All About Multiple Myeloma

What is bone marrow?
The bone marrow is a spongy material found primarily in the center of long bones. It is where blood cells are produced. Bone marrow is comprised of a variety of cells, which gradually mature to form:

- Red blood cells (also known as erythrocytes): carry inhaled oxygen from the lungs to other organs and carry carbon dioxide from the organs to the lungs to be exhaled.
- Platelets (also known as thrombocytes): help form clots.
- White blood cells (also known as leukocytes): come in several varieties: granulocytes, lymphocytes, and monocytes, each of which has a different role in the immune system. Lymphocytes are designated as either B or T lymphocytes.
- Plasma cells: mature form of B-lymphocytes, which produce antibodies, and make up less than 5% of the cells in bone marrow.

There are a large number of different foreign pathogens, such as bacteria or viruses, which can attack your body. When your immune system fights an infection, it needs to make an antibody that specifically targets the pathogen causing that infection. Each plasma cell can only produce one specific kind of antibody. Individual plasma cells can then divide repeatedly to form copies of themselves, known as clones. This group of clones can produce large amounts of a single kind of antibody to fight a specific infection. There are several thousand different groups of plasma cell clones, which then allow the immune system to make a wide variety of antibodies to target many different kinds of pathogens. Antibodies coat the pathogen that they are built to attack, and this invites other immune cells to also attack the pathogen.

What is multiple myeloma?
Multiple myeloma is a cancer of the blood (hematologic cancer) in which one population of clonal (identical) plasma cells starts to reproduce uncontrollably. These cells are known as malignant plasma cells, or myeloma cells. Myeloma cells produce large amounts of one type of antibody, which is known as the monoclonal protein or M-protein. As the number of myeloma cells grows, they begin to overcrowd the bone marrow and prevent normal production of the other blood cell types (red blood cells, platelets, and other white blood cells) in the bone marrow. This also negatively affects the immune system because the bone marrow now predominantly produces only one type of antibody, and can no longer effectively target all pathogens. Thus there is increased risk of infection in patients with multiple myeloma. Anemia results when multiple myeloma prevents the bone marrow from producing enough red blood cells. As the plasma cells continue to multiply, they can invade and damage other organs and bone. The monoclonal protein produced by plasma cells can also damage organs, specifically the kidneys. The acronym "CRAB" is often used to describe symptoms associate with organ damage by multiple myeloma: hypercalcemia (High levels of calcium in the blood), Renal insufficiency (kidney failure), Anemia (low red blood cell counts), and Bone lesions.

Precursors to Multiple Myeloma
Almost all patients with multiple myeloma evolve from an asymptomatic condition called Monoclonal Gammopathy of Unknown Significance (MGUS). However, since MGUS does not cause any symptoms (asymptomatic), they may not know they have it. People with MGUS have an increased number of clonal plasma cells, but not to the degree seen in multiple myeloma, nor do these patients have other symptoms associated with multiple myeloma. However, people with MGUS do have a 1-2% annual risk of developing multiple myeloma or a related blood cancer, such as leukemia or lymphoma. In light of this risk, it is recommended that blood tests be performed to check for elevated monoclonal protein levels every three months initially.

Some patients may be diagnosed with "smoldering multiple myeloma," which is an early stage of multiple myeloma.
Smoldering multiple myeloma meets all the diagnostic criteria for multiple myeloma, but lacks any of the "CRAB" features listed above. The risk of developing symptomatic multiple myeloma is 10% per year for the first 5 years, 3% per year for the next 5 years, and 1.5% per year thereafter. Patients with smoldering myeloma typically do not receive treatment, but are monitored closely for any progression to active myeloma.

**What causes multiple myeloma and am I at risk?**

Approximately 30,770 people will be diagnosed with multiple myeloma in the United States each year. Multiple myeloma comprises approximately 1.8% of all cancers and comprises about 10% of all "blood cancers", which includes leukemia. Multiple myeloma occurs more frequently in men. African Americans are at a much higher risk for developing myeloma compared to other racial/ethnic groups. Multiple myeloma is diagnosed most frequently in people aged 65-74 with a median age at diagnosis of 69.

At this time, the cause of multiple myeloma is not well established. However, there appear to be several factors which increase the risk of developing multiple myeloma, such as extensive exposure to radiation, chemical resins, organic solvents, pesticides, and herbicides. Exposure to radiation (from atomic bomb/nuclear accident) may increase the risk of developing multiple myeloma. Human Herpes Virus 8 (HHV-8) is thought to be related to the development of multiple myeloma. People with a first-degree relative (parent or sibling) who have multiple myeloma may also be at increased risk for developing the disease. However, a clear genetic mutation related to multiple myeloma has not been discovered.

**How can I prevent multiple myeloma?**

Unfortunately, because the exact cause of multiple myeloma is unknown, there are no specific guidelines for the prevention of multiple myeloma. Limiting exposure to radiation, chemical resins, organic solvents, pesticides, and herbicides may decrease the risk for developing multiple myeloma.

If you have MGUS or smoldering multiple myeloma, you should see your healthcare provider regularly to check for progression to multiple myeloma.

**What screening tests are available for multiple myeloma?**

Multiple myeloma is not a cancer that we routinely screen for because it is rather rare (accounting for 1% of all new cancer cases). Regular physicals by your healthcare provider are your best method of screening.

**What are the signs of multiple myeloma?**

The increased number of myeloma cells, as well as the high levels of monoclonal protein that they produce, can cause several symptoms in people with multiple myeloma. The symptoms are related to either infiltration of the bone marrow by plasma cells or organ damage. Because of advances in routine blood work over the last 20 years, patients are more frequently being diagnosed with disease that has no symptoms.

**Bone Pain / Damage**

Multiple myeloma increases bone breakdown and decreases formation of new bone, leading to "lytic lesions," or areas where the bone has been "punched out," which looks like holes on an x-ray. Bone pain is the most common presenting symptom, with up to two-thirds of patients having bone pain at diagnosis. The pain is typically in the back or chest, but can occur in the leg or arm bones. It is usually associated with movement and is not commonly present at night, unless the person moves around in their sleep.

Multiple myeloma can cause osteoporosis, or generalized weakening of the bone, and weakness at the location of the "punched out" bony lesions. This makes people with multiple myeloma more vulnerable to fractures (broken bones). Often fractures can occur with little or no trauma due to the weakening of the bone. Very commonly, the vertebrae (the bones that make up the spine) can develop breaks called "compression fractures." A compression fracture can cause pain or damage to the nerve roots exiting the spinal cord, resulting in numbness. In some cases, these fractures cause no symptoms at all.
Multiple myeloma can also cause bone erosions, which occur when small areas of bone are eaten away. On x-ray, erosions can make the bone appear patchy with the areas of bone loss appearing darker. At diagnosis, about 75% of people with multiple myeloma will have evidence of fractures, bone erosions, or osteoporosis on x-ray. Bisphosphonates, a class of medication that strengthens bone, can be used to help improve bone strength.

**High Calcium Levels**

Bones have high calcium content and as they are broken down, a large amount of calcium is released into the blood. This condition is called hypercalcemia. It can occur in up to 30% of people with multiple myeloma. High levels of calcium in the blood can cause gastrointestinal symptoms, such as nausea, vomiting, and constipation. It can affect the urinary system, causing increased urination and kidney stones, due to the higher calcium concentration in the urine. It can also affect how you feel by causing decreased appetite, increased thirst, restlessness, and confusion.

**Abnormal Blood Counts**

About 70% of people with multiple myeloma will have anemia at the time of diagnosis (low red blood cell count). As the bone marrow becomes overcrowded with myeloma cells, red blood cells cannot be produced in adequate numbers. There are not enough red blood cells in the blood, and this decreases the body's ability to transport oxygen to the tissues and to transport carbon dioxide to the lungs for elimination. Due to this, people with anemia often appear pale and have weakness, fatigue, and shortness of breath.

Individuals with myeloma can also have leukopenia, or too few white blood cells. This can put the person at higher risk for infection. People with myeloma may also have thrombocytopenia, or a low platelet count. This can impact the ability for blood to clot and may result in serious or prolonged bleeding from cuts, scrapes and bruises.

**Increased Blood Thickness (Hyperviscosity syndrome)**

The myeloma cells produce a large amount of monoclonal protein, which can thicken the blood to the point where the blood has problems circulating properly in smaller blood vessels. In general, hyperviscosity is most common with an excess of IgA or IgM, two types of immunoglobulins/antibodies. The most common symptom associated with hyperviscosity syndrome is an increased risk of bleeding. People may have spontaneous bleeding of their gums, nose, or bowel during bowel movements. People may also notice continued bleeding after minor procedures, such as dental work. People may also notice that they bruise easier than they do normally. Hyperviscosity syndrome can cause neurologic symptoms, including changes in vision, such as blurriness or loss of vision, hearing loss, numbness, difficulty with balance, headache, tingling, sleepiness, and even seizures. The thicker blood can also affect the heart and cause symptoms of heart failure, where the heart cannot pump blood well, resulting in fatigue and difficulty breathing.

**Neurologic Impairment**

The spinal cord communicates with the body through a network of nerves. Nerve roots are large bundles of tissue which conduct signals into and out of the spinal cord. Multiple myeloma can weaken the vertebral bones surrounding the spine, leading to fractures, which in turn can compress the nerve roots. Compression can lead to irritation and inflammation of the nerve roots, which is called radiculopathy. These nerves control body movement as well as sensation, thus symptoms of radiculopathy are numbness, tingling, shooting pains, and weakness. The spinal cord, which is protected by the surrounding vertebral bodies, can be compressed by collapsing bone or by the growth of a tumor into the spinal canal. This can occur in 5-10% of patients with multiple myeloma. **Compression of the spinal cord** is a medical emergency, and immediate medical care is necessary to decompress the cord and prevent permanent damage. Cord compression typically causes severe (new or worsening) back pain, leg weakness, urinary retention and/or loss of sensation to the genitals.

Excess proteins can build up and cause irritation to nerves, which can result in a condition called peripheral neuropathy. **Peripheral neuropathy** typically begins with a tingling and/or numbness in the fingers and toes and can progress to painful sensations and extend into the hands and feet.

**Increased Risk of Infection**

Myeloma cell overgrowth in the bone marrow prevents normal plasma cells from producing antibodies. It also prevents
adequate numbers of other white blood cells from being formed in the bone marrow. Due to this, people with multiple myeloma are more susceptible to infections, often caused by bacteria such as Streptococcus pneumoniae, which can cause pneumonia, meningitis, and bloodstream infections. Treatments for the myeloma, including steroids and chemotherapy, can further increase one’s susceptibility to infection. Infection is one of the most common causes of illness and death in multiple myeloma and should be diagnosed and treated promptly.

Plasmacytoma

A plasmacytoma is a collection of myeloma cells that builds up either in the bone or other tissues. Plasmacytomas can develop in the skin anywhere on the body and may appear as purplish lumps. Reports have shown that about 12% of people can develop plasmacytomas in the ribs. Very rarely, plasmacytomas can develop in the brain.

Kidney Failure

Kidney failure is a frequent and serious complication of multiple myeloma. Kidney function can be measured by checking the level of a compound called creatinine in the blood. Normally, the kidneys remove creatinine from the body, so high levels of creatinine (detected in a blood test) indicate that the kidneys are not functioning well. About 25-50% of people with multiple myeloma have an increased level of creatinine in their blood, indicating kidney failure. There are many factors that contribute to kidney failure in multiple myeloma. The most common are deposits of monoclonal protein (produced by myeloma cells) in the kidney's filtration apparatus. This results in the kidney being unable to filter appropriately, leading to kidney failure. High blood levels of calcium caused by bone breakdown, use of NSAIDs, certain chemotherapy agents, and bisphosphonates can also cause kidney failure. Caution should be taken when having CT scans, as the "contrast" used in these tests can cause or worsen renal failure in patients with multiple myeloma.

How is multiple myeloma diagnosed?

Multiple myeloma cannot be diagnosed with any single test result. There are some basic tests which can help to diagnose the disease including a complete blood count (CBC) with differential and platelet counts, serum and urine analysis and a peripheral blood smear. Almost all people with multiple myeloma have monoclonal proteins in their blood or urine, and there are effective tests available to check for them. Other blood tests to check for kidney disease, high calcium levels, and low red blood cell counts (anemia) can also be used screen for the disease. X-rays can be used to detect erosions in bones caused by multiple myeloma.

While blood count and chemistry levels are used, there are a few tests that are less common, but often used in myeloma diagnosis and management:

- **SPEP (serum protein electrophoresis):** test that is used to find the M protein (also called monoclonal immunoglobulin or the abnormal protein that is being produced out of control). This can be a first step in diagnosing myeloma.
- **Immunoelectrophoresis:** a blood test used to determine the type of abnormal immunoglobulin (i.e. IgA, IgG) that was found to be elevated by SPEP.
- **Quantitative Immunoglobulins:** your immune system makes different types of antibodies in the blood (called IgA, IgD, IgE, IgG, and IgM). This blood test measures the levels of these different antibodies. In myeloma, one type may be particularly high, with the others being normal or low.
- **UPEP (Urine protein electrophoresis):** a 24-hour collection of urine is tested to find M protein or Bence-Jones proteins in the urine. Bence-Jones proteins are also called immunoglobulin light chains, which are a part of normal antibodies. When too much is produced, it is filtered by the kidneys and can be detected in the urine.
- **Free Light Chains:** in some myelomas, M proteins cannot be detected by SPEP. SPEP can only measure intact immunoglobulins. However, immunoglobulins can break down into the parts that make them up: 2 heavy chains and 2 light chains. These light chains may be detected in the blood, which can be helpful in myeloma where SPEP cannot detect M proteins.
- **Beta-2 microglobulin:** a blood test to measure the amount of this protein in the blood. High levels can be indicative of more advanced disease.
- **Plasma Cell Labeling Index (PCLI):** a blood test to determine the percentage of the abnormal plasma cells that are
actively reproducing.

- **Bone Marrow Biopsy**: used to determine the percent of abnormal plasma cells in the bone marrow.
- **Immunohistochemistry and Flow Cytometry**: tests used to evaluate the bone marrow sample and detect myeloma cells.
- **Cytogenetics and FISH (fluorescent in situ hybridization)**: tests used to detect chromosomal abnormalities, which can be used to determine prognosis and guide treatment decisions. For instance, abnormalities associated with a better prognosis include trisomies, t(11;14), and t(6;14); those associated with a worse prognosis include 17p deletion, t(14;16), and t(14;20).
- **Skeletal Survey**: x-rays of the entire skeleton that can identify lytic lesions or fractures.
- **Radiology tests**: including bone X-Ray, MRI, CT Scan and PET Scan.

### Diagnosis of Myeloma

There are a specific set of criteria for the diagnosis of multiple myeloma, to help distinguish it from other blood disorders that have similar characteristics to multiple myeloma, such as MGUS, smoldering myeloma, primary amyloidosis, and metastatic carcinoma. A combination of the tests discussed above may be necessary to make a diagnosis.

For a diagnosis of active (symptomatic) multiple myeloma to be made, all of the following criteria must be met:

- $\geq 10$ bone marrow plasma cells or biopsy proven bony or extramedullary plasmacytoma.
- And any one or more of the following:
  - Calcium $>$25 mmol/L ($>$1mg/dL) higher than the upper limit of normal of $>$2.75mmol/L($>$11mg/dL)
  - Renal (kidney) insufficiency (creatinine $>$2 mg/dL) [$>177 \mu$mol/L] or creatine clearance $<$40mL/min
  - Anemia (hemoglobin $<$10g/d or hemoglobin $>$2 g/dL below the lower limit of normal)
  - One or more osteolytic bone lesions on skeletal radiography, CT, or PET/CT
  - Clonal bone marrow plasma cells $\geq 60$
  - Abnormal serum FLC ratio $\geq 100$ (involved kappa) or $\leq 0.01$ (involved lambda)
  - $>$1 focal lesions on MRI studies $\geq 5$ mm

Smoldering (asymptomatic) myeloma is diagnosed if:

- Serum monoclonal protein $>$3 g/dL

Or

- Bence-Jones protein $>$500 mg/24 h

And/or

- Clonal bone marrow plasma cells 10%-60%

And

- Absence of myeloma-defining events or amyloidosis
  - If skeletal

### How is multiple myeloma staged?

Multiple myeloma is disease that can behave very differently in different individuals. It is critically important to identify those patients at high-risk versus low-risk, and tailor treatment accordingly. There are several factors that can predict how aggressive the multiple myeloma will behave and these are incorporated into staging of the disease.

Staging is a way to give a cancer a sort of "rating" that reflects prognosis and helps guide treatment decisions. Staging for myeloma is different than staging for solid tumors (i.e. breast, lung and colon cancer), which typically uses an I-IV stage rating.

The International Staging System (ISS) divides myeloma into three states and is based on the serum beta-2 microglobulin and serum albumin levels. In 2015, the ISS was revised and now includes potential impact of chromosomal abnormalities indicated
via FISH testing and changes to serum LDH level

<table>
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<th>Stage</th>
<th>International Staging System</th>
<th>Revised-ISS (R-ISS)</th>
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<tr>
<td>I</td>
<td>Serum beta-2 microglobulin &lt; 3.5 mg/L</td>
<td>ISS stage I and standard-risk chromosomal abnormalities by FISH</td>
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<tr>
<td></td>
<td>Albumin 3.5 g/dL or greater</td>
<td>(standard risk = no high risk chromosomal abnormality)</td>
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<td></td>
<td>May also include standard risk chromosomal abnormalities and normal LDH</td>
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<td>Serum lactate dehydrogenase (LDH) ≤ the upper limit of normal</td>
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<td>II</td>
<td>Neither Stage I or III</td>
<td>Not R-ISS stage I or III</td>
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<td>ISS stage III and either high risk chromosomal abnormalities by FISH or</td>
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<td>May also include high-risk chromosomal abnormalities and elevated LDH</td>
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<td>Serum LDH &gt; the upper limit of normal</td>
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How is multiple myeloma treated?

**MGUS & Smoldering myeloma**

Treatment is not recommended for MGUS, and no intervention (treatment) has been found to delay or prevent MGUS from progressing to myeloma. Patients with asymptomatic or smoldering myeloma (stage I) should be followed closely, without treatment, because research studies have found that treating asymptomatic myeloma does not improve survival.

**Treatment for Active myeloma**

The past fifteen years has seen unprecedented advances in the treatment of symptomatic myeloma, with most patients responding to initial therapy. Many patients live with myeloma as a chronic cancer for many years. Unfortunately, curative treatment is still lacking. There are a number of treatment options for myeloma, including chemotherapy, steroids, targeted therapy and high dose chemotherapy with stem cell transplant. Your oncology team will work with you to determine the best treatment or combination of treatments for your cancer. Below you will find an introduction to the available treatments.

**High Dose Chemotherapy with Stem Cell Transplant**

Several clinical trials have shown that in patients who are young (age <65 years) and fit enough, high dose chemotherapy and autologous stem cell transplant (using the patient's own stem cells) is a very good treatment option. This may be used as the first line therapy or after the disease has progressed on other therapies. This treatment is not considered a good option for certain high-risk patients with particular DNA abnormalities (chromosome 13 deletion, chromosome 17 translocation), as this may lead to poorer survival.

There are three phases to stem cell transplant therapy: induction therapy, stem cell transplant and maintenance therapy. In transplant candidates, the goal of the initial chemotherapy – called "induction chemotherapy" - is to kill as many myeloma cells as possible without damaging the stem cells. Patients are given several cycles of chemotherapy that typically contains bortezomib combined with dexamethasone and a third agent (thalidomide, carfilzomib, ixazomib, lenalidomide, doxorubicin or cyclophosphamide) and dexamethasone.

Following this "induction chemotherapy," patients will undergo a stem cell collection. Stem cells used to be collected from bone marrow in the operating room. Due to the advances in stem cell collection, they can be taken from the blood, which is done in apheresis unit at a hospital using a procedure similar to dialysis. The patient sits in a recliner chair and, using a catheter in the chest or arm, blood is pulled out and passed through a machine that takes out the stem cells and returns the rest of the blood to the patient. These cells are then frozen until the patient is ready to receive them.
The next part of the transplant is typically done in the hospital. The patient is given high doses of chemotherapy to kill as much of the myeloma as possible. This treatment also damages or kills the stem cells in the patient's body. A day or two after completing the chemotherapy, the previously collected stem cells are thawed and given back to the patient through a catheter. These cells replace the stem cells that were damaged during the high dose chemotherapy, allowing your body to recover from this chemotherapy. In some institutions, the patient will remain in the hospital during the recovery, while others have an apartment or hotel nearby where patients stay and come to the clinic to be checked every day. Talk to the oncology team about their specific procedure.

After transplant, if remission is achieved, patients may require treatment with "maintenance" chemotherapy. It is not currently clear whether maintenance therapy is needed in all patients and your physician may elect instead for observation without maintenance chemotherapy. This is usually a less intense chemotherapy regimen and its goal is to prolong the period of remission. Preferred maintenance therapy is bortezomib or lenalidomide.

Some studies are looking at the benefit of a second transplant (called tandem transplant) for patients who do not achieve a full remission after the first transplant. With this therapy, a second transplant is done within six months of the first. Up to half of patients treated with tandem transplants may have a complete response, however this is still being studied. In some cases, allogeneic transplant (stem cells from a donor) may be a treatment option. Allogeneic transplant has significant side effects and the risks and benefits of this therapy need to be discussed with each potential patient (see more below).

**Allogeneic Stem Cell Transplant**

There are two types of transplants: autologous transplants, where the stem cells to be transplanted come from the person with multiple myeloma, and allogeneic transplants, where stem cells are harvested from a donor who has been matched with the person with multiple myeloma. The role of allogeneic transplant in myeloma is controversial and still being studied.

One theoretical advantage of allogeneic over autologous transplant is that even after induction chemotherapy, there are often still cancer cells in the blood an autologous transplant. Inevitably, during harvesting of stem cells, some of the remaining cancer cells are accidentally collected. Allogeneic cells come from a donor with no cancer; hence the collected stem cells contain no cancer cells.

Allogeneic cells also cause graft versus host phenomenon, which can be good and bad. The donated stem cells form the new immune system for the person receiving the transplant. Unfortunately, this new immune system may perceive the host tissues (the organs of the patient who received the transplant) as foreign and attack them. Typically, the liver, gastrointestinal tract, and skin are most severely affected. However, the new immune system can be used for good since it recognizes the myeloma cells as foreign and can attack any myeloma cells that are left. Graft versus host disease can cause organ failure, and immunosuppression to control graft versus host disease can increase the risk of infection. Hence, there has to be a careful balance when suppressing the new immune system to protect organs, but also allowing the new immune system to destroy any left over myeloma cells.

Another complication of allogeneic transplants is that the donor tissue must be matched to the recipient. Sometimes family members can be donors, but in the event that is not possible, the national registry of bone marrow donors can be searched for a match. Mortality from allogeneic transplant can be as high as 10-20%. Currently, allogeneic transplant as initial therapy should only be considered in the context of a clinical trial.

There is continued investigation of nonmyeloablative transplants ("mini-transplants"), where low doses of chemotherapy are used after stem cell harvest to kill myeloma cells prior to allogeneic transplant. In nonmyeloablative transplants, the goal is to decrease toxicity, but preserve the beneficial graft-versus-myeloma effect. Like other allogeneic transplants, mini-transplants are only recommended when used in the setting of a clinical trial.

**Myeloma treatment for non-transplant candidates**

Patients older than 65 years or with multiple other medical problems may not be candidates for stem cell transplant. In these patients, chemotherapy and targeted therapies may be used. There are several regimen options that include a combination of two or more of these medications:

- Targeted (immunomodulating/proteasome inhibitors) therapies: bortezomib, lenalidomide, thalidomide, ixazomib
Chemotherapy agent: cyclophosphamide
Steroid agents: dexamethasone

Some clinicians feel that melphalan therapy should be avoided because it destroys the bone marrow stem cells and carries an increased risk of developing leukemia or other bone marrow disorders, such as myelodysplastic syndrome. After achieving remission, maintenance chemotherapy may be recommended with bortezomib, lenalidomide, or thalidomide.

Treatment of Relapse

Almost all patients with multiple myeloma eventually relapse, many within 36 months. Management of relapsed myeloma depends on the initial treatment, length of remission, and persisting toxicities and other medical problems. Medications used in relapse for patients who were previously treated for multiple myeloma include: bortezomib, bendamustine, lenalidomide, thalidomide, cyclophosphamide, daratumumab, carfilzomib, daratumumab, etoposide, cisplatin, ixazomib, panobinostat, pomalidomide, bendamustine, vorinostat, and dexamethasone.

An immunotherapy medication, elotuzumab, used in combination with lenalidomide and dexamethasone is also an option for patients who have received previous multiple myeloma treatment.

These medications may be used alone or in combination. The choice of a treatment regimen is based on a number of factors including cytogenetics, staging, lab values, organ/bone involvement, kidney function and other co-morbid medical conditions.

Other Treatment Considerations

Patients with kidney failure at presentation require urgent treatment to improve chances of restoring kidney function. Both bortezomib and lenalidomide have been reported to be effective in reversing kidney damage. Plasmapheresis, a process which separates myeloma cells from the blood, has not been shown to be beneficial.

When there is evidence or suspicion of spinal cord compression, dexamethasone should be started immediately followed by urgent imaging of the spine. A neurosurgeon and/or radiation oncologist should be consulted to consider surgical decompression of the spine or radiation therapy to the spine.

Patients experiencing bone pain due to involvement of myeloma may be treated with low-dose radiation (10-30 Gy) to the bones to relieve pain, improving quality of life. If myeloma involves the bones in the spine (the vertebrae) and a vertebral compression fracture occurs, vertebroplasty or kyphoplasty is recommended. Both procedures involve injecting bone cement into the vertebral body; kyphoplasty also uses a balloon to restore normal height of the bone.

Bisphosphonates are commonly used in patients with myeloma to strengthen bones, prevent fractures and lower calcium levels. Bisphosphonates (pamidronate, zoledronate) inhibit bone breakdown and promote formation of new bone, thus opposing the effects of multiple myeloma on bones. Long-term use of bisphosphonates is associated with a small risk of osteonecrosis of the jaw (death of the jaw bone), atrial fibrillation, unusual fractures, and esophageal cancer. You should have a baseline dental examination before starting bisphosphonate therapy. Usually the benefits of bisphosphonates outweigh the risks, but it is important to discuss risks and benefits as they pertain specifically to you. An alternative to treatment for bone disease with bisphosphonates is the use of denosumab.

Patients with a solitary plasmacytoma (a solid tumor made of myeloma cells) are best treated with radiation therapy as initial (and potentially curative) treatment. Sometimes, surgery is needed after radiation therapy.

Important Side Effects of Multiple Myeloma and It’s Treatments

Myeloma increases one's risk of developing a blood clot in the legs, known as a deep vein thrombosis (DVT). The risk of developing a DVT is even further increased when taking thalidomide or lenalidomide. Fortunately, DVT only happens in 1-3% of people on these medications. However, when used in combination with dexamethasone, this can increase to 10-15%, and if used in combination with dexamethasone and doxorubicin, (a chemotherapy), this number can increase to 25%. DVT in the leg is concerning because the blood clot in the leg can travel to the lungs, causing a serious condition called pulmonary embolus. A pulmonary embolus can cause cough, chest pain, shortness of breath, and even death. Due to the risk of DVT and pulmonary embolism, all patients taking lenalidomide with dexamethasone or any thalidomide-containing therapy should receive
anticoagulation (blood thinners) to prevent formation of a blood clot. Thalidomide and lenalidomide also cause severe life-threatening birth defects. You should not become pregnant or father a child while taking these medications. Bortezomib can increase one’s risk of developing herpes zoster (shingles), so a shingles vaccine is recommended prior to bortezomib therapy. Other side effects of chemotherapy agents include low blood counts, fatigue, constipation, diarrhea and neuropathy (nerve damage, usually manifesting as numbness in the fingers and toes).

Clinical Trials

There are clinical research trials for most types of cancer, and every stage of the disease. Clinical trials are designed to determine the value of specific treatments. Trials are often designed to treat a certain stage of cancer, either as the first form of treatment offered, or as an option for treatment after other treatments have failed to work. They can be used to evaluate medications or treatments to prevent cancer, detect it earlier, or help manage side effects. Clinical trials are extremely important in furthering our knowledge of disease. It is through clinical trials that we know what we do today, and many exciting new therapies are currently being tested. Talk to your provider about participating in clinical trials in your area. You can also explore currently open clinical trials using the OncoLink Clinical Trials Matching Service.

Follow-up care and Survivorship

Follow up appointments to monitor for relapse are an important part of your treatment plan. Generally, after completion of treatment, your provider may ask you to follow up every one to three months. The follow up visit usually entails a physical exam, x-rays, blood tests and urine tests. X-rays are used to check for bone disease and blood and urine tests are used to check for the level of monoclonal proteins. Blood tests to check kidney function, calcium levels, and cell counts are also done routinely. Repeated bone marrow biopsies may also be needed to check for myeloma cells in the bone marrow. Your healthcare provider may also test for minimal residual disease. This measures the number of myeloma cells that remain after therapy is completed. This can help your provider understand more about the remission and potentially how long it may last. Be advised this test is not always covered by insurance as it has not been formally approved by the FDA for use in myeloma. Check your insurance coverage for this test before your care provider orders it.

Treatment options for myeloma have grown exponentially in the past 15 years. As a result, myeloma may be more appropriately viewed as a chronic or long-term cancer. Fear of relapse, relationship challenges, managing financial impact of long term treatment, employment issues, and coping strategies are common emotional and practical issues experienced by myeloma survivors. Your healthcare team can identify resources for support and management of these practical and emotional challenges faced during and after cancer.

Cancer survivorship is a relatively new focus of oncology care. With some 17 million cancer survivors in the US alone, there is a need to help patients transition from active treatment to survivorship. What happens next, how do you get back to normal, what should you know and do to live healthy going forward? A survivorship care plan can be a first step in educating yourself about navigating life after cancer and helping you communicate knowledgeably with your healthcare providers. Create a survivorship care plan today on OncoLink.

Resources

The Leukemia and Lymphoma Society

Provides disease information, support resources and co-pay assistance.

http://www.lls.org/

The International Myeloma Foundation

The International Myeloma Foundation web site provides access to information and services of interest to everyone battling myeloma- patients, their families/caregivers, physicians and scientists.

http://myeloma.org/

Multiple Myeloma Research Foundation
Cutting-edge information on new research and clinical trials for myeloma patients, as well as current treatment information, events for the myeloma community and news from the Foundation.

http://www.themmrf.org/

Life with Multiple Myeloma

An online community to support people living with myeloma.

http://www.lifewithmultiplemyeloma.org/

OncoLink is designed for educational purposes only and is not engaged in rendering medical advice or professional services. The information provided through OncoLink should not be used for diagnosing or treating a health problem or a disease. It is not a substitute for professional care. If you have or suspect you may have a health problem or have questions or concerns about the medication that you have been prescribed, you should consult your health care provider.