

Multiple Myeloma Questions and Answers

What is Multiple Myeloma?

Multiple myeloma is a cancer of the plasma cells, which are a type of B-lymphocyte, or white blood cell, that is normally found in the bone marrow. They may also be found in the bloodstream in low numbers whenever the immune system is activated. In myeloma, a single defective plasma cell, called a myeloma cell, arises, and over the course of months to years divides into many other myeloma cells, filling the bone marrow space.

The bone marrow is the “factory” that produces all of your blood cells, including red cells, white cells, and platelets. As the myeloma cells take up more and more space in the marrow, it becomes less able to grow other blood cells in normal amounts. This results in a weakened immune system, as well as anemia and, in some cases, decreased levels of platelets, which normally help the blood to clot. As the myeloma cells continue to multiply, they can damage surrounding bone and soft tissues, such as nerves and muscles. They can also travel through the blood stream from one bone marrow site to another, leading to the name multiple myeloma (multiple bone marrow sites). Sometimes, myeloma cells can also be found outside of bony areas, where they form masses called plasmacytomas.

Multiple myeloma is the second most common type of cancer of blood-forming cells. According to the American Cancer Society, about 20,580 new cases will be diagnosed in the U.S. in 2009, which is more than double the number seen 25 years ago. This is in part due to the aging of the American population, since myeloma is most commonly diagnosed in patients who are 65-70 years of age, and there are more people in the U.S. of this age now than in the past. Myeloma occurs slightly more often in males, and is more common in African Americans than Caucasians, less common in Hispanic Americans, and least common in Asian Americans. The exact cause of multiple myeloma is unknown, but a history of exposure to radiation or certain chemicals does increase the risk of developing this cancer.

What are the symptoms of Multiple Myeloma?

Fractures

Bone damage is the most serious concern at the time myeloma is diagnosed. Bone damage occurs because myeloma cells produce substances called cytokines, which can trigger bone cells (osteoclasts) to destroy surrounding bone, and reduce the activity of bone-forming cells (osteoblasts). When more than 30% of the bone has been destroyed, x-rays will show either a thinning of the bone (osteoporosis) or the presence of dark holes (lytic lesions), which are areas

of decreased bone density and strength. The weakened area of bone can break, which is called a pathological fracture. To prevent bone destruction and reduce the risk of a fracture, your doctor may recommend giving you drugs that prevent osteoclasts from destroying bone (e.g. Zometa[®] or Aredia[®]). However, these drugs do have some risks, including a small possibility of kidney damage and jaw osteonecrosis, or damage to the jaw bone. Your doctors and nurses will monitor your kidney function regularly, but be sure to tell them in advance if you are planning on having any dental work performed when you are on these drugs.

Bone Pain

This is especially common in the middle and/or lower back, rib cage or hips. The pain can be mild, moderate, or severe, depending on the size of the lesion, the speed with which it has developed, and whether or not a fracture or nerve compression has occurred. Typically, movement makes the pain much worse. Fortunately, pain can be treated either with non-steroidal anti-inflammatory agents (NSAIDs), such as aspirin and ibuprofen, or prescription medications. Also, in some cases, radiation may be helpful if one or a small number of areas are especially involved. Finally, surgery may help in the case of a bone fracture, or in an area where a fracture seems likely to happen, while procedures known as a kyphoplasty or vertebroplasty can be performed on vertebrae in the spine that have fractured and collapsed.

Fatigue

Because the myeloma cells crowd out the other blood cells in the bone marrow, the number of red cells in the blood decreases. This leads to symptoms of tiredness or fatigue. Anemia can be treated with blood transfusions, and in some cases with injections of growth factors to stimulate more red blood cell production from the bone marrow.

Infection

Because the myeloma cells crowd out normal white blood cells, which fight infection, there is a risk of infection. Symptoms of infection depend upon where the infection is located.

Pneumonia, bladder or kidney infections, sinusitis, and skin infections occur with increased frequency in myeloma. Patients may benefit from vaccinations to decrease the risk of some of these infections, and should discuss this with their doctor or nurse.

Hypercalcemia

Hypercalcemia is a high amount of calcium in the blood stream. When the bone is destroyed, calcium is released into the bloodstream. As the amount increases, the kidneys are unable to get rid of the calcium in the urine. Symptoms of hypercalcemia include thirst, nausea, constipation, and mental confusion. This can be treated with intravenous (IV) fluids and Zometa[®] or Aredia[®], and often requires admission to the hospital to help improve this condition rapidly.

What are the common tests used to evaluate Multiple Myeloma?

If you have one or more of the symptoms in the above section, a doctor will order initial blood tests. If the blood tests show abnormalities, such as high calcium or protein levels, he or she may order more specific tests to confirm a diagnosis of multiple myeloma.

Blood and Urine Tests

Blood and urine tests are needed to determine calcium levels and changes in the level of different abnormal proteins that myeloma produces. In the blood, these proteins are called “paraproteins” or “M-proteins,” and in the urine they are called “Bence-Jones proteins.” These paraproteins are measured in the blood by a test called serum protein electrophoresis (or SPEP). The Bence-Jones protein is measured in the urine by collecting a 24-hour urine sample and running a urine protein electrophoresis (or UPEP).

If these proteins cannot be detected by serum electrophoresis or by urine electrophoresis, an additional test, called immunofixation (or IFE), is performed to detect even small traces of these abnormal proteins.

Another blood test, called a serum free light chain assay, is also now available, and measures the levels of serum free light chains (or sFLCs) in the blood, and can sometimes detect abnormalities even when the SPEP and UPEP are normal.

Bone Marrow Aspiration

A bone marrow aspiration is used to determine the number of plasma cells present in the bone marrow. Normal bone marrow contains less than 5% plasma cells, and these are all different from each other, whereas in myeloma, plasma cells account for more than 10% of cells being produced, and these are all similar to each other. However, it is important to know that multiple myeloma is considered a “spotty” disease, especially in its early stages. This means that you can find a spot in your marrow that is packed with myeloma cells, and move a few centimeters away and find a spot that is relatively clean and free of myeloma cells.

Samples from the bone marrow aspiration are also used to perform cytogenetic studies, such as routine karyotyping and fluorescence in situ hybridization (or FISH). These studies look for the presence of abnormal chromosomes that contribute to the development of multiple myeloma. Some of these abnormalities can influence the outcome of myeloma, and also influence decisions about the best type of treatment.

Biopsy

Myeloma can be present as single or multiple tumors in the bone, or soft tissues around the bone. These tumors are called plasmacytomas. Direct biopsy of one of these plasmacytomas usually shows 90-100 percent myeloma cells.

Bone Survey

Bone x-rays, or surveys will be done to look for lytic lesions or osteoporosis. In some cases, other more detailed tests may be required, such as a bone density scan, magnetic resonance imaging (MRI), or positron emission tomography (PET). These tests may find very early or small lytic lesions missed by bone x-rays.

What is Myeloma staging?

Once multiple myeloma is diagnosed, the doctor will determine the stage of the disease. Staging is a way of determining how much disease is in the body, and the doctor needs this information to decide the best way to treat the cancer. Once staging is determined at diagnosis, it does not change regardless of response to chemotherapy or disease activity.

Multiple myeloma is staged using the International Staging System. This system is based upon the results of two blood tests, one of which is the albumin, while the other is the beta-2-microglobulin (or β 2m).

Stage I patients have essentially normal levels of albumin and β 2m

Stage II patients have a low albumin, or a moderately elevated β 2m

Stage III patients have high levels of β 2m

The stage influences the prognosis of multiple myeloma, and is another factor that is sometimes used to help decide on the best therapy for the disease.

What are the different treatments for Multiple Myeloma?

The treatment depends on the stage of disease, and also on whether patients have disease-related symptoms such as anemia, hypercalcemia, kidney damage, bone damage, or less frequent symptoms such as bacterial infections, amyloidosis, or hyperviscosity. For some patients who do not have any symptoms, a period of watchful waiting may be recommended, since it may be months to years before treatment is needed, and starting chemotherapy before symptoms appear does not seem to be helpful. These patients are said to have asymptomatic myeloma, which was also in the past sometimes called smoldering myeloma.

For patients who do need treatment because of the presence of one or more of the symptoms described above, this may consist of chemotherapy, radiation therapy, and/or bone marrow or stem cell transplantation. Your healthcare team will discuss your treatment plan in more detail. You will also be scheduled for chemotherapy classes in the Lymphoma & Myeloma Center, if appropriate.

Chemotherapy

Chemotherapy destroys the myeloma cells directly, and may be given over a period of months. Often, chemotherapy may be received outside the hospital, and many drugs used against myeloma, such as cyclophosphamide (Cytosan[®]), dexamethasone (Decadron[®]), lenalidomide (Revlimid[®]), melphalan (Alkeran[®]), prednisone, and thalidomide (Thalomid[®]) are available in an oral form.

During therapy, patients will be monitored by their healthcare team for any side effects, and usually visit the clinic at least once a month. Other chemotherapy drugs are given in an

intravenous (IV) form, such as bortezomib (Velcade[®]) and doxorubicin (Adriamycin[®] or Doxil[®]), and generally can be given on an outpatient basis. In some cases, it may be necessary to receive therapy in the hospital. All of the drugs are given in cycles, giving the patient's immune system and normal cells time to recover in between treatments. By destroying the cancer cells, chemotherapy can also relieve many of the symptoms of the disease.

Radiation Therapy

This is usually used to treat a specific area where there is bone destruction and pain, or a local mass of plasma cells, or plasmacytoma. Radiation can kill cancer cells more quickly than chemotherapy and has fewer side effects. For this reason, it is often used to get quicker pain relief and control severe bone loss.

Autologous and Allogeneic Transplantations

There are two types of stem cell transplants: **autologous** and **allogeneic**. These procedures allow patients to receive higher doses of chemotherapy than would normally be possible, and these high doses are helpful because they kill more myeloma cells. Since these doses also kill normal bone marrow cells, the transplant procedure restores the ability of the marrow to produce normal blood cells. In an autologous transplant, patients receive their own stem cells. The stem cells are collected from the patient before he or she receives their high dose chemotherapy, which protects them from the effects of these drugs. In an allogeneic transplant, patients receive stem cells from a donor, who typically has not received any chemotherapy to damage their stem cells. The donor may be related (usually a matched sibling) or unrelated (non-family) individual.

Stem cells can be collected in two ways: 1.) collected or harvested directly from the hip bone or bone marrow of the patient or donor, or more commonly 2.) collected through the peripheral or circulating blood through a process called **apheresis**, which is similar to donating platelets. Therefore, a stem cell transplant is a transplant where stem cells are collected/harvested directly from the patient or donor. A peripheral blood stem cell transplantation (PBSCT) is a transplant where stem cells are collected through the peripheral bloodstream by apheresis.

Often, myeloma patients who undergo autologous transplants will have their stem cells collected by apheresis because it is easier on the patient and requires a shorter recovery time. Patients will receive two daily injections of hormone growth factor over a few days to stimulate the bone marrow, and “squeeze” the stem cells from the bone marrow into the peripheral blood. During this process, patients are connected to a machine that will remove their blood and selectively collect their stem cells. Once the stem cells are collected, the blood is returned to the patient. Each apheresis session takes about 4 hours. Depending on how many stem cells are collected with each session, the entire process may take 1 to 3 days or more. Collected stem cells are frozen and stored until the patient is ready to receive them.

Chemotherapy destroys the cancer cells, but it will also destroy “good” cells. By collecting the stem cells in advance, intense or high-dose chemotherapy can be given safely. After the patient receives the high-dose chemotherapy, and it has had a chance to kill myeloma cells and then leave the patient's body, they receive their collected stem cells back. By infusing (returning)

these stem cells, patients are able to recover their blood counts and “bounce back” much more quickly.

The most common side effects of the high-dose chemotherapy given prior to stem cell transplantation include:

- Low blood counts (white cells, red cells and platelets),
- Nausea
- Vomiting
- Hair loss
- Mouth sores
- Diarrhea

When patients have low blood counts, they are more susceptible to getting infections, suffering from fatigue, and bleeding. Although patients may have some side effects during chemotherapy, they usually feel worse a few days after receiving chemotherapy, when their blood counts drop to their lowest. During this time, they are monitored closely for any fevers (infections), the need for any blood or platelet transfusions, and the need for fluid and electrolyte replacement.

Allogeneic transplantation for myeloma is not as common because fewer patients have matched donors, and because it is associated with a higher risk of death. It is mostly for patients who relapse after an autologous transplant, or for those with very aggressive myeloma. When patients receive stem cells from a donor, they are essentially receiving a new immune system that may help fight the myeloma. The high risk of allogeneic transplantation is in part from **graft-versus-host disease (GVHD)**. GVHD occurs when the new bone marrow (the graft) recognizes the tissues of the patient’s body as foreign, and reacts against the body like it would against an infection. Graft-versus-host disease can vary from mild and temporary, to serious and chronic, or even life threatening. Signs and symptoms include: a rash, dry eyes, dry mouth, nausea, vomiting, diarrhea, or liver enzymes abnormalities.

A newer type of allogeneic transplant, which is sometimes called a non-myeloablative, or “mini” allogeneic transplant, may also be considered. This one uses lower doses of chemotherapy, and carries with it a lower risk of death, though GVHD is still possible.

Your healthcare team will talk to you about your specific treatment plan, and will provide you with patient information sheets describing each drug or treatment, and a treatment calendar to put in your Lymphoma & Myeloma New Patient Education Manual.

Once treated, can Multiple Myeloma come back?

Although there is currently no cure for myeloma, it is a highly treatable disease. Many patients go on to lead full lives for years, even decades, after diagnosis, and the survival of patients with this disease has doubled in just the past 10 years. After initial treatment, patients will sometimes receive maintenance therapy to help prolong or maintain remission. Maintenance therapy may be systemic chemotherapy, injections, or medicine by mouth.

Because there is always a chance that the cancer may come back (recur) or progress, it is very important to see your doctor regularly for follow-up exams. If the cancer returns and is found early, the chances of controlling it are better. If it progresses, it may be necessary to change your treatment plan. Your doctor will tell you more about the chances of relapse or progression of cancer and will explain your need for follow up visits.

Are clinical trials available for multiple myeloma patients?

Because myeloma is not yet cured in most patients by our currently available therapies, your healthcare team may talk to you about participating in a clinical trial. This is a way to give you more options for therapy than just the standard ones that are available in many places. Clinical trials may focus on newly diagnosed patients, or on patients with disease that has relapsed after prior therapies. There are many different types of trials. For example, some trials will use drugs that may have already been approved for therapy of multiple myeloma, but are being combined in a new and different way. Other trials may use drugs that are not yet approved, but have shown promising activity against myeloma either in other patients, or in laboratory models of multiple myeloma, or both. As is the case for standard therapies, clinical trials have their risks and benefits, so be sure to discuss these with your healthcare team. If you decide to participate in a study, please be assured that you have the right to withdraw at any time, and will then be given the best standard care possible.

If you have any questions or concerns, please talk to your health care team.

Lymphoma and Myeloma Center

Monday through Friday, 7:30 a.m. – 5 p.m.

Main Building, Floor 6 near Elevator B

713-792-3510