Multiple Myeloma Early Detection, Diagnosis, and Staging

Detection and Diagnosis

Catching cancer early often allows for more treatment options. Some early cancers may have signs and symptoms that can be noticed, but that is not always the case.

- Can Multiple Myeloma Be Found Early?
- Signs and Symptoms of Multiple Myeloma
- Tests to Find Multiple Myeloma
- Diagnosing Multiple Myeloma from Test Results

Stages and Outlook (Prognosis)

After a cancer diagnosis, staging provides important information about the extent of cancer in the body and anticipated response to treatment.

- Multiple Myeloma Stages
- Survival Rates by Stage for Multiple Myeloma

Questions to Ask About Multiple Myeloma

Here are some questions you can ask your cancer care team to help you better understand your diagnosis and treatment options.

- What Should You Ask Your Doctor About Multiple Myeloma?

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.

- **References**

[See all references for Multiple Myeloma](#)

Last Medical Review: May 22, 2014 Last Revised: January 19, 2016

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**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 [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.

References

See all references for Multiple Myeloma

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.

- References
  See all references for Multiple Myeloma

Diagnosing Multiple Myeloma from Test Results

Although multiple myeloma is often diagnosed based on tests, 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

References

See all references for Multiple Myeloma

Last Medical Review: May 22, 2014 Last Revised: January 19, 2016
Multiple Myeloma Stages

After someone is diagnosed with cancer, doctors will try to figure out if it has spread, and if so, how far. This process is called staging. The stage of a cancer describes how much cancer is in the body. It helps determine how serious the cancer is and how best to treat it. Doctors also use a cancer’s stage when talking about survival statistics.

The Revised International Staging System

Multiple myeloma is staged using the Revised International Staging System (RISS) that is based on 4 factors:

- The amount of albumin in the blood
- The amount of beta-2-microglobulin in the blood
- The amount of LDH in the blood
- The specific DNA abnormalities (cytogenetics) of the cancer.

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<tr>
<th>RISS Stage Group</th>
<th>Factors</th>
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<tbody>
<tr>
<td>I</td>
<td>Serum beta-2 microglobulin is less than 3.5 (mg/L) &lt;br&gt; AND &lt;br&gt; Albumin level is 3.5 (g/dL) or greater &lt;br&gt; AND &lt;br&gt; Cytogenetics are considered “not high risk” * &lt;br&gt; AND &lt;br&gt; LDH levels are normal</td>
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<tr>
<td>II</td>
<td>Not stage I or III</td>
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<tr>
<td>III</td>
<td>Serum beta-2 microglobulin is 5.5 (mg/L) or greater &lt;br&gt; AND &lt;br&gt; Cytogenetics are considered “high-risk”* &lt;br&gt; AND/OR &lt;br&gt; LDH levels are high</td>
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*The bone marrow may be sent for tests to look at the chromosomes in the cancer cells. This test may also be called cytogenetics. Certain chromosome changes can mean a poorer outlook. For example, loss of a piece of chromosome 17 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. A translocation involving chromosomes 14 and 16 is also linked to a poorer outcome. These 3 specific chromosome changes are considered “high risk.” Other chromosome abnormalities are considered “standard risk” or not high risk.

Cancer staging can be complex, so ask your doctor to explain it to you in a way you understand.

**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.

**Overall Health**

Someone’s overall health can affect the outlook of someone with myeloma. Poorly controlled health conditions, such as diabetes or heart disease, for example, can predict a worse prognosis.

- **References**


  See all references for Multiple Myeloma

Last Medical Review: December 18, 2017 Last Revised: December 18, 2017

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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**
  - Stage I: 62 months
  - Stage II: 44 months
  - Stage III: 29 months

- **Median Survival**
  - 62 months
  - 44 months
  - 29 months

- **References**
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.