Multiple Myeloma

What is multiple myeloma?

Cancer starts when cells in the body begin to grow out of control. Cells in nearly any part of the body can become cancer, and can spread to other areas of the body. To learn more about how cancers start and spread, see *What Is Cancer?*

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 made up 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. The major types of lymphocytes are 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 are in many areas of the body, such as lymph nodes, the bone marrow, the intestines, and the bloodstream. Plasma cells, however, are mainly found in the bone marrow. Bone marrow is the soft tissue inside some hollow bones. In addition to plasma cells, normal bone marrow has cells that make the different normal blood cells.

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 someone has only a single plasma cell tumor, the disease is called an *isolated* (or *solitary*) *plasmacytoma*. If someone has more than one plasmacytoma, they have *multiple myeloma*.

Multiple myeloma is characterized by several features, including:

Low blood counts

In multiple myeloma, the overgrowth of plasma cells in the bone marrow can crowd out normal blood-forming cells, leading to low blood counts. This can cause anemia – a shortage of red blood cells. People with anemia 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.

Bone and calcium problems

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 can also raise calcium levels in the blood. (Problems caused by high calcium levels are discussed in the section "How is multiple myeloma diagnosed?")

Infections

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 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's because the myeloma cells are just many copies of the same plasma cell – all making copies of the same exact (or monoclonal) antibody.

Kidney problems

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

Monoclonal gammopathy

Having many copies of the same antibody is known as a *monoclonal gammopathy*. This condition can be found with a blood test. Although people with multiple myeloma have a monoclonal gammopathy, not everyone with monoclonal gammopathy has multiple myeloma. It can also occur in other diseases, such as Waldenstrom macroglobulinemia and some lymphomas. It can also occur in a disorder known as *monoclonal gammopathy of undetermined significance (MGUS),* which does not cause problems like multiple myeloma does. However, some people with MGUS will eventually go on to develop multiple myeloma or other diseases.

Light chain amyloidosis

Antibodies are made up of protein chains joined together – 2 short light chains and 2 longer heavy chains. In light chain amyloidosis, abnormal plasma cells make too many light chains. These light chains can deposit in tissues, where they build up. This accumulation of light chains can lead to an abnormal protein in tissues known as amyloid. The buildup of amyloid in certain organs can lead them to enlarge and not work well. For example, when amyloid builds up in the heart, it can cause an irregular heart beat and cause the heart to enlarge and get weaker. A weak heart can lead to a condition called *congestive heart failure*, with symptoms like shortness of breath and swelling in the legs. Amyloid in the kidneys can cause them to work poorly. This may not cause symptoms early on, but the poor kidney function may be found on blood tests. If it gets worse, amyloid in the kidney can lead to kidney failure. See the section "Signs and symptoms of multiple myeloma" for more information about the signs and symptoms of light chain amyloidosis.

Other names for light chain amyloidosis include *AL* and *primary amyloidosis*. This is sometimes considered a separate disease from multiple myeloma, but because treatment is often similar to that of myeloma, we will discuss it in this document.

Light chain amyloidosis is only one of the diseases where amyloid builds ups and causes problems. Amyloidosis can also be caused by a genetic (hereditary) disease called *familial amyloidosis*. Long-standing (chronic) infection and/or inflammation can also cause amyloidosis. This is known as *secondary* or *AA amyloidosis*. This document does not talk about these other kinds of amyloidosis.

Monoclonal gammopathy of undetermined significance

In monoclonal gammopathy of undetermined significance (MGUS), abnormal plasma cells produce many copies of the same antibody (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's most often found when a routine blood test finds a high level of protein in the blood and further testing shows the protein is a monoclonal antibody. 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.

Some people with MGUS will eventually develop multiple myeloma, lymphoma, or amyloidosis. Each year, about 1% of people with MGUS develops one of these diseases. The risk 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 that of normal plasma cells. This suggests that these cells are

truly malignant, not just slow growing. Because people with MGUS are generally 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* plasmacytoma.

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 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 143 (0.7%).

The American Cancer Society's estimates for multiple myeloma in the United States for 2016 are:

- About 30,330 new cases will be diagnosed (17,900 in men and 12,430 in women).
- About 12,650 deaths are expected to occur (6,430 in men and 6,220 in women).

Visit the American Cancer Society's Cancer Statistics Center for more key statistics.

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 lung cancer 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 as people age. Less than 1% of cases are diagnosed in people younger than 35. Most people diagnosed with this cancer are at least 65 years old.

Gender

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

Race

Multiple myeloma is more than twice as common in African Americans than in white Americans. The reason is not known.

Radiation

People who were exposed to radiation from an atomic bomb blast had a higher risk of multiple myeloma. Exposure to lower levels of radiation may also increase the risk of multiple myeloma. At most, this accounts for a very small number of cases.

Family history

Multiple myeloma seems 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

Studies looking at workplace exposures and multiple myeloma risk have found no clear links.

Obesity

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

Having 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 make plasma cells 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 make cells die at the right 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 *MYC*) develop early in the course of plasma cell tumors. Changes in other oncogenes (such as the *RAS* genes) are more often found in myeloma cells in the bone marrow after treatment, and changes in tumor suppressor genes (such as the gene for *p53*) are associated with spread to other organs.

Myeloma cells also show abnormalities in their chromosomes. In human cells, DNA is packaged into chromosomes. Although normal human cells contain 46 chromosomes, some cancer cells may have extra chromosomes (called a *duplication*) or have all or part of a chromosome missing (called a *deletion*). 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.

In about half of all people with myeloma, part of one chromosome has switched with part of another chromosome in the myeloma cells. This is called a *translocation*. When this occurs in a crucial area next to an oncogene, it can turn the oncogene 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. Excessive production of IL-6 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 are known for the majority of cases. For example, smoking causes most lung cancers. This provides an opportunity for prevention. For other cancers, such as cervical cancer, pre-cancers can be detected early by a screening test (such as the Pap test) and treated before they develop into an invasive cancer.

With multiple myeloma, few cases are linked to risk factors that can be avoided. There is no known way to prevent multiple myeloma from developing in those people with monoclonal gammopathy of undetermined significance or solitary plasmacytomas.

Can multiple myeloma be found early?

It’s difficult to diagnose multiple myeloma early. Often, multiple myeloma causes no symptoms until it reaches an advanced stage. Sometimes, it might 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.

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

Such as:

- Pain, which can be in any bone, but is most often in the back, the hips, and skull
- Bone weakness, either all over (osteoporosis), or where there is a plasmacytoma
- Broken bones (fractures), sometimes from only a minor stress or injury

Low blood counts

Shortages of red blood cells, white blood cells, and blood platelets are common in multiple myeloma.

- 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 levels of calcium

High levels of calcium in the blood (called *hypercalcemia*) can cause:

- Extreme thirst, leading to drinking a lot of fluids
- Urinating (peeing) a lot
- Dehydration
- Kidney problems and even kidney failure

- Severe constipation,
- Abdominal (belly) pain
- Loss of appetite
- Weakness
- Feeling drowsy
- Confusion

If the level of calcium gets high enough, you can even lapse into a coma.

Nervous system symptoms

If myeloma weakens the bones in the spine, they can collapse and press on spinal nerves. This is called *spinal cord compression* and can cause

- Sudden severe back pain,
- Numbness, most often in the legs
- Muscle weakness, most often in the legs.

This is a medical emergency and you should contact your doctor right away or go to the emergency room.

Nerve damage

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

Hyperviscosity

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
- Symptoms of a stroke, like weakness on one side of the body and slurred speech

Patients with these symptoms should call their doctor. Removing the protein from the blood using a procedure called *plasmapheresis* can rapidly reverse this problem. (Note: This is not something that can be treated with drugs known as “blood thinners.”)

Kidney problems

Myeloma protein can damage the kidneys. Early on, this doesn't cause any symptoms, but signs of kidney damage may be seen on a blood test or a urine 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
- Shortness of breath
- Itching
- Leg swelling.

Infections

Myeloma patients are much more likely to get infections. When someone with myeloma gets an infection, they may be 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.

Signs and symptoms of light chain amyloidosis

Patients with amyloidosis (discussed in the section "What is multiple myeloma?") can have some of the same problems as patients with myeloma, such as kidney problems and nerve damage. They also can have other problems, such as:

- **Heart problems**: Some patients develop an irregular heartbeat. The heart may enlarge and become weaker. In some people, the heart becomes so weak that fluid builds up in the lungs, making them feel short of breath. Fluid may also build up in the legs and feet (*edema*). This is called *congestive heart failure*.
- **Enlarged liver and spleen**: The person may feel the liver below the right ribs and the spleen below the left ribs. When these get large they can press on the stomach and so the person feels full after eating only a small amount of food.
- **Enlarged tongue**: When amyloid builds up in the tongue it can get larger. This can lead to problems swallowing and problems breathing during sleep (sleep apnea).
- **Skin changes**: Such as changes in the color or texture, easy bruising, and bleeding into the skin around the eyes ("raccoon eyes")
- **Diarrhea**
- **Carpal tunnel syndrome**: Which causes numbness and weakness in the hands.

Tests to find multiple myeloma

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.

Laboratory tests

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 there are too many myeloma cells in the bone marrow, some of these blood cell levels will be low. The most common finding is a low red blood cell count (anemia).

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 (all the exact same antibody). *Serum protein electrophoresis* (SPEP) is a test that measures the immunoglobulins in the blood and can find a monoclonal immunoglobulin. Then, another test, such as *immunofixation* or *immunoelectrophoresis*, is used to determine the exact type of abnormal antibody (IgG or some other type). Finding a monoclonal immunoglobulin in the blood may be the first step in diagnosing 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, known as *Bence-Jones protein*, is the part of the immunoglobulin called the *light chain*. The tests used for finding a monoclonal immunoglobulin in urine are called *urine protein electrophoresis* (UPEP) and *urine immunofixation*. These are done most often on urine that has been collected over a 24-hour period, not just on a routine urine sample.

Free light chains

This test measures the amount of light chains in the blood, being a possible sign of myeloma or light chain amyloidosis.

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.

This test also measures the *light chain ratio* which is used to see if one type of light chain is more common than the other. There are 2 kinds of light chains: kappa and lambda. Normally, they are present in equal amounts in the blood, giving a ratio of 1 to 1. If one kind of light chain is more common than the other, the ratio will be different, which can be a sign of myeloma.

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 mean the disease is more advanced and maybe a worse prognosis.

Blood chemistry tests

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

BUN and 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 used to check the bone marrow is called a *bone marrow biopsy* and *aspiration*. It can be done either at the doctor's office or at the hospital.

In bone marrow aspiration, the back of the pelvic bone is numbed with local anesthetic. Then, 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. Patients may feel some pressure during the biopsy, but it usually isn't painful. 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 look at the bone marrow tissue under a microscope 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 the immunohistochemistry test, the flow cytometry 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 make them 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 lets doctors evaluate the chromosomes (long strands of DNA) in normal bone marrow cells and myeloma cells. Some myeloma cells may have too many chromosomes, too few chromosomes, or other chromosome abnormalities. The cells are looked at under a microscope to see if the chromosomes have any changes, such as translocations (where part of one chromosome has broken off and is now attached to another chromosome) or deletions (where part or all of a chromosome is missing), as sometimes happens in multiple myeloma. Finding these changes can sometimes help in predicting a person’s prognosis.

Cytogenetic testing usually takes about 2 to 3 weeks because the cells must grow in lab dishes for a couple of weeks before their chromosomes are ready to be seen 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 and deletions) 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 as well as bone marrow samples. It's very accurate and because the cells don't have to grow in a dish first, results are often available within a couple of days.

Biopsy tests for amyloid

Amyloid can build up in any tissue, and a biopsy of any of these may be able to diagnose this disease. Sometimes it can be seen on a bone marrow biopsy. The biopsy done most often to look for amyloid uses a needle to remove some fat from the wall of the abdomen (belly). This is after the skin over the biopsy site is numbed with medicine. A doctor uses a special stain on the fat removed to look for amyloid.

Because amyloid often affects the heart and kidneys, they may also be biopsied to look for amyloid. This is rarely needed to find out if a patient has light chain amyloidosis, but it is sometimes done in someone with amyloid if it isn't clear that their heart or kidney problems are caused by the amyloid or some other problem.

Other tests are often done as well, to help confirm that the patient has light chain amyloidosis and not some other kind. These include a bone marrow biopsy, free light chains, and electrophoresis of the urine (these were discussed earlier in this section).

Other biopsy tests

If an area looks abnormal on an x-ray, a biopsy may be needed to confirm that it's 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 abnormal area (tumor) is deep inside the body, the needle can be guided while it's watched on a computed tomography (CT) scan (see discussion of imaging tests later in this section). The main advantage of FNA is that it doesn't 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 tests

Bone x-rays

X-rays can detect bone destruction caused by the myeloma cells. 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 scans

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 rotates around you, taking many pictures of the part of your body being studied. 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.

A CT scanner has been described as a large donut, with a narrow table in the middle opening. You will need to lie still on the table while the scan is being done. CT scans take longer than regular x-rays, and you might feel a bit confined by the ring while the pictures are being taken.

You might be asked to drink 1 to 2 pints of a solution of contrast material before the test. This helps outline the intestine so that it is not mistaken for tumors. You might 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 contrast material 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 contrast agents damage the kidneys of people with myeloma.

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

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. Because MRI can find plasmacytomas that can't be seen on regular x-rays, they can be helpful if the patient has pain in a bone but nothing abnormal is seen on the x-ray. 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 are placed inside tunnel-like equipment, which is confining and can upset some people. The machine also makes a thumping noise that could be disturbing. Some places provide headphones with music to block this out.

Positron emission tomography scans

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. Like MRI scans, PET scans can find plasmacytomas that can't be seen on regular x-rays, so they are helpful if the patient has pain in a bone but the x-ray result is negative.

Echocardiogram

Amyloidosis often affects the heart, so if your doctor diagnoses or suspects you have this disorder, an echocardiogram may be ordered. This test uses sound waves to look at the heart muscle and how well it's working. The echocardiogram can see if the heart size is normal and if it is pumping normally. It also is especially helpful if amyloid is suspected because amyloid in the heart muscle can change the appearance of the heart muscle.

Diagnosing multiple myeloma from test results

Although multiple myeloma is often diagnosed based on test results (tests for multiple myeloma were discussed in the previous section), the patient's symptoms and the doctor's physical examination of the patient are also important. A diagnosis of multiple myeloma requires either:

1. A plasma cell tumor (proven by biopsy) OR at least 10% of the cells in the bone marrow are plasma cells, AND at least one of the following:

- High blood calcium level
- Poor kidney function
- Low red blood cell counts (anemia)
- Holes in bones from tumor growth found on imaging studies
- An abnormal area in the bones or bone marrow on an MRI scan
- Increase in one type of light chains in the blood so that one type is 100 times more common than the other

OR

2. 60% or more plasma cells in the bone marrow

Smoldering myeloma

This term is used to mean early myeloma that is not causing any symptoms or problems. People with smoldering myeloma have some signs of multiple myeloma, such as any of the following

- Plasma cells in the bone marrow between 10 and 60%
- High level of monoclonal immunoglobulin (M protein) in the blood
- High level of light chains in the urine (also called Bence-Jones protein)

But they have normal blood counts, normal calcium levels, normal kidney function, no bone or organ damage, and no signs of amyloidosis. Smoldering myeloma often does not need to be treated right away.

Light chain amyloidosis

A diagnosis of light chain amyloidosis is made when the patient has both:

- Signs and symptoms of amyloidosis, and
- A biopsy that shows amyloid made up of light chains,

PLUS any of the following:

- Elevated free light chains in the blood,
- Elevated light chains in the urine (also called Bence-Jones protein),
- Abnormal plasma cells in the bone marrow

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 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 can be 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 carries oxygen in red blood cells. Low hemoglobin levels mean you are anemic and can indicate that the myeloma cells occupy much of the bone marrow and that not enough space is left for the normal marrow cells to make enough 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 is only slightly below normal (but still above 10 g/dL)
- Bone x-rays appear normal or show only 1 area of bone damage
- Calcium levels in the blood are normal (less than 12 mg/dL)
- Only a relatively small amount of monoclonal immunoglobulin is 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 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 3.5 (g/dL) or greater

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 5.5 or greater.

Factors other than stage 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 mean a poorer outlook. For example, loss of a copy of chromosome 13 is linked to a poorer outcome. Another genetic abnormality that predicts a poor outcome is an exchange of material from chromosomes 4 and 14. This is called a *translocation.* Having extra copies of a certain area on chromosome 1 (an amplification of 1q21) is also linked to a poorer outcome.

Survival rates by stage for multiple myeloma

Doctors often use survival rates 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 won't find the numbers helpful, or might not want to know them. If you decide that you don't want to know them, stop reading here and skip to the next section.

"Median survival" means the time it took for half of the patients in that group to die. By definition, half the patients lived longer than the median survival. It's important to remember that the median is just a kind of average researchers use. 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 your outlook, such as your age and general health, the

treatment you received, and how well your cancer responds to treatment. Your doctor is familiar with your situation and can tell you how the numbers below apply to you.

The numbers below are the approximate overall median survival using the International Staging System. These survival times are measured from the point that treatment, such as 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?

After multiple myeloma is found and staged, your cancer care team will discuss treatment options with you. The treatment for multiple myeloma may include:

- Chemotherapy and other drugs
- Bisphosphonates
- Radiation
- Surgery
- Stem cell transplant
- Plasmapheresis

It is important to discuss all of your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. It's also very important to ask questions if you're not sure about something. You can find some good questions to ask in the section "What should you ask your doctor about multiple myeloma?"

For information about some of the most common approaches used based on the extent of the disease, see the section "Treatment of multiple myeloma, by stage."

You should take a reasonable amount of time to think about all of the choices. Getting 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.

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-of-the art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service at 1-800-303-5691 for a list of studies that meet your medical needs, or see Clinical Trials to learn more.

Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your cancer or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used along with your regular medical care. Alternative treatments are used instead of a doctor's medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be dangerous.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision. See *Complementary and Alternative Medicine* to learn more.

Help getting through cancer treatment

Your cancer care team will be your first source of information and support, but there are other resources for help when you need it. Hospital- or clinic-based support services are an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, support groups, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained specialists on call 24 hours a day, every day.

The treatment information given here is not official policy of the American Cancer 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.

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

Chemo drugs that may be used to treat multiple myeloma include

- Melphalan
- Vincristine (Oncovin)
- Cyclophosphamide (Cytoxan)
- Etoposide (VP-16)
- Doxorubicin (Adriamycin)
- Liposomal doxorubicin (Doxil)
- Bendamustine (Treanda)

Combinations of these drugs are more effective than any single drug. Often these drugs are combined with other types of drugs like corticosteroids or immunomodulating agents (drugs that will change the patient's immune response).

Chemo side effects

Chemo drugs kill cancer cells but also can damage normal cells. They are given carefully 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:

- Increased risk of serious infection (from low white blood cell counts)

- Easy bruising or bleeding (from low blood platelets or *thrombocytopenia*)
- Feeling excessively tired or short of breath (from low red blood cells or *anemia*).

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 chemo to prevent or reduce nausea and vomiting.

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

Corticosteroids

Corticosteroids, such as dexamethasone and prednisone, are an important part of the treatment of multiple myeloma. They can be used alone or combined with other drugs as a part of treatment. Corticosteroids are also used to help decrease the nausea and vomiting that chemo may cause.

Common side effects of these drugs include

- High blood sugar
- Increased appetite and weight gain
- Problems sleeping
- Changes in mood (some people become irritable or “hyper”)

When used for a long time, corticosteroids also suppress the immune system. This leads to an increased risk of serious infections. They can also weaken bones.

Most of these side effects go away over time after the drug is stopped.

Immunomodulating agents

The way immunomodulating agents affect the immune system isn’t entirely clear. Three immunomodulating agents are used to treat multiple myeloma. The first of these drugs to be developed, thalidomide, caused severe birth defects when taken during pregnancy. Because the other immunomodulating agents are related to thalidomide, there’s concern that they could also cause birth defects. That’s why all of these drugs can only be obtained through a special program run by the drug company that makes them.

Because these drugs can increase the risk of serious blood clots, they are often given along with aspirin or a blood thinner.

Thalidomide (Thalomid) was first used decades ago as a sedative and as a treatment for morning sickness in pregnant women. 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 can include drowsiness, fatigue, severe constipation, and painful nerve damage (neuropathy). The neuropathy can be severe, and might 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.

Lenalidomide (Revlimid) is a similar to thalidomide. It works well in treating 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.

Pomalidomide (Pomalyst) is also related to thalidomide and is used to treat multiple myeloma. Some common side effects include low red blood cell counts (anemia) and low white blood cell counts. The risk of nerve damage is not as severe as it is with the other immunomodulating drugs, but it's also linked to an increased risk of blood clots.

Proteasome inhibitors

Proteasome inhibitors work by stopping enzyme complexes (proteasomes) in cells from breaking down proteins important for keeping cell division under control. They appear to affect tumor cells more than normal cells, but they are not without side effects.

Bortezomib (Velcade) was the first of this type of drug to be approved, and it's often used to treat multiple myeloma. It may be especially helpful in treating myeloma patients with kidney problems. It's injected into a vein (IV) or under the skin, once or twice a week.

Common side effects of this drug include nausea and vomiting, tiredness, diarrhea, constipation, fever, decreased appetite, and lowered blood counts. The platelet count (which can cause easier bruising and bleeding) and the white blood cell count (which can increase the risk of serious infection) are most often affected. Bortezomib can also cause nerve damage (peripheral neuropathy) that can lead to problems with numbness, tingling, or even pain in the hands and feet. Some patients develop shingles (herpes zoster) while taking this drug. To help prevent this, your doctor may have you take an anti-viral medicine (like acyclovir) while you take bortezomib.

Carfilzomib (Kyprolis) is a newer proteasome inhibitor that can be used to treat multiple myeloma in patients who have already been treated with bortezomib and an immunomodulating agent. It's given as an injection into a vein (IV), often in a 4 week cycle. To prevent problems like allergic reactions during the infusion, the steroid drug dexamethasone is often given before each dose in the first cycle.

Common side effects include tiredness, nausea and vomiting, diarrhea, shortness of breath, fever, and low blood counts. The blood counts most often affected are the platelet count (which can cause easier bruising and bleeding) and the red blood cell count (which can lead to tiredness, shortness of breath, and being pale). People on this drug can also

have more serious problems, such as pneumonia, heart problems, and kidney or liver failure.

Ixazomib (Ninlaro) is a proteasome inhibitor that is taken by mouth as a capsule, typically once a week for 3 weeks, followed by a week off. This drug is usually used after other drugs have been tried.

Common side effects of this drug include nausea and vomiting, diarrhea, constipation, rash, swelling in the hands or feet, back pain, and a lowered blood platelet count (which can cause easier bruising and bleeding). This drug can also cause nerve damage (peripheral neuropathy) that can lead to problems with numbness, tingling, or even pain in the hands and feet.

Histone deacetylase (HDAC) inhibitors

HDAC inhibitors are a group of drugs that can affect which genes are active inside cells. They do this by interacting with proteins in chromosomes called *histones*.

Panobinostat (Farydak) is an HDAC inhibitor that can be used to treat patients who have already been treated with bortezomib and an immunomodulating agent. It is taken as a capsule, typically 3 times a week for 2 weeks, followed by a week off. This cycle is then repeated.

Common side effects include diarrhea (which can be severe), feeling tired, nausea, vomiting, loss of appetite, swelling in the arms or legs, fever, and weakness. This drug can also affect blood cell counts and the levels of certain minerals in the blood. Less common but more serious side effects can include bleeding inside the body, liver damage, and changes in heart rhythm, which can sometimes be life threatening.

Monoclonal antibodies

Antibodies are proteins made by the body's immune system to help fight infections. Man-made versions, called *monoclonal antibodies*, can be designed to attack a specific target, such as a substance on the surface of myeloma cells.

Daratumumab (Darzalex) is a monoclonal antibody that attaches to the CD38 protein, which is found on myeloma cells. This is thought to both kill the cells directly and to help the immune system attack the cells. This drug is used mainly in patients who have already had several other treatments for their myeloma. It's given as an infusion into a vein (IV).

This drug can cause a reaction in some people while it is being given or within a few hours afterward, which can sometimes be severe. Symptoms can include coughing, wheezing, trouble breathing, tightness in the throat, a runny or stuffy nose, feeling dizzy or lightheaded, headache, rash, and nausea.

Other side effects can include fatigue, nausea, back pain, fever, and cough. This drug can also lower blood cell counts, which can increase the risk of infections and bleeding or bruising.

Elotuzumab (Empliciti) is a monoclonal antibody that attaches to the SLAMF7 protein, which is found on myeloma cells. This is thought to help the immune system attack the cells. This drug is used mainly in patients who have already had other treatments for their myeloma. It's given as an infusion into a vein (IV).

This drug can cause a reaction in some people while it is being given or within several hours afterward, which can sometimes be severe. Symptoms can include fever, chills, feeling dizzy or lightheaded, rash, wheezing, trouble breathing, tightness in the throat, or a runny or stuffy nose.

Other common side effects with this drug include fatigue, fever, loss of appetite, diarrhea, constipation, cough, nerve damage resulting in weakness or numbness in the hands and feet (peripheral neuropathy), upper respiratory tract infections (such as a cold), and pneumonia.

Interferon

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. In people who have been treated with other drugs that put the myeloma in remission, interferon is sometimes used to try to prolong the remission.

This drug can cause side effects that include fatigue and other symptoms similar to the flu. Some patients have trouble tolerating this treatment, but overall the benefits of longer remission and fewer myeloma symptoms may outweigh the side effects.

Using these drugs together to treat multiple myeloma

Although a single drug may be used to treat multiple myeloma, more often different kinds of drugs are used in combination. For example:

- Melphalan and prednisone (MP), with or without thalidomide or bortezomib
- Vincristine, doxorubicin (Adriamycin), and dexamethasone (called VAD)
- Thalidomide (or lenalidomide) and dexamethasone
- Bortezomib, doxorubicin, and dexamethasone,
- Bortezomib, dexamethasone, and thalidomide (or lenalidomide)
- Liposomal doxorubicin, vincristine, dexamethasone
- Carfilzomib, lenalidomide, and dexamethasone
- Dexamethasone, cyclophosphamide, etoposide, and cisplatin (called DCEP)
- Dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and etoposide (called DT-PACE), with or without bortezomib

- Panobinostat, bortezomib, and dexamethasone
- Ixazomib, lenalidomide, and dexamethasone
- Elotuzumab, lenalidomide, and 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 certain drugs, like melphalan, that can damage the bone marrow.

For more information about chemotherapy and its side effects, see *A Guide to Chemotherapy*.

Bisphosphonates for multiple myeloma

Myeloma cells can dissolve, weaken, and even break bones. 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®) and zoledronic acid (Zometa®). These drugs are given intravenously (IV or 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 doesn't heal. It can also lead to tooth loss in that area. The jaw bone can also become infected. Doctors aren't sure why this happens or how best to prevent it, but having jaw surgery or having a tooth removed can trigger this problem. Avoid these procedures while you are taking a bisphosphonate. 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 cancer cells. Radiation may be used to treat areas of bone damaged by myeloma that have not responded to chemotherapy and are causing pain. It's 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.* 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 can continue for several weeks.

Side effects of radiation can include:

- Skin changes in the area being treated, which can range from redness to blistering and peeling
- Fatigue (tiredness)
- Nausea
- Diarrhea (if the belly or pelvis is being treated)
- Low blood counts

These symptoms improve once treatment is over.

For more information about radiation therapy and its side effects, see our document *Understanding Radiation Therapy: A Guide for Patients and Families*.

Surgery for multiple myeloma

Although surgery is sometimes used to remove single plasmacytomas, it’s rarely used to treat 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 or treat fractures.

Stem cell transplant for multiple myeloma

In a stem cell transplant, the patient gets high-dose chemotherapy (sometimes with radiation to the whole body) to kill the cells in the bone marrow (including the myeloma cells). Then the patient receives new, healthy blood-forming stem cells. When stem cell transplants were first developed, the new stem cells came from bone marrow, and so this was known as a *bone marrow transplant*. Now, stem cells are more often gathered from the blood (a peripheral blood stem cell transplant).

Stem cell transplant is commonly used to treat multiple myeloma. Before the transplant, drug treatment is used to reduce the number of myeloma cells in the patient's body (see the section "Chemotherapy and other drugs for multiple myeloma").

Stem cell transplants (SCT) are autologous and allogeneic.

Autologous transplants

For an autologous stem cell transplant, the patient's own stem cells are removed from his or her bone marrow or peripheral blood before the transplant. The cells are stored until they are needed for the transplant. Then, the person with myeloma gets treatment such as high-dose chemotherapy, sometimes with radiation, to kill the cancer cells. When this is complete, the stored stem cells are infused back into the patient's blood.

This type of transplant is a standard treatment for patients with multiple myeloma. Still, while an autologous transplant can make the myeloma go away for a time (even years), it doesn't cure the cancer, and eventually the myeloma returns.

Some doctors recommend that patients with multiple myeloma have 2 autologous transplants, 6 to 12 months apart. This approach is called *tandem transplant*. Studies show that this may help some patients more than a single transplant. The drawback is that it causes more side effects and so is riskier.

Allogeneic transplants

In an allogeneic stem cell transplant, the patient gets blood-forming stem cells from another person – the donor. The best treatment results occur when the donor's cells are closely matched to the patient's cell type and the donor is closely related to the patient, such as a brother or sister. Allogeneic transplants are much riskier than autologous transplants, but they may be better at fighting the cancer. That's because transplanted (donor) cells may actually help destroy myeloma cells. This is called a *graft vs. tumor effect*. Still, in studies of multiple myeloma patients, those who got allogeneic transplants often did worse in the short term than those who got autologous transplants. At this time, allogeneic transplants are not considered a standard treatment for myeloma, but may be done as a part of a clinical trial.

Side effects

The early side effects from a stem cell transplant (SCT) are similar to those from chemotherapy and radiation, only more severe. One of the most serious side effects is low blood counts, which can lead to risks of serious infections and bleeding.

The most serious side effect from allogeneic transplants is *graft-versus-host disease* (or GVHD). This occurs when the new immune cells (from the donor) see the patient's tissues as foreign and so attack them. GVHD can affect any part of the body and can be life threatening.

For more information about stem cell transplants, including details about the processes and side effects, see our document *Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants)*.

Supportive treatments for patients with multiple myeloma

Intravenous immunoglobulin (IVIG)

Patients with multiple myeloma often have low levels of the normal antibodies (immunoglobulins) needed to fight infection. This can lead to problems with lung and/or sinus infections that keep coming back. The patient's level of antibodies in the blood can be tested, and if it's low, antibodies from donors can be given into a vein (IV) to raise the levels and help prevent infections. The antibodies given are called *IVIG* or intravenous immunoglobulin. IVIG is often given once a month at first, but may be able to be given less often based on blood tests of antibody levels.

Treatment for low blood cell counts

Some patients develop low red blood cell counts (anemia) from multiple myeloma or its treatment. They feel tired, light headed, or short of breath while walking. Anemia that's causing symptoms can be treated with transfusions. These are often given on an outpatient basis.

Erythropoietin (Procrit®) and darbepoietin (Aranesp®) are drugs 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 these drugs are used much less often because they have been linked to poorer survival in some patients with lymphoid cancers, such as multiple myeloma.

Plasmapheresis

Plasmapheresis can be used to remove myeloma protein from the blood. It's helpful when certain myeloma proteins build up, thicken the blood, and interfere with circulation (called *hyperviscosity*).

Most often, this procedure is done through a large catheter placed in a vein in the neck, under the collarbone, or in the groin. This catheter is hooked up to a machine, and blood flows into the machine. The machine separates the blood cells from the blood plasma (liquid part of the blood), and then returns the blood cells to the patient with either salt solution or donor plasma. The plasma that's removed contains the abnormal antibody protein produced by the myeloma cells and is discarded.

Although plasmapheresis lowers the protein level and can relieve symptoms for a time, it does not kill the myeloma cells. That means that without further treatment, the protein will just build-up again. For this reason, plasmapheresis is often followed by chemotherapy or some other type of drug treatment to kill the cells that make the protein.

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. Chemotherapy (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. For many patients, starting treatment early does not seem to help them live longer. These patients are often watched closely without starting chemo or other treatments for myeloma. They may be started on a bisphosphonate if they have bone disease.

Based on how abnormal the plasma cells look under the microscope and the levels of immunoglobulins, some patients with early myeloma have a high risk of progressing to active myeloma and needing treatment. In one study, treating these patients with lenalidomide (Revlimid) and dexamethasone before they developed symptoms or problems helped them live longer.

Active (symptomatic) myeloma

Patients whose myeloma is stage II or higher or who have light chain amyloidosis are often given drug therapy. The drugs chosen depend on the patient's health (including their kidney function) and whether a transplant is planned. (These drugs are discussed in more detail in the section "Chemotherapy and other drugs for multiple myeloma.")

Often, a combination containing bortezomib (Velcade), thalidomide or lenalidomide, and dexamethasone is used. Combinations containing bortezomib are especially helpful in patients with kidney problems and those whose myeloma cells contain certain high risk chromosome abnormalities.

Other combinations may be considered, including vincristine, doxorubicin (Adriamycin), and dexamethasone (VAD). If the patient is not expected to have a transplant, chemotherapy with melphalan and prednisone (MP) may be used, and can be combined with thalidomide.

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

Patients with multiple myeloma also receive supportive treatments, such as transfusions to treat low blood cell counts, and antibiotics and sometimes intravenous immunoglobulin (IVIG) for infections.

A stem cell transplant may be part of treatment. Options for stem cell transplant are discussed in the section "Stem cell transplant for multiple myeloma."

Some patients are given additional cycles of treatment after transplant. This is called *consolidation treatment* and increases the chance of a complete response (where signs and symptoms of the disease go away).

Some patients (even some who didn't have a stem cell transplant) may be given long-term treatment with thalidomide, lenalidomide, or bortezomib. This is known as *maintenance treatment,* and helps delay the return of the myeloma, but it can cause serious side effects.

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

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. They want to answer all of your questions, no matter how minor they might seem. You should ask any question you have. Among the questions you might want to ask are:

- What's my stage of multiple myeloma? What does that mean?
- What are my treatment choices?
- Based on what you've learned about my cancer, how long do you think I'll survive?
- What side effects can I expect from 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 the cancer will come back after treatment (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 give you 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's very important to go to 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 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's 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's important that you be able to give your new doctor the details of your diagnosis and treatment. Gathering these details soon after treatment may be easier than trying to get them at some point in the future. Make sure you have this information handy:

- A copy of your pathology report(s) from any biopsies or surgeries
- Copies of imaging tests (CT or MRI scans, etc.), which can usually be stored on a CD, DVD, etc.
- 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 drug treatment (such as chemotherapy or immunotherapy), a list of the drugs, drug doses, and when you took them
- If you had radiation, a copy of the treatment summary

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

Can I get another cancer after having multiple myeloma?

Cancer survivors can be affected by a number of health problems, but often their greatest concern is facing cancer again. If a cancer comes back after treatment it is called a "recurrence." But some cancer survivors may develop a new, unrelated cancer later. This is called a "second cancer." No matter what type of cancer you have had, it is still possible to get another (new) cancer, even after surviving the first.

Unfortunately, being treated for cancer doesn't mean you can't get another cancer. People who have had cancer can still get the same types of cancers that other people get. In fact, certain types of cancer and cancer treatments can be linked to a higher risk of certain second cancers.

Survivors of multiple myeloma can get any type of second cancer, but they have an increased risk of:

- Kaposi sarcoma
- Chronic myeloid leukemia (CML)
- Acute myeloid leukemia (AML)
- Myelodysplastic syndrome (MDS)

Follow-up

Patients with multiple myeloma need to see their doctors regularly. Treatment doesn't cure this cancer, but can cause it to regress or go away for a time. Then, if the cancer comes back or worsens, treatment may begin again. Let your doctor know about any new symptoms or problems, because they could be caused by the myeloma or by a new disease or second cancer.

All people with multiple myeloma should avoid tobacco smoke, as smoking increases the risk of many cancers.

To help maintain good health, survivors should also:

- Achieve and maintain a healthy weight

- Adopt a physically active lifestyle
- Consume a healthy diet, with an emphasis on plant foods
- Limit consumption of alcohol to no more than 1 drink per day for women or 2 per day for men

These steps may also lower the risk of some cancers.

See *Second Cancers in Adults* for more information about causes of second cancers.

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.

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 might 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. A person who has never exercised will not be able to take on the same amount of exercise as someone 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, please see *Fatigue in People With Cancer* and *Anemia in People With Cancer*. The "Additional resources for multiple myeloma" section has a list of some other documents about dealing with symptoms and side effects that you may find helpful.

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'll 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's 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 don't 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's 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've 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's 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 the 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 documents called *Hospice Care* and *Nearing the End of Life*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there's 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 world. Each year, scientists find out more about what causes the disease and how to improve treatment. Many new drugs are being tested.

Researchers have found that bone marrow-support tissues and bone cells produce growth factors that increase the growth of myeloma cells. In turn, the myeloma cells produce

substances that cause bone cells to undergo changes that weaken the bones. These discoveries are helping the researchers develop new drugs to block these growth factors, slow down the cancer, and reduce bone destruction. For example, bone marrow support (*stromal)* cells produce interleukin-6 (IL-6). Because IL-6 is a strong growth factor for multiple myeloma cells and eventually destroys bone, some current research efforts are focused on developing ways to block IL-6 function.

A form of arsenic, arsenic trioxide, is used to treat a certain kind of leukemia, and is also being tested to treat myeloma.

Drugs that act differently than the ones in use are being studied. For example, a drug called panobinostat is a histone deacetylase (HDAC) inhibitor, which means it affects the proteins in chromosomes. It has shown promising results when used in combination with bortezomib (Velcade) and dexamethasone, and it is now approved for use along with these drugs.

A test called *gene expression profiling* has been studied in recent years in multiple myeloma. This test looks to see what genes are active in cancer cells, and 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

We have a lot more information that you might find helpful. Explore www.cancer.org or call our National Cancer Information Center toll-free number, 1-800-227-2345. We're here to help you any time, day or night.

National organizations and websites*

Along with the American Cancer Society, other sources of information and support include:

International Myeloma Foundation
Toll-free number: 1-800-452-2873 (1-800-452-CURE)
Website: www.myeloma.org

> Support includes a Myeloma Hotline staffed by NCI-trained coordinators; extensive myeloma literature for patients and caregivers, Patient & Family Interactive Seminars, a videotape lending library of myeloma presentations by myeloma experts, and a network of myeloma support groups worldwide

The Leukemia & Lymphoma Society
Toll-free number: 1-800-955-4572
Website: www.lls.org

> Has a variety of service programs and resources available throughout the US and Canada including: the Information Resource Center, staffed by healthcare professionals, available via the toll-free number; free publications on all forms of

blood cancer, including multiple myeloma, and related topics; First Connection, a telephone-based peer support network for patients and survivors; family support groups; education teleconferences and web-casts – a schedule is on the website.

Multiple Myeloma Research Foundation (MMRF)
Telephone: 203-229-0464
Website: www.themmrf.org

Offers internet programming, live symposia, teleconferences, and print materials (including brochures and a quarterly newsletter); website also has general information about multiple myeloma, a calendar of MMRF events, and current information about multiple myeloma clinical trials via the Clinical Trials Monitor

National Cancer Institute (NCI)
Toll-free number: 1-800-422-6237 (1-800-4-CANCER)
TTY: 1-800-332-8615
Website: www.cancer.gov

Their "Cancer Information Service" offers a wide variety of free, accurate, up-to-date information about cancer to patients, their families, and the general public; also can help people find clinical trials in their area

National Coalition for Cancer Survivorship ((NCCS)
Toll-free number: 1-888-650-9127
Website: www.canceradvocacy.org

Has publications on many cancer-related topics; also offers the Cancer Survival Toolbox – a free program that teaches skills that can help people with cancer meet the challenges of their illness

**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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1-800-227-2345 or www.cancer.org