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# Multiple Myeloma Early Detection, Diagnosis, and Staging

Know the signs and symptoms of multiple myeloma. Find out how multiple myeloma is tested for, diagnosed, and staged.

#### **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?

# Can Multiple Myeloma Be Found Early?

It can be hard 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. Sometimes, multiple myeloma is found early when a routine blood test shows an abnormally high amount of protein in the blood.

People with		
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# Signs and Symptoms of Multiple

# Myeloma

- Bone problems
- Low blood counts
- High blood levels of calcium
- Nervous system symptoms
- Kidney problems
- Infections
- Signs and symptoms of light chain amyloidosis

Some people with multiple myeloma have no symptoms at all. But sometimes multiple myeloma does cause symptoms.

### **Bone problems**

- Bone pain, which can be in any bone, but is most often in the back, the hips, or skull
- Bone weakness, either all over (osteoporosis), or where there is a tumor
- 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, and might lead to other symptoms.

- Anemia: Having too few red blood cells can cause weakness, a reduced ability to exercise, shortness of breath, and dizziness.
- Leukopenia: Having too few white blood cells can lower resistance to infections such as pneumonia.
- Thrombocytopenia: Having too few blood platelets may cause serious bleeding even with minor scrapes, cuts, or bruises. .

# 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, or even kidney failure
- Severe constipation
- Abdominal (belly) pain
- Loss of appetite
- Weakness
- Feeling drowsy
- Confusion

If the level of calcium gets high enough, a person can even slip 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 it can cause:

- Sudden severe back pain
- Numbness, most often in the legs
- Muscle weakness, most often in the legs

This is a medical emergency, so you should contact your doctor right away or go to the emergency room if you have any of these symptoms. If spinal cord compression is not treated right away, there is a possibility of permanent paralysis.

#### Nerve damage

Sometimes, the abnormal proteins produced by myeloma cells can damage nerves. This can lead to weakness and numbness and sometimes a "pins and needles" sensation. This is called **peripheral neuropathy**.

#### **Hyperviscosity**

In some people, large amounts of myeloma protein can cause the blood to "thicken." This is called **hyperviscosity**. It can slow blood flow to the brain, which can cause:

Confusion

- Dizziness
- Symptoms of a stroke, like weakness on one side of the body and slurred speech

People with these symptoms need to 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 most likely won't cause any symptoms, but signs of kidney damage may be seen on a blood test or a urine test. If the kidneys start to fail, they lose the ability to get rid of excess salt, fluid, and body waste products. This can lead to symptoms such as:

- Weakness
- Shortness of breath
- Itching
- Leg swelling

#### **Infections**

People with myeloma 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 people with myeloma.

# Signs and symptoms of light chain amyloidosis

People with amyloidosis (discussed in What Is Multiple Myeloma?<sup>1</sup>) can have some of the same health issues as people with myeloma, such as kidney problems and nerve damage. They can also have other problems, such as:

- Heart problems: 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: A person may feel the liver below the right ribs. When this gets

large it can press on the stomach, so the person might feel 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:** Symptoms can include changes in the color or texture of the skin, easy bruising, and bleeding into the skin around the eyes ("raccoon eyes")
- Carpal tunnel syndrome: This can cause numbness and weakness in the hands.

### **Hyperlinks**

1. <u>www.cancer.org/cancer/types/multiple-myeloma/about/what-is-multiple-myeloma.html</u>

#### References

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# **Tests for Multiple Myeloma**

If signs, symptoms, or the results of certain lab tests suggest a person might have multiple myeloma, other tests will be done to find out for sure.

If multiple myeloma is found, further tests might also be done to learn more about it and help decide the best treatments.

A routine urine sample is checked for myeloma protein that has filtered through the kidney.

You most likely also will be asked to give a sample of urine that has been collected over a 24-hour period, to measure how much myeloma protein is present (see Electrophoresis, below). You will be given instructions on how to do this.

#### **Quantitative immunoglobulins**

This test measures the blood levels of the different antibodies (immunoglobulins), including 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**

Finding a monoclonal antibody in the blood is often a first step in diagnosing multiple myeloma. A test known as electrophoresis can be done on blood or urine samples to find these antibodies. The antibodies made by myeloma cells are abnormal because they are all the same (monoclonal). This abnormal protein is known by several different names, including monoclonal immunoglobulin, monoclonal protein (M protein), M spike, or paraprotein.

**Serum protein electrophoresis (SPEP)** is a test that measures the antibodies in the blood and can find a monoclonal antibody.

Another test, called **immunofixation** or **immunoelectrophoresis**, can be used to determine the exact type of abnormal antibody (IgG, IgA, or some other type).

Antibodies are made up of chains of proteins, including 2 long (heavy) chains and 2 shorter (light) chains. Sometimes pieces of the abnormal myeloma protein are filtered through the kidney and into the urine. This urine protein, known as **Bence Jones protein** 

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) antibodies, it cannot measure the amount of light chains only.

This test can also be used to calculate the serum free light chain ratio, which can

special lab-made antibodies (immune proteins) that cause color changes on the cells if they contain certain proteins. This can be used to help identify myeloma cells.

- Flow cytometry: This test also uses antibodies, but it uses a special machine to see if the antibodies attached to the cells.
- Cytogenetics (karyotyping): This test looks at the chromosomes (long strands of DNA) in the cells. Sometimes myeloma cells have too many chromosomes, too few chromosomes, or other chromosome abnormalities, such as translocations (the swapping of DNA between chromosomes) or deletions (loss of part of a chromosome). Finding these changes can sometimes help predict a person's prognosis (outlook). Cytogenetic testing usually takes about 2 to 3 weeks to get a result.

**Fluorescent in situ hybridization (FISH):** This test uses special fluorescent dyes that only attach to specific parts of chromosomes. It can find most chromosome changes (such as translocations and deletions) that can be seen with standard

### **Imaging tests**

Imaging tests use sound waves, x-rays, magnetic fields, or radioactive substances to create pictures of the inside of your body. Imaging tests may be done for a number of reasons, such as:

- To look at suspicious areas that might be cancer
- To learn how far cancer has spread
- To help determine if treatment is working

#### Bone x-rays

<u>X-rays</u><sup>3</sup> can detect bone destruction caused by 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 (CT) scan

A <u>CT scan</u><sup>4</sup> uses x-rays taken from different angles, which are combined by a computer to make detailed pictures of the inside of your body. Sometimes, this test can help tell if your bones have been damaged by myeloma. It can also be used to guide a biopsy needle into an area of concern.

#### Magnetic resonance imaging (MRI) scan

Like CT scans, MRIs<sup>5</sup> show detailed images of soft tissues in the body. But MRIs use radio waves and strong magnets instead of x-rays.

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 a person 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 people with multiple myeloma.

### Positron emission tomography (PET) scan

For this test, a form of radioactive sugar is put into a vein and travels throughout the body. Cancer cells absorb high amounts of this sugar. A special camera then takes pictures that show the areas where the sugar collected throughout the body. A PET scan is often combined with a CT scan (known as a **PET/CT scan**).

Like MRI scans, PET scans can find plasmacytomas (tumors) that can't be seen on regular x-rays, so they are helpful if a person has pain in a bone but the x-ray doesn't show anything.

#### **Echocardiogram (ECHO)**

<u>Amyloidosis</u><sup>6</sup> often affects the heart, so if your doctor suspects you have this disorder, an echocardiogram (ECHO) may be done.

This test is an ultrasound of the heart. It uses sound waves to look at the heart muscle and see how well it's working. The echocardiogram can see if the heart size is normal and if it is pumping normally. It also is helpful if amyloid is suspected because amyloid in the heart muscle looks different from normal heart muscle.

## Diagnosing multiple myeloma

Multiple myeloma is often diagnosed based on test results, a person's symptoms, and the results of the physical exam. A diagnosis of multiple myeloma requires:

Either a plasma cell tumor (proven by biopsy) OR at least 10% plasma cells in the bone marrow, AND

At least one of the following:

- High blood calcium level
- Poor kidney function
- Low red blood cell count (anemia)
- Holes in the bones from tumor(s) found on imaging tests (CT, MRI, PET scan)
- Increase in one type of light chain in the blood so that one type is at least 100 times more common than the other
- 60% or more plasma cells in the bone marrow

# Diagnosing smoldering myeloma

This term is used to describe early myeloma that is not causing any symptoms. 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 do not meet the requirements for multiple myeloma, as defined above. That is, they have normal blood counts, normal calcium levels, normal kidney function, and no bone or organ damage. They also have no signs of amyloidosis.

# Diagnosing monoclonal gammopathy of undetermined significance (MGUS)

To be diagnosed with MGUS, a person must have ALL of these:

- Higher than normal level of monoclonal immunoglobulin (M protein) in the blood, but less than that for smoldering myeloma
- Less than 10% plasma cells in the bone marrow
- None of the requirements for multiple myeloma, as defined above. That is, they have normal blood counts, normal calcium levels, normal kidney function, and no bone or organ damage. They also have no signs of amyloidosis.

# Diagnosing light chain amyloidosis

A diagnosis of light chain amyloidosis is made when a person has ALL of the following:

- Evidence of amyloid-related damage to an organ or system (such as the kidneys, heart, liver, digestive tract, or nerves)
- A biopsy that shows amyloid in any tissue (fat, bone marrow, or an organ such as the heart)
- A positive test showing the amyloid is a light chain protein
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for amyloid. This is rarely needed to find out if a person has light chain amyloidosis, but it is sometimes done in someone with amyloidosis if it isn't clear what is causing their heart or kidney problems.

Other tests are often done as well to help confirm that a person has light chain amyloidosis and not some other type of amyloidosis. These include a bone marrow biopsy, serum free light chains, and electrophoresis of the urine (discussed earlier in this section).

### **Hyperlinks**

- 1. <u>www.cancer.org/cancer/diagnosis-staging/tests/understanding-your-lab-test-results.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts/anemia.html</u>
- 3. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/x-rays-and-other-radiographic-tests.html</u>
- 4. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ct-scan-for-cancer.html</u>
- 5. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/mri-for-cancer.html
- 6. <u>www.cancer.org/cancer/types/multiple-myeloma/about/what-is-multiple-myeloma.html</u>

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# **Multiple Myeloma Stages**

- The amount of albumin in the blood
- The amount of beta-2-microglobulin in the blood
- The amount of LDH in the blood

A translocation involving chromosomes 14 and 16

These 3 specific chromosome changes are considered **high risk**. Most 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 can affect survival

Other factors can also be important in helping to determine a person's prognosis (outlook), although it's important to keep in mind that each person is different.

#### **Kidney function**

The blood creatinine level shows how healthy the kidneys are. The kidneys remove this chemical from the blood. When they are damaged by the monoclonal immunoglobulin,

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# **Survival Rates for Multiple Myeloma**

- What is a 5-year relative survival rate?
- Where do these numbers come from?
- 5-year relative survival rates for myeloma
- Understanding the numbers

Survival rates tell you what percentage of people with the same type and stage of cancer are still alive a certain amount of time (usually 5 years) after they were diagnosed. They can't tell you how long you will live, but they may help give you a better understanding about how likely it is that your treatment will be successful.

Keep in mind that survival rates are estimates and are often based on previous outcomes of large numbers of people who had a specific cancer, but they can't predict what will happen in any particular person's case. These statistics can be confusing and may lead you to have more questions. Ask your doctor, whois familiar with your situation, how these numbers may apply to you.

# What is a 5-year relative survival rate?

A **relative survival rate** compares people with the same type and stage of cancer to people in the overall population. For example, if the **5-year relative survival rate** for a

specific stage of multiple myeloma is 60%, it means that people who have that cancer are, on average, about 60% as likely as people who don't have that cancer to live for at least 5 years after being diagnosed.

#### Where do these numbers come from?

The American Cancer Society relies on information from the Surveillance, Epidemiology, and End Results (SEER) database, maintained by the National Cancer Institute (NCI), to provide survival statistics for different types of cancer.

The SEER database tracks 5-year relative survival rates for myeloma in the United States, based on how far the cancer has spread. The SEER database, however, does not group cancers by the Revised International Staging System (stage 1, stage 2, or stage 3). Instead, it groups cancers into localized, regional, and distant stages:

- Localized: Only one tumor (a <u>solitary plasmacytoma</u><sup>1</sup>) is growing in the bone or outside the bone.
- **Regional:** This stage does not apply to myeloma, because this type of cancer does not spread to the lymph nodes.
- **Distant:** Many tumors are found inside or outside the bones, or multiple myeloma has been diagnosed.

# 5-year relative survival rates for myeloma

These numbers are based on people diagnosed with plasmacytomas or multiple myeloma between 2012 and 2018.

SEER Stage	5-year Relative Survival Rate
Localized (solitary plasmacytoma)	79%
Regional	Not applicable
Distant (multiple myeloma)	57%
All SEER stages combined	58%

**American Cancer Society** 

Once treatment begins, you'll need to know what to expect and what to look for. Not all of these questions may apply to you, but asking the ones that do may be helpful.

- How will we know if the treatment is working?
- Is there anything I can do to help manage side effects?
- What symptoms or side effects<sup>5</sup> should I tell you about right away?
- How can I reach you on nights, holidays, or weekends?
- Do I need to change what I eat during treatment?
- Are there any limits on what I can do?
- Can I exercise during treatment<sup>6</sup>? If so, what kind should I do, and how often?
- Can you suggest a mental health professional I can see if I start to feel overwhelmed, depressed, or distressed?
- What if I need social support during treatment because my family lives far away?

#### After treatment

- Do I need a special diet after treatment?
- Are there any limits on what I can do?
- What other symptoms should I watch for?
- What kind of exercise should I do now?

- 1. www.cancer.org/cancer/diagnosis-staging/tests.html
- 2. <a href="www.cancer.org/cancer/types/multiple-myeloma/treating.html">www.cancer.org/cancer/types/multiple-myeloma/treating.html</a>
- 3. <a href="www.cancer.org/cancer/managing-cancer/finding-care/seeking-a-second-opinion.html">www.cancer.org/cancer/managing-cancer/finding-care/seeking-a-second-opinion.html</a>
- 4. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html
- 5. www.cancer.org/cancer/managing-cancer/side-effects.html
- 6. <u>www.cancer.org/cancer/survivorship/be-healthy-after-treatment/physical-activity-and-the-cancer-patient.html</u>
- 7. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html
- 8. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 9. <u>www.cancer.org/cancer/managing-cancer/finding-care/the-doctor-patient-relationship.html</u>

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