



# Multiple Myeloma

## 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 multiple myeloma?

Multiple myeloma is a cancer formed by malignant plasma cells. Normal plasma cells are found in the bone marrow and are an important part of the immune system.

The immune system is composed of several types of cells that work together to fight infections and other diseases. Lymphocytes (lymph cells) are the main cell type of the immune system. There are 2 major types of lymphocytes: T cells and B cells.

When B cells respond to an infection, they mature and change into plasma cells. Plasma cells make the antibodies (also called *immunoglobulins*) that help the body attack and kill germs. Lymphocytes can be found in many areas of the body, such as lymph nodes, the bone marrow, and the bloodstream. Plasma cells, however, are mainly found in the bone marrow. Bone marrow is the soft tissue inside some hollow bones.

When plasma cells become cancerous and grow out of control, they can produce a tumor called a *plasmacytoma*. These tumors generally develop in a bone, but they are also rarely found in other tissues. If there is only a single plasma cell tumor, it is called an isolated (or solitary) plasmacytoma. When there is more than one plasma cell tumor, it is called *multiple myeloma*.

In multiple myeloma, the overgrowth of plasma cells in the bone marrow can crowd out the normal blood-forming cells, leading to low blood counts. This can cause *anemia* — a shortage of red blood cells. Anemia causes people to become pale, weak, and fatigued. Multiple myeloma can also cause the level of platelets in the blood to become low (called *thrombocytopenia*). This can lead to increased bleeding and bruising. Another condition that can develop is *leukopenia* — a shortage of normal white blood cells. This can lead to problems fighting infections.

Myeloma cells also interfere with cells that help keep the bones strong. Bones are constantly being remade to keep them strong. Two major kinds of bone cells normally work together to keep bones healthy and strong. The cells that lay down new bone are

called *osteoblasts*. The cells that break down old bone are called *osteoclasts*. Myeloma cells make a substance that tells the osteoclasts to speed up dissolving the bone. Since the osteoblasts do not get a signal to put down new bone, old bone is broken down without new bone to replace it. This makes the bones weak and they break easily. Fractured bones are a major problem in people with myeloma. This increase in bone break-down also causes calcium levels in the blood to get too high (problems caused by high calcium levels are discussed in the section “How is multiple myeloma diagnosed?”).

Abnormal plasma cells do not protect the body from infections. As mentioned before, normal plasma cells produce antibodies that attack germs. For example, if you developed pneumonia, normal plasma cells would produce antibodies that are aimed at the specific bacteria that were causing the illness. These antibodies help the body attack and kill the bacteria. In multiple myeloma, the myeloma cells crowd out the normal plasma cells, so that antibodies to fight the infection can't be made. The antibody made by the myeloma cells does not help fight infections. That is because the myeloma cells are just many copies of the same plasma cell — all making copies of the same exact (or *monoclonal*) antibody.

The antibody made by myeloma cells can harm the kidneys. This can lead to kidney damage and even kidney failure.

Having many copies of the same antibody is known as a *monoclonal gammopathy*. This condition can be found with a blood test. Having a monoclonal gammopathy does not mean you have multiple myeloma. It occurs in other diseases, such as *Waldenstrom macroglobulinemia* and *light chain amyloidosis*. Also, some people have a monoclonal gammopathy but it does not cause problems like multiple myeloma does. This condition is called *monoclonal gammopathy of undetermined significance (MGUS)*. Some people with MGUS go on to develop multiple myeloma or other diseases.

## Monoclonal gammopathy of undetermined significance

In monoclonal gammopathy of undetermined significance (MGUS), abnormal plasma cells produce excess amounts of a monoclonal antibody protein. However, these plasma cells do not form an actual tumor or mass and do not cause any of the other problems seen in multiple myeloma. MGUS usually does not affect a person's health. In particular, it doesn't cause weak bones, high calcium levels, kidney problems, or low blood counts. It is most often found because a routine blood test finds a high level of protein in the blood and further testing shows the protein is a monoclonal immunoglobulin. In MGUS, the number of plasma cells may be increased, but they still make up less than 10% of the cells in the bone marrow.

Over time, many people with MGUS eventually develop multiple myeloma, lymphoma, or a disease called amyloidosis. The rate of this happening is about 1% per year. The risk of this happening is higher in people whose protein levels are particularly high. Patients with MGUS don't need treatment, but they are watched closely to see if they get a disease that does need to be treated, such as multiple myeloma.

Recently, scientists have studied the genes of the plasma cells in patients with MGUS. They found that the genetic make-up of these plasma cells resembles myeloma plasma cells more than it resembles normal plasma cells. This suggests that these cells are truly malignant, not just slow growing. Because, in general, people with MGUS are elderly, they may not live long enough for it to transform into myeloma.

## Solitary plasmacytomas

This is another type of abnormal plasma cell growth. Rather than many tumors in different locations as in multiple myeloma, there is only one tumor, hence the name solitary plasmacytomas.

Most often, a solitary plasmacytoma develops in a bone, where it may be called an *isolated plasmacytoma of bone*. When a plasmacytoma starts in other tissues (such as the lungs or the lining of the sinuses, throat, or other organs), it is called an *extramedullary plasmacytoma*. Solitary plasmacytomas are most often treated with radiation therapy. Sometimes surgery may be used for a single extramedullary plasmacytoma. As long as no other plasmacytomas are found later on, the patient's outlook is usually excellent. However, since many people with a solitary plasmacytoma will develop multiple myeloma, these people are watched closely for signs of this disease.

## What are the key statistics about multiple myeloma?

Multiple myeloma is a relatively uncommon cancer. In the United States, the lifetime risk of getting multiple myeloma is 1 in 159 (0.63%).

The American Cancer Society's most recent estimates for multiple myeloma in the United States are for 2012:

- About 21,700 new cases will be diagnosed (12,190 in men and 9,510 in women).
- About 10,710 deaths are expected to occur (6,020 in men and 4,690 in women).

The 5-year relative survival rate for multiple myeloma is around 40%. Survival is higher in younger people and lower in the elderly. Of course, 5-year survival rates are based on patients diagnosed and initially treated more than 5 years ago. The recent improvements in treatment may result in a more favorable outlook for recently diagnosed patients.

The *5-year survival rate* refers to the percentage of patients who live at least 5 years after their cancer is diagnosed. Five-year survival rates are used to produce a standard way of discussing prognosis. Of course, many people live much longer than 5 years. *Five-year relative survival rates* assume that some people will die of other causes and compare the observed survival with that expected for people without the cancer. This is a more accurate way to describe the outlook for patients with a particular type and stage of cancer.

# What are the risk factors for multiple myeloma?

A *risk factor* is anything that changes a person's 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 who have no risk factors can still get the disease. Also, having a risk factor, or even several, does not mean that a person will get the disease.

Scientists have found few risk factors that may affect someone's chance of getting multiple myeloma.

## Age

The risk of multiple myeloma goes up with age. Less than 1% of cases are diagnosed in people younger than 35. Most people diagnosed with this cancer are over 65 years old.

## Gender

Men are slightly more likely to develop multiple myeloma than women.

## Race

Multiple myeloma is almost twice as common among black Americans as white Americans. The reason is not known.

## Radiation

Exposure to radiation may increase the risk of multiple myeloma. At most, this accounts for a very small number of cases.

## Family history

Multiple myeloma does seem to run in some families. Someone who has a sibling or parent with myeloma is 4 times more likely to get it than would be expected. Still, most patients have no affected relatives, so this accounts for only a small number of cases.

## Workplace exposures

Some studies have suggested that workers in certain petroleum-related industries may be at a higher risk.

## Obesity

A study by the American Cancer Society has found that being overweight or obese increases a person's risk of developing myeloma.

## Other plasma cell diseases

Many people with monoclonal gammopathy of undetermined significance (MGUS) or solitary plasmacytoma will eventually develop multiple myeloma.

## Do we know what causes multiple myeloma?

Scientists still do not know exactly what causes most cases of multiple myeloma. However, they have made progress in understanding how certain changes in DNA can cause plasma cells to become cancerous. DNA is the chemical that carries the instructions for nearly everything our cells do. Some *genes* (parts of our DNA) contain instructions for controlling when our cells grow and divide. Certain genes that promote cell division are called *oncogenes*. Others that slow down cell division or cause cells to die at the appropriate time are called *tumor suppressor genes*. Cancers can be caused by mistakes, or defects, in the DNA called *mutations* that turn on oncogenes or turn off tumor suppressor genes.

Recent studies have found that abnormalities of some oncogenes (such as c-myc) develop early in the course of plasma cell tumors. Changes in other oncogenes (such as N-ras and K-ras) are more often found in myeloma after it has come back in the bone marrow after treatment, and changes in tumor suppressor genes (such as p53) are associated with spread to other organs.

Myeloma cells also show abnormalities in their chromosomes. Normal human cells contain 46 chromosomes—pieces of DNA and protein that control cell growth and metabolism. One fairly common finding in myeloma cells is that parts of chromosome number 13 are missing. These deletions appear to make the myeloma more aggressive and resistant to treatment.

About half of all people with myeloma have abnormally translocated chromosomes in their myeloma cells. This means that a part of one chromosome has switched with part of another chromosome. This often occurs in a crucial area next to an oncogene, which causes it to be turned on.

Researchers have found that patients with plasma cell tumors have important abnormalities in other bone marrow cells and that these abnormalities may also cause excess plasma cell growth. Certain cells in the bone marrow called *dendritic cells* release a hormone called interleukin-6 (IL-6), which stimulates normal plasma cells to grow. Excess IL-6 production by these cells appears to be an important factor in development of plasma cell tumors.

## Can multiple myeloma be prevented?

For some types of cancer, risk factors that account for the majority of cases are known. For example, smoking causes most lung cancers. This provides an opportunity for prevention. For other cancers, such as cervical cancer, precancerous changes can be detected early by the Pap test and treated before they develop into an invasive cancer.

With multiple myeloma, there are no risk factors you can avoid that are known to be responsible for most cases. And for those people with monoclonal gammopathy of undetermined significance or solitary plasmacytomas there is no known way to prevent multiple myeloma from developing.

## Can multiple myeloma be found early?

It is difficult to diagnose multiple myeloma early. Often, multiple myeloma causes no symptoms until it has reached an advanced stage. In some cases, it may cause vague symptoms that at first seem to be caused by other diseases. Rarely, multiple myeloma is found early when a routine blood test shows an abnormally high amount of protein in the blood.

## How is multiple myeloma diagnosed?

### Signs and symptoms of multiple myeloma

Although some patients with multiple myeloma have no symptoms at all, the following are the most common symptoms of this disease:

#### **Bone problems**

Normally, the 2 major kinds of bone cells work together to keep bones healthy and strong. The cells that lay down new bone are called *osteoblasts*. The cells that break down old bone are called *osteoclasts*. Myeloma cells make a substance that tells the osteoclasts to speed up the dissolving of bone. The osteoblasts do not get a signal to put down new bone, so old bone is being broken down without new bone to replace it. This can cause areas of bone weakness that are painful. Any bone can be affected, but pain in the bones in the back, the hips, and skull is particularly common with this disease. These changes also increase the chance that the bones will break (fracture). Sometimes bones break from only a minor stress or injury.

#### **Low blood counts**

When myeloma cells replace normal blood-forming marrow cells, shortages of red blood cells, white blood cells, and blood platelets result. A reduced number of red blood cells, a condition called *anemia*, causes weakness, reduced ability to exercise, shortness of breath, and dizziness. Too few white blood cells (a condition called *leukopenia*) lowers

resistance to infections such as pneumonia. When blood platelet counts are low (a condition called *thrombocytopenia*), even minor scrapes, cuts, or bruises may cause serious bleeding.

## **High blood calcium**

When the myeloma cells dissolve bone, calcium is released. This can lead to high blood levels of calcium (called *hypercalcemia*). Symptoms include feeling very thirsty, drinking a lot of fluids, and urinating (peeing) a lot. This can cause dehydration and even kidney failure. High calcium can also cause severe constipation and loss of appetite. It can make people feel weak, drowsy, and confused. If the level of calcium gets high enough, it can even cause you to lapse into a coma.

## **Nervous system symptoms**

If myeloma weakens the bones in the spine, they can collapse and press on spinal nerves. This can cause sudden severe pain, numbness, and/or muscle weakness. This is a medical emergency and you should contact your doctor right away or go to the emergency room.

Sometimes, the abnormal proteins produced by myeloma cells can be toxic to the nerves. This damage can lead to weakness and numbness.

In some patients, large amounts of myeloma protein can cause the blood to "thicken." This thickening is called *hyperviscosity*. It can slow blood flow to the brain and cause confusion, dizziness, and stroke-like symptoms. Patients with these symptoms should call their doctor. Removing the protein from the blood by a procedure called *plasmapheresis* can rapidly reverse this problem.

## **Kidney problems**

Myeloma protein can damage the kidneys. Early on, this doesn't cause any symptoms, but can be found with a blood test. As the kidneys start to fail, they lose the ability to dispose of excess salt, fluid, and body waste products. This can lead to symptoms like weakness and leg swelling.

## **Infections**

Myeloma patients are about 15 times more likely to get infections. This happens because the body is unable to make the antibodies that help fight infection. Often, once someone with myeloma gets an infection, it is slow to respond to treatment. That person may stay sick for a long time. Pneumonia is a common and serious infection seen in myeloma patients.

## **Laboratory tests**

If symptoms suggest that a person might have multiple myeloma, lab tests on blood and/or urine, x-rays of the bones, and a bone marrow biopsy are usually done.

## **Blood counts**

The complete blood count (CBC) is a test that measures the levels of red cells, white cells, and platelets in the blood. If myeloma cells occupy too much of the bone marrow, levels of these blood cells will be low.

## **Quantitative immunoglobulins**

This test measures the blood levels of the different antibodies. There are several different types of antibodies in the blood: IgA, IgD, IgE, IgG, and IgM. The levels of these immunoglobulins are measured to see if any are abnormally high or low. In multiple myeloma, the level of one type may be high while the others are low.

## **Electrophoresis**

The immunoglobulin produced by myeloma cells is abnormal because it is monoclonal. *Serum protein electrophoresis (SPEP)* is a test to measure the total amount of immunoglobulin in the blood and find any abnormal immunoglobulin. Then, another test, such as *immunofixation* or *immuno-electrophoresis*, is used to determine the exact type of antibody that is abnormal (IgG or some other type). Finding a monoclonal immunoglobulin in the blood may be the first step in making the diagnosis of multiple myeloma. This abnormal protein is known by several different names, including *monoclonal immunoglobulin*, *M protein*, *M spike*, and *paraprotein*.

Immunoglobulins are made up of protein chains: 2 long (heavy) chains and 2 shorter (light) chains. Sometimes the kidneys excrete pieces of the M protein into the urine. This urine protein is the part of the immunoglobulin called the *light chain*. It is also known as *Bence-Jones protein*. The tests used for finding a monoclonal immunoglobulin in urine are called *urine protein electrophoresis (UPEP)* and *urine immunofixation*.

## **Free light chains**

This test measures the amount of light chains in the blood. This is most helpful in the rare cases of myeloma in which no M protein is found by SPEP. Since the SPEP measures the levels of intact (whole) immunoglobulins, it cannot measure the amount of light chains.

## **Beta-2 microglobulin**

This is another protein produced by the malignant cells. Although this protein itself doesn't cause problems, it can be a useful indicator of a patient's prognosis (outlook). High levels indicate more advanced disease and maybe a worse prognosis.

## **Blood chemistry tests**

Levels of blood urea nitrogen (BUN) and creatinine, albumin, calcium, and other electrolytes will be checked

- BUN and creatinine (Cr) levels show how well your kidneys are working. Higher levels mean that kidney function is impaired. This is common in people with myeloma.
- Albumin is a protein found in the blood. Low levels can be a sign of more advanced myeloma.
- Calcium levels may be higher in people with advanced myeloma. High calcium levels can cause severe symptoms of fatigue, weakness, and confusion.
- Levels of electrolytes such as sodium and potassium may be affected as well.

## Bone marrow biopsy

People with multiple myeloma have too many plasma cells in their bone marrow. The procedure to check the bone marrow is called a *bone marrow biopsy and aspiration*. It can be either done at the doctor's office or at the hospital.

In this procedure, the back of the pelvic bone is numbed with local anesthetic. Then, to do the bone marrow aspiration, a needle is inserted into the bone, and a syringe is used to remove a small amount of liquid bone marrow. This causes a brief sharp pain. Then for the biopsy, a needle is used to remove a tiny sliver of bone and marrow, about 1/16-inch across and 1-inch long. There is some soreness in the biopsy area when the numbing medicine wears off. Most patients can go home immediately after the procedure. A doctor will use a microscope to look at the bone marrow tissue to see the appearance, size, and shape of the cells, how the cells are arranged and to determine if there are myeloma cells in the bone marrow and, if so, how many. The aspirate may also be sent for other tests, including immunohistochemistry and flow cytometry, and chromosome analyses, including karyotype and fluorescent *in situ* hybridization (also known as FISH).

## Immunohistochemistry

In this test, a part of the biopsy sample is treated with special antibodies (man-made versions of immune system proteins) that attach only to specific molecules on the cell surface. These antibodies cause color changes, which can be seen under a microscope. This test may be helpful in telling different types of cells apart and in finding myeloma cells.

## Flow cytometry

Like immunohistochemistry, this test looks for certain substances on the outside surface of cells that help identify what types of cells they are. But this test can look at many more cells than immunohistochemistry.

For this test, a sample of cells is treated with special antibodies that stick to the cells only if certain substances are present on their surfaces. The cells are then passed in front of a laser beam. If the cells now have antibodies attached to them, the laser will cause them to give off light, which can be measured and analyzed by a computer. Groups of cells can be separated and counted by these methods.

This is the most commonly used test for immunophenotyping — classifying cells according to the substances (antigens) on their surfaces. Different cells and cell types have different antigens on their surface. These antigens may also change as each cell matures.

Flow cytometry can help determine if there are abnormal cells in the bone marrow and if they are myeloma cells, lymphoma cells, some other cancer, or a non-cancerous disease.

## **Cytogenetics**

This technique allows doctors to evaluate the chromosomes (long strands of DNA) in normal bone marrow cells and myeloma cells. The cells are looked at under a microscope to see if the chromosomes have any translocations (where part of one chromosome has broken off and is now attached to another chromosome), as can happen in some cases of multiple myeloma. Some myeloma cells may have too many chromosomes, too few chromosomes, or other chromosome abnormalities. Finding these changes can sometimes help in predicting prognosis.

Cytogenetic testing usually takes about 2 to 3 weeks because the lymphoma cells must grow in lab dishes for a couple of weeks before their chromosomes are ready to be viewed under the microscope.

## **Fluorescent in situ hybridization**

Fluorescent in situ hybridization (FISH) is similar to cytogenetic testing. It uses special fluorescent dyes that only attach to specific parts of chromosomes. FISH can find most chromosome changes (such as translocations) that can be seen under a microscope in standard cytogenetic tests, as well as some changes too small to be seen with usual cytogenetic testing.

FISH can be used to look for specific changes in chromosomes. It can be used on regular blood or bone marrow samples. It is very accurate and can usually provide results within a couple of days, which is why this test is now used in many medical centers.

## **Other biopsy tests**

If an area looks abnormal on an x-ray, a biopsy may be needed to confirm that it is a plasmacytoma. Most often, a needle biopsy is used.

## **Fine needle aspiration biopsy**

Fine needle aspiration (FNA) uses a very thin needle and an ordinary syringe to withdraw a small amount of tissue from a tumor or lymph node. The doctor can aim the needle while feeling an enlarged node near the surface of the body. If the tumor is deep inside the body, the needle can be guided while it is viewed on a computed tomography (CT) scan (see discussion of imaging tests later in this section). The main advantage of FNA is that it does not require surgery. The disadvantage is that in some cases the thin needle

cannot remove enough tissue for a definite diagnosis. FNA can be useful in diagnosing cancers that have spread to nodes from other organs.

## **Core needle biopsy**

This test is similar to FNA, but a larger needle is used and a larger tissue sample is removed.

## **Imaging studies**

### **Bone x-rays**

Bone destruction caused by the myeloma cells can be detected with x-rays. Often doctors will do a series of x-rays that includes most of the bones. This is called a *bone survey* or *skeletal survey*.

### **Computed tomography**

The computed tomography (CT) scan (also known as a CAT scan) is an x-ray procedure that produces detailed cross-sectional images of your body. Instead of taking one picture, like a conventional x-ray, a CT scanner takes many pictures of the part of your body being studied as it rotates around you. A computer then combines these pictures into an image of a slice of your body. Sometimes, this test can help tell if your bones have been damaged by myeloma.

You may be asked to drink 1 to 2 pints of a solution of contrast material before the scan. This helps outline the intestine so that it is not mistaken for tumors. You may also receive an intravenous (IV; in the vein) line through which a different contrast dye is injected. This helps better outline structures in your body. The injection can cause a feeling of warmth throughout the body (flushing). Some people are allergic to the IV contrast and get hives. Rarely, more serious reactions like trouble breathing and low blood pressure can occur. Medicine can be given to prevent and treat allergic reactions. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays. If IV contrast is being used, it is important you tell the radiology people that you have myeloma. Some of these contrast agents can damage the kidneys of people with myeloma.

CT scans take longer than regular x-rays, and you usually need to lie still on a table a while they are being done. Also, you might feel a bit confined by lying within the equipment while the pictures are being taken. But just like other computerized devices, they are getting faster and your stay might be pleasantly short. Some modern scanners can complete the study in seconds.

CT scans can also be used to guide a biopsy needle precisely into a suspected tumor. For this procedure, called a *CT-guided needle biopsy*, the patient remains on the CT scanning table while a radiologist advances a biopsy needle toward the location of the tumor. CT scans are repeated until the doctors are confident that the needle is within the mass. A

fine needle biopsy sample (tiny fragment of tissue) or a core needle biopsy sample (a thin cylinder of tissue about ½-inch long and less than 1/8 inch in diameter) is removed and examined under a microscope.

## **Magnetic resonance imaging**

MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of tissue and by certain diseases. A computer translates the pattern of radio waves given off by the tissues into a very detailed image of parts of the body. Not only does this produce cross-sectional slices of the body like a CT scanner, it can also produce slices that are parallel with the length of your body. A dye (contrast material) might be injected just as with CT scans but is used less often.

MRI scans are very helpful in looking at bones, the brain, and the spinal cord. They might be able to find plasmacytomas that cannot be seen on regular x-rays. MRI can also be used to look at the bone marrow in patients with multiple myeloma. MRI scans are a little more uncomfortable than CT scans. First, they can take an hour or longer. Also, you have to be placed inside tunnel-like equipment, which is confining and can upset some people. The machine also makes a thumping noise that may be disturbing. Some places provide headphones with music to block this out.

## **Positron emission tomography**

In this test, which is also called a PET scan, radioactive glucose (sugar) is injected into the patient's vein to look for cancer cells. Because cancers use glucose (sugar) at a higher rate than normal tissues, the radioactivity will tend to concentrate in the cancer. A scanner is used to spot radioactive deposits. When a patient appears to have a solitary plasmacytoma, a PET scan may be used to look for other plasmacytomas.

## **Interpreting test results**

Results of any single test are not enough to make a diagnosis of multiple myeloma. Diagnosis is based on a combination of factors, including the patient's description of symptoms, the doctor's physical examination of the patient, and the results of blood tests and x-rays. The diagnosis of multiple myeloma requires either:

- A plasma cell tumor (proven by biopsy)

OR

- At least 10% of the cells in the bone marrow be plasma cells.

AND one of the following:

- M protein over a certain level in the blood (3g/dL)

OR

- M protein in the urine over a certain level (1g/dL)

OR

- Holes in bones due to tumor growth are found on imaging studies.

## Smoldering myeloma

This term used to mean early myeloma that is not causing any symptoms or problems. People with smoldering myeloma have normal blood counts, normal calcium levels, normal kidney function, and no bone or organ damage. Smoldering myeloma does not need to be treated right away.

## How is multiple myeloma staged?

*Staging* is the process of finding out how much the cancer has advanced. It is important for treatment options and prognosis. *Prognosis* is a prediction of the course of disease—the outlook for the chances of survival. Knowing all you can about staging lets you take a more active role in making informed decisions about your treatment.

Multiple myeloma may be staged using the Durie-Salmon system. Although some doctors use this system, its value is becoming limited because of newer diagnostic methods. Recently, a new staging system called the *International Staging System for Multiple Myeloma* has been developed. It relies mainly on levels of albumin and beta-2-microglobulin in the blood. Other factors that may be important are kidney function, platelet count and the patient's age.

## The Durie-Salmon staging system

This system is based on 4 factors:

- The amount of abnormal monoclonal immunoglobulin in the blood or urine: Large amounts of monoclonal immunoglobulin indicate that many malignant plasma cells are present and are producing that abnormal protein.
- The amount of calcium in the blood: High blood calcium levels are also related to advanced bone damage. Because bone normally contains lots of calcium, bone destruction releases calcium into the blood.
- The severity of bone damage based on x-rays: Multiple areas of bone damage seen on x-rays indicate an advanced stage of multiple myeloma.
- The amount of hemoglobin in the blood: Hemoglobin is the substance in red blood cells that carries oxygen. Low hemoglobin levels indicate that the myeloma cells occupy much of the bone marrow and that not enough space is left for the normal marrow cells that produce red blood cells.

This system uses these factors to divide myeloma into 3 stages. Stage I indicates the smallest amount of tumor, and stage III indicates the largest amount of tumor:

## **Stage I**

A relatively small number of myeloma cells are found. All of the following features must be present:

- Hemoglobin level only slightly below normal (still above 10 g/dL)
- Bone x-rays appear normal or show only 1 area of bone damage
- Normal blood calcium levels (less than 12 mg/dL)
- Relatively small amount of monoclonal immunoglobulin in blood or urine

## **Stage II**

A moderate number of myeloma cells are present. Features are between stage I and stage III.

## **Stage III**

A large number of myeloma cells are found. One or more of the following features must be present:

- Low hemoglobin level (below 8.5 g/dL)
- High blood calcium level (above 12 mg/dL)
- 3 or more areas of bone destroyed by the cancer
- Large amount of monoclonal immunoglobulin in blood or urine

## **The International Staging System**

This system divides myeloma into 3 stages based only on the serum beta-2 microglobulin and serum albumin levels.

### **Stage I**

Serum beta-2 microglobulin is less than 3.5 (mg/L) and the albumin level is above 3.5 (g/L)

### **Stage II**

Neither stage I or III, meaning that either:

- The beta-2 microglobulin level is between 3.5 and 5.5 (with any albumin level),
- OR
- The albumin is below 3.5 while the beta-2 microglobulin is less than 3.5

### **Stage III**

Serum beta-2 microglobulin is greater than 5.5.

## Other factors that affect survival

### **Kidney function**

The blood creatinine (Cr) level shows how healthy the kidneys are. Kidneys eliminate this chemical from the body. When they are damaged by the monoclonal immunoglobulin, blood creatinine levels rise, predicting a worse outlook.

### **Age**

Age is also important. In the studies of the international staging system, older people with myeloma do not live as long.

### **Labeling index**

The *myeloma cell labeling index*, sometimes called the *plasma cell labeling index*, indicates how fast the cancer cells are growing. This test is done in specialized labs, using myeloma cells from bone marrow samples. A high labeling index can predict a more rapid accumulation of cancer cells and a worse outlook.

### **Chromosome studies**

The bone marrow may be sent for tests to look at the chromosomes in the malignant cells. Certain chromosome changes can indicate a poorer outlook. For example, changes in chromosome 13 will lower the chances for survival. Another genetic abnormality that predicts a poor outcome is an exchange of material from chromosomes 4 and 14. This is called a *translocation*.

## Survival rates by stage

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some patients with cancer may want to know the survival statistics for people in similar situations, while others may not find the numbers helpful, or may even not want to know them.

Median survival refers to the time it took for half of the patients to die. By definition, half the patients lived longer than the median survival. It is important to remember that the median is just a kind of average used by researchers. No one is "average" and many people have much better outcomes than the median.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any particular person's case. Many other factors can affect a person's outlook, such as those discussed in the next section. Your doctor can tell you how the numbers below may apply to you, as he or she is familiar with the aspects of your particular situation.

The numbers below are the approximate overall median survival for the International Staging System stages. These times are measured from the point that treatment, usually chemotherapy, first started. Many patients, such as those with indolent or smoldering myeloma, have a good deal of time after diagnosis before treatment is started. Also, these patients were treated anywhere from 5 to 25 years ago. Treatment since then has improved considerably and modern results are likely to be better.

International Staging System Stage	Median Survival
Stage I	62 months
Stage II	44 months
Stage III	29 months

## How is multiple myeloma 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.*

After multiple myeloma is found and staged, your cancer care team will discuss treatment options with you. You should take a reasonable amount of time to think about all of the choices. Seeking a second opinion can provide more information and help you feel more confident about the chosen treatment plan. Some insurance companies require a second opinion before they will agree to pay for certain treatments.

## Chemotherapy and other drugs for multiple myeloma

Chemotherapy (chemo) is the use of drugs to destroy or control cancer cells. These drugs can be taken by mouth or given in a vein or a muscle. They enter the bloodstream and reach all areas of the body, making this treatment useful for cancers such as multiple myeloma that often spread widely.

Many different types of drugs are used to treat multiple myeloma.

## **Traditional chemo**

Chemotherapy drugs that may be used to treat multiple myeloma include melphalan, vincristine, cyclophosphamide, carmustine, and doxorubicin (and liposomal doxorubicin). Combinations of these drugs are more effective than any single drug. Sometimes these drugs are combined with other types of drugs like corticosteroids or immunomodulating agents.

## **Corticosteroids**

Corticosteroids are an important part of the treatment of multiple myeloma and can be used alone or combined with other drugs. Corticosteroids also help decrease the nausea and vomiting that other chemotherapy may cause. These drugs have side effects for patients including high blood sugar, increased appetite, and problems sleeping. When used for a long time, corticosteroids also suppress the immune system. This leads to an increased risk of serious infections. Most of these side effects go away with time after the drug is stopped. The drugs most often used in treating myeloma are dexamethasone and prednisone.

## **Immunomodulating agents**

**Thalidomide:** The drug thalidomide was first used as a sedative. When it was found to cause birth defects, it was taken off the market. Later, it became available again as a treatment for multiple myeloma. Side effects of thalidomide include drowsiness, fatigue, severe constipation, and neuropathy (painful nerve damage). The neuropathy can be severe, and may not go away after the drug is stopped. There is also an increased risk of serious blood clots (that start in the leg and can travel to the lungs). Because thalidomide causes severe birth defects if taken during pregnancy, this drug can only be obtained through a special program run by the drug company that makes it.

**Lenalidomide** (Revlimid<sup>®</sup>) is a newer drug that is similar to thalidomide. It works well in multiple myeloma. The most common side effects of lenalidomide are thrombocytopenia (low platelets) and low white blood cell counts. It can also cause painful nerve damage. The risk of blood clots is not as high as that seen with thalidomide, but it is still increased. Like thalidomide, access to lenalidomide is also tightly controlled out of concern about possible serious birth defects.

## **Other drugs**

Bortezomib (Velcade<sup>®</sup>) is a newer type of drug known as a proteasome inhibitor. It works by stopping enzyme complexes (proteasomes) in cells from breaking down proteins important for keeping cell division under control. It appears to affect tumor cells more than normal cells, but it is not without side effects.

Common side effects of this drug include nausea and vomiting, tiredness, diarrhea, constipation, decreased platelet blood count (causing easier bruising and bleeding), fever,

and decreased appetite. Bortezomib can also cause peripheral neuropathy (numbness or tingling in the arms and legs).

## **Drug treatment**

These drugs can be used alone or in combination. Often different classes of drugs are combined for treatment. For example:

- Melphalan and prednisone (MP), with or without thalidomide or bortezomib
- Vincristine, doxorubicin (Adriamycin<sup>®</sup>), and dexamethasone (called VAD)
- Thalidomide (or lenalidomide) and dexamethasone
- Bortezomib and dexamethasone, with or without doxorubicin or thalidomide
- Liposomal doxorubicin, vincristine, dexamethasone

The choice and dose of drug therapy depend on many factors, including the stage of the cancer and the age and kidney function of the patient. If a stem cell transplant is planned, most doctors avoid using a drug like melphalan that can damage the bone marrow.

## **Side effects**

Chemotherapy drugs kill cancer cells but can also damage normal cells. Careful attention is given to avoid or reduce the side effects of chemotherapy. These side effects depend on the type and dose of drugs given and the length of time they are taken. Common side effects of chemotherapy include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea, and vomiting
- Low blood counts

Chemotherapy often leads to low blood counts, which can cause the following:

- Lowered resistance to infection (low white blood cell counts)
- Easy bruising or bleeding (low blood platelets)
- Fatigue (low red blood cells).

Most side effects are temporary and go away after treatment is finished.

If you have side effects, your cancer care team can suggest steps to ease them. For example, drugs can be given along with the chemotherapy to prevent or reduce nausea and vomiting.

In addition to these temporary side effects, some chemotherapy drugs can permanently damage certain organs such as the heart or kidneys. These possible risks are carefully balanced against their benefits, and the health of these organs is carefully monitored during treatment. If serious organ damage occurs, the drug that caused it is stopped and replaced with another.

## Bisphosphonates for multiple myeloma

Myeloma cells can cause bone to dissolve, weaken, and even break. Drugs called bisphosphonates can help bones stay strong by slowing down this process.

The standard bisphosphonates for treating bone problems in people with myeloma are pamidronate (Aredia<sup>®</sup>) and zoledronic acid (Zometa<sup>®</sup>). These drugs are given intravenously (into a vein). Most patients are treated once a month at first, but they may be able to be treated less often later on if they are doing well. Treatment with a bisphosphonate helps prevent further bone damage in multiple myeloma patients.

Bisphosphonate treatment does have a rare but serious side effect called osteonecrosis of the jaw (ONJ). Patients complain of pain and doctors find that part of the jaw bone has died. This can lead to an open sore that does not heal. It can also lead to loss of teeth in that area. The jaw bone can also become infected. Doctors aren't sure why this happens or how best to prevent it. The only factor that seems to increase the risk of this problem is having jaw surgery or having a tooth removed. These procedures should be avoided while a patient is on bisphosphonate therapy. Many doctors recommend that patients have a dental checkup before starting treatment. That way, any dental problems can be taken care of before starting the drug. If ONJ does occur, the doctor will stop the bisphosphonate treatment.

One way to avoid these dental procedures is to maintain good oral hygiene by flossing, brushing, making sure that dentures fit properly, and having regular dental checkups. Any tooth or gum infections should be treated promptly. Dental fillings, root canal procedures, and tooth crowns do not seem to lead to ONJ.

## Radiation therapy for multiple myeloma

Radiation therapy uses focused high-energy x-rays or particles that penetrate the tissues of the body to reach and destroy cancerous cells. Radiation may be used to treat areas of bone damaged by myeloma that have not responded to chemotherapy and are causing pain. It is also the most common treatment for solitary plasmacytomas.

If myeloma severely weakens the vertebral (back) bones, these bones can collapse and put pressure on the spinal cord and spinal nerves. Symptoms include a sudden change in sensation (such as numbness or tingling), sudden weakness of leg muscles, or sudden problems with urination or moving the bowels. This is a medical emergency; patients with these symptoms should call their doctor right away. Prompt treatment with radiation therapy and/or surgery is often needed to prevent paralysis.

The type of radiation therapy most often used to treat multiple myeloma or solitary plasmacytoma is called *external beam radiation therapy*. For this type, the radiation is aimed at the cancer from a machine outside the body. Having radiation therapy is much like having a diagnostic x-ray except that each treatment lasts longer, and the course of treatment may continue for several weeks.

## Surgery for multiple myeloma

Although surgery is sometimes used to remove single plasmacytomas, it is rarely used in treating multiple myeloma. When spinal cord compression causes paralysis, severe muscle weakness, or numbness, emergency surgery may be needed. Non-emergency (elective) surgery to attach metal rods or plates can help support weakened bones and may be needed to prevent fractures.

## Biologic therapy for multiple myeloma

Biologic therapy uses proteins that are normally found in the body to fight disease, even cancer.

*Interferon* is a hormone-like substance released by some white blood cells and bone marrow cells. When given as a drug, it can slow the growth of myeloma cells. Interferon is sometimes given to patients who have been treated with chemotherapy so that the myeloma is in remission. Interferon seems to prolong remission. This drug can cause side effects that include fatigue and other symptoms similar to those from a flu infection. Some patients have trouble tolerating this, but overall the benefits of longer remission and fewer myeloma symptoms may outweigh these side effects.

*Erythropoietin* is a drug that can help correct anemia from low red blood cells and reduce the need for blood transfusions in some patients who are getting chemotherapy. But the FDA warns that some patients with lymphoid cancers, such as multiple myeloma, had shorter survival or their cancers re-grew when they used this type of drug.

## Stem cell transplant for multiple myeloma

This has become a standard treatment for younger myeloma patients in otherwise good health. Many centers are using this treatment for older patients as well. Several studies have shown that this treatment increases survival compared to standard chemotherapy.

The first step is to treat the myeloma to reduce the amount of cancer in a patient's body. Many different drug combinations can be used (see the section, "Chemotherapy and other drugs").

There are 2 types of stem cell transplant (SCT): autologous and allogeneic.

### **Autologous stem cell transplant**

This type of transplant uses the patient's own blood-forming stem cells. These transplants are fairly safe and have a low risk of serious complications. To collect the patient's stem cells, often the drug cyclophosphamide and a white blood cell stimulating drug are given. Then blood-forming stem cells are removed from the patient's blood by a process called *leukapheresis*. In this process, blood is removed from the patient or donor, the stem cells are separated by a machine, and then the blood is returned to the patient. In some patients, the stem cells come from their bone marrow.

The stem cells are preserved by being frozen while the patient receives high-dose chemotherapy. This chemotherapy destroys almost all the cells in the patient's bone marrow. This includes the blood-forming stem cells as well as plasma cells. After the chemo, the frozen stem cells are given back to the patient. Stem cells are given IV (in a vein) like a blood transfusion. They travel to the bone marrow and start to grow and make new blood cells.

The chemotherapy can cause many problems. Many patients have high fevers from infections. These are treated with IV antibiotics. Another common problem is mouth sores which can be very painful. Morphine may be given to reduce the pain. The chemotherapy also kills cells in the intestines, which may lead to cramps and diarrhea. Also, since bone marrow is unable to make blood cells, transfusions of red blood cells and platelets are often needed. When the new stem cells start making new blood cells, the transfusions are no longer needed.

Because this type of transplant is fairly safe with a low risk of serious complications, it can be used in elderly patients. Unfortunately, even high-dose chemotherapy doesn't kill all the myeloma cells, so the myeloma eventually comes back. Some patients are free of myeloma for quite a long time, but they aren't really cured.

Some doctors are recommending that patients have 2 autologous transplants, 6 to 12 months apart. This approach is called *tandem transplant*. Studies show that this may help patients live longer than a single transplant. The drawback, of course, is that it causes more side effects.

Autologous transplants are better than traditional chemo at treating myeloma and can help patients live longer. They are a standard part of myeloma treatment.

## **Allogeneic stem cell transplant**

This type of transplant has more risks than autologous transplants, and so it is used much less often to treat multiple myeloma. For this type of transplant, the stem cells come from someone else. The donor is usually a close relative (like a brother or sister). Less often, an unrelated donor is used, someone whose tissue type is closely matched to the patient. Allogeneic transplants are much riskier than autologous transplants, but they may be better at fighting the cancer. That is because transplanted (donor) cells may actually help destroy myeloma cells. This is called a *graft vs. tumor effect*. A patient must be fairly young and healthy to withstand the side effects of this kind of transplant (most myeloma patients are elderly). The transplant also requires a donor matched to the patient. These factors tend to limit the use of this type of transplant in myeloma.

**Non-myeloablative stem cell transplant:** This is a type of allogeneic transplant in which low doses of certain kinds of chemotherapy drugs are used. The chemo doesn't completely wipe out the bone marrow, but it does enough to let the transplanted stem cells take hold. Then it is hoped that the new cells will kill the myeloma cells (*graft vs. tumor effect*). Because lower doses of chemo are used, this type of transplant is sometimes called a *mini transplant*. The lower chemo doses mean that this type of transplant can be done on older patients.

## Plasmapheresis for multiple myeloma

In this treatment, blood is removed from a vein. The blood cells are separated from the blood plasma (liquid part of the blood) and then returned to the patient. The discarded plasma contains the abnormal antibody protein produced by the myeloma cells. It can be replaced with a salt solution and plasma from donors.

Plasmapheresis is helpful when certain myeloma proteins build up, thicken the blood, and interfere with circulation (called *hyperviscosity*). Although plasmapheresis can relieve some symptoms, it does not kill the myeloma cells. For that reason, plasmapheresis is often followed by chemo or some other type of drug treatment to kill the cells that make the protein.

## Clinical trials for multiple myeloma

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](http://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](http://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 multiple myeloma

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 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.

# Treatment options for multiple myeloma by stage

## **Solitary plasmacytomas**

These are often treated with radiation therapy. If the plasma cell tumor is not in a bone, it may be removed with surgery. Chemo is only used if multiple myeloma develops.

## **Early myeloma**

Early myeloma includes smoldering myeloma and stage I disease. Patients with early myeloma can do well for years without treatment. Starting treatment early does not seem to help them live longer. These patients are often watched closely without starting chemo. Patients with bone disease from myeloma are often started on a bisphosphonate.

## **Advanced myeloma**

Patients whose myeloma is stage II or higher are often given drug therapy. The drugs chosen depend on the patient's health (including their kidney function) and whether or not a transplant is planned. (These drugs are discussed in more detail in the section, "Chemotherapy and other drugs.")

If the patient is not expected to have a transplant, chemotherapy with melphalan and prednisone (MP) may be used. Sometimes thalidomide is given with MP, but other drug combinations can be used as well.

Because it can have long-term effects on the bone marrow, MP is used less often if a transplant is planned. The combination of vincristine, doxorubicin (Adriamycin), and dexamethasone (VAD) once was often used before transplant, but now newer drugs are used more often. Most often a combination containing bortezomib (Velcade), thalidomide, or lenalidomide (Revlimid) plus dexamethasone is used.

Bisphosphonate treatment is often started along with chemo. If the areas of damaged bone continue to cause symptoms, radiation therapy may be used.

For an autologous transplant, stem cells are collected from the patient. Often this means treatment with chemo followed by daily doses of a drug that signals the body to make white blood cells. The stem cells are removed from the blood with a pheresis machine and stored until they are needed. Then, high doses of chemo are given to kill the myeloma cells. Most often, melphalan is the chemo drug used. Later, the patient gets back their own stem cells. The transplant may be repeated in 6 to 12 months if myeloma cells are still present.

Another possible treatment is allogeneic SCT. This may be able to cure the myeloma, but it has more severe side effects than the autologous transplant. Because they are so toxic, allogeneic transplants are only offered to younger patients who are otherwise in good health. The non-myeloablative allogeneic transplant may be a better option for some patients, such as those who are older.

Some patients are given additional cycles of treatment after transplant. This, called *consolidation*, increases the chance for a complete response (where signs and symptoms of the disease go away). This may be followed by long-term treatment with thalidomide or bortezomib. This is known as *maintenance treatment*, and helps delay the return of the myeloma, but it can cause serious side effects. The use of consolidation and maintenance treatment after standard drug therapy (without stem cell transplant) is being studied.

Many drug combinations can be useful in treating myeloma. If a drug stops working (or the myeloma comes back), others can be tried.

## More treatment information for multiple myeloma

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 some of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. They are available on the NCCN Web site ([www.nccn.org](http://www.nccn.org)).

The NCI provides treatment information by telephone (1-800-4-CANCER) and its Web site ([www.cancer.gov](http://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](http://www.cancer.gov).

## What should you ask your doctor about multiple myeloma?

As you deal with your cancer and the process of treatment, you need to have frank, open discussions with your cancer care team. You should ask any question on your mind. Among the questions you might want to ask are

- What is my stage of multiple myeloma? What does the staging mean to me?
- What treatment choices do I have?
- Based on what you've learned about my cancer, how long do you think I'll survive?
- What side effects can I expect from my treatment?
- How long will it take me to recover from treatment?
- When can I go back to work or resume other activities after treatment?
- What are the chances that my cancer will recur?
- Does one type of treatment reduce the risk of recurrence more than another?
- What should I do to be ready for treatment?
- Should I get a second opinion?

You will no doubt have other questions about your personal situation. Be sure to write down your questions so that you remember to ask them during each visit with your cancer care team. Also keep in mind that doctors are not the only ones who can provide you with information. Other health care professionals, such as nurses and social workers, may have the answers you seek.

# What happens after treatment for multiple myeloma?

For most people, multiple myeloma never goes away completely. These people may get regular treatments with chemotherapy and other drugs, radiation therapy, or other therapies to try to help keep the cancer in check. Although there may be a time when they stop treatment for a time, most patients never really finish treatment. Follow up is needed for the doctor to know when to start treatment again. This can help prevent problems that can interfere with daily life.

Learning to live with cancer that does not go away can be difficult and very stressful. Our document, *When Cancer Doesn't Go Away*, talks more about this.

## Follow-up care

During and after treatment, it is very important to keep all follow-up appointments. During these visits, your doctors will ask about symptoms, examine you, and order blood tests or imaging studies such as CT scans or x-rays. Follow-up is needed to see if more treatment is needed, and to check for any side effects. This is the time for you to talk to your cancer care team about any changes or problems you notice and any questions or concerns you 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 cancer 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. Myeloma is rarely curable at this time. It may go away for a while, but the disease is likely to come back again. When that happens, the last thing you want is to have to worry about paying for treatment. The American Cancer Society document, *When Your Cancer Comes Back: Cancer Recurrence* gives you information on how to manage and cope with this phase of your treatment.

## Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know anything about 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 the following information handy:

- A copy of your pathology report(s) from any biopsies or surgeries
- Copies of your lab results
- If you had surgery, a copy of your operative report(s)
- If you were in the hospital, a copy of the discharge summary that doctors prepare when patients are sent home
- If you had radiation, a copy of the treatment summary

- 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 multiple myeloma

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 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 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 multiple myeloma 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 when your cancer was first found 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, as you feel 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 multiple myeloma stops working**

If cancer keeps growing or comes back after one kind of treatment, it is possible that another treatment plan might still cure the cancer, or at least shrink it enough to help you live longer and feel better. But when a person has tried many different treatments and the cancer has not gotten any better, the cancer tends to become resistant to all 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 cancer — 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 many cases, your doctor can estimate how likely it is the cancer will respond to treatment you are considering. For instance, the doctor may say that more chemo or radiation 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 multiple myeloma research and treatment?**

Important research into multiple myeloma is being done in many university hospitals, medical centers, and other institutions around the country. Each year, scientists find out more about what causes the disease and how to improve treatment. Many new drugs are being tested.

Researchers have discovered that bone marrow-support tissues called *stromal cells* produce interleukin-6 (IL-6). Because IL-6 is a strong growth factor for multiple myeloma cells and eventually results in bone destruction, some current research efforts are focused on developing ways to block the function of IL-6.

Another growth factor called RANKL has been discovered. It stimulates the cells responsible for dissolving bone. RANKL appears to be made in larger than normal amounts in the bone marrow of people with multiple myeloma. A drug called *denosumab*

that blocks RANKL was studied in patients with multiple myeloma. Although early studies were promising, in later studies multiple myeloma patients treated with denosumab were more likely to die than those treated with bisphosphonates.

A form of arsenic, arsenic trioxide, is also being tested as a treatment for myeloma.

Drugs that block blood vessel growth are also being studied in myeloma patients. Another type of drug being tested in myeloma blocks an important molecule in tumor growth called farnesyl transferase.

Research is also being directed toward improving transplants. A newer approach is to follow an autologous (self) transplant with an allogeneic one (donor). So far, results have been mixed, and more studies are needed.

An entirely new test called *gene expression profiling* has developed in the last several years. This test may be able to tell if and when a patient with multiple myeloma will need to have chemotherapy. Much more work lies ahead though, before this test can be used routinely.

## **Additional resources for multiple myeloma**

### **More information from your American Cancer Society**

We have some related information that may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

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

Bone Marrow and Peripheral Blood Stem Cell Transplant

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

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

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

When Cancer Doesn't Go Away

### **Books**

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

Cancer Caregiving: A to Z

Eating Well, Staying Well During and After Cancer

What Helped Get Me Through

## National organizations and web sites\*

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

### **International Myeloma Foundation**

Toll-free number: 1-800-452-2873 (1-800-452-CURE)

Web site: [www.myeloma.org](http://www.myeloma.org)

### **The Leukemia & Lymphoma Society**

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

Web site: [www.lls.org](http://www.lls.org)

### **Multiple Myeloma Research Foundation**

Telephone number: 203-229-0464

Web site: [www.multiplemyeloma.org](http://www.multiplemyeloma.org)

### **National Cancer Institute**

Toll-free number: 1-800-422-6237 (1-800-4-CANCER)

TTY: (800) 332-8615

Web site: [www.cancer.gov](http://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](http://www.cancer.org).

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For additional assistance please contact your American Cancer Society  
1 · 800 · ACS-2345 or [www.cancer.org](http://www.cancer.org)