



Myelodysplastic Syndromes

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called metastasis. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called benign. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

What is myelodysplastic syndrome?

Myelodysplastic syndrome (MDS) is the name of a group of conditions that occur when the blood-forming cells in the bone marrow are damaged. This damage leads to low numbers of one or more type of blood cells.

Normal bone marrow

Bone marrow is found inside certain bones, including the skull, ribs, pelvis, and spine. It is made up of blood-forming cells, fat cells, and supporting tissues that help the blood-forming cells grow. A small fraction of the blood-forming cells are a special type of cell known as blood *stem cells*. Stem cells are needed to make new cells. When a stem cell divides it makes 2 cells: one cell that stays a stem cell, and another cell that can keep changing and dividing to make blood cells. There are 3 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 people 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. The 2 major types of white blood cells are *lymphocytes* and *granulocytes*.

Lymphocytes are immune cells that are found in the bone marrow, the blood, and in lymph nodes. They make the antibodies that help the body fight germs. They can also directly kill invading germs by producing toxic substances that damage the cells. Lymphocytes are not usually abnormal in MDS.

Granulocytes are a group of white blood cells that destroy bacteria. They are called granulocytes because they contain granules that can be seen under the microscope. These

granules are made up of enzymes and other substances that can destroy germs that cause infections. In the bone marrow, granulocytes develop from young cells called *myeloblasts*. The most common type of granulocyte is the neutrophil; this cell is crucial in fighting bacteria. Other types of granulocytes are basophils and eosinophils. When the number of neutrophils in the blood is low, it is called *neutropenia*. This can lead to severe infections.

Monocytes, which are related to the granulocyte family, are also important in protecting the body against bacteria. The cells in the bone marrow that turn into monocytes are called *monoblasts*. Monocytes can leave the bloodstream to become macrophages in some of the body's organs. Macrophages can destroy germs by surrounding and digesting them. They are also important in helping lymphocytes recognize germs and begin producing antibodies to fight them.

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 cell called the *megakaryocyte*. Pieces of this cell break off and enter the bloodstream as platelets. Platelets are needed 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 syndrome

In MDS, some of the cells in the bone marrow are damaged and have problems making new blood cells. Many of the blood cells that are formed by the damaged bone marrow cells are defective. The body destroys many of these abnormal blood cells, leaving the patient with low blood counts because there aren't enough normal blood cells.

In about one-third of patients, MDS can progress to a rapidly growing cancer of bone marrow cells called acute myeloid leukemia. Because most patients do not get leukemia, MDS was previously 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. The major reason is that MDS is a clonal disease, which means that there is a large population of abnormal cells that all came from a single, abnormal cell. These abnormal cells have the same genes -- just like identical twins -- and they share abnormal growth properties. Clonal growth is typical of cancer.

In the past, MDS was referred to as pre-leukemia and smoldering leukemia. Since most MDS patients do not get leukemia, these terms are not accurate and are no longer used.

Our document, *Leukemia: Acute Myeloid (Myelogenous)*, provides more information about the leukemia that develops in some MDS patients.

Types of myelodysplastic syndrome

The original classification of myelodysplastic syndrome (MDS) was developed more than 20 years ago at an international conference attended mostly by doctors from France, the

United States, and Great Britain. This system was known as the French-American-British (FAB) classification.

The system used today is the World Health Organization (WHO) classification. This system seems to be more helpful than the FAB classification in predicting prognosis (outlook). There are 7 categories of MDS in the WHO system:

- Refractory cytopenia with unilineage dysplasia (RCUD)
- Refractory anemia with ringed sideroblasts (RARS)
- Refractory cytopenia with multilineage dysplasia (RCMD)
- Refractory anemia with excess blasts-1 (RAEB-1)
- Refractory anemia with excess blasts-2 (RAEB-2)
- Myelodysplastic syndrome, unclassified (MDS-U)
- Myelodysplastic syndrome associated with isolated del(5q)

Most of these categories are determined by the appearance of the cells in the blood and the bone marrow. One category is defined by a certain chromosome change in the bone marrow cells. Because small differences in the way the cells look can change the diagnosis, doctors may sometimes disagree on the exact MDS category for a patient's disease.

Chronic myelomonocytic leukemia (CMML) was considered a type of MDS in the FAB classification, but is not in the WHO classification. Information about CMML can be found in our document, *Leukemia: Chronic Myelomonocytic*.

Refractory cytopenia with unilineage dysplasia (RCUD)

People with RCUD have low numbers of one type of blood cell, but normal numbers of the other 2 types. Examples of RCUD include refractory anemia (RA), refractory neutropenia (RN), and refractory thrombocytopenia (RT). Refractory anemia (RA) is the most common type of RCUD. People with RA have low numbers of red blood cells (anemia), but have normal numbers of white blood cells and platelets. In the bone marrow of RA patients, only the cells that grow to become red blood cells look abnormal. In the bone marrow of RCUD patients, at least 10% of the early cells of the affected cell type look abnormal (show *dysplasia*), but the other types of cells in the bone marrow look normal. 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. About 5% to 10% of all MDS patients have RCUD. This type of MDS seldom, if ever, progresses to acute myeloid leukemia. Patients with this type of MDS can live a long time.

Refractory anemia with ringed sideroblasts (RARS)

This condition is similar to refractory anemia except that 15% or more of the early red blood cells in the bone marrow contain circles of iron deposits (rings) around the nucleus

(these cells are called *ringed sideroblasts*). About 10% to 15% of all people with MDS have this type. This type rarely turns into leukemia, and the outcome for people with this type is generally the same as for those with refractory anemia.

Refractory cytopenia with multilineage dysplasia (RCMD)

In this condition, the counts of at least 2 types of blood cells are low. In the bone marrow, those same types of cells look abnormal under the microscope (dysplasia). Ringed sideroblasts may or may not be present. The number of blasts in the bone marrow is less than 5% and none of the blasts contain Auer rods (an abnormality seen in some leukemia cells). Blasts are rare or absent in the blood. About 40% of people with MDS have this type. It changes into leukemia in about 10% of patients. Having this type of MDS will shorten a person's life. One estimate is that half of patients will die within 2 years of diagnosis.

Refractory anemia with excess blasts-1 (RAEB-1)

One or more cell types are low in the blood and look abnormal in the bone marrow. The number of blasts in the bone marrow is increased; but is still less than 10%. The blasts do not contain Auer rods. Blasts may be present in the blood, but they make up less than 5% of the white blood cells. The chance of RAEB-1 turning into acute myeloid leukemia is about 25%. This type of MDS has a poor outlook and most patients die within 2 years.

Refractory anemia with excess blasts-2 (RAEB-2)

This type of MDS is similar to RAEB-1 except the bone marrow contains more blasts -- between 10% and 20% of the bone marrow cells are blasts. The blood also contains more blasts - between 5 and 19% of the white blood cells in the blood are blasts. The blasts may contain Auer rods. Any one (or more) of the cell types can be low in the blood and look abnormal in the bone marrow. The chance of RAEB-2 turning into acute myeloid leukemia may be as high as 50%.

Myelodysplastic syndrome, unclassified (MDS-U)

This type of MDS is uncommon. For a case to be considered MDS-U, the findings in the blood and bone marrow can't fit any other type of MDS. 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. The cells in the bone marrow have at least one certain chromosome abnormality that is only seen in MDS or leukemia. The number of blasts in the bone marrow is less than 5%. Because this type is so rare, it has not been studied well.

MDS associated with isolated del(5q)

In this type of MDS, the chromosomes of the bone marrow are normal except they show a missing part of chromosome number 5. In the blood, the red cell counts are low, but the white blood cell counts are normal. Often the platelet count is increased. The number of

blasts in the bone marrow is less than 5%. For unknown reasons, patients with this type of MDS have a very good prognosis (outlook). They often live a long-time and rarely go on to develop leukemia.

Clinical classification of MDS

The WHO system defines types of MDS based on the cells in the blood and bone marrow. This is called a cellular classification system. Cases of MDS can also be classified based on the underlying cause. This is known as a clinical classification. If no cause can be identified, it is called *primary MDS*. When the cause of the disease is known, it is called *secondary MDS*. Secondary MDS is often called *treatment-related MDS*, because the most common cause is prior cancer treatment. This is discussed further in the section, "What are the risk factors for myelodysplastic syndrome?" Identifying MDS as primary or secondary is important because the secondary type is much less likely to respond to treatment.

What are the key statistics about myelodysplastic syndrome?

In the United States, myelodysplastic syndrome (MDS) occurs at a rate of 4.4 cases for every 100,000 people. That works out to about 12,000 new cases of MDS each year. The number of new cases diagnosed each year seems to be increasing as the average age of the population has increased.

About 80% to 90% of all patients with MDS are older than 60 years. It is rare in young adults.

What are the risk factors for myelodysplastic syndrome?

A risk factor is anything that changes your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for cancer of the lung and many other cancers. But risk factors don't tell us everything. People without any risk factors can still get the disease. And having a risk factor, or even several, does not mean that you will get the disease.

Cancer treatment

Prior treatment with chemotherapy is the most important risk factor for MDS. Patients who have been treated with certain chemotherapy drugs for cancer are more likely to develop MDS. When MDS is caused by cancer treatment it is called *secondary MDS* or *treatment-related MDS*.

Some of the drugs that can lead to MDS include:

- Mechlorethamine (nitrogen mustard)
- Procarbazine
- Chlorambucil
- Etoposide, teniposide
- Cyclophosphamide and ifosfamide
- Doxorubicin

Combining these drugs with radiation therapy increases the risk further. Secondary MDS seems to be more common after treatment for Hodgkin disease, non-Hodgkin lymphoma, or childhood acute lymphocytic leukemia. It develops less often after treatment of breast, lung, ovarian, testicular, gastrointestinal system, or other cancers. MDS is also seen in patients who have had stem cell transplants (bone marrow transplants) because these patients receive very high doses of chemotherapy. Still, only a small percentage of people who are treated with these medicines will eventually develop MDS.

Genetic syndromes

Some bone marrow problems are caused by abnormal (mutated) genes that have been passed on from one or both parents. People with certain inherited syndromes are more likely to develop MDS. These disorders include Fanconi anemia, Shwachman-Diamond syndrome, familial platelet disorder, and severe congenital neutropenia.

Familial MDS

In some families, MDS has been found to occur more often than would be expected.

Smoking

Smoking increases the risk of MDS. Many people know that smoking can cause cancers of the lungs, mouth, throat, larynx, and other organs, but few realize that it can also affect areas that do not come into direct contact with smoke. Cancer-causing substances in tobacco smoke are absorbed into the blood as it passes through the lungs. Once in the bloodstream, these substances spread to many parts of the body.

Environmental exposures

Environmental risk factors, such as radiation and certain chemicals, have been linked to MDS. High-dose radiation exposure (such as surviving an atomic bomb blast or nuclear reactor accident) increases the risk of developing MDS. Long-term workplace exposure to benzene and certain chemicals used in the petroleum and rubber industries can also increase the risk of developing MDS.

Age

The risk of MDS increases with age. This disease is rare in people younger than 40, with most cases found in those older than 60.

Sex

MDS is more common in men.

Do we know what causes myelodysplastic syndrome?

Some cases of myelodysplastic syndrome (MDS) are linked to known risk factors, but for most, the cause is unknown.

Over the past few years, scientists have made great progress in understanding how certain changes in DNA of bone marrow cells may cause MDS to develop. DNA is the chemical that carries the instructions for nearly everything our cells do. We usually look like our parents because they are the source of our DNA. But DNA affects more than the way we look.

Some genes (parts of DNA) contain instructions for controlling a cell's growth and division process. Certain genes that promote cell division are called *oncogenes*. Other genes called *tumor suppressor genes* can slow down cell division or even cause cells to die at an appropriate time. Cancers can be caused by DNA *mutations* (gene defects) that turn on oncogenes or turn off tumor suppressor genes.

Exposure to radiation or certain chemicals can cause mutations that lead to MDS. Sometimes these gene changes occur for no apparent reason. Every time a cell prepares to divide into 2 new cells, it must copy its DNA. This process is not perfect, and copying errors can occur. Fortunately, cells have *repair enzymes* that read and fix DNA. However, some errors may slip past, especially if the cells are growing rapidly.

Human DNA is packaged in 23 pairs of chromosomes. Often, MDS cells contain altered chromosomes. Tests to identify these chromosome problems can help predict the prognosis of patients with MDS. Sometimes part of one chromosome attaches to a different chromosome. This is called a *translocation*. Like mutations, translocations can turn on oncogenes or turn off tumor suppressor genes. Translocations that develop during life are quite common in some forms of leukemia and MDS. Another chromosome abnormality that can be seen in MDS is called a *deletion*. This is where part or all of a chromosome is lost, or deleted. Another type of chromosome abnormality is called a *duplication*. This means there is an extra copy of part or all of a chromosome.

Can myelodysplastic syndrome be prevented?

Since smoking is linked to the development of leukemia and myelodysplastic syndrome (MDS), not smoking can lower the risk of these diseases. Of course, nonsmokers are also less likely than smokers to develop many other types of cancers, as well as heart disease, stroke, and other diseases.

Treating cancer with chemotherapy and radiation can cause MDS. Doctors are studying ways to minimize the risk of MDS developing in patients who receive these treatments. In some cancers, doctors may try to avoid using the chemotherapy drugs that are more likely to lead to MDS. Some cancers, however, may need these specific drugs. Often, the obvious benefits of treating life-threatening cancers with chemotherapy and radiation therapy must be balanced against the small chance of developing MDS several years later.

Avoiding known cancer-causing industrial chemicals, such as benzene, might lower your risk of developing MDS. However, most people with MDS do not have any known preventable exposure to occupational and environmental radiation and chemicals.

Can myelodysplastic syndrome be found early?

Currently, no special tests are recommended for early detection of myelodysplastic syndromes (MDS) in the general population.

Follow-up physical exams and blood tests may help find some cases of MDS in cancer survivors previously treated with certain chemotherapy drugs.

How is myelodysplastic syndrome diagnosed?

Signs and symptoms

Shortages of one or more types of blood cells cause many of the signs and symptoms of myelodysplastic syndrome (MDS):

- Shortage of red blood cells (*anemia*) can lead to excessive tiredness, shortness of breath, and pale skin.
- Not having enough normal white blood cells (*leukopenia*) can lead to frequent or severe infections; often the neutrophil is the type of white blood cell that is low - this condition is called *neutropenia*.

- Shortage of blood platelets (*thrombocytopenia*) can lead to easy bruising and bleeding. Some people notice frequent or severe nosebleeds or bleeding from the gums.

Other symptoms can include weight loss, fever, and loss of appetite. Of course, these problems not only occur with MDS but are more often caused by something other than cancer.

Tests to diagnose and classify MDS

If signs and symptoms suggest you may have MDS, the doctors will look at cells from your blood and bone marrow to confirm this diagnosis.

Blood cell counts and blood cell examination

The complete blood count (CBC) is a test that measures the different cells in the blood, such as the red blood cells, the white blood cells, and the platelets. The CBC is often done with a *differential count* (or "diff"), which is a count of the different types of white blood cells in the blood sample. In a blood *smear*, some of the blood is put on a slide to see how the cells look under the microscope.

Patients with MDS often have too few red blood cells. They may have shortages of white blood cells and blood platelets as well. Patients with RAEB (refractory anemia with excess blasts) may have a small number of myeloblasts in the blood. Blasts are very early cells that are produced by bone marrow stem cells and are normally only found in bone marrow. When blasts are present in the blood it is always abnormal and often signals a bone marrow problem. Blood cells from MDS patients may also have certain abnormalities in size, shape, or other features that can be seen under the microscope.

Blood abnormalities may suggest MDS, but the doctor cannot make an exact diagnosis without examining a sample of bone marrow cells.

Other blood tests

The doctor may also order tests to check for other possible causes of low blood counts, such as low levels of vitamin B12 and folate.

Bone marrow tests

Bone marrow samples are obtained from a bone marrow aspiration and biopsy, 2 tests that are usually done at the same time. The samples are usually taken from the back of the pelvic (hip) bone. These tests are used first for diagnosis and classification and may be repeated later to tell if the MDS is responding to therapy or is transforming into an acute leukemia.

For a bone marrow *aspiration*, you lie on a table (either on your side or on your belly). After cleaning the area, the skin over the hip and the surface of the bone is numbed with local anesthetic, which may cause a brief stinging or burning sensation. A thin, hollow

needle is then inserted into the bone and a syringe is used to suck out a small amount of liquid bone marrow (about 1 teaspoon). Even with the anesthetic, most patients still have some brief pain when the marrow is removed.

A bone marrow *biopsy* is usually done just after the aspiration. A small piece of bone and marrow (about 1/16 inch in diameter and 1/2 inch long) is removed with a needle that is twisted as it is pushed down into the bone. The biopsy may also cause some brief pain. Once the biopsy is done, pressure will be applied to the site to help prevent bleeding.

A pathologist (a doctor specializing in the diagnosis of diseases using laboratory tests) examines the bone marrow samples under a microscope. A hematologist (a doctor specializing in medical treatment of diseases of the blood and blood-forming tissues) or an oncologist (a doctor specializing in medical treatment of cancer) usually reviews these as well.

The doctors will look at the size and shape of the cells and see whether the red cells contain iron particles or whether the other cells contain granules (microscopic packets of enzymes and other chemicals that help white blood cells fight infections). The percentage of marrow cells that are blasts is particularly important. Blasts are very early cells that are produced by bone marrow stem cells. Blasts eventually mature into normal blood cells. In MDS, the blasts do not mature properly, so there may be too many blasts and not enough mature cells. For a diagnosis of MDS, a patient must have less than 20% blasts in the bone marrow. A patient who has more than 20% blasts in the bone marrow is considered to have acute leukemia.

Different types of tests that are done on the bone marrow help the doctor diagnose MDS:

Cytochemistry: Cells from the bone marrow sample are placed on glass microscope slides and then exposed to stains (dyes) that are attracted to certain chemicals present in only certain types of cells. For example, one stain causes the granules inside the cells to appear as black spots when seen under the microscope, but it does not cause other types of cells to change colors.

Immunocytochemistry: Cells from the bone marrow sample are treated with special antibodies that cause certain types of cells change color. The color change can be seen only under a microscope. This testing is helpful in distinguishing different types of MDS or leukemia from one another and from other diseases.

Flow cytometry: This technique is sometimes used to examine the cells from bone marrow and blood samples. It is very helpful in diagnosing and classifying the type of MDS. It is also used in diagnosing leukemia and lymphoma. A sample of cells is treated with special antibodies and passed in front of a laser beam. Each antibody sticks only to certain types of cells. If the sample contains those cells, the laser will cause them to give off light. The instrument detects the light, and a computer counts the cells. This test may not be needed for all patients.

Cytogenetics: This test looks at the chromosomes inside the cells. DNA in human cells is packed into chromosomes. Each cell should have 46 chromosomes (23 pairs). Abnormal chromosomes are common in MDS. Sometimes parts of chromosomes or even whole

chromosomes are missing. MDS cells may also have extra copies of all or part of some chromosomes. Chromosome translocations (portions of chromosomes may trade places with each other) may also be seen.

Cytogenetic testing can take several weeks because the bone marrow cells need time to grow in laboratory dishes before their chromosomes can be viewed under the microscope. The results of cytogenetic testing are written in a shorthand form that describes which chromosome changes are present. For example:

- A minus sign (-) or the abbreviation "del" is used to mean a deletion. For example, if a copy of chromosome 7 is missing, it can be written as -7 or del(7). Often, only a part of the chromosome is lost. There are 2 parts to a chromosome, called p and q. Thus the loss of the q part of chromosome 5 is written 5q- or del(5q).
- A plus sign is used when there is an extra copy of all or part of a chromosome. +8, for example, means that chromosome 8 has been duplicated, and too many copies of it are found within the cell.
- The letter t is used to indicate a translocation

Chromosome changes commonly seen in MDS include deletions in chromosomes 5 and 7 or an extra chromosome 8. Certain chromosome changes, such as del(5q) (a deletion of a part of chromosome 5), can predict a better outcome (as long as there are no other chromosome changes). Other changes, such as deletions of chromosome 7 or changes in 3 or more chromosomes, have a poorer outlook.

Molecular genetic studies: These tests are another way to find chromosome and gene abnormalities. An example of this is *fluorescent in situ hybridization* - more commonly called FISH. In FISH, specific gene sequences are tagged with a fluorescent dye. These may correspond to a certain area of a chromosome or even a certain translocation. An advantage of FISH is that it doesn't require actively dividing cells. This allows the testing to go a bit faster than cytogenetic testing. FISH is very good for finding translocations-- it can even find some that may be too small to be seen with usual cytogenetic testing. This sophisticated testing is not needed to make a diagnosis in most cases of MDS, but it can be useful in determining a person's outlook.

How is myelodysplastic syndrome staged?

Doctors often group cancers into different stages based on the size of the tumor and how far the cancer has spread from the original site in the body. The stage of a cancer can help predict the outlook for a cancer. Often, the stage of a cancer is used to decide which treatment is needed.

However, myelodysplastic syndrome (MDS) is a disease of the bone marrow. It cannot be staged by looking at the size of a tumor like some other cancers. In MDS, other factors are used instead. These factors include the patient's blood counts, the appearance of their bone marrow, their age, and certain chromosome changes.

International Prognostic Scoring System

The International Prognostic Scoring System (IPSS) is a system developed for staging MDS. It was intended for use with the FAB classification system. It rates 3 factors:

- The percentage of blasts in the bone marrow (scored on a scale from zero to 2)
- Chromosome abnormalities (scored from zero to 1)
- The patient's blood counts. (scored as zero or 0.5)

Each factor is given a score, with the lowest scores having the best outlook. Then the scores for the factors are added together to make the IPSS score. The IPSS puts people with MDS into 4 groups:

- Low risk
- Intermediate - 1 risk (Int-1)
- Intermediate - 2 risk (Int-2)
- High risk

Below is a table for the outlook for each group:

IPSS risk group	5-year survival*	Risk of leukemia +
Low	55%	15%
Int-1	35%	30%
Int-2	7%	65%
High	0%	100%

*The 5-year survival rate refers to the percentage of people who live at least 5 years after they are diagnosed with MDS. The 5-year rate is used to produce a standard way of discussing outlook. Of course, many people live much longer than 5 years.

+The percentage of people who will develop leukemia within 5 years of diagnosis of MDS.

WHO Prognostic Scoring System (WPSS)

More recently, a scoring system was developed based on 3 factors:

- The type of MDS based on the WHO classification
- Chromosome abnormalities
- Whether or not the patient requires blood transfusions

	No points	1 point	2 points	3 points
WHO type	RA, RARS, (del)5q	RCMD, RCMD-RS	RAEB-1	RAEB-2
Chromosomes	Good	Intermediate	Poor	
Needs Transfusions	No	Yes		

This system puts patients with MDS into 5 groups

- Very low risk (score = 0)
- Low risk (score = 1)
- Intermediate (score = 2)
- High risk (score = 3 or 4)
- Very high risk (score = 5 or 6)

These risk groups can also be used to predict outlook

Risk Group	Median Survival*	Risk of Leukemia (within 5 years)+
Very low	12 years	3%
Low	5.5 years	14%
Intermediate	4 years	33%
High	2 years	54%
Very high	9 months	84%

*Median survival is the amount of time for half the patients in the group to die. This is a middle value -- half the patients live longer than this, and half do not live this long. Median survival is another standard way to indicate outlook.

+ The percentage of people who will develop leukemia within 5 years of being put into this risk group.

How is myelodysplastic syndrome treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

Myelodysplastic syndrome (MDS) isn't just one disease; it is a group of related diseases. The different types of MDS vary in their prognosis and response to treatment. Treatment is based on the type of MDS, as well as the patient's age and health. Patients with these diseases are treated by specialists, such as a hematologist or an oncologist.

Chemotherapy for myelodysplastic syndrome

Chemotherapy (chemo) is the use of drugs for treating a disease such as cancer. The drugs can be swallowed as pills, or they can be injected by needle into a vein or muscle. These drugs enter the bloodstream and reach most areas of the body and are considered systemic treatment. This type of treatment is useful for diseases such as myelodysplastic syndrome (MDS) that are not localized to one part of the body. The purpose of the chemo is to eliminate the abnormal stem cells and allow normal ones to grow back.

Conventional chemotherapy

Because MDS can progress to acute leukemia, patients with MDS may receive the same treatment as leukemia patients. Chemotherapy drugs often used for MDS and acute myeloid leukemia include cytarabine with idarubicin, cytarabine with topotecan, and cytarabine with fludarabine. This type of treatment can help some patients, but it has many severe side effects. Complications from chemo may hasten death, particularly in the elderly. Still, this treatment may be an option for some patients with advanced MDS.

Another option is to use lower doses of chemo drugs. This approach can lower the chance of serious side effects.

Chemotherapy drugs can cause many side effects. The side effects depend on the type and dose of the drugs that are given and how long they are taken. Common side effects include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting

- Low blood counts

Chemotherapy often slows blood production, leading to low blood counts. In MDS, this problem is usually made worse before it gets better. It can lead to lowered resistance to infection (due to low white blood cell counts), easy bruising and bleeding (due to low platelet counts), and fatigue (due to low red blood cell counts).

At times during treatment when their white blood cell counts are very low, patients can reduce their risk of infection by avoiding exposure to bacteria, fungi, or viruses. Wearing a surgical mask around crowds and construction areas may be recommended. During this time, patients should be very careful about washing hands, and avoiding fresh flowers and uncooked fruit and vegetables, as well as other foods that might carry germs. Another important way to protect patients with low white blood cell counts against infection is treatment with powerful antibiotics. These may be given before signs of infection or at the earliest sign that an infection may be developing.

While their platelet counts are low, patients may receive platelet transfusions as to prevent or treat bleeding. Likewise, fatigue caused by low red blood cell counts can be treated with red blood cell transfusions or with growth factors, such as erythropoietin (discussed below), to raise red blood cell counts.

Most side effects are temporary and will go away after treatment is finished. Your health care team often can suggest ways to lessen side effects. For example, other drugs can be given along with the chemotherapy to prevent or reduce nausea and vomiting.

Chemotherapy drugs can also damage organs such as the kidneys, liver, testicles, ovaries, brain, heart, and lungs. With careful monitoring, such side effects are rare. If serious side effects occur, the chemotherapy treatments may have to be reduced or stopped, at least temporarily.

Carefully monitoring and adjusting drug doses are important because some of these side effects can be permanent.

Hypomethylating agents

These drugs are actually a form of chemotherapy that affect the way genes are controlled. They help in MDS by slowing down genes that promote cell growth. They also kill cells that are dividing rapidly. Examples of this type of drug include azacytidine (Vidaza[®]) and decitabine (Dacogen[®]). In some MDS patients, these drugs improve blood counts, lower the chance of getting leukemia, and even prolong life. Red blood cell counts may improve enough to stop transfusions.

These drugs have some of the same side effects as regular chemotherapy, but these side effects are usually mild. They include:

- Nausea/vomiting
- Diarrhea or constipation
- Fatigue and weakness

- Low blood counts (most often the white blood cells or platelets)

Immune treatments

Immune modulating drugs: The drugs *thalidomide* and *lenalidomide* (Revlimid®) belong to the class of drugs known as immunomodulating drugs (or IMiDs). Thalidomide was used first in treating MDS. It helped some patients, but many people stopped taking the drug because of side effects. Lenalidomide is a newer drug related to thalidomide that has fewer side effects. It seems to work well in low-grade MDS, eliminating the need for transfusions in about half the patients treated. The drug seems to work best in people whose MDS cells are missing a part of chromosome number 5 (this is called del(5q) or 5q-) and is approved by the FDA to treat these patients. It can also help MDS patients that do not have this abnormal chromosome.

Side effects include:

- Decreased blood counts (most often the white cell count and platelet count)
- Diarrhea or constipation
- Fatigue and weakness

Both of these drugs can also increase the risk of serious blood clots that start in the veins in the legs (called deep venous thrombosis or DVT). Part of a DVT can break off and travel to the lungs (called a pulmonary embolus or PE), where it can cause problems with breathing or even death. Many experts feel that patients getting this drug should also get some kind of treatment to prevent blood clots.

When thalidomide was first released in the 1960s, it was found to cause serious birth defects if given to pregnant women. This led to the drug being taken off the market for many years. Now, it is only available through a special program of the drug company. Lenalidomide hasn't been shown to cause birth defects, but concern about this risk has limited the availability of this drug as well. It is also only available through a program from the company that makes it.

Immunosuppression: Drugs that suppress the immune system can help some patients with MDS. These drugs are used more often in patients with aplastic anemia, a condition where the immune system attacks the bone marrow, leading to low blood counts.

A drug called *anti-thymocyte globulin* (ATG) has helped some people, usually younger ones, with MDS. The drug is an antibody against a type of white blood cell called the T-lymphocyte. T-lymphocytes help control immune reactions. In some patients with MDS, T-lymphocytes interfere with normal blood cell production. ATG is given as an infusion through a vein. It must be given in the hospital because it can sometimes cause severe allergic reactions leading to low blood pressure and problems breathing.

Another drug that works by suppressing the immune system is called *cyclosporine*. It was first used to block immune responses in people who have had organ or bone marrow transplants, but, it has helped some patients with MDS. Side effects of cyclosporine include loss of appetite and kidney damage.

Growth factors for myelodysplastic syndrome

Hematopoietic growth factors are hormone-like substances that stimulate bone marrow to produce blood cells. These substances occur naturally in the body, but scientists have found a way to make them outside of the body in large amounts. This allows patients to receive these factors in larger doses than would be produced by their own body.

Shortages of blood cells cause most of the symptoms in people with myelodysplastic syndrome (MDS), and growth factors can help the blood counts to become more normal. The growth factors *granulocyte colony stimulating factor* (G-CSF, Neupogen[®], or filgrastim) and *granulocyte macrophage-colony stimulating factor* (GM-CSF, Leukine[®], or sargramostim) can improve white blood cell production. These can benefit some MDS patients whose main problem is a shortage of white blood cells, who suffer from frequent infections. Pegfilgrastim (Neulasta[®]) is a long-acting form of G-CSF. It works in the same way but can be given less often.

Erythropoietin (Epo[®] or Procrit[®]), a growth factor that promotes red blood cell production, can help avoid red blood cell transfusions in some patients. For some patients, giving both erythropoietin and G-CSF improves the response to the erythropoietin. Darbepoetin alfa (Aranesp[®]) is a long-acting form of erythropoietin. It works in the same way, but can be given less often.

A drug called *oprelvekin* (Neumega[®], interleukin-11, or IL-11) can be used to stimulate platelet production after chemotherapy and in some other diseases. This drug can help increase the platelet counts of some MDS patients for a time, but then the counts go back down again. For most MDS patients, this drug is not very helpful.

More studies are under way to find the best way to predict which patients will benefit from growth factors and the best way to combine growth factors with each other and with other treatments, such as chemotherapy or hormones. Patients usually receive the growth factors through subcutaneous (under the skin) injections. Your health care team can give the injections, or you or your family members can learn to give them.

Androgens, or male hormones, can boost blood cell production that is abnormally low due to certain diseases. A few people with MDS may be helped by androgens, but most do not improve. If no other treatment options are appropriate for a patient, some doctors recommend trying androgens. However, these hormones can cause side effects, such as liver problems or muscle cramps. In women, androgens can produce male features such as growth of facial and body hair and can increase the sex drive.

Supportive therapy for myelodysplastic syndrome

For many patients with myelodysplastic syndrome (MDS) the main goal of treatment is to prevent the problems caused by low blood cell counts. For example, low red blood cell counts (anemia) can cause severe fatigue. Patients with MDS and anemia often benefit from receiving red blood cell transfusions if erythropoietin isn't helping them.

Some people are concerned about a slight risk of infection (hepatitis or HIV) spread by blood transfusion, but this possibility is very unlikely, and the benefits of the transfused cells greatly outweigh this risk.

Blood transfusions can cause excess iron to build up in the body. This extra iron can deposit in the liver and heart, causing the organs to function poorly. Iron build up is usually seen only in people who receive many transfusions over a period of years. Drugs called *chelating agents* (substances that bind with metal so that the body can get rid of it) can be used in patients who may develop iron overload from transfusions. The most commonly used drug is desferoxamine. This drug helps treat and prevent iron overload. This is given intravenously or as an injection under the skin. It is inconvenient because the injection must be given slowly (over several hours) 5 to 7 times per week. In some patients, treatment continues for years. Deferasirox (Exjade[®]) is a newer drug that is taken by mouth once a day to treat iron overload. It has been used more for patients with certain congenital anemias (like thalassemia), but it can also help some MDS patients.

MDS patients with bleeding problems resulting from a shortage of platelets may benefit from platelet transfusions.

Patients with low white blood cell counts are very susceptible to infections. They should be especially cautious to avoid cuts and scrapes or to care for them without delay. They should tell their doctors immediately about any fever, signs of pneumonia (cough, shortness of breath), or urinary infection (burning when urinating). Doctors will treat known or suspected infections with antibiotics. For serious infections, a white blood cell growth factor may also be used. This drug can help raise the white blood cell count so that the body can fight the infection.

Stem cell transplant for myelodysplastic syndrome

Stem cell transplant (SCT) is the only treatment that can cure MDS. In this treatment, the patient receives high-dose chemotherapy and/or total body irradiation to kill the cells in the bone marrow (including the abnormal bone marrow cells). Then the patient receives new, healthy blood-forming stem cells. There are 2 main types of SCT: *allogeneic* and *autologous*.

In an autologous stem cell transplant, after the bone marrow is destroyed, the patient gets back their own stem cells. This type of transplant is not a standard treatment for patients with MDS because their bone marrow contains abnormal stem cells.

For an allogeneic stem cell transplant, the patient receives blood-forming stem cells from another person - the donor. The donor's cells must be matched to the patient's cell type. The best results are seen when the donor is related to the patient, such as a brother or sister. Less often, the donor is matched to the patient, but is not related. Stem cells for the transplant can be taken from multiple bone marrow samples. More often, the blood-forming stem cells are separated and removed from the peripheral (circulating) blood by a method known as *apheresis*.

Allogeneic stem cell transplant can have serious, even fatal, side effects and so is rarely used in elderly patients. Because of these side effects, some doctors restrict this treatment to people younger than a certain age.

A special type of allogeneic transplant, called *non-myeloablative allogeneic stem cell transplant* may be an option for older patients. This type of transplant is sometimes called a mini-transplant or a mini-allo. For this kind of transplant, the doses of chemotherapy and/or radiation that are given are lower than those used for a standard allogeneic transplant. These doses are not high enough to kill all the bone marrow cells, but they are just enough to allow the donor cells to take hold and grow in the bone marrow. The lower doses of chemotherapy and/or radiation cause fewer side effects, but some serious side effects remain, particularly graft-versus-host disease.

Side effects from a SCT are generally divided into early and long-term effects. The early complications and side effects are the same as those caused by any other type of high-dose chemotherapy. They may include:

- Damage to the lungs from radiation (this is rare)
- Damage to the ovaries causes infertility and abrupt menopause, usually with symptoms such as hot flashes and loss of menstrual periods.
- Damage to the thyroid gland may produce problems with metabolism.
- Cataracts, clouding of the lens of the eye that can decrease vision, may occur.

The most serious side effect from allogeneic transplants is called *graft-versus-host disease* (or GVHD). This occurs when the new immune cells (from the donor) attack the patient's tissues because they see them as foreign. This is more common if the donor is unrelated or if the cells aren't completely matched. GVHD can occur early in the transplant process - this is called *acute GVHD*. It can also start later and last a long time - this is called *chronic GVHD*. Common sites of GVHD include the skin, where it can cause a rash, blistering, or open sores. When GVHD affects the intestines, it can cause diarrhea, which can be severe. It can also cause liver and lung problems. Drugs to suppress the immune system are given as part of the transplant to prevent GVHD. If GVHD develops despite these drugs, additional treatments to suppress the immune system may be needed.

Joint damage called *aseptic necrosis* is a rare complication; however, if damage is severe, the patient will need to have part of the bone and joint replaced.

Although allogeneic SCT is currently the only treatment that can cure some patients with MDS, not all patients who get a transplant are cured. In addition, patients may die from complications of this treatment. Your chance for cure is higher if you are young and your MDS hasn't begun to transform into leukemia. Still, doctors recommend waiting until the MDS develops into a more advanced stage before considering transplant.

For more information about stem cell transplants, see our document *Bone Marrow and Peripheral Blood Stem Cell Transplant*.

Clinical trials for myelodysplastic syndrome

You may have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is choosing which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our Web site at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials.

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the-art cancer treatment. They are the only way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

You can get a lot more information on clinical trials in our document called *Clinical Trials: What You Need to Know*. You can read it on our Web site or call our toll-free number (1-800-227-2345) and have it sent to you.

Complementary and alternative therapies for myelodysplastic syndrome

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and Web sites may offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help

relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not to be helpful, and a few have even been found to be harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at.

The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

General approach to treatment of MDS

Stem cell transplant (SCT) is usually considered the only curative option for patients with MDS, and may be the treatment of choice for younger patients when a matched donor is available. This is the recommended treatment for nearly all children. For older patients, either the high-dose or low-dose approach can be used. For either of these options, it appears best to wait until the disease is advanced before performing the SCT.

When SCT is not an option, MDS is not considered curable. In that case, the goal is to relieve symptoms and avoid complications and side effects of treatment. Patients with

mild low blood counts and few symptoms may be carefully watched without treatment for a while. If low blood counts are causing problems, treatments such as transfusions, blood cell growth factors, and possibly androgens may be helpful.

If a person has the 5q- type of MDS, then lenalidomide is often used as the first treatment. If this drug doesn't help, treatment with azacytidine or decitabine is often the next option.

Treatment with azacytidine or decitabine is often the first choice for patients with MDS without the 5q- chromosome problem. Azacytidine can be given as injections under the skin, often for 7 consecutive days every month. The standard dosing of decitabine is to give the drug as an injection into a vein (IV) every 8 hours for 3 days every 6 weeks. Since this means that the patient has to stay in the hospital for treatment, studies were done to see if the drug would still work on a different schedule. One option that seems to work well is to give the drug IV daily for 5 days every 4 weeks. This allows it to be given in an outpatient clinic. The major side effect of these drugs is an early drop in blood counts, as seen with most chemotherapy drugs. If the drug is successful, blood counts will improve to levels that are better than those seen before treatment was started.

A major benefit for patients receiving azacytidine or decitabine is that they need fewer transfusions and have a better quality of life. In particular, if they respond, they have less fatigue and are able to function more normally. Finally, these drugs can increase life span in some patients.

Other drugs, such as those mentioned previously, have helped some patients. It may be worth joining a clinical trial or receiving these agents outside a trial, if none is available.

Careful general medical care and measures to prevent and treat infections are very important. Patients should think about taking part in clinical trials of new treatments.

More treatment information for myelodysplastic syndrome

For more details on treatment options -- including some that may not be addressed in this document -- the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. Those are available on the NCCN Web site (www.nccn.org).

The NCI provides treatment information via telephone (1-800-4-CANCER) and its Web site (www.cancer.gov). Information for patients as well as more detailed information intended for use by cancer care professionals is also available on www.cancer.gov.

What should you ask your doctor about myelodysplastic syndrome?

It is important to have frank, open, and honest discussions with your doctor about your condition. Your doctor and the rest of the health care team want to answer all of your questions. For instance, consider these questions:

- What type of myelodysplastic syndrome do I have?
- What is my prognostic score?
- What treatment choices do I have?
- Which treatment, if any, do you recommend, and why?
- What are the side effects of the treatments that you recommend?
- How can I help reduce the side effects I may have from the treatment?
- What is the outlook for my survival?
- Should I get a second opinion, and whom do you recommend as an expert in this field?

What happens after treatment for myelodysplastic syndrome?

Since myelodysplastic syndrome (MDS) is rarely cured, most patients never actually complete treatment. Patients may go through a series of treatments with rest in between. Some people stop active treatment in favor of supportive care.

Follow-up care

Even if you have stopped your treatment for MDS, it is still very important to keep all follow-up appointments. During these visits, your doctors will ask about symptoms, do physical exams, and order blood tests. They will continue to watch for signs of infection and progression to leukemia, as well as for short-term and long-term side effects of treatment. This is the time for you to ask your health care team any questions you need answered and to discuss any concerns you might have.

Almost any cancer treatment can have side effects. Some may last for a few weeks to several months, but others can be permanent. Don't hesitate to tell your care team about any symptoms or side effects that bother you so they can help you manage them.

It is also important to keep your medical insurance. With a chronic disease like MDS, your treatment may never really be over. You don't want to have to worry about paying for it. Many people have been bankrupted by medical costs.

Seeing a new doctor

At some point after your diagnosis and treatment, you may find yourself in the office of a new doctor who does not know your medical history. It is important that you be able to give your new doctor the details of your diagnosis and treatment. Make sure you have this information handy:

- A copy of your pathology report(s) from any biopsies or surgeries
- If you had surgery, a copy of your operative report(s)
- If you were in the hospital, a copy of the discharge summary that doctor prepare when patients are sent home
- Finally, since some drugs can have long-term side effects, a list of your drugs, drug doses, and when you took them

The doctor may want copies of this information for his records, but always keep copies for yourself.

Lifestyle changes after having myelodysplastic syndrome

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life -- making choices to help you stay healthy and feel as well as you can. This can be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even start during cancer treatment.

Making healthier choices

For many people, a diagnosis of cancer helps them focus on their health in ways they may not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on the alcohol, or give up tobacco. Even things like keeping your stress level under control may help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society at 1-800-227-2345 for information and support. This tobacco cessation and coaching service can help increase your chances of quitting for good.

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after cancer treatment. Treatment may change your sense of taste. Nausea can be a problem. You may

not feel like eating and lose weight when you don't want to. Or you may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment caused weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do after cancer treatment is put healthy eating habits into place. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of cancer, as well as having many other health benefits.

Rest, fatigue, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a "bone-weary" exhaustion that doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to exercise and do other things they want to do. But exercise can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it is normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis twice a week. If you haven't exercised in a few years, you will have to start slowly – maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, try to find an exercise buddy so you're not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, you will need to balance activity with rest. It is OK to rest when you need to. Sometimes it's really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. (For more information on dealing with fatigue, please see *Fatigue in People With Cancer* and *Anemia in People With Cancer*.)

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- Along with a good diet, it will help you get to and stay at a healthy weight.
- It makes your muscles stronger.

- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.
- It can make you feel happier.
- It helps you feel better about yourself.

And long term, we know that getting regular physical activity plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

How does having myelodysplastic syndrome affect your emotional health?

At some point, you may find yourself overcome with many different emotions. This happens to a lot of people. You may have been going through so much at first that you could only focus on getting through each day. Now it may feel like a lot of other issues are catching up with you.

You may find yourself thinking about death and dying. Or maybe you're more aware of the effect the cancer has on your family, friends, and career. You may take a new look at your relationship with those around you. Unexpected issues may also cause concern. For instance, if you start feeling better and have fewer doctor visits, you will see your health care team less often and have more time on your hands. These changes can make some people anxious.

Almost everyone who has been through cancer can benefit from getting some type of support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or one-on-one counselors. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or good for you to try to deal with everything on your own. And your friends and family may feel shut out if you do not include them. Let them in, and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you.

If treatment for myelodysplastic syndrome stops working

If your myelodysplastic syndrome (MDS) does not improve with one treatment, it is often possible to try another treatment plan to help you live longer and feel better. But if you have tried many different treatments without improvement, your disease may be resistant

to treatment. If this happens, it's important to weigh the possible limited benefits of a new treatment against the possible downsides. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with MDS -- when you have been through many medical treatments and nothing's working anymore. Your doctor may offer you new options, but at some point you may need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment for as long as you can, you need to think about the odds of treatment having any benefit and how this compares to the possible risks and side effects. In some cases, your doctor can estimate how likely it is the MDS will respond to the treatment you are considering. For instance, the doctor may say that chemo might have about a 1% chance of working. Some people are still tempted to try this. But it is important to think about and understand your reasons for choosing this plan.

No matter what you decide to do, you need to feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative care*.

Palliative care helps relieve symptoms, but is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose - the main purpose of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using drugs to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat cancer. For instance, radiation might be used to help relieve bone pain caused by cancer that has spread to the bones. Or chemo might be used to help shrink a tumor and keep it from blocking the bowels. But this is not the same as treatment to try to cure the cancer.

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. In hospice the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. You can learn more about hospice in our document called *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that are filled with happiness and meaning. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do. Though the cancer may be beyond your control, there are still choices you can make.

What's new in myelodysplastic syndrome research and treatment?

Genetics and biology of MDS

Research on the causes, diagnosis, and treatment of MDS is being done at many cancer research centers. Scientists are making progress in understanding how a series of changes in a person's DNA can cause normal bone marrow cells to develop into myelodysplastic cells.

Scientists are also learning how bone marrow stromal cells influence MDS cells. Bone marrow stromal cells are cells that are found in the bone marrow but do not develop into blood cells. Instead, they help support, nourish, and regulate the blood-forming cells. Recent 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 design new drugs or eventually in developing gene therapy. This approach replaces the abnormal DNA of cancer cells with normal DNA to restore normal control of cell growth.

Chemotherapy

Studies are being done to find drug combinations that work well without serious side effects. New drugs are continually being developed and tested. The drugs sapacitabine and clofarabine have both shown promise. Research is under way to see if there is a group of patients that may benefit from more intensive chemotherapy.

Immune suppression

Researchers are also looking at different ways to block patients' immune systems. The drug alemtuzumab (Campath), which is more often used to treat lymphoma and a certain type of chronic leukemia, acts by attacking T-cells. This suppresses the immune system, and was helpful in a recent study in MDS.

Targeted therapy

Targeted therapy is a newer type of cancer treatment that uses drugs or other substances to identify and attack cancer cells while doing little damage to normal cells. These therapies attack the cancer cells' inner workings -- the programming and gene changes that make them different from normal, healthy cells. Each type of targeted therapy works differently, but all alter the way a cancer cell grows, divides, repairs itself, or interacts with other cells.

Some targeted therapy drugs, called *angiogenesis inhibitors*, work by preventing growth of new blood vessels. This type of drug has been helpful in treating some types of cancer that form tumors, but may also be helpful in cancers like leukemia and MDS that grow in the bone marrow. Other types of targeted therapy drugs target certain abnormal genes in cancer cells. Some drugs that have been studied in MDS include bevacizumab, aflibercept, everolimus, sorafenib, sunitinib, and midostaurin.

Stem cell transplant

Scientists continue to refine this procedure to increase its effectiveness, reduce complications, and determine which patients are likely to be helped by this treatment.

Drugs to help blood counts

Romiplostim (Nplate[®]) is a new drug that raises platelet counts. It is approved to treat patients who have a disease in which their immune system attacks and destroys their platelets (called ITP), but in more recent studies it has helped raise platelet counts in people with MDS.

Additional resources for myelodysplastic syndrome

More information from your American Cancer Society

We have some related information that might also be helpful to you. These materials may be ordered from our toll-free number (1-800-227-2345) or viewed on our Web site.

After Diagnosis: A Guide for Patients and Families (also available in Spanish)

Blood Product Donation and Transfusion

Bone Marrow and Peripheral Blood Stem Cell Transplant (also available in Spanish)

Caring for the Patient With Cancer at Home: A Guide for Patients and Families (also available in Spanish)

Infections in People With Cancer

Leukemia: Acute Myeloid (Myelogenous)

Second Cancers Caused by Cancer Treatment

Understanding Chemotherapy: A Guide for Patients and Families (also available in Spanish)

The following book is available from the American Cancer Society. Call us at 1-800-227-2345 to ask about costs or to place your order.

Caregiving: A Step-By-Step Resource for Caring for the Person with Cancer at Home.
American Cancer Society, Atlanta, GA.

National organizations and Web sites*

In addition to the American Cancer Society, other sources of patient information and support include:

The National Marrow Donor Program

Toll-free number: 1-800-MARROW2 (1-800-627-7692)

Web site: www.marrow.org

Aplastic Anemia & MDS International Foundation, Inc.

Toll-free number: 1-800-747-2820

Web site: www.aamds.org

The Leukemia & Lymphoma Society

Toll-free number: 1-800-955-4572

Web site: www.leukemia-lymphoma.org

The Myelodysplastic Syndromes Foundation

Toll-free number: 1-800-MDS-0839

Web site: www.mds-foundation.org

National Cancer Institute

Toll-free number: 1-800-4-CANCER

TTY: 1-800332-8615

Web site: www.cancer.gov

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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