NATIONAL MARROW DONOR PROGRAM®

Myelodysplastic Syndromes (MDS)

Myelodysplastic syndromes (MDS) are a group of diseases that affect the bone marrow and blood. Some types of MDS are mild and easily managed, while other types are severe and life-threatening. Mild MDS can grow more severe over time. It can also develop into a fast-growing leukemia called acute myelogenous leukemia.

MDS Causes, Symptoms and Diagnosis

About 10,000 to 15,000 people are diagnosed with myelodysplastic syndromes in the United States each year. Although MDS can affect people of any age, more than 80% of cases are in people over age 60. MDS is more common in men than in women.

Causes of MDS

In MDS, the bone marrow does not make enough normal blood cells for the body. One, two or all three types of blood cells – red blood cells, white blood cells and platelets – may be affected. The marrow may also make unformed cells called blasts. Blasts normally develop into red blood cells, white blood cells or platelets. In MDS, the blasts are abnormal and do not develop or function normally.

Most often the cause of the changes to the bone marrow is unknown. This is called de novo MDS. In a small number of people, MDS might be linked to heavy exposure to some chemicals, such as certain solvents or pesticides, or to radiation. MDS can also be caused by treatment with chemotherapy or radiation therapy for other diseases. This is called treatment-related MDS or secondary MDS. Treatment-related MDS is often more severe and difficult to treat than de novo MDS.

MDS Symptoms

The symptoms of MDS depend on how severe the disease is. Many people with MDS have no symptoms when they are diagnosed. Their disease is found through a routine blood test. If a person does have symptoms, they are caused by low numbers of blood cells:

- Red blood cells carry oxygen throughout the body. Low numbers can lead to anemia – feeling tired or weak, being short of breath and looking pale. Anemia is the most common symptom of MDS.
- White blood cells fight infection. Low numbers can lead to fever and frequent infections.
- Platelets control bleeding. Low numbers can lead to easy bleeding or bruising.

In severe MDS, infection or uncontrolled bleeding can be life-threatening.

Diagnosis

MDS is one of several diseases with these symptoms. Doctors look at samples of blood and bone marrow to diagnose MDS. They also look for changes in the chromosomes of bone marrow cells (cytogenetics).

MDS can be hard to diagnose. Careful study of blood and marrow samples is needed to tell MDS apart from other diseases with similar signs and symptoms, such as aplastic anemia. Blood and marrow samples are often tested several times over two or more months to find out whether the disease is stable or getting worse.

MDS is a group of diseases that have many differences. It is important to diagnose the type of MDS to make the best treatment choices. With some types of MDS, a person may live with few symptoms for years, while other types can be life-threatening within months. In addition, some types of MDS are more likely than others to develop into acute myelogenous leukemia (AML). AML that develops from MDS can be hard to treat.

MDS Types and Risk Scores

Types of MDS

The likely course of MDS can be very different for different people. Experience has shown that certain disease factors affect a person's prognosis – his or her chances of long-term survival and risk of developing AML. Researchers use these factors to classify MDS into types.

The FAB system uses several disease factors to classify MDS. One important factor is the percent of blasts in the bone marrow (Table 1). A higher percent of blasts is linked to a higher likelihood of developing AML and a poorer prognosis.

The two more common types of MDS are refractory anemia (RA) and refractory anemia with ringed sideroblasts (RARS). These are also the less severe forms of MDS. They have a lower risk of turning into AML. Some patients with these forms of MDS may live with few symptoms and need little treatment for many years.

The other types of MDS tend to be more severe and more difficult to treat successfully. The refractory anemia with excess blasts (RAEB) and refractory anemia with excess blasts in transformation (RAEB-t) forms of MDS also have a high risk of turning into AML.

Table 1. MDS Types in the FAB System

Type of MDS	**Percent of blasts in marrow (less than 5% is normal)**
Refractory anemia (RA)	Less than 5% (normal amount)
Refractory anemia with ringed sideroblasts (RARS)	Less than 5% (normal amount), plus more than 15% of abnormal red blood cells called ringed sideroblasts
Refractory anemia with excess blasts (RAEB)	5% to 20%
Refractory anemia with excess blasts in transformation (RAEB-t)	21% to 30%
Chronic myelomonocytic leukemia (CMML)	5% to 20%, plus a large number of a type of white blood cell called monocytes

Although the type of MDS can help predict the course of a person's disease, people with the same type of MDS may respond to the disease and to treatment differently.

To try to better predict people's outcomes, researchers developed another system for defining types of MDS. The newer World Health Organization (WHO) system divides MDS into eight types. Today a doctor may use either the FAB or WHO system to determine the type of MDS a person has. Either system can be helpful in planning a patient's treatment.

MDS Risk Scores

Researchers have developed one other system for classifying MDS. This system is called the international prognostic scoring system (IPSS). The IPSS risk score describes the risk that a person's disease will develop into AML or become life-threatening.

A doctor may use the IPSS risk score along with the MDS type to plan treatment. The IPSS risk score is based on three factors that have been shown to affect a patient's prognosis:

- The percent of cells in the bone marrow that are blasts.
- Whether one, two or all three types of blood cells are low (also called cytopenias). The three types are red blood cells, white blood cells and platelets.
- Changes in the chromosomes of bone marrow blood cells. This may be called cytogenetics (the study of chromosome abnormalities). It may also be called the karyotype (a picture of the chromosomes that shows whether they are abnormal).

A person may have an IPSS risk score of low, intermediate-1, intermediate-2 or high risk. Doctors can use the risk score to plan treatment. Someone with low-risk disease may be likely to survive for years with few symptoms. That person may need less intense treatment. Someone with intermediate-1, intermediate-2 or high-risk disease may be likely to survive only if he or she receives aggressive treatment, such as a transplant.

However, people with the same risk score and type of MDS can still respond differently to treatment. A person's age, overall health and other factors all influence his or her response to the disease and treatment. A doctor will also look at all these factors when planning treatment. If you have MDS, it is important to talk with your doctor about what type of MDS you have and your risk score. Ask how this information affects your treatment options.

Treatment Options

The best treatment for a person with MDS depends on his or her type of MDS, risk level, age, overall health and his or her own preferences. The treatment options include:

- Supportive care – the goal is to manage disease symptoms and related problems. Supportive care includes blood transfusions and growth factors
- Bone marrow or cord blood transplant (BMT) – discussed further below
- Induction chemotherapy – this intensive chemotherapy uses drugs to destroy abnormal cells or stop them from growing
- Newer drug therapies – many newer drug therapies have been shown to bring a response in some patients with MDS

Whichever treatment you and your doctor decide on, you may choose to be part of a clinical trial. Even standard treatments continue to be studied in clinical trials. These studies help doctors improve treatments so that more patients can have better results.

Bone Marrow or Cord Blood Transplant for MDS

The only known treatment that can bring a long-term remission from MDS is a bone marrow or cord blood transplant (also called a BMT). A transplant replaces the abnormal cells in the bone marrow with healthy blood-forming cells from a family member or unrelated donor or cord blood unit.

The standard transplant for MDS is allogeneic, which uses blood-forming cells from a family member, an unrelated donor or a cord blood unit. The donor for a transplant must closely match the patient's tissue type. The best donor is usually a matched sibling. For patients who do not have a suitable donor in their family, doctors may search the National Marrow Donor Program (NMDP) Registry for a matching adult volunteer donor or cord blood unit.

A transplant can offer some people the chance for a long-term remission of disease and a longer life, but it is not an option for all patients. A transplant may be a good option for people who have a suitable donor or cord blood unit and are healthy enough to tolerate a transplant. In general, younger patients tend to do better after a transplant than older patients. However, advances in transplant have enabled more older patients to undergo a transplant successfully.

Reduced-Intensity Transplant for MDS

Before a transplant, a patient receives a preparative regimen of high-dose chemotherapy with or without radiation therapy. Many patients with MDS are older and have other health problems that may make them unable to tolerate this high-dose regimen. However, some may be able to tolerate a reduced-intensity regimen, which uses lower doses of chemotherapy and low-dose or no radiation therapy.

Reduced-intensity transplant is a newer approach to transplant for MDS, and early results have been encouraging. The use of reduced-intensity transplant to treat MDS is growing. This approach may offer the chance for long-term survival to some patients, especially those who are older or have other health problems.

Autologous Transplant for MDS

Another type of transplant is an autologous transplant, which uses the patient's own blood-forming cells. An autologous transplant is a standard treatment for some diseases and is being studied in clinical trials as a treatment for MDS. An autologous transplant may be an option for patients who do not have a suitable donor for an allogeneic transplant.

In an autologous transplant, blood-forming cells are collected from the patient. After treatment with high-dose chemotherapy and possibly radiation therapy, the patient receives his or her own cells back.

Autologous transplants have risks of serious side effects, but these risks are lower than for allogeneic transplants. However, a patient has higher risks of a relapse of MDS after an autologous transplant. This may be because disease cells may be returned to the patient along with his or her blood-forming cells.

Transplant Success Rates

Transplants have risks of serious complications, but a transplant offers some patients the best chance for a long-term remission. If transplant is an option for you, talk with your about the possible risks and benefits of a transplant.

Making Treatment Choices

If you are diagnosed with MDS, it is important to talk with a doctor who has experience treating MDS. Ask about the type of MDS you have, your risk factors and treatment options, and discuss your own treatment goals. There are a variety of treatment options available, including newer treatments being studied in clinical trials. The best treatment for you will depend on your type of MDS, risk score, age, overall health and your own preferences.

The NMDP's Office of Patient Advocacy (OPA) continually develops resources and materials to help patients, family members and doctors with questions about marrow or cord blood transplantation. In addition to print, audio and visual materials, OPA has bilingual (Spanish/English) case managers and LanguageLine interpreter services available for callers. All OPA materials and services are free and confidential. Call the OPA toll-free at 1 (888) 999-6743. Outside the United States call (612) 627-8140, or visit marrow.org/patient