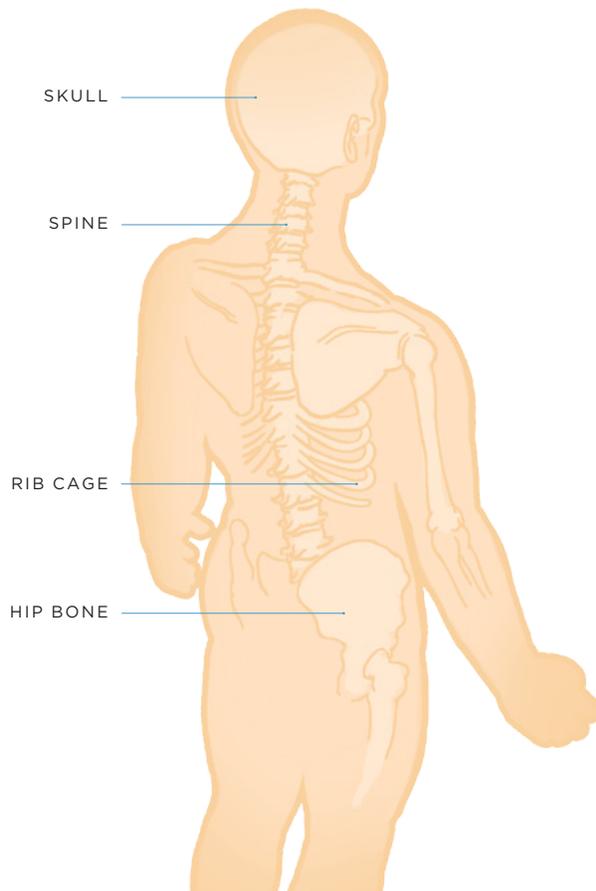


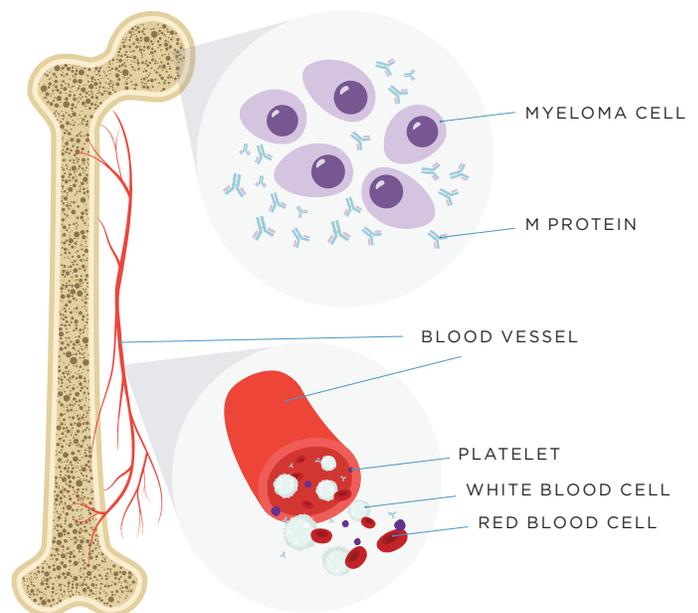
MULTIPLE MYELOMA

What is multiple myeloma (MM)?

BONES THAT ARE OFTEN AFFECTED BY MULTIPLE MYELOMA



CANCEROUS PLASMA (MYELOMA) CELLS AND BLOOD CELLS ARE PRODUCED IN THE BONE MARROW



Multiple myeloma is a cancer of the plasma cells

- Red blood cells, white blood cells, and platelets are formed in the bone marrow by stem cells
- Plasma cells are a type of white blood cell that produce proteins called antibodies (immunoglobulins) to fight infections. When plasma cells transform into cancer cells, they are called myeloma cells. When myeloma cells form in many different parts of the body, it is called multiple myeloma
- Myeloma cells frequently produce an abnormal, nonfunctional antibody
- The abnormal antibodies produced by myeloma are called monoclonal proteins, or M proteins (also known as paraproteins)

ELEVATED CALCIUM

Signs and symptoms of multiple myeloma

Multiple myeloma is a cancer of the plasma cells in your bone marrow (the soft tissues inside your bones). Plasma cells are specialized white blood cells that produce antibodies, which are responsible for fighting infection in your body. Bone is a living tissue that is constantly being rebuilt, with specialized cells that make new bone (osteoblasts) and other specialized cells that break down existing bone (osteoclasts). Myeloma cells interfere with this process.

Cause of elevated calcium

- Calcium is a mineral found in bones. Myeloma cells increase the breakdown of the bone, which raises calcium levels in the blood
- High levels of calcium in the blood is called hypercalcemia, which can cause damage to the kidneys
- If left untreated, hypercalcemia may cause other serious or life-threatening problems

Signs and symptoms of elevated calcium

- Trouble thinking clearly, confusion
- Feeling thirsty
- Constipation
- Urinating a lot
- Loss of appetite
- Nausea
- Weakness
- Arrhythmias

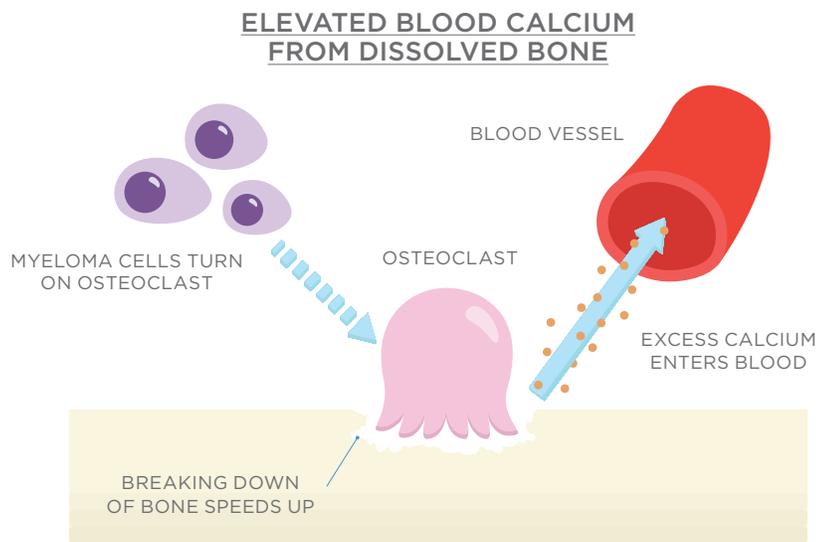
How elevated calcium levels are diagnosed and monitored

- A serum calcium test shows how much calcium is in your blood. Your doctor may ask for additional blood and/or urine tests
- Continual monitoring of calcium levels with blood tests is an important part of myeloma care

Treatment options

Your healthcare team may give the following advice and treatment

- Drink plenty of fluids (for mild hypercalcemia)
- Avoid calcium-containing foods
- Remain active
- Give fluids intravenously (through a tube into a vein)
- Your healthcare professional may prescribe medicine to stop the breakdown of bone and the release of calcium into the blood
- If there is kidney damage, perform dialysis to help with kidney function, including removing excess calcium from the blood



KIDNEY DISEASE

Signs and symptoms of multiple myeloma

Multiple myeloma is a cancer of the plasma cells in your bone marrow (the soft tissues inside your bones). Plasma cells are specialized white blood cells that produce antibodies, which are responsible for fighting infection in your body. Myeloma can also damage your kidneys, as described below.

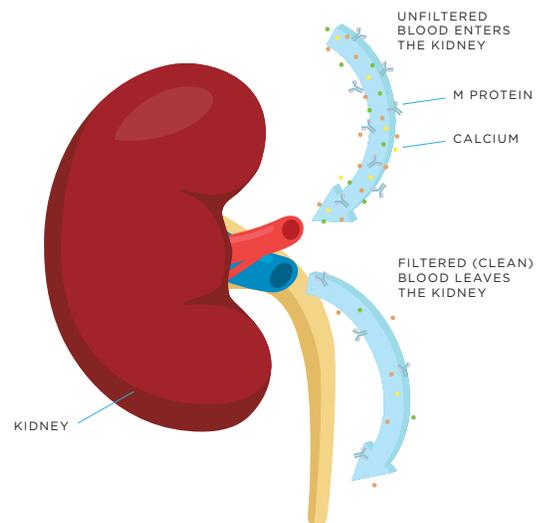
Causes of kidney disease in multiple myeloma

- Myeloma can damage your kidneys by producing too much abnormal antibody protein (called M protein), which can accumulate in the kidney tubes
- Too much calcium in the blood from broken-down bone caused by myeloma can also harm the kidney
- Kidney damage makes it harder for your body to get rid of excess salt, fluids, and waste products in the urine

Signs and symptoms of kidney disease

- Feeling tired
- Trouble thinking clearly
- Loss of appetite
- Itching
- Nausea
- Sleep problems
- Vomiting
- Changes in urination
- Hiccups
- Cramps
- Breath odor
- Easy bruising and bleeding
- Sexual dysfunction
- Shortness of breath
- Swelling of legs
- Fluid in the lungs

NORMAL KIDNEY FUNCTION



Diagnosis and monitoring of kidney disease

Two tests are used to determine how well your kidneys are working:

- Blood urea nitrogen (BUN) test—poor kidney function can result in high levels of a chemical called urea in your blood
- Creatinine test—poor kidney function also causes the level of a chemical called creatinine to rise in both your blood and urine. Your healthcare professional may ask you for a sample of blood or urine for different creatinine tests. You may also be asked to collect all of your urine over 24 hours for a test called creatinine clearance

Treatment options

Your healthcare team may recommend the following:

- Discuss all medications with your healthcare provider before taking them (including prescription and nonprescription medications, and herbal or dietary supplements). The dose of some medications may need to be adjusted, as some medications may contribute to kidney damage
- Discuss your fluid intake and diet with your healthcare professional to see whether you have special needs
- When possible, avoid the use of IV contrast dye in certain imaging tests like MRIs
- Plasmapheresis, a procedure that reduces the excess M proteins in the blood

BLOOD MONITORING

Signs and symptoms of multiple myeloma

Multiple myeloma is a cancer of the plasma cells in your bone marrow (the soft tissues inside your bones). Plasma cells are specialized white blood cells that produce antibodies, which are responsible for fighting infection in your body. A plasma cell becomes cancerous (called a myeloma cell) when the DNA mutates and makes continuous copies of itself. Because myeloma cells grow in the bone marrow, they can cause a number of abnormalities in the blood.

Causes of blood abnormalities in multiple myeloma

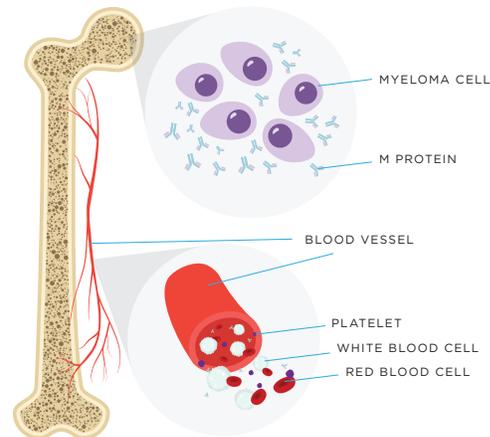
- Antibodies are also called immunoglobulins and are made by plasma cells
- Myeloma cells produce an abnormal antibody protein called **M protein**, which can be used to confirm a diagnosis of myeloma
- Myeloma cells growing in the bone marrow crowd out other blood cells that are also produced in the marrow, causing changes in the blood

Various laboratory tests can be used to detect the abnormal proteins, myeloma cells, mutated DNA, and abnormalities in the blood. Some of them are listed here:

M protein analysis and evaluation

- All antibodies are made of 2 identical heavy protein chains and 2 identical light protein chains
- There are 5 types of heavy chains (IgG, IgA, IgM, IgD, IgE)
- There are 2 types of light chains (kappa and lambda)
- In multiple myeloma, myeloma cells are producing too many of one type of immunoglobulin (IgA, for example)
- These proteins, called M proteins, can be measured in the blood and/or urine and can be measured by the following lab tests:
 - Serum protein electrophoresis
 - Urine protein electrophoresis
 - Immunofixation electrophoresis
 - Free serum light chain testing
- Knowing the type of immunoglobulin being overproduced is important for diagnosis, monitoring, and treatment

CANCEROUS PLASMA (MYELOMA) CELLS AND BLOOD CELLS ARE PRODUCED IN THE BONE MARROW



- Some patients only make light chains and these proteins can be monitored by the free serum light chain test or urine protein electrophoresis

Bone marrow biopsy and evaluation

- Your healthcare professional may remove a tissue sample from your bone marrow
- The tissue sample will be evaluated to see whether you have myeloma cells and to test for abnormal chromosomes

Chromosomal abnormalities in multiple myeloma

- Chromosomes are long strands of DNA that contain genetic information
- When there are missing, misplaced, or abnormal chromosomes, cancer and other harmful effects in cells can result
- Certain chromosomal abnormalities may be associated with poor outcomes
- Your healthcare team may ask for one of these tests to see whether you have missing or abnormal chromosomes

- Karyotyping

- FISH test

- These tests may tell important information about how your multiple myeloma will progress and the best way to treat it

Anemia related to multiple myeloma

- Myeloma cells in your bone marrow can prevent your body from producing enough red blood cells (RBCs), resulting in anemia
- Symptoms common to many types of anemias include the following:
 - Easy fatigue and loss of energy
 - Rapid heartbeat, particularly with exercise
 - Shortness of breath
- Your healthcare professional will assess you for anemia using a test called a complete blood count (CBC). This test measures how many RBCs and other types of cells are in your blood
- You may get medicine to treat anemia or a blood transfusion

Ask your healthcare team if you have questions about any of the listed lab tests.

BONE LESIONS

Signs and symptoms of multiple myeloma

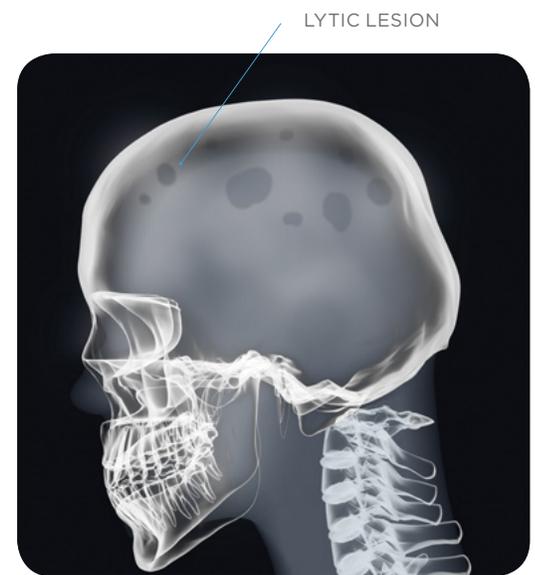
Multiple myeloma is a cancer of the plasma cells in your bone marrow (the soft tissues inside your bones). Plasma cells are specialized white blood cells that produce antibodies, which are responsible for fighting infection in your body. Myeloma cells in the bone marrow can also turn off the cells that build up bone and turn on the cells that break down bone.

Cause of bone lesions

- Bone remodeling is the balance of bone formation and bone breakdown
- As myeloma cells grow in the marrow, this balance is disrupted and bone breakdown increases
- As bone breakdown progresses, people can get soft spots on their bones that show up on imaging as lytic lesions
- Lytic lesions weaken the bone, causing pain and increasing the risk of broken bones

Signs and symptoms of bone lesions

- Back pain
- Lytic bone lesions
- Broken bones
- Too much calcium in the blood (known as hypercalcemia)
- Compression of the spinal cord, which can cause numbness in the hands and feet; bladder and/or bowel dysfunction; and sometimes paralysis



X-RAY OF LYTIC BONE LESIONS IN SKULL

How bone lesions are diagnosed and monitored

Bone lesions show up on imaging tests. Your healthcare professional may diagnose your condition and monitor the disease by asking for:

- Bone x-rays show if damage has been caused by myeloma cells. You may get a skeletal survey, which is an x-ray of most of your bones
- CT scan—a type of x-ray that shows a 3-dimensional picture
- MRI uses radio waves and strong magnets to form a 3-dimensional picture
- PET CT—tests that use radioactive sugar to identify and locate cancer cells (as they absorb the sugar) in the body

Treatment options

There are several therapies your healthcare team may use to treat bone disease caused by multiple myeloma, including:

- Medication to prevent the breakdown of bone
- Spinal injections—vertebroplasty or kyphoplasty
- Surgery
- Radiation
- Remain active under physician supervision
- Pain medication

NEUROLOGICAL EFFECTS

Signs and symptoms of multiple myeloma

Multiple myeloma is a cancer of the plasma cells in your bone marrow (the soft tissues inside your bones). Plasma cells are specialized white blood cells that produce antibodies, which are responsible for fighting infection in your body. Myeloma cells can also cause damage to other parts of your body such as the nerves.

Causes of nerve problems in multiple myeloma

- Multiple myeloma can cause bone damage to your spine, making it weak and creating soft spots, or lesions, in the bone. This can lead to spinal cord compression. This compression can damage the nerves in your spine
- Abnormal proteins produced by myeloma cells can also damage your nerves and disrupt the signals your brain sends to other parts of the body
 - In some people, the abnormal proteins can cause the blood to thicken. This can slow the flow of blood to the brain and cause many of the signs and symptoms of nerve damage listed below:

Signs and symptoms of spinal cord compression

- Back or buttock pain
- Limb pain
- Limb weakness/numbness
- Urinary retention and stool incontinence
- Paralysis

Signs and symptoms of the abnormal protein nerve effects

- Pain
- Numbness, especially in the legs and feet
- Limb heaviness, muscle weakness
- Abnormal sensations, usually in the hands or feet

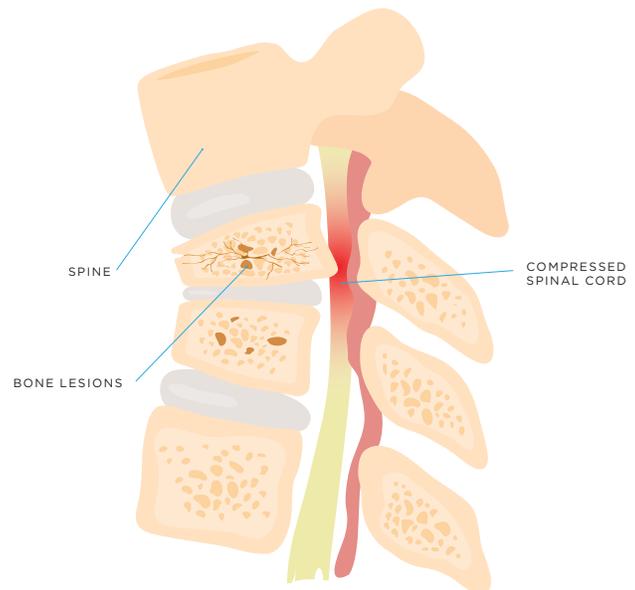
Diagnosis and monitoring of nerve problems

- Keep a record of the listed signs and symptoms of nerve problems and report them to your healthcare team
- Bone damage causing nerve problems may show up on imaging tests. Your healthcare team can diagnose the condition and monitor its progress with these tests:
 - MRI—uses radio waves and strong magnets to form a 3-dimensional picture
 - CT scan—a type of x-ray that shows a 3-dimensional picture
 - PET CT—tests that use radioactive sugar to identify and locate cancer cells (as they absorb the sugar) in the body
- Nerve conduction studies—tests to rule out other conditions that have signs and symptoms of nerve damage similar to those in multiple myeloma

Treatment options

- Your healthcare professional may make the following recommendations for treating bone disease caused by multiple myeloma
 - Medications
 - Surgery
 - Radiation
- You may be treated with a process called plasmapheresis to reduce the level of abnormal proteins in the blood

BONE LESIONS RESULTING IN SPINAL CORD COMPRESSION



UNDERSTANDING SLiM CRAB

Diagnostic criteria for active multiple myeloma

SLiM and CRAB are acronyms healthcare professionals use to recognize the signs and symptoms of multiple myeloma.

- CRAB has traditionally been the set of 4 criteria used by healthcare professionals to diagnose active multiple myeloma. These symptoms were the results of damage from the disease
- Recent studies showed that evidence of multiple myeloma characterized by special biomarkers can be detected by advanced lab tests and imaging. These biomarkers—summarized as SLiM—appear before the CRAB symptoms
- Testing for these biomarkers allows healthcare professionals to diagnose and treat multiple myeloma earlier and help prevent organ damage
- The current recommendation by the International Myeloma Working Group (IMWG) is to use both the SLiM biomarkers and CRAB symptoms for diagnosis. These criteria are summarized below:

ACRONYM	LAB RESULT	CRITERIA
S	Sixty percent (60%) or greater of bone marrow plasma cells	There is excessive multiplication of abnormal plasma cells in the bone marrow
Li	Light chain ratio of 100 or greater in serum	There are 2 types of light chains (kappa and lambda free light chains [FLC]) of immunoglobulins that circulate freely in blood serum. When the ratio—or percentage—of 1 of these chains is abnormally larger than the other, it indicates excessive plasma cell production
M	MRI with more than 1 focal lesion	Magnetic resonance imaging shows that an abnormality has formed in part of the bone or bone marrow

ACRONYM	SYMPTOM	WHAT CAUSES IT	HOW IT AFFECTS YOU
C	Calcium levels increased in blood	Myeloma cells increase the rate at which bones dissolve and decrease the rate of bone repair and growth. This releases calcium into the blood	Confusion, thirst, constipation, urinating a lot, loss of appetite, nausea, weakness, arrhythmias
R	Renal (kidney) problems	Excess M protein and calcium in the blood damage the kidneys as they filter blood. The amount of urine can increase and the kidneys may fail to work properly	Fatigue/weakness, changes in urination, swelling in legs and feet, nausea, vomiting
A	Anemia	Myeloma cells can suppress the formation of red blood cells, decreasing the number of red blood cells	Fatigue, shortness of breath, rapid heartbeat, dizziness
B	Bone damage	Myeloma cells can turn on cells that destroy bone and turn off cells that repair bone	Bone pain, pathological fractures, elevated calcium, spinal cord compression



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