

## Multiple Myeloma

Multiple myeloma is a cancer of the plasma cells—a type of white blood cell. It is normally found in the bone marrow. Low numbers of these cells may also be found in the bloodstream whenever the immune system is triggered. A myeloma cell develops from a single flawed plasma cell. Over the course of months to years, it divides forming other myeloma cells that can fill the bone marrow space.

All of your red and white blood cells and platelets are produced by the bone marrow. When the myeloma cells divide and fill the bone marrow space, other blood cells cannot grow in normal amounts. As a result, the immune system becomes weak. This can lead to anemia and a decrease in platelets. Platelets help the blood to clot.

Myeloma cells can damage surrounding bone and soft tissues, such as nerves and muscles, if they continue to grow and divide. These cells can also travel through the blood stream from one bone marrow site to another (multiple bone marrow sites). This is why it is called “multiple myeloma”. Sometimes, these cells can be found outside of bony areas in formed masses called “plasmacytomas”.

This disease is typically diagnosed in people between the ages of 65 to 70 years. It is more common in males and among African Americans. While the cause is unknown, exposure to high levels of radiation or certain chemicals increases the risk of developing this cancer.

### Symptoms

There are several symptoms associated with multiple myeloma. These include fractures, bone pain, fatigue, infection, and hypercalcemia.

### Fractures

Bone damage is a serious concern with myeloma. Bone damage occurs because myeloma cells produce substances called cytokines. Cytokines can trigger bone cells (osteoclasts) to destroy nearby bone and reduce bone-forming cell (osteoblasts) activity. X-rays will show either a thinning of the bone (osteoporosis) or the presence of dark holes (lytic lesions) when more than 30 percent of the bone has been destroyed. This leads to areas of decreased bone density and strength. The weakened area of bone is more prone to breaks (fractures).

Your doctor may recommend taking drugs, such as Zometa<sup>®</sup>, Aredia<sup>®</sup>, or Xgeva<sup>®</sup>, to prevent bone damage and reduce the risk of a fracture. While these drugs prevent osteoclasts from destroying bone, they do have some possible side effects, including damage to the kidney and the jaw bone (osteonecrosis). Your care team will monitor your kidney function on a regular basis. Be sure you tell your doctor or nurse ahead of time if you plan to have any dental work done while taking these drugs.

## **Bone Pain**

Bone pain in the middle and lower back, rib cage, or hips is common. It can be mild, moderate, or severe. This depends on the lesion size, how fast it develops, and whether or not a fracture or nerve compression has occurred. Movement usually makes the pain much worse. Pain can be treated with non-steroidal anti-inflammatory agents (NSAIDs), such as aspirin and ibuprofen, or prescription medicines. In some cases, radiation may be helpful if one or a small number of areas are mainly involved. Surgery may help with a bone fracture or in an area where a fracture seems likely to happen. Procedures, such as a kyphoplasty or vertebroplasty, can be done on vertebrae in the spine that have fractured and collapsed.

## **Fatigue**

Red cells in the blood decrease because the myeloma cells crowd them out in the bone marrow. This can lead to anemia (too few red blood cells) and cause you to feel tired or fatigued. Anemia can be treated with blood transfusions. Sometimes, growth factor injections are given to stimulate the bone marrow to produce more red blood cells.

## **Infection**

There is a risk of infection because the myeloma cells crowd out normal white blood cells. White blood cells fight infection. Symptoms depend on where the infection is located. Pneumonia, sinusitis, and bladder, kidney, and skin infections occur more often in myeloma patients. Vaccines may help decrease the risk of some of these infections. Talk with your doctor or nurse to learn more.

## **Hypercalcemia**

Hypercalcemia is a high amount of calcium in the blood stream. Calcium is released into the bloodstream when the bone is destroyed. As the levels increase, the kidneys are unable to remove the excess calcium in the urine. Symptoms include thirst, nausea, constipation, and confusion. This condition is treated with IV fluids and Zometa<sup>®</sup> or Aredia<sup>®</sup>. Often, it requires a hospital stay to help improve this condition quickly.

## **Tests**

Your doctor will order blood and/or urine tests if you have one or more of the symptoms listed above. If the results are abnormal, such as high calcium or protein levels, your doctor may order more tests to confirm a cancer diagnosis. These additional tests include bone marrow aspiration, biopsy, and bone survey.

## **Blood and Urine**

Blood and urine tests are needed to determine calcium levels and changes of different abnormal protein levels produced by the myeloma. "Paraproteins" or "M-proteins" are found in the blood. "Bence-Jones" proteins are found in the urine. A test called serum protein electrophoresis (SPEP) is done to measure the paraproteins in the blood. A test called urine protein electrophoresis (UPEP) is done to measure the Bence-Jones protein in the urine. A 24-hour urine collection is needed for this test.

If both tests cannot detect these proteins, another test, called immunofixation (IFE), is done. It can detect small traces of these abnormal proteins.

A serum-free light chain assay is another blood test that may be done. It measures the serum-free light chains (sFLCs) levels in the blood. Sometimes, it can detect abnormal levels even when the other blood tests are normal.

## **Bone Marrow Aspiration**

Blood cells are produced mainly in the bone marrow. The marrow is the soft, spongy, center part of the bone. A bone marrow aspiration test can show the number of plasma cells present in the bone marrow. Normal bone marrow has less than five percent of plasma cells that are all different from each other. With myeloma, the bone marrow contains more than 10 percent of plasma cells, which are all similar to each other.

Myeloma is considered a “spotty” disease, mainly in its early stages. This means that a spot in your marrow can be packed with myeloma cells. But, if you were to move a few centimeters away, that spot could be free of myeloma cells.

Bone marrow aspiration samples are also used to perform cytogenetic studies, such as karyotyping and fluorescence in-situ hybridization (FISH). These studies look for the presence of abnormal chromosomes that play a part in the development of myeloma. Some of these abnormal chromosomes can influence the outcome of myeloma and decisions about the best type of treatment.

## **Biopsy**

Myeloma can present as a single tumor or as many tumors in the bone or soft tissues around the bone. These tumors are called plasmacytomas. A biopsy of a tumor usually shows 90 to 100 percent myeloma cells.

## **Bone Survey**

A bone survey is an X-ray that looks for lytic lesions or osteoporosis. In some cases, other more detailed tests may be needed, such as a bone density scan, magnetic resonance imaging (MRI), or positron emission tomography (PET). These additional tests may show very early or small lytic lesions missed by the X-rays.

## **Cancer Staging**

The doctor will determine the stage of the disease once myeloma is diagnosed. This is known as staging. The stage describes the extent to which the disease has spread in the body. Staging is important because it helps the doctor determine the best treatment approach.

This disease is staged using the International Staging System. It is based on the results of two blood tests (albumin and beta-2-microglobulin or B2m).

- Stage I: Patients have, for the most part, normal levels of albumin and B2m.
- Stage II: Patients have a low albumin or a somewhat elevated B2m.
- Stage III: Patients have high levels of B2m.

## **Treatment**

Myeloma treatment depends on the stage of disease and whether you have disease-related symptoms. Watchful waiting for a period of time may be used if you do not have any symptoms. This is called asymptomatic myeloma. It is sometimes referred to as “smoldering myeloma.” It may be months or years before treatment is needed. Starting chemotherapy before symptoms appear does not seem to help.

Treatment for patients who do have symptoms may include chemotherapy, radiation therapy, and bone marrow or stem cell transplant. Your care team will talk with you about your treatment plan.

## **Chemotherapy**

Chemotherapy (chemo) is the use of medicines to treat cancer. Chemo kills or slows the growth of cancer. There are many types of chemo medicines used to treat myeloma. Doctors may prescribe a single chemo medicine or use a combination of many. Depending on the drug, chemo can be given as an outpatient or as an inpatient.

Some chemo medicines can be taken by mouth. These include cyclophosphamide (Cytosan<sup>®</sup>), dexamethasone (Decadron<sup>®</sup>), lenalidomide (Revlimid<sup>®</sup>), melphalan (Alkeran<sup>®</sup>), prednisone, and thalidomide (Thalomid<sup>®</sup>). Other chemo medicines are given intravenously (IV), such as bortezomib (Velcade<sup>®</sup>) and doxorubicin (Adriamycin<sup>®</sup> or Doxil<sup>®</sup>).

You will visit the clinic at least once a month during treatment. This allows the care team to monitor you for any side effects. Chemo is given in cycles to give your immune system and normal cells time to recover in between treatments. As the chemo destroys the cancer cells, it can also help to ease cancer symptoms.

## **Radiation Therapy**

Radiation is a special kind of energy carried by waves or a stream of energy particles. It may be delivered by a radiation machine or from radioactive substances injected into the bloodstream. It works by killing the cells in the area where the radiation is directed. It can kill cancer cells faster than chemo and has fewer side effects. It is often used for quick pain relief and to control severe bone loss.

## **Stem Cell Transplant**

Autologous, allogeneic, and peripheral blood stem cell transplants (SCT) are procedures that restore the supply of normal cells that are destroyed by high-dose chemo and radiation. In an autologous transplant, the bone marrow or blood stem cells are collected from the patient. In an allogeneic transplant, the bone marrow or blood stem cells are collected from a matched donor who may or may not be related to you.

Stem cells can be collected or harvested directly from inside the donor or patient's hip bone. They can also be obtained through a process called apheresis, which is similar to donating blood. This type of peripheral blood stem cell transplant is most common.

Often, myeloma patients who have an autologous transplant will have their stem cells collected by apheresis. It is an easy process for the patient and has a shorter recovery time. Two daily hormone growth factor injections are given over a few days. These injections stimulate the bone marrow to "squeeze" the stem cells into the peripheral blood. During this process, the patient's central venous catheter (CVC) is connected to a machine. The patient's blood flows through the CVC and then through the machine. The machine collects the stem cells and the blood is returned back to the patient's body.

Each apheresis session takes about four hours. The total collection process may take one to three days or more depending on the number of stem cells collected with each session. Once collected, the stem cells are frozen and stored until the patient is ready to receive them.

When we are able to collect stem cells in advance, intense or high-dose chemo, which destroys the cancer cells along with good, healthy cells, can be given more safely.

After you receive high-dose chemo, it will need a chance to kill the myeloma cells and leave your body. Then, you will receive your collected stem cells back. You are able to recover your blood counts and “bounce back” faster when we infuse (return) the stem cells.

During this time, we will monitor you for low blood counts. Low blood counts could lead to infection (fever), fatigue, and bleeding. We will also watch you for other side-effects, such as nausea, vomiting, hair loss, mouth sores, and diarrhea. You may also need blood or platelet transfusions and fluid and electrolyte replacements.

Allogeneic transplants are not a common myeloma treatment because there are not many matched donors for patients. There is also a higher risk of death in those who relapse after an autologous transplant or for those with very aggressive disease. Patients that have an allogeneic transplant are really getting a new immune system from their donor to help fight the disease.

### **Graft Versus Host Disease (GVHD)**

After an allogeneic transplant, the patient is at high risk for graft versus host disease (GVHD). The stem cells (the graft) you receive will form your new immune system to fight infection. The new immune system may recognize you (the host) as being different. Instead of protecting your body, the graft reacts as though the body is “foreign” and attacks the body. This may cause GVHD. Signs and symptoms of GVHD can vary from mild and temporary, to serious and chronic, or even be fatal. These include rash, dry eyes, dry mouth, nausea, vomiting, diarrhea, or abnormal liver enzyme levels.

A non-myeloablative or “mini” allogeneic transplant may also be considered. It uses a lower dose of chemo and has a lower risk of death. Yet, GVHD is still possible.

Your doctor or nurse will talk to you about your specific treatment plan. You will receive a handout that describes each drug or treatment and a treatment calendar.

### **Relapse or Recurrence**

There is no cure for myeloma, but it can be treated successfully. Many patients are treated and go into remission for years, even decades. Sometimes, patients may need maintenance therapy after their initial treatment to help prolong or stay in remission. Maintenance therapy may be general chemo, injections, or taking medicine by mouth.

There is always a chance that cancer may return. So, it is very important to see a doctor for regular follow up exams. If the cancer returns and it is found early, you have a better chance of controlling it. Your doctor will explain the chances of relapse and your plan for follow up visits.

### **Clinical Trials**

Your care team may talk with you about taking part in a clinical trial. Clinical trials may offer more options for therapy than just the available standard treatments. A trial may focus on newly diagnosed patients or on patients with relapsed disease.

There are many different types of trials. Some may use drugs that have already been approved for myeloma, but are being combined in a new and different way. Other trials may use drugs that are not yet approved, but have shown good results in other patients, myeloma lab models, or both. Clinical trials have risks and benefits just like with standard treatment. Be sure to talk with your care team about the risk and benefits. If you decide to take part in a study, you have the right to stop your participation at any time. We will still treat you with the best standard care possible.

Talk to your care team if you have any questions or concerns.

### **Resources**

Here are some websites for additional information.

National Cancer Institute at [www.cancer.gov](http://www.cancer.gov)

National Institutes of Health at [www.nih.gov](http://www.nih.gov).

National Heart, Lung, and Blood Institute at <http://www.nhlbi.nih.gov>.

American Society of Clinical Oncologists at [www.asco.org](http://www.asco.org).

Leukemia and Lymphoma Society at [www.lls.org](http://www.lls.org).

International Myeloma Foundation at [www.myeloma.org](http://www.myeloma.org).

American Society of Hematology at [www.bloodthevitalconnection.org](http://www.bloodthevitalconnection.org).

American Society for Radiation Oncology (ASTRO) at [www.ranswers.org](http://www.ranswers.org).

American Cancer Society at [www.cancer.org](http://www.cancer.org) or call the national number for information and services at 1.800.ACS.2345.