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## What are Myelodysplastic Syndromes (MDS)?

Myelodysplastic Syndromes (MDS) are a group of diverse bone marrow disorders in which the bone marrow does not produce enough healthy blood cells. MDS is often referred to as a "bone marrow failure disorder". MDS is primarily a disease of the elderly, but MDS can affect younger patients as well.

In the early stages, patients can have low blood counts or may need blood transfusions. But at more advanced stages, patients have a condition which is not dissimilar to **Acute Myeloid Leukaemia**.

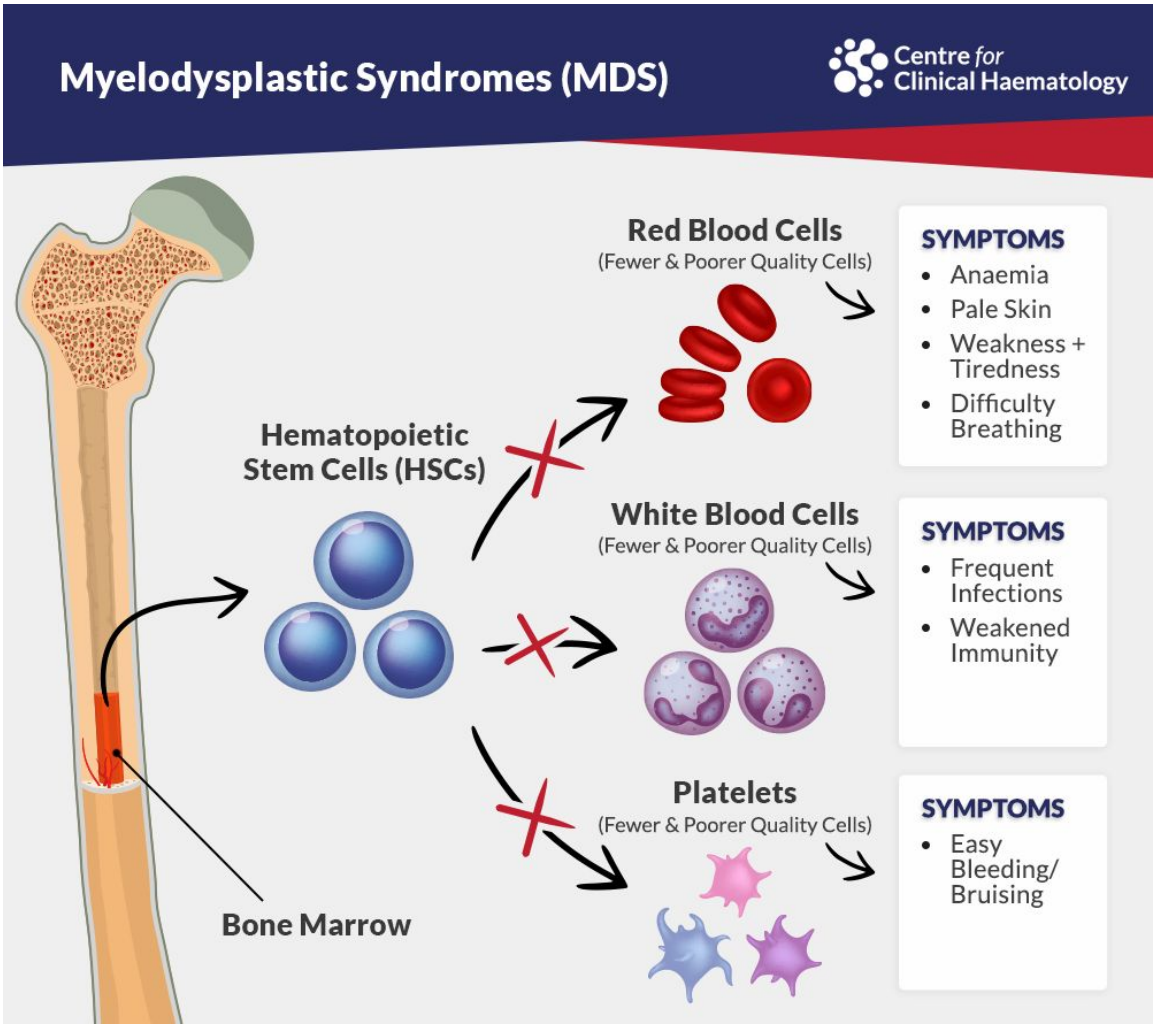
## What are the causes of MDS?

In most cases, the exact cause of Myelodysplastic syndromes may not be known. This is known as Primary MDS. When patients develop MDS after radiotherapy or chemotherapy, it is known as Secondary MDS or Treatment-related MDS.

Some factors are known to increase the risk of developing MDS:

- **Age**: The incidence of Myelodysplastic syndromes is higher in people above 60 years of age.
- **Exposure to toxic chemicals**: Exposure to harmful chemicals can cause damage to the bone marrow and trigger abnormal cancerous changes that can lead to MDS. Some of these chemicals include:
    - Ionizing radiation, benzene and other industrial solvents.
    - Toxic chemicals present in cigarette smoke and pesticides.
    - Heavy metals like mercury and lead.
- **Exposure to Cancer Treatment Drugs**: Patients receiving radiation therapy or chemotherapy for cancer treatment are more likely to subsequently develop Myelodysplastic syndromes. MDS has been associated in particular in patients receiving prior treatment with a class of chemotherapy known as alkylating agents.

## What are the signs & symptoms of MDS?




Myelodysplastic syndromes may not cause any signs and symptoms in the initial stages. As the disease progress, patients may experience symptoms related to impaired function of the blood such as:

- Difficulty in breathing.
- Persistent weakness and tiredness.
- Tendency for bruising or bleeding due to thrombocytopenia or a low blood platelet count. This may also present as small red spots just beneath the skin called petechiae.
- Unusual paleness of the skin due to anaemia or a low red blood cell count.
- Frequent infections due to a low white blood cell count.

## How is MDS diagnosed?

- **Blood tests**
  Blood tests can help to detect abnormalities in the blood cells counts. A reduced blood count can raise the suspicion of blood or marrow disorders.

  Blood tests can also help to detect any abnormalities in the size, appearance, and shape of the blood cells.

- **Bone marrow biopsy**
  A **bone marrow biopsy** and aspiration involve the insertion of a thin needle into a long bone of the body to withdraw a small amount of marrow. The sample can be tested in a laboratory to detect any abnormalities linked to MDS.Specific tests are performed on the bone marrow aspirate including:
    - **Immunophenotyping**
      Immunophenotyping is a specialist test that is performed on either a blood sample or bone marrow aspirate sample. The patient sample is analysed through a machine known as a flow cytometer, which allows identification of abnormal markers which are present on the surface of white cells.
      Immunophenotyping allows for the detection of blood cancers, and aids in the classification of the sub-type of the blood cancers. In addition, as the test can detect even small amounts of residual disease in the blood or bone marrow, it is used following treatment to assess disease response.

    - **Cytogenetic tests**
      Genetic tests of the bone marrow can help to confirm the diagnosis of MDS. The results of these studies can also be useful for determining how the disease will progress in the future.
      This test involves the examination of the chromosomes in the cells of the marrow sample taken during a biopsy. It can help to detect mutations in the chromosomes that can affect the functions of the bone marrow and trigger the development of MDS.

    - **Molecular testing**
      Increasingly, there are several recognised molecular genetic abnormalities (mutations) in MDS cells that are linked to prognosis. Molecular testing provides information on the risk group of MDS patients. In addition, monitoring of the level of known mutations in patients often also allows us to measure the response of patients to therapy, even when there may be only very small levels of MDS disease in the bone marrow.

## How is MDS treated?

The treatment for Myelodysplastic syndromes depends on the stage of the disease, your age, and your performance status. It may involve one or a combination of therapies.

- **Growth Factor Injections**
  Growth Factor Injections work by causing stimulation of the bone marrow. These drugs encourage the bone marrow to form an increased number of healthy white and red blood cells in the blood.

  Growth factor injections containing erythropoietin may be recommended for patients who have a low red cell count. Erythropoietin can help to increase the production of red cells in the marrow and decrease the number of blood transfusions you might need.

  A Growth Factor called G-CSF is usually administered to patients who have a low white cell count to stimulate the production of these cells.

- **Blood Transfusions**
  **Blood transfusions** include the transfusion of red cells or platelets aimed at improving the counts in the blood and relieve symptoms.

  Transfusion of red cells is recommended for patients who experience severe symptoms of anaemia, such as unusual fatigue and shortness of breath. Patients who have received multiple blood transfusions are at risk of an accumulation of iron in the body resulting in an increased risk of longer term organ damage. Iron chelation may be required in such cases to remove the excess iron and reduce the iron overload.

  Transfusions of platelets are recommended for reducing the risk of excessive bleeding due to a low platelet count. However, since platelets survive only for a few days, patients may need platelet transfusions more frequently.

- **Immune Modulating Agents**
  Administration of Immune Modulating Agents such as thalidomide, anti-thymoglobulin, and steroids are sometimes used in the treatment of low-risk MDS

  For example, Thalidomide can be effective in reducing or eliminating the need for blood transfusions in some patients with myelodysplastic syndromes. Thalidomide possesses anti-angiogenesis properties which means it can inhibit the formation of new blood vessels in the affected tissues, thereby preventing the survival of abnormal cells in the marrow. This would reduce the production of immature blood cells.

- **Epigenetics Agents**
  Epigenetic agents work by inhibiting cellular processes controlled by specific genes involved in the development of MDS. Epigenetic agents may reverse the genes that were suppressed in the bone marrow and help to restore the healthy functions of the bone marrow.

  One of the epigenetic agents – 5-azacitidine, remains the only drug to have shown to improve overall survival in patients with MDS. 5-azacitidine is usually used in MDS patients with advanced disease, or MDS patients with low blood counts who may need blood product transfusions.

- **Stem Cell Transplant**
  **Stem cell transplant** involves the infusion of stem cells from the patient's bone marrow or a donor. Stem cell transplantation is usually recommended for patients who have high-risk MDS. It is aimed at improving the long-term survival of patients.

  A "matched related donor", preferably a biological brother or sister of the patient having a similar genetic makeup, is considered the best source of stem cells for this procedure.

## What is the prognosis for MDS?

The prognosis of MDS is determined by several factors including the risk category, the presence of other medical conditions as well as age.

One of the most established prognostic scoring systems is the **IPSS-R** (International Prognostic Scoring System – Revised). This score is based on various patient factors including the haemoglobin level, neutrophil count, platelet count, bone marrow blasts and the cytogenetic category. The score helps to determine if a patient has low risk MDS or high risk MDS. Patients with low risk MDS tend to live for longer without the need for intervention. However, patients with high risk MDS generally require treatment sooner and may have a shorter life expectancy.