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About Myelodysplastic Syndromes

Overview and Types

If you have been diagnosed with a myelodysplastic syndrome or are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

- [What Are Myelodysplastic Syndromes?](#)
- [Types of Myelodysplastic Syndromes](#)

Research and Statistics

See the latest estimates for new cases of myelodysplastic syndromes in the US and what research is currently being done.

- [Key Statistics for Myelodysplastic Syndromes](#)
- [What's New in Myelodysplastic Syndrome Research?](#)

What Are Myelodysplastic Syndromes?

Myelodysplastic syndromes (MDS) are conditions that can occur when the blood-forming cells in the bone marrow become abnormal. This leads to low numbers of one or more types of blood cells. MDS is considered a type of [cancer](#)¹.

Normal bone marrow

Bone marrow is found in the middle of certain bones. It is made up of blood-forming cells, fat cells, and supporting tissues. A small fraction of the blood-forming cells are blood *stem cells*. Stem cells are needed to make new blood cells.

There are 3 main types of blood cells: red blood cells, white blood cells, and platelets.

Red blood cells pick up oxygen in the lungs and carry it to the rest of the body. These cells also bring carbon dioxide back to the lungs. Having too few red blood cells is called *anemia*. It can make a person feel tired and weak and look pale. Severe anemia can cause shortness of breath.

White blood cells (also known as leukocytes) are important in defending the body against infection. There are different types of white blood cells:

- **Granulocytes** are white blood cells that have granules that can be seen under the microscope. In the bone marrow, granulocytes develop from young cells called *myeloblasts*. The most common type of granulocyte is the **neutrophil**. When the number of neutrophils in the blood is low, the condition is called *neutropenia*. This can lead to severe infections.
- **Monocytes** are also important in protecting the body against germs. The cells in the bone marrow that turn into monocytes are called *monoblasts*.
- **Lymphocytes** make proteins called *antibodies* that help the body fight germs. They can also directly kill invading germs. Lymphocytes are not usually abnormal in MDS.

Platelets are thought of as a type of blood cell, but they are actually small pieces of a cell. They start as a large cell in the bone marrow called the *megakaryocyte*. Pieces of this cell break off and enter the bloodstream as platelets. You need platelets for your blood to clot. They plug up damaged areas of blood vessels caused by cuts or bruises. A shortage of platelets, called *thrombocytopenia*, can result in abnormal bleeding or bruising.

Myelodysplastic syndromes

In MDS, some of the cells in the bone marrow are abnormal (dysplastic) and have problems making new blood cells. Many of the blood cells formed by these bone marrow cells are defective. Defective cells often die earlier than normal cells, and the body also destroys some abnormal blood cells, leaving the person without enough normal blood cells. Different cell types can be affected, although the most common finding in MDS is a shortage of red blood cells (anemia).

There are several different [types of MDS](#)², based on how many types of blood cells are affected and other factors.

In about 1 in 3 patients, MDS can progress to a rapidly growing cancer of bone marrow cells called [acute myeloid leukemia \(AML\)](#)³. In the past, MDS was sometimes referred to as *pre-leukemia* or *smoldering leukemia*. Because most patients do not get leukemia, MDS used to be classified as a disease of low malignant potential. Now that doctors have learned more about MDS, it is considered to be a form of cancer.

Hyperlinks

1. <https://www.cancer.org/content/cancer/en/cancer/cancer-basics/what-is-cancer.html>
2. <https://www.cancer.org/content/cancer/en/cancer/myelodysplastic-syndrome/about/mds-types.html>
3. <https://www.cancer.org/content/cancer/en/cancer/acute-myeloid-leukemia.html>

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Types of Myelodysplastic Syndromes

Myelodysplastic syndromes (MDS) are classified using the World Health Organization (WHO) classification system, which was most recently updated in 2016. It divides MDS into types based mainly on how the cells in the bone marrow look under the

microscope, as well as some other factors:

- How many early forms of cell types in the bone marrow (red blood cells, white blood cells, or platelets) show **dysplasia** (look abnormal under the microscope).
- How many types of **low blood cell counts** (cytopenias) a person has.
- What portion of early red blood cells are **ring sideroblasts** (cells that contain rings of iron deposits around the nucleus).
- The portion of **blasts** (very early forms of blood cells) in the bone marrow or blood.
- Certain **chromosome changes** in the bone marrow cells.

Based on these factors, the WHO system recognizes 6 main types of MDS:

- **MDS with multilineage dysplasia (MDS-MLD)**
- **MDS with single lineage dysplasia (MDS-SLD)**
- **MDS with ring sideroblasts (MDS-RS)**
- **MDS with excess blasts (MDS-EB)**
- **MDS with isolated del(5q)**
- **MDS, unclassifiable (MDS-U)**

Because small differences in the way the cells look can change the diagnosis, doctors may sometimes disagree on a patient's exact type of MDS.

MDS with multilineage dysplasia (MDS-MLD)

In MDS-MLD:

- Dysplasia is seen in at least 10% of the early cells of **2 or 3 cell types** (red blood cells, white blood cells, and/or megakaryocytes [the cells that make platelets]) in the bone marrow.
- The person has low numbers of at least 1 type of blood cell.
- There is a normal number (less than 5%) of very early cells called blasts in the bone marrow, and blasts are rare (or absent) in the blood.

This is the most common type of MDS. In the past, it was referred to as *refractory cytopenia with multilineage dysplasia* (RCMD).

MDS with single lineage dysplasia (MDS-SLD)

In MDS-SLD:

- Dysplasia is seen in at least 10% of the early cells of **1 cell type** (either red blood cells, white blood cells, or megakaryocytes [the cells that make platelets]) in the bone marrow.
- The person has low numbers of 1 or 2 types of blood cells, but normal numbers of the other type(s).
- There is a normal number (less than 5%) of very early cells called blasts in the bone marrow, and blasts are rare (or absent) in the blood.

This type of MDS is not common. It seldom, if ever, progresses to [acute myeloid leukemia \(AML\)](#)¹. Patients with this type of MDS can often live a long time, even without treatment.

This was referred to as *refractory cytopenia with unilineage dysplasia* (RCUD) in the previous classification system. It includes **refractory anemia** (RA), **refractory neutropenia** (RN), and **refractory thrombocytopenia** (RT), depending on which cell type is affected.

MDS with ring sideroblasts (MDS-RS)

In this type of MDS, many of the early red blood cells are ring sideroblasts. For this diagnosis, at least 15% of the early red blood cells must be ring sideroblasts (or at least 5% if the cells also have a mutation in the *SF3B1* gene).

This condition is further divided into 2 types, based on how many of the cell types in the bone marrow are affected by dysplasia:

- **MDS-RS with single lineage dysplasia (MDS-RS-SLD):** dysplasia in only one cell type
- **MDS-RS with multilineage dysplasia (MDS-RS-MLD):** dysplasia in more than one cell type

This type of MDS is not common. It rarely turns into [AML](#)², and the outcome for people with this type is generally better than for some other types of MDS. This was previously referred to as *refractory anemia with ring sideroblasts* (RARS).

MDS with excess blasts (MDS-EB)

In this type of MDS, there are more blasts than normal in the bone marrow and/or blood. The person also has low numbers of at least one type of blood cell. There may or may not be severe dysplasia in the bone marrow.

This condition is further divided into 2 types, based on how many of the cells in the bone marrow or blood are blasts:

- **MDS-EB1:** blasts make up 5% to 9% of the cells in the bone marrow, or 2% to 4% of the cells in the blood
- **MDS-EB2:** blasts make up 10% to 19% of the cells in the bone marrow, or 5% to 19% of the cells in the blood

This type accounts for about 1 in 4 cases of MDS. It is one of the types most likely to turn into [AML](#)³, with the risk being higher for MDS-EB2 than for MDS-EB1. This was previously referred to as *refractory anemia with excess blasts* (RAEB).

MDS with isolated del(5q)

In this type of MDS, the chromosomes of the bone marrow cells are missing part of chromosome number 5. (There may also be one other chromosome abnormality, as long as it isn't a loss of part or all of chromosome 7.) The person also has low numbers of 1 or 2 types of blood cells (usually red blood cells), and there is dysplasia in at least 1 cell type in the bone marrow.

This type of MDS is not common. It occurs most often in older women. For reasons that aren't clear, patients with this type of MDS tend to have a good prognosis (outlook). They often live a long time and rarely go on to develop [AML](#)⁴.

MDS, unclassifiable (MDS-U)

This type of MDS is uncommon. For MDS-U, the findings in the blood and bone marrow don't fit any other type of MDS. For example, the numbers of any one of the cell types may be low in the blood, but less than 10% of that type of cell looks abnormal in the bone marrow. Or the cells in the bone marrow have at least one certain chromosome abnormality that is only seen in MDS or leukemia.

This type is rare, so it has not been studied well enough to predict prognosis (outlook).

Clinical classification of MDS

Along with the WHO classification, MDS can also be classified based on the underlying cause. This is known as a *clinical classification*.

- If no cause can be identified, it's called **primary MDS**. (This type is more common.)
- When the cause of the disease is known, it's called **secondary MDS**.

Secondary MDS is often related to prior cancer treatment, or it develops in someone who already had a different bone marrow disease. This is discussed further in [Risk Factors for Myelodysplastic Syndrome⁵](#).

Identifying MDS as primary or secondary is important because the secondary type is much less likely to respond to treatment.

Hyperlinks

1. <https://www.cancer.org/content/cancer/en/cancer/acute-myeloid-leukemia.html>
2. <https://www.cancer.org/content/cancer/en/cancer/acute-myeloid-leukemia.html>
3. <https://www.cancer.org/content/cancer/en/cancer/acute-myeloid-leukemia.html>
4. <https://www.cancer.org/content/cancer/en/cancer/acute-myeloid-leukemia.html>
5. <https://www.cancer.org/content/cancer/en/cancer/myelodysplastic-syndrome/causes-risks-prevention/risk-factors.html>

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Key Statistics for Myelodysplastic Syndromes

The number of people diagnosed with myelodysplastic syndromes (MDS) in the United States each year is not known for sure. Some estimates have put this number at about 10,000, while other estimates have been much higher.

MDS is uncommon before age 50, and the risk increases as a person gets older. It is most commonly diagnosed in people in their 70s. The number of new cases diagnosed each year is likely increasing as the average age of the US population increases.

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What's New in Myelodysplastic

Syndrome Research?

Research into the causes, diagnosis, and treatment of myelodysplastic syndromes (MDS) is being done at many cancer research centers around the world.

Genetics and biology of MDS

Scientists are making progress in understanding how changes in the DNA (genes) inside normal bone marrow cells can cause them to develop into myelodysplastic cells. It's also clear that not all cases of MDS have the same gene changes. An improved understanding of this is helping to better classify different [types of MDS](#)¹ and to determine a person's likely prognosis (outlook). It might also help determine which patients might benefit most from different types of treatment.

Scientists are also learning how bone marrow stromal cells influence MDS cells. Stromal cells in the bone marrow do not develop into blood cells. Instead, they help support, nourish, and regulate the blood-forming cells. Some studies suggest that although the stromal cells in MDS patients are not cancerous, they are not normal either, and seem to have a role in causing MDS. Scientists have identified some of the chemical signals that are exchanged between stromal cells and MDS cells.

As more information from this research unfolds, it may be used to help develop new drugs or other types of treatment.

Chemotherapy

Studies are being done to find new drugs and drug combinations that might work better, as well as having less serious side effects.

Drugs called [hypomethylating agents](#)², such as azacitidine (Vidaza) and decitabine (Dacogen), are currently some of the most effective drugs in treating MDS. But they're not helpful for everyone, and they eventually stop working for most people.

Guadecitabine is a newer drug that is related to decitabine, but it stays inside cells longer, so in theory it might work better. It has helped some people in early studies, and is now being tested in a larger study.

Researchers are also testing oral (by mouth) forms of azacitidine and decitabine, which might be easier for patients to take.

Research is also under way to see if there are some patients who might benefit from

more intensive chemotherapy.

Immune suppression

In some people with MDS, the immune system seems to interfere with normal blood cell production. Some [medicines](#)³, such as ATG and cyclosporine, are already being used to treat some people with MDS. Researchers are now looking at other ways to suppress the immune system in people with MDS to see if this might be helpful.

Targeted therapy

Targeted therapy drugs work differently from standard chemotherapy drugs. They affect specific parts of cancer cells that make them different from normal, healthy cells. Targeted drugs might work in some cases where chemotherapy doesn't, and they tend to have different (and sometimes less severe) side effects. Targeted drugs are now part of the treatment for many types of cancer, and they are being studied for use in MDS as well.

For example, **luspatercept** is a new drug that blocks cellular proteins that are part of the TGF-beta superfamily. These proteins slow down red blood cell production. In early studies, this drug has shown a lot of promise in raising red blood cell levels in people with lower-risk forms of MDS. Further studies of this and similar drugs are under way.

Rigosertib is a new drug that targets several different proteins that normally help cancer cells grow. This drug has been shown to help some people with high-risk MDS in early studies, and is now being studied for use by itself and along with azacitidine.

Other new targeted drugs now being studied for use in MDS include:

- **Imetelstat**, a telomerase inhibitor
- **Pevonedistat**, an NAE inhibitor
- **Selinexor**, an XPO1 inhibitor
- **Glasdegib**, a smoothened (SMO) inhibitor

Many other targeted therapy drugs are now being studied as well.

More general information on this type of treatment can be found in [Targeted Therapy](#)⁴.

Stem cell transplant

Scientists continue to refine this procedure to increase its effectiveness, reduce complications, and determine which patients are most likely to be helped by [this treatment](#)⁵.

Hyperlinks

1. <https://www.cancer.org/content/cancer/en/cancer/myelodysplastic-syndrome/about/mds-types.html>
2. <https://www.cancer.org/content/cancer/en/cancer/myelodysplastic-syndrome/treating/chemotherapy.html>
3. <https://www.cancer.org/content/cancer/en/cancer/myelodysplastic-syndrome/treating/chemotherapy.html>
4. <https://www.cancer.org/content/cancer/en/treatment/treatments-and-side-effects/treatment-types/targeted-therapy.html>
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