking for help is the first step. There are many resources that may help you manage each day.

1. First, it is important to make the most of your relationship with your health care team. This will improve your participation in making decision about your health and treatment. Communication among and between the members of your health care team will improve your health.
2. Explore the BBoH-MPN to learn more about MPNs and the resources available for each specific disease or symptom.
3. The MDS Foundation is currently developing a mobile app, MPN Manager, to help patients and caregivers keep track of their symptoms, blood counts and medications. It will also provide easy access to MPN resources.

We have included links to specific resources from several well-respected cancer advocacy organizations that provide general information for cancer patients.

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

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

Helpline 800-227-2345

Cancer Care: www.cancercare.org/contact

Services: 800-813-HOPE (4673)

https://media.cancercare.org/publications/original/178-helping_hand.pdf?1442411382

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

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

Memory and concentration problems

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

Organizing health information by using MPN manager can help you in organizing your thoughts. The symptom tracker may help you keep track of symptoms you're experiencing in between visits to your health care provider.

Things you can do:

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

Additional resources:

Cancer.net: Attention, Thinking or Memory Problems

www.cancer.net/navigating-cancer-care/side-effects/attention-thinking-or-memory-problems

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

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

Mobility

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

Things you can do:

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

Additional resources:

Cancer.net: Nutrition, Physical Activity and You

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

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

Mouth sores/mucositis

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

There are a number of things you can do to improve oral health and reduce pain associated with mucositis.

Things you can do:

1. Keep a log of symptoms that you are concerned about. Discuss these with your health care team.
2. Keep all your appointments as scheduled.
3. If you are experiencing pain in the mouth making it difficult to chew or swallow, or if there is any bleeding from the mouth, contact your health care providers immediately. You may need medication.
4. See your dentist regularly, however, speak to your health care team prior to any dental procedures.
5. Rinse with salt water and baking soda and water. You can't make this at home by simply combining a tablespoon of salt to a quart of water in one solution and a tablespoon of baking soda and water in a second solution. Rinse with the saltwater first and then spit it out. Follow-up with a rinse of baking soda and water and spit it out. You can do this several times a day.
6. Avoid alcohol-based mouth washes.
7. Use a soft toothbrush.
8. Stop using dental floss if your mouth is painful. Dental floss can be continued unless your blood counts are too low. Speak to your health care team about when to stop using dental loss.
9. Avoid alcohol.
10. Avoid eating coarse or acidic foods.

Additional resources:

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

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

American Cancer Society: Mouth sores

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

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

Nausea and vomiting

Nausea is a symptom that is often described as an unpleasant feeling associated with flushing, tachycardia, and the urge to vomit. Vomiting is a physical phenomenon that involves contraction of the abdomen, chest wall muscles, and movement of the diaphragm followed by expulsion of the stomach contents.

Things you can do:

1. Meeting with a dietician may be helpful in finding a diet that works best for you.
2. Make a note of any symptoms of nausea that you have or episodes of vomiting. Discuss these with your health care provider at your next visit.
3. If you experience vomiting more than 5–6 times in a 24-hour period, notice any blood when you vomit, or are not able to keep food or liquids down, and be sure to contact your health care provider immediately. Talk with your health care provider about when and how to call in case of more severe symptoms.
4. Discuss how many of each type of anti-emetic you can safely use each day and what side effects they may cause. Some of the medications used to treat or prevent nausea and vomiting may increase the risk of developing constipation.
5. Drink 2–3 liters of fluid a day—avoid caffeine or high sugar drinks.
6. Eat small, frequent meals.
7. Avoid: fatty foods, greasy foods, spicy foods, foods that are hard to digest (hard fruits, meats, hard cheese, popcorn), alcohol, caffeine, chocolate, and foods with strong odors.
8. Brush your teeth more frequently and use non-alcohol-based mouth washes to reduce the symptoms of dry mouth and bad taste.
9. Peppermint and ginger supplements have been found to be helpful for some patients.
10. Relaxation, imagery, and meditation may help some patients. Ask your health care team about any resources available.
11. Ask for help from family and friends.

Additional resources:

Cancer.net: American Cancer Society: Nausea

<https://www.cancer.org/treatment/survivorship-during-and-after-treatment/staying-active/nutrition/nutrition-during-treatment/nausea.html>

Cancer Care: Nausea and Vomiting from Chemotherapy

www.cancercare.org/publications/7-coping-with-nausea-and-vomiting-from-chemotherapy

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

Pain

Many patients experience pain during and after cancer treatment. It may help to know that cancer pain can be treated successfully for most patients. It is important to focus on managing pain during all phases of cancer treatment. Bone pain and abdominal pain may be a result of the inflammatory nature of MPNs or due to an enlarged spleen or liver. Treatment of the MPN may help to reduce these symptoms.

Things you can do:

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

Additional resources:

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

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

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

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

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

Sexuality and intimacy

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

Questions you should ask your health care provider:

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

Additional resources:

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

Oncolink: Women's guide to sexuality www.oncolink.org/support/sexuality-fertility/sexuality/women-s-guide-to-sexuality-during-after-cancer-treatment

Oncolink: Men's guide to sexuality www.oncolink.org/support/sexuality-fertility/sexuality/men-s-guide-to-sexuality-during-after-cancer-treatment

Shortness of Breath

The feeling that you are not able to get a good breath or are not getting enough oxygen can be alarming and uncomfortable. Shortness of breath, or dyspnea, may be a result of several underlying problems. In patients with MPNs, anemia may predispose you to feeling short of breath with activity. Splenomegaly may cause pressure on the diaphragm, making it difficult to take a deep breath. Deconditioning due to inactivity may also predispose you to shortness of breath with activity.

Things you can do:

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

Additional resources:

Cancer.net: Shortness of Breath or Dyspnea

<https://www.cancer.net/navigating-cancer-care/side-effects/shortness-breath-or-dyspnea>

American Cancer Society: Shortness of Breath

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

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

Skin Changes including rash, pruritus, or leg ulcers

The most common skin changes for patients with MPNs is itching or pruritus. The itching can be intense and unrelenting in some patients. Treatment of the MPN is usually the best way to reduce the intensity of pruritus. Avoidance of aggravating factors and use of supportive medications may also be helpful.

A rash is a change of the skin which affects its color, appearance, or texture. A rash may be localized in one part of the body or affect all the skin. Rash is generally caused by a skin irritation that can result from chemotherapy, allergy, infection, or skin problem. Certain skin changes may indicate more severe skin infections, such as shingles.

Leg ulcers, often on the ankles, may develop if you are taking Hydroxyurea over an extended period. These can be painful and may increase the risk of secondary infection. If you notice an ulcer, report this immediately to your health care team. You may need to modify your MPN treatment.

Things you can do:

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

Additional resources:

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

American Cancer Society: Getting help for skin changes

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

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

Oncolink: Nail and Skin Changes: www.oncolink.org/support/side-effects/nail-and-skin-changes

Sleep and insomnia

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

How much sleep is enough? The general recommendation is 7–9 hours of sleep per night, according to the National Sleep Foundation. However, like exercise, sleep needs are individual. One person may function well with 7 hours of sleep, while another may need 10 hours.

Things you can do:

1. Keep a log of symptoms that you are concerned about. Discuss these with your health care team.
2. Keep all your appointments as scheduled.
3. Discuss problems sleeping with the health care team. Medications for anxiety, depression, and insomnia may be necessary.
4. If sleep is altered by symptoms related to MPN, discuss these symptoms with the health care team.
5. Keep regular bedtime and awakening hours.
6. Avoid stimulants and caffeine 2 hours prior to bedtime.
7. Exercise for 30 minutes three to five times per week.
8. Limit day time napping to 30 minutes.
9. Spend 30 minutes to an hour of quiet time prior to going to bed.

Additional resources:

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

American Cancer Society: Sleep Problems

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

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

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

Spirituality

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

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

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

Things you can do:

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

Additional resources:

American Cancer Society: Sources of Support

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

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

Oncolink: Spirituality www.oncolink.org/support/practical-and-emotional/integrative-therapies-spirituality/tips-in-a-minute-addressing-spiritual-concerns-across-the-cancer-continuum

Transportation resources

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

Air Charity Network

877-621-7177 www.aircharitynetwork.org

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

American Cancer Society's Road to Recovery Program

800-227-2345 www.cancer.org

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

Angel Wheels to Healing

800-768-0238 www.angelwheels.org

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

Cancer Care

www.cancercares.org/publications/303-transportation_resources

CancerCare provides limited financial assistance for treatment-related transportation to people affected by cancer.

Fisher House Foundation

www.fisherhouse.org

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

Good Days

877-968-7233 www.mygooddays.org

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

The Patient Travel Referral Program

www.patienttravel.org

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

Urinary symptoms

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

Things you can do:

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

Additional resources:

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

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

Acute

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

Acute Myeloid Leukemia (AML)

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

Synonyms: acute myeloblastic leukemia, acute myelocytic leukemia

Allogeneic Stem Cell Transplant

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

Anaphylaxis

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

Synonym: anaphylactic shock

Anemia

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

Antibiotics

Medications used to treat bacterial infections and other similar microorganisms.

Antibodies

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

Anticoagulant

(ant-i-ko-AG-yuh-lunt) See blood thinner.

Anti-thymocyte globulin (ATG)

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

Apheresis

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

Aplastic Anemia

A rare and serious condition in which the bone marrow does not make enough blood cells: red blood cells, white blood cells, and platelets. Anemia is a condition that happens when the red blood cell count is low. Most scientists believe that aplastic anemia happens when the immune system attacks the bone marrow stem cells. Aplastic anemia can be acquired (begin any time in life) or

can be hereditary (less common, passed down from parent to child).

Synonyms: acquired aplastic anemia, hereditary aplastic anemia

Apoptosis

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

Autoimmune Disease

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

Basic Research

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

Basophil

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

Benzene

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

Bilirubin

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

Biologic Agent

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

Synonyms: biologic, biological drug

Blast Cells

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

Synonym: precursor cell

Blood Clot

A clot or small cluster of blood cells that forms when platelets stick together. A combination of platelets and fibrin that form a mesh with the intention of preventing bleeding in response to an injury or illness. The term thrombus describes a blood clot that develops

and attaches to a blood vessel. Blood clots are more common in Paroxysmal Nocturnal Hemoglobinuria (PNH) or in people with blood clotting disorders.

Synonym: thrombus

Blood Tests

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

Blood Thinner

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

Synonyms: anticoagulant, anti-clotting

Blood Transfusion

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

Bone Marrow

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

Bone Marrow Aspirate

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

Bone Marrow Aspiration

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

Bone Marrow Biopsy

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

Synonym: Bone Marrow Trepine Biopsy

Bone Marrow Failure

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

Bone Marrow Transplant (BMT)

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

CD 55 and CD 59

Protein antibodies

Cellularity

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

Chemotherapy

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

Chronic Illness

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

Chromosomes

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

Clinical Trial

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

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

Clone

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

Coagulate

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

Combination Chemotherapy

The use of more than one drug during cancer treatments.

Comorbidities

Additional medical conditions beyond MDS.

Complement System

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

Complete Blood Count (CBC)

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

Complex Karyotype

Three or more abnormalities in the chromosomes being evaluated.

Conditioning Treatment

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

Cytogenetics

Testing that is performed on bonemarrow samples and examines the chromosomes of the cells. Your cytogenetic results are used to identify the type of MDS you have and to calculate the International Prognostic Scoring System (IPSS) and the revised IPSS (IPSS-R) risk category. Common abnormalities include:

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

Synonyms: Chromosomes, Karyotype, DNA

Cytogenetic Remission

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

Cytokines

Proteins

Cytopenia

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

Cytotoxic Agent

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

D-dimer

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

del(5q)

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

De Novo

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

Differentiation

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

Dietary Supplement

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

DNA Methylation

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

Dysplasia

Abnormal shape and appearance or morphology, of a cell.

Synonym: dysplastic

Embolus

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

Engraftment

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

Epidemiology

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

Erythroid Response

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

Erythrocyte

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

Erythropoietin (EPO)

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

Erythropoietin-stimulating Agent (ESA)

A medicine used to help the bone marrow make more red blood cells. Epoetin alfa (Epogen, Procrit) and darbepoetin alfa (Aranesp) are erythropoiesis-stimulating agents that can help boost the

red blood cell count of some bone marrow failure patients. These medicines are given via an injection. Also called red blood cell growth factor.

Eosinophil

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

Etiology

The cause or origin of a disease.

FAB Classification

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

Fanconi Anemia

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

Fatigue

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

Synonyms: tired, exhaustion, lethargy, malaise

Ferritin

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

Fibrosis

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

Flow Cytometry

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

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

Fluorescence In Situ Hybridization (FISH)

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

Folate

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

Gene Expression

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

Graft-Versus-Host Disease (GVHD)

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

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

Graft-Versus-Leukemia Effect

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

Granulocyte

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

Growth Factor

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

Haploidentical Stem Cell Transplantation

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

Hematocrit (HCT)

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

Synonyms: packed cell volume, PCV

Hematologist

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

Hematopoiesis

The formation and development of blood cells.

Hemochromatosis

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

Hemoglobinuria

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

Hemolytic Anemia

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

Hemolysis

The destruction of red blood cells.

HLA

See human leukocyte antigen.

Hormone

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

Human Leukocyte Antigen

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

Hypercellular

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

Hypocellular

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

Hypomethylating Agent

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

Synonym: demethylating agent

Idiopathic

Usually refers to any condition with no known cause.

Immature Blood Cells

May be called stem cells, progenitor cells or blasts.

Immune Deficiency

A decreased ability of the immune system to fight infection.

Immune System

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

Immunocompromised

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

Synonym: immune compromised

Immunosuppressive Drug

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

Intravenous Infusion

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

Synonym: IV infusion

Investigational New Drug

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

IPSS/IPSS-R

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

Iron Chelation Therapy

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

Iron Overload

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

Ischemia

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

Lactate DeHydrogenase

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

Leukocyte

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

Lymphatic System

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

Lymphocyte

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

Matched Related Donor

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

Mean Corpuscular Volume

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

Megakaryocyte

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

Mini Transplant (aka reduced intensity transplant)

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

Minimal Residual Disease

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

Monosomy 7

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

Monoclonal Antibody

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

Monocyte

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

Morphology

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

Multilineage Dysplasia

Abnormalities in more than one type of blood cell

Mutation

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

Myelo

A Greek word meaning marrow.

Myelodysplastic Syndromes (MDS)

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

- **Anemia:** low red blood cells (oxygen carrying cells)
- **Thrombocytopenia:** low platelets (cells that help to clot the blood)
- **Leukopenia:** low white blood cells (WBC) (help to fight infection)
- **Neutropenia:** low neutrophils (most important type of WBC for fighting infection)

Natural Killer Cells

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

Neutropenia

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

Neutropenic Diet

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

Occlusion

Obstruction; blockage.

Off Label Drug

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

Oncologist

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

Over-the-Counter (OTC) Medicine

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

Packed RBCs

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

Pancytopenia

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

Paroxysmal Nocturnal Hemoglobinuria (PNH)

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

Pathophysiology

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

Pediatric MDS

MDS is rare in children; but it does happen.

Peripheral Blood Stem Cell (PBSC) Transplant

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

Petechiae

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

Phagocyte

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

Pharmacist

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

Placebo

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

Platelets

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

Platelet Transfusion

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

Prophylactic

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

Protocol

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

Pulmonary Embolism

(PULL-muh-nerr-ee EM-buh-liz-um) A blockage of an artery that carries blood to the lungs. See Embolus.

Pure Red Cell Aplasia (PRCA)

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

Red Blood Cell

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

Red Blood Cell Growth Factor

See erythropoietin-stimulating agent.

Red Blood Cell (RBC) Transfusion

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

Reduced Intensity Transplant

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

Refractory

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

Reticulocyte

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

Remission

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

Revised IPSS (IPSS-R)

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

Ring Sideroblast

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

Secondary MDS

A type of MDS that is caused by a previous treatment for another disorder or disease. Treatments typically associated with secondary MDS include radiation therapy and chemotherapy used to treat cancer. Also called therapy-related MDS, T-MDS.

Synonyms: T-MDS, therapy-related MDS

Serum Erythropoietin

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

Serum Sickness

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

Single Lineage Dysplasia

Abnormalities in only one type of blood cell.

Social Worker

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

Somatic Mutation

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

Stem Cells

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

Stem Cell Transplant (SCT)

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

Subcutaneous Injection

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

Synonyms: shot, injection

Supportive Care

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

Synonyms: palliative care, symptom management

T cell

See lymphocyte

T lymphocyte

See lymphocyte

Therapy-Related MDS

See Secondary MDS

Thrombus

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

Thrombosis

The process of forming a blood clot.

Thrombocytopenia

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

Transfusion

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

Transfusion Independence

No longer needing any type of blood transfusion.

Treatment Failure

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

Unrelated Donor

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

Venous thrombosis

Blood clot in a vein.

Vitamin B12

A complex vitamin found in animal products. Vitamin B12 helps maintain healthy red blood cells and nerve cells. A shortage of Vitamin B12 and folate can reduce blood cell production in the

bone marrow. Also called B complex vitamins. Levels of B12 can be measured in the blood.

White Blood Cells (WBC)

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

World Health Organization (WHO) Classification

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

WHITE BLOOD CELLS

ANC (absolute neutrophil count)

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

Basophil

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

Eosinophil

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

Granulocyte

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

Lymphocytes

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

Monocyte

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

Neutrophil

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

BONE MARROW BIOPSY

Biopsy

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

Iliac Crest

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

BONE MARROW TRANSPLANT

Allogeneic Stem Cell Transplantation

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

Allograft

An allogeneic stem cell collection used for transplant.

Autograft

An autologous stem cell collection used for transplant.

Autologous Stem Cell Transplantation

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

Bone Marrow Transplant

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

Cord Blood Transplant

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

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. Also called *nonmyeloablative transplant* or *reduced intensity transplant*.

Reduced Intensity Transplant

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

Unrelated Donor

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

MEDICATIONS

Adverse Event (AE)

Any undesired actions or effects of a drug or treatment.
Synonyms: side effect, toxicity

Antibiotic Therapy (AB)

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

Antithymocyte Globulin (ATG)

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

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 transfusion dependent iron overload. It is an iron-chelating drug that is administered subcutaneously (under the skin).

Erythropoietin (EPO)

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

Exjade® (deferasirox)

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

Growth Factors (hematopoietic)

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

Synonym: cytokine

Hycamtin® (topotecan hydrochloride)

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 anemia by increasing the red blood cell production.

Reblozyl® (luspatercept-aamt)

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

Revlimid® (lenalidomide)

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

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 to interfere with other proteins (cytokines) that promote premature death of cells in the bone marrow. It's 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, hemoglobin, white blood cells, platelets, and/or decreases the amount of blast cells within the bone marrow. It is categorized as a DNA hypomethylating agent and can be administered intravenously (IV) or subcutaneously (under the skin).

THE MDS FOUNDATION, INC.

The MDS Foundation, Inc. is a global non-profit advocacy 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
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Tracey Iraca
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Deborah Murray
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THE MDS FOUNDATION, INC.

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About the MDS Foundation, Inc.

The MDS Foundation is a non-profit patient advocacy organization that seeks to increase awareness and foster research of the Myelodysplastic Syndromes. The MDS Foundation was established in 1994 by a global group of physicians and researchers. It was the first organization dedicated solely to improving outcomes for patients with MDS.

Every day approximately 238 people worldwide are diagnosed with MDS. The MDS Foundation assists the MDS community by providing awareness, patient and physician education, facilitating global working groups and assisting with clinical research.

Patient Advocacy & Education

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

We also provide various printed and electronic patient resources and handbooks that are available in multiple languages. In addition to the education component, the MDS Foundation develops patient support groups, hosts Quality-of-Life Patient and Family Forums, and provides access to a full-time Patient Liaison who is available to advise and refer patients to the appropriate resources, studies, and/or specialists.

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

Professional Education

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

We also hold a Biennial MDS International Symposium. Since its inception, we have conducted 14 international educational symposia for healthcare professionals in Austria, England, the United States (Chicago, Washington DC), Spain (Barcelona, Valencia), Czech Republic, Sweden, France, Japan, Italy, Greece, Scotland, and Germany. The 15th International Symposium on MDS will be held in Copenhagen, Denmark on May 8-11, 2019. For these symposia, we host an average of 1,000 healthcare professionals and hold three workshops dedicated to specific MDS-related research developments, 10-12 plenary scientific sessions, which consist of abstract presentations, roundtables and debates, as well as an abstract poster viewing. We also offer the opportunity to include corporate satellite symposia, pharmacist and nursing sessions, as well as medical pipeline sessions.

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

Global Working Groups

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

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

International Nurse Leadership Board (NLB) – Composed of more than 30 members worldwide, and includes 3 subcommittees: *Professional Education, Patient Education, and Quality of Life.*

Research

From 2012–2017, we have awarded more than \$300,000 in grants through our Young Investigator Grant program. These funds have helped to make great strides in research into areas such as aberrant mRNA splicing induced by ZRSR2 mutation in the pathogenesis of myelodysplastic syndromes, unraveling the role of alternative splicing in normal and MDS hematopoietic stem and progenitor cells, HIF-1a as a central pathobiologic mediator of myelodysplastic syndromes, and targeting TP53 gene mutations in myelodysplastic syndromes through functional reconstitution and immune activation. Providing the resources for these research projects directly improves the quality of life of MDS patients and their caregivers.

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

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



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Staff

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).

Audrey Hassan Patient Liaison

Audrey joined the MDS Foundation in 2002 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 has been associated with the Foundation since 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.

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, patient programs, 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.

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The International Nurse Leadership Board (NLB)

The International Nurse Leadership Board (NLB) is composed of more than 30 members worldwide and includes 3 subcommittees: Professional Education, Patient Education, and Quality of Life. It is important to note that all nurse members of this Leadership Board participate on a volunteer basis.

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

Mission

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

Accomplishments to date:

- Formalization of the NLB with international representation.
- Facilitation of patient forums in the US and Europe.
- Development of an MDS Nurse Mentorship Program including facilitation/presentation at 6 regional meetings.
- Nursing sessions at international MDSF symposia.
- Poster presentations for QOL data on behalf of the Foundation (at ASH and MDSF symposia).
- Development of Nursing Education Slide Modules for Europe.
- MDS Foundation Newsletter contributions.
- Development and updates of patient and caregiver guides, including our *Building Blocks of Hope: Strategies for Patients and Caregivers LIVING with MDS (BBoH)*.
- Modification of the content for Patient Forums with incorporation of Building Blocks of Hope program information for patients and caregivers – including a new mobile application for patients to track and manage their treatments – MDS Manager.
- ONS Symposia with release of the CJON supplement dedicated to MDS, developed by the NLB.
- MDS Glossary pocket guide to be distributed at patient forums and included in the BBoH.

Goals:

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

Patient Services

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

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

In-Person patient and caregiver forums

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

- Registration is required to attend. Learn the latest on the diagnosis and treatment of MDS from leading experts in the field and meet patients and caregivers just like you. Complimentary breakfast and lunch.
- Visit the MDS Foundation website for more information at www.mds-foundation.org/patient-and-family-forums

MDS Foundation Patient Liaison

Audrey Hassan

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

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

1-609-298-0590 fax

email: patientliaison@mds-foundation.org

ahassan@mds-foundation.org

Online patient and caregiver message board

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

Global patient support groups

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

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

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

MDS Foundation's MDS Centers of Excellence

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

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

Please contact the Foundation for further information.

The MDS Foundation currently has 70 MDS Centers of Excellence throughout the US and 110 MDS Centers of Excellence in 36 countries outside the US. These numbers are continually increasing as more centers are approved.

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



Online Resources

US-Based Resources

MDS Foundation, Inc.

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

www.mds-foundation.org

Aplastic Anemia and MDS International Foundation

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

www.aamds.org

Be The Match

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

www.bethematch.org

Leukemia and Lymphoma Society

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

www.lls.org

MDS Alliance

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

www.mds-alliance.org

MPN Advocacy and Education International

An organization dedicated to providing the knowledge, support, and resources patients will need as they adjust to living with an MPN through educational symposia in several cities each year, website access, free webcasts of each program, collateral materials, and direction to people, resources and other organizations that can help.

www.mpnadvocacy.com

MPN Research Foundation

Partner. Advocate. Friend. At the MPN Research Foundation, we're committed to standing with you in the fight against polycythemia vera (PV), essential thrombocythemia (ET) and myelofibrosis (MF) – the group of blood cancers collectively known as myeloproliferative neoplasms.

www.mpnresearchfoundation.org

NCCN Patient and Caregiver Resources

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

www.nccn.org/patients

Patient Worthy

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

www.patientworthy.com

Internationally-Based Resources

AAMAC (Canada)

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

www.aamac.ca/e

Denmark MDS Patientstotte Gruppe (Denmark)

This site is for those who have just established the familiarity with the abbreviation MDS, for those who are going to learn to live with MDS and for those who want to keep up with the latest news from the research front.

<http://dkpsg.mds-and-you.info/>

Hematon (The Netherlands)

A patient organization for patients with a haematological-oncological disorder and / or people who have undergone a stem cell transplant. Our goal is to support them in all aspects that life with and after cancer entails. We are also there for relatives and donors of patients. Companion contact, advocacy and information provision are our spearheads. Hematon bundles knowledge and experience.

www.hematon.nl

Leukaemie Hilfe Rhein-Main (Germany)

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

www.leukaemihilfe-rhein-main.de

Lyle (Denmark)

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

www.lyle.dk

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

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

www.mds-patienten-ig.org

UK MDS Patient Support Group (United Kingdom)

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

www.mdspatientsupport.org.uk

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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 Hematological malignancies, including MDS and MPNs. The colors of the Building Blocks of Hope include Tucson Teal, Navajo Red, and Desert Sand. They are reminiscent of a Southwest landscape with the beauty of the night sky over the sand swept deserts and stunning mountain ranges. The colors represent welcoming, warmth, stability, healing, passion, and protection. These colors form the base for the Building Blocks of Hope logo constructed in a wave-like pattern indicating the fluidity of life, health and illness. The single red band which continues up into the plant symbolizes strength and improvement in bone marrow function. The idea of hope for the future and extension of life is emulated in the sprouting plant.

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

A special thanks to 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 myeloid malignancies, including MDS and MPNs, and other bone marrow failure diseases. 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 and MPNs 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 MPNs patients. Most importantly, we hope the Building Blocks of Hope will empower MPN patients and their caregivers to **LIVE** with MPNs.



Best regards and best wishes,
Sandy Kurtin

Thank you to Incyte Corporation for supporting this resource.



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