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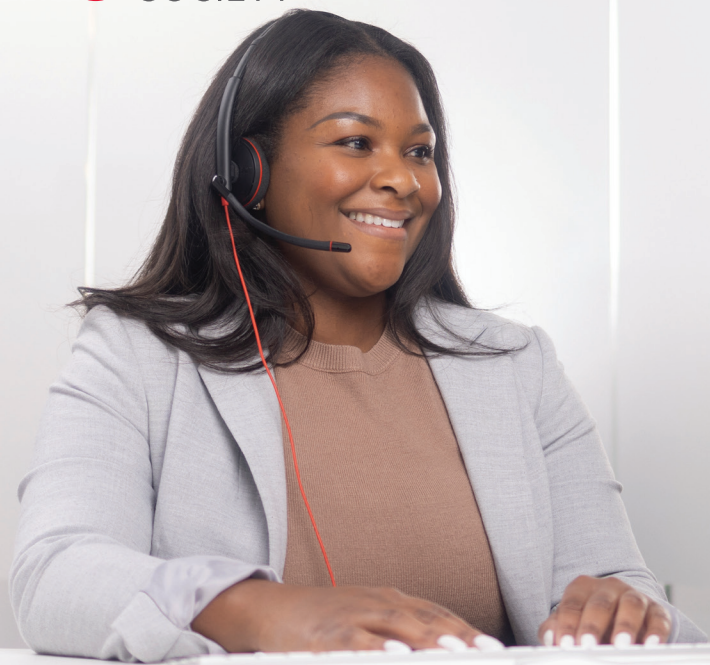
# Myeloma: In Detail

**A companion to the book  
Myeloma: The Basics**



Revised **2025**

*Formerly titled Myeloma*



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# Introduction

Myeloma is a blood cancer that starts in a plasma cell, a type of white blood cell. It typically develops in the bone marrow, the soft spongy tissue inside bones where blood cells are made. Because myeloma often occurs in many locations in the bone marrow, it is frequently called “multiple myeloma.”

**For easy-to-read, general information about myeloma for yourself, family or friends, visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Myeloma: The Basics*.**

Over the past decade, advances in the treatment of myeloma have resulted in improved remission rates, quality of life and survival. More work, however, needs to be done. Researchers continue to study and develop new therapies in clinical trials to treat myeloma.

The more you know about myeloma, the better you can take care of yourself—your body, your mind and your health. This booklet provides information about the diagnosis and treatment of myeloma. It also includes brief descriptions of blood and bone marrow as well as definitions of health terms related to myeloma.

We hope that you will keep this booklet handy and that, should you ever feel alone in confronting problems, you will turn to it for information and guidance to find the support and resources you need.

We are here to help.



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# Myeloma Basics

The human body is made up of trillions of cells. Normally these cells grow and multiply to form new cells as the body needs them. When cells become damaged or grow old, they usually die, and new cells take their place.

Cancer starts when a gene or several genes in a cell mutate and create a cancerous cell. This abnormal cancer cell grows and divides instead of dying. As cancer cells multiply, they can spread into, or invade, nearby tissue and make it hard for the body to work as it should. Cancer often spreads from where it started to other areas in the body.

Cancer can start in almost any cell anywhere in the body. Myeloma is a blood cancer that begins in a type of white blood cell called a plasma cell. Plasma cells are mainly found in the bone marrow, the soft, spongy tissue in the center of bones where most blood cells are made.

Plasma cells develop from B lymphocytes (B cells), a type of white blood cell that is part of the body's immune system. Normally when bacteria or viruses enter the body, some B cells mature and change into plasma cells. Plasma cells then make antibodies (also called immunoglobulins) that help the body fight infection. For more information on immunoglobulins, see **Figure 1** on page 5.

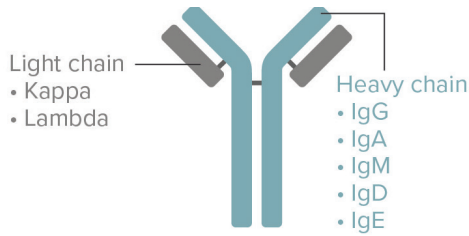
Myeloma happens when there is damage to the DNA of a plasma cell. This damage is called a “gene mutation.” Gene mutations can build up in a plasma cell. When a plasma cell has too many mutations, it becomes a type of cancer cell called a “myeloma cell.”

Myeloma cells grow more quickly and live longer than normal plasma cells. They copy their DNA and divide to make more and more myeloma cells. Over time, the myeloma cells build up in the bone marrow and may crowd out and slow down the production of different red blood cells, white blood cells and platelets. As a result, the body may not have enough healthy blood cells.

Myeloma cells can travel through the bloodstream and collect in other bones in the body. In most patients with myeloma, the disease involves multiple sites at the time of diagnosis. Because myeloma frequently occurs at many sites in the bone marrow, it is often referred to as “multiple myeloma” or “active myeloma.”

While myeloma cells are most commonly found in multiple bones, an abnormal mass of myeloma cells may develop in just one location. This is called a “solitary plasmacytoma.” A solitary plasmacytoma often develops in a bone. When a plasmacytoma starts in soft tissue outside a bone, it is called an “extramedullary plasmacytoma.” An extramedullary plasmacytoma can affect soft tissue throughout the body, but it often affects the lungs, skin and neck. A solitary plasmacytoma is often treated with radiation therapy, although it may recur or later develop into multiple myeloma.

**Figure 1. Immunoglobulins**



Healthy plasma cells make immunoglobulins (abbreviated as Ig) to fight infections. Immunoglobulins are antibodies (proteins) that attach to foreign substances entering the body. Immunoglobulins identify germs and help the immune system destroy them.

In healthy individuals, plasma cells normally produce proteins called “polyclonal immunoglobulins.” These are antibodies that protect the body against all kinds of different invading viruses, bacteria or other infectious agents (antigens).

Each type of plasma cell makes a single type of immunoglobulin, which is made of two larger pieces (heavy chains) and two smaller pieces (light chains) that are attached to each other. There are five types of heavy chains, and each type is represented by a specific letter: IgG, IgA, IgM, IgD and IgE. There are two types of light chains, kappa (k) and lambda (λ).

Myeloma cells, which are cancerous plasma cells, make large numbers of a single abnormal immunoglobulin. Unlike a normal immunoglobulin, the abnormal immunoglobulin does not help fight infection. This abnormal immunoglobulin is known by several different names, including M protein, monoclonal immunoglobulin, M spike and paraprotein.

Like normal immunoglobulins, M proteins are also made of a pair of heavy chains and a pair of light chains. The most common type of myeloma immunoglobulin is IgG kappa. In IgG kappa myeloma, the myeloma cells produce an immunoglobulin made from two IgG heavy chains bound to two kappa light chains.

Immunoglobulins can be measured in the following ways: (1) an SPEP (serum protein electrophoresis) assay looking for the M protein in the blood, (2) serum free light chain assay that looks for the abnormal kappa or lambda light chains in the blood, or (3) UPEP (urine protein electrophoresis) that looks for light chains from the M protein in the urine.

In some people with myeloma, the immunoglobulin components get distorted or do not fully join together: in these cases, the M protein test may be normal but the abnormal light chain (kappa or lambda) is detectable. In other myeloma patients, the myeloma cells only produce light chains, either kappa or lambda. These unattached “free” light chains enter the blood and are excreted in the urine where they can be detected. Light chains in the urine are referred to as “Bence Jones proteins.” In both cases, SPEP or UPEP tests for M proteins may not detect M proteins, but the abnormal light chains (kappa or lambda) are detectable in the blood.

A small number of patients have “oligosecretory myeloma,” in which the tests above are only slightly abnormal, or “non-secretory myeloma,” in which no monoclonal protein can be detected. About 2 to 3 percent of patients have non-secretory myeloma. In these cases, bone marrow biopsies can be used to look for the cancerous myeloma cells and to see if treatment is working. Even more rare, “macrofocal myeloma” means that plasmacytomas (masses of myeloma cells) occur in several bones without any bone marrow biopsy abnormalities. Here, imaging tests like MRI scans are the best way to track the disease.

Myeloma cells, like normal plasma cells, also make immunoglobulins. Myeloma cells release a large amount of a single type of abnormal immunoglobulin known as monoclonal protein or M protein. Unlike normal immunoglobulins, M proteins do not help fight infection. The proteins can build up in the blood and pass through the urine, where they can cause renal (kidney) problems. High levels of M proteins can lead to serious health complications.

**Complications of Myeloma.** Most of the complications and symptoms of myeloma are caused by the build-up of myeloma cells in the bone marrow and the presence of M proteins. Complications of myeloma include:

- **Low Blood Cell Counts.** Healthy bone marrow produces blood cells that circulate through the body: red blood cells that carry oxygen, white blood cells that fight infection and platelets that help prevent bleeding. In myeloma, the myeloma cells become so numerous in the bone marrow that they can crowd out and slow down the production of healthy blood cells. As a result, people with myeloma may not have enough healthy red blood cells, white blood cells and/or platelets.

When this happens, the body’s organs and tissues may not receive enough oxygen to work properly due to decreased red blood cells. Also, the body may not be able to fight infections, due to decreased white blood cells. A decreased number of platelets may result in easy bruising or bleeding, or the inability to form blood clots when they are needed.

Medical Term	Definition
<b>Anemia</b>	Low number of red blood cells
<b>Thrombocytopenia</b>	Low number of platelets (“thrombocyte” is another word for platelet)
<b>Neutropenia</b>	Low number of neutrophils (a neutrophil is a type of white blood cell)



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Side Effect Management: Managing Low Blood Cell Counts*.

- **Bone Damage and Pain.** Myeloma cells can damage bones, causing bone pain, osteoporosis (weakened bones) and fractures (breaks). Myeloma cells can build up in the bone marrow and form masses called “plasmacytomas.” The growth of these masses can weaken bones and cause pain. The pain may be dull or aching. It is often felt in the lower back and ribs.

Myeloma cells also release substances that break down bones. Old bone is dissolved without new bone to replace it, causing small holes in the bone called “lytic lesions.” This causes bones to become weaker and increases the risks of fractures. Without treatment, bones with larger lesions may break easily from activities as simple as coughing. The pain is usually constant and made worse by movement. Bone lesions are present in about 80 percent of



myeloma patients, most commonly in the skull, collarbone, ribs, spine and pelvis, but any bone may be affected.

Fractures that occur in the vertebrae (the bones that make up the spine), are called “spinal fractures.” Spinal fractures can cause vertebrae to collapse, putting pressure on the spinal cord. This can damage the nerves of the spinal cord and cause pain, weakness, numbness and tingling in the arms and legs and incontinence (inability to control urine or stool).

- **Hypercalcemia (high blood calcium levels).** Calcium is a mineral needed for healthy teeth, bones and other body tissue. Most of the body’s calcium is stored in the bones, but some of it is in the blood. When myeloma cells damage bones, calcium is released from the bones into the bloodstream. If this release happens too quickly, high blood calcium levels can occur. This can cause kidney failure, cardiac arrest or a coma.
- **Impaired Kidney Function and Damage.** The kidneys are two bean-shaped organs that are located just below the rib cage, one on each side of the spine. Healthy kidneys remove waste and extra water from the blood, which are then carried away in the urine. In people with myeloma, too much M protein, light chains and calcium in the blood can overwork and damage the kidneys as they filter blood. When the kidneys are damaged, fluid and waste products can build up in the body. This can cause nausea, loss of appetite, fatigue, swelling in the ankles and shortness of breath.
- **Hyperviscosity Syndrome.** If M protein levels in the blood become too high, the blood may become viscous (thick), resulting in “hyperviscosity syndrome.” Hyperviscosity syndrome can cause bleeding, headaches, chest pain, decreased alertness and shortness of breath. This rarely occurs and is more common when the myeloma produces certain classes of antibodies, such as immunoglobulin types A or M.
- **Amyloidosis.** Some people with myeloma develop a condition called “amyloidosis.” Amyloidosis occurs when light chains produced by myeloma cells form clumps with each other called “amyloid fibrils.” These clumps build up in tissues and organs throughout the body, disrupting their normal functions. Patients with amyloidosis can sometimes have kidney, heart or nerve issues. Amyloidosis is very rare.

**Precursors to Myeloma.** Before developing active myeloma (myeloma that causes symptoms), patients pass through two earlier stages: monoclonal gammopathy of undetermined significance (MGUS) and smoldering myeloma. These two pre-cancerous plasma cell disorders may develop into active myeloma.

- **Monoclonal Gammopathy of Uncertain Significance (MGUS).** MGUS is a condition in which there is a higher-than-normal level of M protein in the blood. MGUS does not cause any symptoms. Consequently, more than 50 percent of people who are diagnosed with MGUS have had the condition

for many years prior to the diagnosis. Usually, MGUS is discovered as an incidental finding of routine laboratory tests. Only 20 percent of people diagnosed with MGUS eventually develop myeloma. The risk of progression to myeloma is approximately 1 percent per year. Patients with MGUS are usually monitored with blood tests once or twice a year to determine if there is any change in their level of M protein.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Monoclonal Gammopathy of Undetermined Significance (MGUS) and Related Conditions*.

- **Smoldering Myeloma.** The stage between MGUS and active myeloma is called “smoldering myeloma.” People with smoldering myeloma have M protein in their blood at higher levels than MGUS but lower levels than active myeloma. People with smoldering myeloma usually have no symptoms but need to be checked often for signs of progression to active myeloma. The risk of progression of smoldering myeloma to myeloma is approximately 10 percent per year over the first 5 years following diagnosis, 3 percent per year over the next 5 years, and 1.5 percent per year afterwards. Some people with smoldering myeloma may have a higher risk of progression to active myeloma. Talk to your doctor to find out more about clinical trials that may be available for patients who have high-risk smoldering myeloma.

## Signs and Symptoms

Signs and symptoms are changes in the body that may indicate the presence of disease. A “sign” is a change that the doctor sees during a physical exam or in a laboratory or imaging test. A “symptom” is a change that a patient feels or experiences.

In the early stages of myeloma, some patients have no symptoms of the disease. Myeloma or its early precursors (MGUS and smoldering myeloma) are sometimes only suspected after a routine blood or urine test.

Myeloma is a difficult cancer to diagnose because many patients present with non-specific symptoms such as back and bone pain, fatigue and repeated infections. These symptoms are common in many other conditions. As a result, patients can go back and forth between doctors, which can lead to delays in diagnosis. Speak with your doctor if you experience any of the symptoms listed in **Table 1** on page 9 to ensure proper diagnosis and treatment.

**Symptoms of Myeloma.** Most of the symptoms of myeloma are caused by the build-up of myeloma cells in the bone marrow and the presence of M protein in the body. See **Table 1** below for a list of common myeloma symptoms.

**Table 1. Common Symptoms of Myeloma**

<b>Anemia (low red blood cell count)</b> <ul style="list-style-type: none"><li>○ Fatigue</li><li>○ Shortness of breath during normal physical activities</li><li>○ Dizziness</li><li>○ Pale complexion</li></ul>	<b>Hyperviscosity Syndrome</b> <ul style="list-style-type: none"><li>○ Headaches</li><li>○ Fatigue</li><li>○ Bruising easily</li><li>○ Vision problems</li></ul>
<b>Neutropenia (low number of neutrophils, a type of white blood cell important in fighting infection)</b> <ul style="list-style-type: none"><li>○ Frequent infections</li><li>○ Fever</li><li>○ Chills</li></ul>	<b>Kidney Failure</b> <ul style="list-style-type: none"><li>○ Decreased urine output</li><li>○ Leg and ankle swelling</li><li>○ Confusion</li><li>○ Nausea</li><li>○ Fatigue</li></ul>
<b>Thrombocytopenia (low platelet count)</b> <ul style="list-style-type: none"><li>○ Bruising easily</li><li>○ Prolonged bleeding from minor cuts</li><li>○ Chronic nosebleeds</li></ul>	<b>Other Symptoms of Myeloma</b> <ul style="list-style-type: none"><li>○ Sudden and severe back pain</li><li>○ Muscle weakness</li><li>○ Numbness</li><li>○ Feeling of pins and needles</li></ul>
<b>Bone Disease</b> <ul style="list-style-type: none"><li>○ Bone pain</li><li>○ Fractures (broken bones)</li></ul>	
<b>High Calcium Levels</b> <ul style="list-style-type: none"><li>○ Frequent urination</li><li>○ Increased thirst</li><li>○ Fatigue</li><li>○ Headaches</li><li>○ Nausea, vomiting, loss of appetite</li></ul>	

**Signs of Myeloma.** Doctors sometimes refer to the acronym **CRAB** to describe the four most common signs of myeloma. Doctors look for these signs in blood tests and imaging tests. CRAB stands for the following criteria:

**C**, increased calcium in the blood. This condition is called “hypercalcemia”

**R**, renal (kidney) failure

**A**, anemia (low red blood cell count)

**B**, bone lesions

## Testing for Myeloma

While certain signs and symptoms may indicate that a person has myeloma, laboratory tests are needed to confirm the diagnosis. An accurate diagnosis is important because it helps the doctor to:

- Estimate how the disease will progress
- Determine the appropriate treatment

### **Talk to your doctor about:**

- The tests that are being done
- What the results mean
- Getting copies of the results

A person who has signs or symptoms that suggest the possibility of myeloma is referred to a specialist called a “hematologist-oncologist.” This is a doctor who has special training in diagnosing and treating blood disorders and blood cancers such as leukemia, lymphoma and myeloma. In some large medical centers, there are hematologist-oncologists who specialize in treating myeloma.

To diagnose myeloma, doctors use a variety of tests to analyze bone marrow, blood and urine. A pathologist—a doctor who specializes in identifying diseases by studying cells under a microscope—will examine the blood cells and the bone marrow cells. The samples should also be examined by a hematopathologist, a pathologist who specializes in diagnosing blood and bone marrow diseases.

Along with bone marrow, blood and urine tests, imaging tests can help diagnose and monitor myeloma. Imaging tests can identify bone damage linked to myeloma.

The following are some of the tests done to diagnose myeloma. These tests may be repeated during and after treatment to determine if treatment is working.

**Medical History.** Your doctor will take a thorough medical history. The history may include information about past illnesses, injuries, treatments and medications. Myeloma often causes symptoms, so it is important to tell your doctor about any symptoms that you are experiencing. Some illnesses run in families, so the doctor may also ask about the health of your blood relatives.

**Physical Examination.** Your doctor will perform a physical examination. During the examination, the doctor may listen to your lungs and heart and carefully examine your body for signs of infection or disease. To check your internal organs, the doctor may feel different parts of your body. For example, your doctor may feel your abdomen to see if you have an enlarged liver or spleen, and check the lymph nodes in your neck, armpits and groin (top inner part of the thigh). Your doctor will also look for signs of other problems such as bruising, muscle weakness or neuropathy (numbness/tingling/pain in your hands and feet).

**Blood Tests.** Blood tests are routinely done during the diagnosis and treatment of myeloma.

**Complete Blood Count (CBC) With Differential.** This test is used to measure the number of red blood cells, white blood cells and platelets in a sample of blood. It also measures the amount of hemoglobin, a protein inside red blood cells that carries oxygen from the lungs to tissues in the body. The CBC should include a differential, which measures the numbers of the different types of white blood cells in the sample. When myeloma cells accumulate in the bone marrow, there is often less room for healthy blood cells to develop. As a result, people with myeloma often have low blood cell counts. The most common finding is a low red blood cell count.

**Serum Quantitative Immunoglobulins.** This test measures the amount of each common immunoglobulin (IgA, IgG and IgM) in the blood. These measurements, however, include both the polyclonal (normal) immunoglobulins made by healthy plasma cells and the monoclonal (myeloma-related M protein) immunoglobulins. If this test finds an increase in any one of the immunoglobulins, further testing with electrophoresis is needed to determine if the high level is due to a monoclonal immunoglobulin.

**Serum Protein Electrophoresis (SPEP).** SPEP uses an electric current to separate proteins based on their electrical charge, size and shape. It can measure the amount of M proteins in the blood. Finding M protein in the blood is the first step in diagnosing myeloma. SPEP is usually paired with another test, called **serum immunofixation electrophoresis (SIFE)**, which is used to identify the type of abnormal immunoglobulin (IgG, IgA, IgM, IgE or IgD).

**Serum Free Light Chain (SFLC) Assay.** Immunoglobulins are usually made of heavy chains and light chains (either kappa or lambda) that are bound together. Normally plasma cells make a small amount of extra light chains that do not bind with heavy chains. These unlinked chains are known as “free light chains.” An

SFLC assay measures the amount of lambda and kappa free light chains in the blood.

A person without myeloma normally has the same number of kappa and lambda light chains in the blood. In this case, the SFLC assay would show a ratio of one to one. In some patients, the myeloma cells only produce one type of light chain, either kappa or lambda. If there is more of one type of light chain than the other, the ratio will be different, which can be a sign of myeloma.

In some patients with myeloma, only free light chains are produced. SFLC assay is helpful in the rare cases of myeloma in which no monoclonal proteins (M spike) are found in the blood using SPEP.

**Blood Chemistry Tests.** Abnormal levels of certain chemicals may indicate that an organ is not working properly, or they may be caused by cancer or other health conditions. Tests are done to measure the levels of the following substances in the blood:

- Blood urea nitrogen (BUN) is a waste product made by the liver that is filtered out of the blood and into the urine. This level must be monitored carefully in myeloma patients, since too much urea in the blood raises the risk for developing kidney disease. A high BUN level may be a sign of kidney damage.
- This test measures the level of calcium in the blood. Bone destruction causes calcium to leave the bones and enter the blood, where it may reach an elevated level. This can damage many organs, including the brain, nerves, muscles, gut and kidneys.
- Creatinine is a waste product from muscles that is also filtered out of the blood and into urine by the kidneys. A high creatinine level may be a sign of kidney damage.
- Glomerular filtration rate (GFR) is a test that calculates kidney function.
- Albumin is the main protein in blood plasma. A low level of this protein may be a sign of advanced myeloma, or indicate the presence of amyloidosis, malnutrition or chronic disease and inflammation.
- Total protein level is a measure of all the proteins in the blood, including the myeloma proteins. The level is often elevated on diagnosis and may go down with treatment, though it is not as specific as the SPEP for measuring myeloma proteins.
- Beta 2 ( $\beta_2$ )-microglobulin is a small protein made by many types of cells, especially B cells. A high level of  $\beta_2$ -microglobulin may be a sign of a high number of myeloma cells. The levels of this protein and albumin are significant and will be considered when staging myeloma.
- Lactate dehydrogenase (LDH) is a protein made by many different types of cells, including myeloma cells. A high LDH level may be an indication of advanced myeloma. This finding is also used in staging myeloma.

- Electrolytes such as sodium, calcium, potassium and chloride are minerals needed for healthy organ function. When there is kidney damage, there may be abnormal levels of these chemicals.
- Uric acid is a chemical released when cancer cells die. Very high levels of uric acid in the blood can damage the kidneys and other organs.
- Liver function tests measure the level of certain proteins and enzymes in the blood. Abnormal levels may indicate liver disease or damage.

**Urine Tests.** In addition to blood tests, urine tests can also reveal signs of myeloma and can help check kidney function. Urine tests are also used to measure the amount of myeloma in the body.

A 24-hour urine collection can be performed to help measure protein in the urine. **Urine protein electrophoresis (UPEP)** is a test that measures the amount of M protein and light chains (called Bence Jones proteins) in the urine. **Urine immunofixation electrophoresis (UIFE)** is a test that identifies the type of M proteins and light chains present in the urine.

A 24-hour urine test is a lot of work because the patient has to collect urine with every void and store it in a refrigerator or cooled environment. This test is normally used only in the case of amyloidosis (where amyloid fibrils can cause kidney damage), which is quite rare. Certain clinical trials may require 24-hour urine specimens as well. In recent years, these urine tests have been mostly replaced by the serum free light assay which is designed to identify and measure light chains in the blood.

**Bone Marrow Aspiration and Biopsy.** Myeloma usually starts in the bone marrow, the spongy tissue inside the center of most bones. When blood tests show low blood cell counts or the presence of M proteins, your doctor may recommend a test of the bone marrow to see whether your bone marrow is healthy and making normal amounts of blood cells. Doctors use the results from these tests to diagnose and monitor blood and bone marrow diseases, including myeloma.

Bone marrow has both a liquid and a solid component.

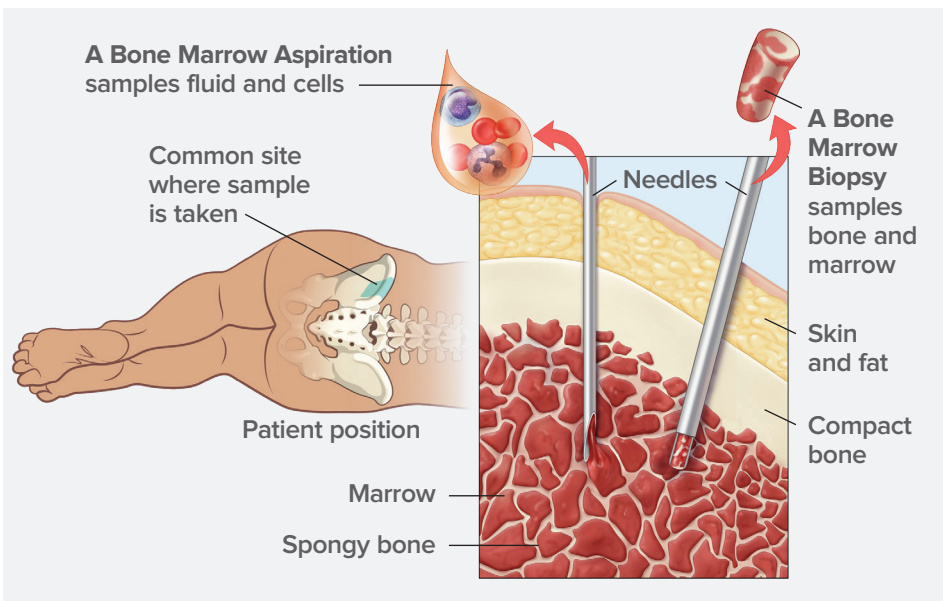
- Bone marrow aspiration is a procedure to remove a sample of the liquid part of the bone marrow.
- Bone marrow biopsy is a procedure to remove a small sample of the solid, spongy part of the bone marrow.

Both tests are frequently done in the same visit, either at the doctor's office or in a hospital. Both samples are usually taken from the large hip bone in the lower back. You will likely lie on your stomach or side.

For many patients, this is a painful procedure, so you will receive medicine to numb the skin and the surface of the bone. You may also have the option to take medicine before the procedure to help you relax. Some patients may be given a sedative so that they will feel less pain and have no memory of the procedure.

For a bone marrow aspiration, a special, hollow needle is inserted through the hip bone and into the bone marrow to aspirate (remove) a liquid sample of cells. For a bone marrow biopsy, a wider needle is used to remove a sample of solid bone that contains bone marrow. Both needles are inserted through the skin, generally in the same area. Both bone marrow samples are sent to the laboratory where they are examined under a microscope. See **Figure 2** for an illustration of the bone marrow tests.

**Figure 2. Bone Marrow Aspiration and Biopsy**



**Left:** The place on the back of the patient’s hip bone where a bone marrow aspiration or biopsy is done. **Right:** One needle goes into the bone marrow to get a liquid sample for aspiration (the needle on the left) and the other needle goes inside the bone for a bone marrow biopsy (the needle on the right). The needle for the aspiration is thinner than the one for the biopsy.



Visit [www.LLS.org/3D](http://www.LLS.org/3D) and click on “**Bone Marrow Biopsy and Aspiration**” to view an interactive 3D model that will help you visualize and better understand the bone marrow aspiration and biopsy procedures.



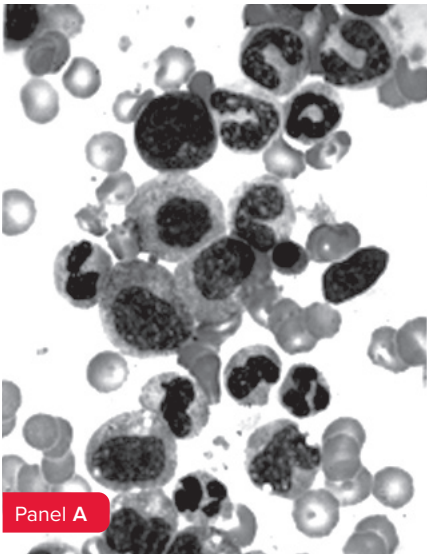
**Cell Assessment.** At the laboratory, a hematopathologist examines the blood, urine and bone marrow samples. A “hematopathologist” is a doctor who has special training in identifying blood diseases by studying cells under a microscope and performing specialized tests on the samples.

The hematopathologist looks at the bone marrow cells under a microscope to count the number of the different types of blood cells and to examine their size and shape to see whether they look normal or abnormal (see **Figure 3**).

In testing for myeloma, it is important to find out the percentage of cells in the bone marrow that are plasma cells. Plasma cells typically make up less than 5 percent of the cells in the bone marrow. Generally, a diagnosis of myeloma requires a finding of 10 percent or more of plasma cells in the bone marrow.

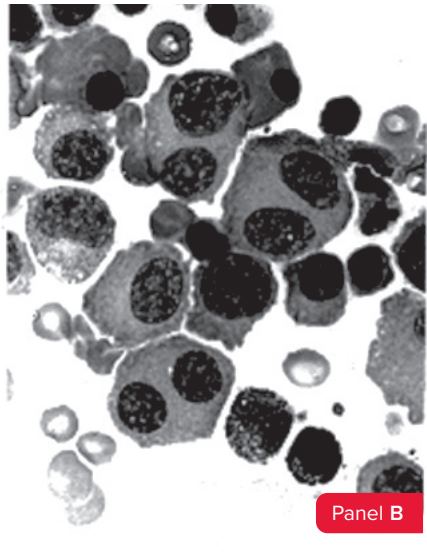
### Figure 3. Normal Cells versus Myeloma Cells

#### Normal Cells



Panel A

#### Myeloma Cells



Panel B

**Panel A** is a photograph of normal bone marrow cells. The variations in the shape and appearance of the cells are characteristic of the developmental stages of normal cells. **Panel B** is a photograph of bone marrow cells from a person with myeloma. The normal bone marrow cells are replaced by plasma cells. Several cells have two nuclei, which may be a sign of abnormal plasma cells (myeloma cells).

The hematopathologist will conduct additional tests on the bone marrow sample to gather more information about the abnormal plasma cells.

**Biomarker Testing.** These laboratory tests look for biomarkers, which are molecules found in the blood, other body fluids or tissues that are signs of a normal or abnormal process, or of a condition or disease. Biomarkers provide information about a person’s cancer. Each person’s cancer has a unique pattern of biomarkers.

Biomarker testing is used to help diagnose some types of cancer. It may also be used to help plan treatment, make a prognosis or predict whether cancer will come back or spread to other parts of the body. It may also be used to monitor treatment. Biomarker tests may include:

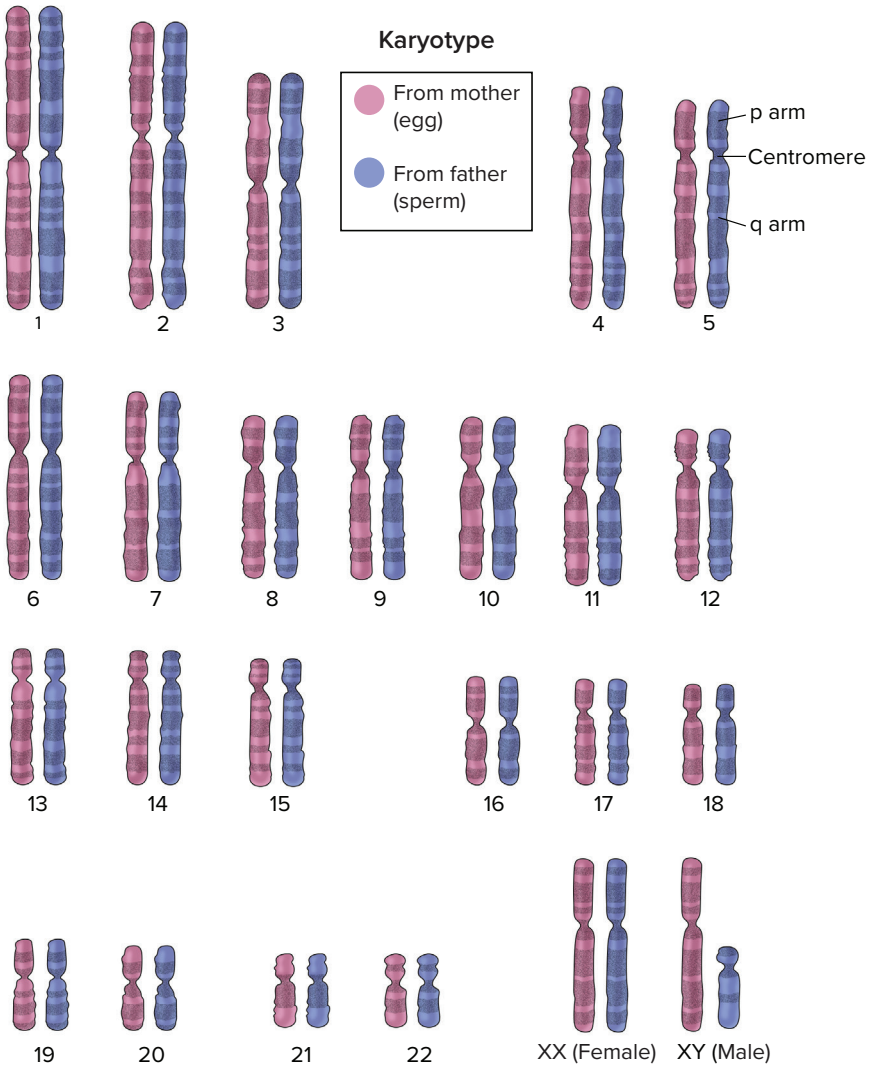
**Flow Cytometry (Immunophenotyping).** This lab test identifies cancer cells based on markers called “antigens.” Antigens are proteins found either on the surface of or within white blood cells. Finding (or not finding) certain antigens can help identify cancer cells. The pattern of the surface proteins is called the “immunophenotype.” Flow cytometry can detect abnormal plasma cells by identifying certain antigens on the outer surface of cells. Flow cytometry is not always done at diagnosis, but it can be used to see if there are any residual cancer cells remaining in the body after treatment. This is called measurable residual disease (MRD). For more information on MRD, see page 28.

**Fluorescence In Situ Hybridization (FISH).** Cancer is a disease caused by mutations (changes) to the genetic material inside of cells. This genetic material is called DNA. Inside cells, DNA is packaged into thread-like structures called “chromosomes.” In people with myeloma, FISH is used to look for abnormal changes in the chromosomes of myeloma cells.

Human cells normally contain 23 pairs of chromosomes, for a total of 46 chromosomes. Chromosomes are passed from the parents to a child. Every person inherits 23 chromosomes from their mother’s egg cell, and 23 chromosomes from their father’s sperm cell.

Each pair of chromosomes has a certain size, shape and structure. Each chromosome is divided into two sections or “arms.” The short arm of the chromosome is labeled the “p arm.” The long arm of the chromosome is labeled the “q arm.” See **Figure 4** on page 17 for an illustration of human chromosomes lined up in pairs, an arrangement called a karyotype.

**Figure 4. Normal Karyotype**



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In some cases of myeloma, the chromosomes of the myeloma cells have abnormalities. These abnormalities can be “numerical” or “structural.” A numerical abnormality is when there is a different number of chromosomes in the cells than usually found. For example, instead of the typical 46 chromosomes in each cell, there may be 45 or 47 chromosomes in the myeloma cell. One type of numerical abnormality found in myeloma cells is a trisomy, the presence of three copies of a chromosome instead of the usual two copies.

A structural abnormality occurs when the chromosome's structure has been altered in one of several ways including:

- Translocation, which occurs when a piece of one chromosome breaks off and attaches to another chromosome. Sometimes pieces from two different chromosomes trade places with each other.
- Deletion, which occurs when part of the chromosome is missing.
- Amplification, which occurs when a specific area of a chromosome is duplicated, leading to an increased number of copies of a particular gene.

Chromosomal abnormalities are used to classify myeloma as either “high risk” or “standard risk.” High-risk myeloma is associated with shorter remissions. People with high-risk myeloma may need more intensive treatment or may benefit from treatment with new therapies. High-risk chromosomal abnormalities may include:

- Del(1p32), deletion of the short arm (upper part) of chromosome 1
- t(4;14), translocation of genetic material between chromosomes 4 and 14
- t(14;16), translocation of genetic material between chromosomes 14 and 16
- t(14;20), translocation of genetic material between chromosomes 14 and 20
- Del(17p), deletion of the short arm of chromosome 17
- +1q21, copies (duplication/amplification) in the long arm (lower part) of chromosome 1

**Next-Generation Sequencing (NGS).** Next-generation sequencing, also called “molecular testing” or “genomic testing,” refers to a number of different laboratory tests that examine the exact sequence (order) of DNA or RNA. This makes it possible to identify a variety of genetic changes in a patient’s cancer cells. With NGS, researchers can sequence DNA and RNA much more quickly and cost effectively than they could with older technologies. It identifies mutations present in the genes of the myeloma cells. Next-generation sequencing is being done now on a research basis but may soon be used in routine clinical practice. NGS can also be used to test for measurable residual disease (MRD). See page 28, for more information on MRD.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Understanding Genetics*.

**Imaging Tests.** Imaging tests make detailed pictures of areas inside the body. Because myeloma cells may reside in any bone in the body, it is important to have a whole-body scan. Imaging tests of your bones help your doctor diagnose myeloma and monitor the disease during treatment. The following imaging tests are a very important part of the diagnosis, staging and management of myeloma:

- **Whole Body Low-Dose Computed Tomography (CT) Scan.** In CT scans,

many pictures of different areas inside the body are taken from different angles using x-rays. A computer combines all the images to create a single, clear and detailed picture. The amount of radiation used for this scan is much lower than that used for standard CT scans.

- **PET-CT Scan.** PET and CT scans are two types of imaging tests. PET-CT scan is a procedure that combines the images from a positron emission tomography (PET) scan and a computed tomography (CT) scan. A whole-body PET-CT scan is very good at showing where myeloma is located in the body. A small amount of radioactive glucose (sugar) is injected into a vein, and a scanner is used to make detailed computerized pictures of areas inside the body where glucose is taken up. Because cancer cells often take up more glucose than normal cells, the pictures can be used to find cancer cells in the body. It can also help show bone damage from myeloma and can identify active myeloma versus healing bone more accurately than a CT scan alone.
- **Magnetic Resonance Imaging (MRI) Scan.** This test uses radio waves and a powerful magnet to make a series of detailed pictures of areas inside the body. This imaging test is done in select cases. It is useful for detecting abnormal areas where myeloma cells have replaced bone marrow. Unlike CT or PET-CT scans, an MRI does not use any radiation.
- **Bone/Skeletal Survey.** X-rays of all the bones in the body are taken and examined to identify areas of decreased bone density and bone lesions. Bone surveys have mostly been replaced by low-dose CT scans, which show bone damage better than regular x-rays.

Certain imaging tests may be done depending on the situation. For example, MRI has been found to be a very sensitive method to evaluate bone involvement (for example, when looking for spinal cord compression); PET-CT is the most sensitive option for detecting extramedullary disease outside the bone marrow; and a whole-body low-dose CT scan is preferred for its lower cost.

The latest clinical guidelines from the International Myeloma Working Group (IMWG) recommend replacing conventional skeletal survey with whole-body low-dose CT as the standard imaging technique for assessing bone lesions. Given that there must be significant bone destruction, sometimes up to 70 percent, before it can be visible on x-ray skeletal survey, more advanced techniques such as low-dose CT and PET-CT scans are recommended for staging disease and monitoring treatment.

## Questions to Ask Your Doctor About Testing

- What tests are necessary before I start treatment?
- When will the tests take place?
- Where will the tests take place?
- How long will the tests take?
- Will my insurance provider pay for all my tests? If not, is there someone who can help me to find out how I can get the cost of my tests covered?
- What are my options if my insurance plan does not cover the cost of the tests that are needed?
- Will the tests need to be repeated after the end of the initial treatment?



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Understanding Lab and Imaging Tests*.

## Diagnosis

An accurate diagnosis is one of the most important aspects of a person's medical care. It will help the healthcare team to:

- Estimate how the disease will progress
- Determine the appropriate treatment

For a diagnosis of myeloma, a specific set of diagnostic criteria must be met. These criteria were updated in 2014 by the International Myeloma Working Group (IMWG). A myeloma diagnosis requires both of the following criteria:

1. A plasmacytoma proven by a biopsy or at least 10 percent of bone marrow made up of cancerous plasma cells *and*
2. At least one of the following myeloma-associated findings:
  - Hypercalcemia (high calcium levels in the blood)
  - Kidney damage
  - Anemia (low red blood cell counts)
  - Bone lesions
  - Bone marrow where at least 60 percent of the cells are cancerous plasma cells
  - A large ratio between kappa and lambda free light chains, whereby one is over 100 times higher than the other

- More than one focal lesion on an MRI. Focal lesions are abnormal areas that signal the development of a lytic lesion (small hole in the bone) within 18 to 24 months.

## Treatment Planning

**Choosing a Hospital and Doctor.** When you find out that you have cancer, you want to get the best possible medical care and treatment. Myeloma is associated with a wide range of outcomes, so it is essential to seek treatment in a center with hematologist-oncologists who have significant experience in the care of patients with myeloma.

A local oncologist may only see a few myeloma patients. In large medical centers, there are hematologist-oncologists who specialize in treating myeloma. These myeloma specialists see hundreds of myeloma patients, and they develop experience and expertise in diagnosing and treating myeloma. They can also better anticipate treatment-related side effects of myeloma and provide therapies to prevent or manage side effects.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Choosing a Specialist or Treatment Center*.

**Getting a Second Opinion.** If you have been diagnosed with myeloma, you may want to consult one or more myeloma specialists before proceeding with a treatment plan to make sure that you receive the therapy that is right for you. When you go to the appointment for a second opinion, make sure that all your medical records are available for examination (including laboratory and imaging test results and bone marrow aspiration and biopsy findings). Upon review of your medical records, the specialist you see for a second opinion can confirm a proposed treatment plan and/or suggest modifications, as well as potentially offer a clinical trial that may only be available at certain institutions. This review may reassure you that you have explored all of your options.

If you are either unsure about getting a second opinion or feel uncomfortable about how to tell your doctor you are seeking one, call our Information Specialists at (800) 955-4572 to discuss an approach that makes you feel comfortable. You may also want to check with your insurance company to be sure that your plan covers the cost of getting a second opinion and to see if specific doctors or centers are recommended.

**Staging.** Doctors use laboratory and imaging tests to determine the extent of your myeloma. This determination is called “staging,” and it provides important information for treatment planning and for prognosis. There is significant variation in myeloma patient outcomes, depending on a series of factors that include the stage, the presence of chromosomal abnormalities, a patient’s

baseline organ function and fitness, and the patient’s response to treatment. Thus, stage alone does not determine the treatment plan.

For decades, a myeloma staging system called the “Durie-Salmon Staging System” has been used. The Durie-Salmon system evaluates the following factors:

- Hemoglobin level in the blood
- Level of blood calcium
- Presence of bone lesions detected with imaging studies to determine the extent of the myeloma
- Amount of M protein in the blood and urine
- Level of kidney function

A newer “International Staging System” (ISS) for multiple myeloma uses the levels of beta 2 ( $\beta_2$ )-microglobulin and albumin in the blood to stage myeloma. The ISS was revised (R-ISS) in 2015 to include an elevated lactate dehydrogenase (LDH) level or the presence of high-risk cytogenetic abnormalities to make this prognostic index. These measurements allow the doctor to classify the patient’s myeloma as stage I, stage II or stage III. See **Table 2** on page 23, for more information on the two staging systems for myeloma.



**Table 2. Myeloma Staging Systems**

Stage	Durie-Salmon Staging System	Revised International Staging System (R-ISS)	5-Year Overall Survival Rates for R-ISS
I	<p><b>All of the following:</b></p> <ul style="list-style-type: none"> <li>○ Hemoglobin concentration &gt;10 g/dL</li> <li>○ Serum calcium value normal or &lt;10.5 mg/dL</li> <li>○ X-ray studies of bone showing normal bone structure (scale 0) or solitary bone plasmacytoma only</li> <li>○ Low M-component production rate IgG value &lt;5 g/dL IgA value &lt;3 g/dL</li> <li>○ Urine light chains &lt;4 g/24 hours</li> </ul>	<p><b>All of the following:</b></p> <ul style="list-style-type: none"> <li>○ Serum beta 2 (<math>\beta_2</math>)-microglobulin &lt;3.5 mg/L</li> <li>○ Serum albumin <math>\geq</math>3.5 g/dL</li> <li>○ Standard-risk chromosomal abnormalities</li> <li>○ Normal serum lactate dehydrogenase level</li> </ul>	82%
II	<p><b>Neither stage I nor stage III</b></p> <ul style="list-style-type: none"> <li>○ A – No renal failure (creatinine <math>\leq</math>2 mg/dL)</li> <li>○ B – Renal failure (creatinine &gt;2 mg/dL)</li> </ul>	<p><b>Neither stage I nor stage III</b></p>	62%
III	<p><b>One or more of the following:</b></p> <ul style="list-style-type: none"> <li>○ Hemoglobin concentration &lt;8.5 g/dL</li> <li>○ Serum calcium value &gt;12 mg/dL</li> <li>○ X-ray studies of bone showing advanced lytic bone lesions (scale 3)</li> <li>○ High M protein production rate IgG value &gt;7 g/dL IgA value &gt;5 g/dL</li> <li>○ Urine light chains &gt;12 g/24 hours</li> </ul>	<p><b>Both of the following:</b></p> <ul style="list-style-type: none"> <li>○ Serum beta 2 (<math>\beta_2</math>)-microglobulin <math>\geq</math>5.5 mg/L</li> <li>○ AND one of the following                             <ul style="list-style-type: none"> <li>○ High-risk chromosomal abnormalities</li> <li>○ High serum lactate dehydrogenase level</li> </ul> </li> </ul>	40%

**Key:** del, deletion; dL, deciliter; g, gram; Ig, immunoglobulin; L, liter; M-component, monoclonal component; M protein, monoclonal (myeloma) protein; mg, milligram; t, a translocation between chromosomes.

**Sources:** Rajkumar SV. Multiple myeloma: 2024 update on diagnosis, risk stratification, and management. *American Journal of Hematology*.

Shah, D. Multiple Myeloma Workup. Medscape reference.

Palumbo A, Avete-Loiseau H, Olivia S, et al. Revised international staging system for multiple myeloma: a report from international myeloma working group. *American Society of Clinical Oncology*.

# Treatment

New treatments may have been approved since this booklet was printed. Check [www.LLS.org/DrugUpdates](http://www.LLS.org/DrugUpdates) or call (800) 955-4572.

Before you begin treatment, you and your doctor will discuss your treatment options. One option may be a clinical trial. A clinical trial is a type of research study that tests how well new medical approaches work in people. Like all treatment options, clinical trials have possible risk and benefits. By considering all your treatment options, including a clinical trial, you will be taking an active role in a very important decision that affects you. For more information on clinical trials, see page 35.

## Talk to your doctor about:

- Your treatment options and the results you can expect from treatment
- The possibility of participating in a clinical trial

Treatment for myeloma focuses on both fighting the cancer and relieving symptoms. While myeloma cannot be cured for most, it can be managed for years with the right care. Patients are treated and generally go into remission, followed by relapses. But these remissions can last for long periods of time, and many people have a number of remissions and relapses during their lifetime.

The goals of treatment:

- Reduce the amount of M protein (as measured by protein electrophoresis) or light chains (as measured by free light chain assay)
- Eliminate myeloma cells from the bone marrow (as measured by bone marrow testing)
- Reduce symptoms
- Achieve long remission
- Lengthen survival while preserving quality of life

**Treatment Planning.** Myeloma that is causing symptoms is called “active myeloma.” Treatment for active myeloma is based on a number of factors, including:

- Extent and characteristics of the disease, such as chromosomal abnormalities and stage
- Rate of disease progression
- Patient’s age and fitness (note: the patient’s overall health is considered in determining ability to tolerate intensive therapy, rather than age alone)

- Presence of other conditions, such as heart or kidney disease, diabetes or neuropathy
- Risk of treatment-related complications

Treatment has significantly progressed over the last decade with the development of novel agents and combinations of different drug therapies, as well as autologous stem cell transplantation and chimeric antigen receptor (CAR) T-cell therapy.

There are several treatments for myeloma, and new ones continue to be developed. Not everyone with myeloma receives the same treatment. You and your doctor will discuss the most appropriate treatment option for you. Your treatment will depend on the aggressiveness of your myeloma and other factors such as your age and overall health.

One of the first considerations for a newly diagnosed myeloma patient is whether they may be a candidate for autologous stem cell transplantation after completing initial therapy (called induction). Please see page 29 for more information on stem cell transplantation. Not everyone can have a stem cell transplant. It is an intense treatment with high-dose chemotherapy that can cause life-threatening side effects in some patients. Eligibility for transplant depends on multiple factors including disease status, age and overall health. It is important for patients considering a stem cell transplant to have an in-depth conversation with their doctor to understand the risks and benefits, and to be evaluated at a transplant center to determine eligibility.

**Supportive Care.** Supportive care refers to specialized medical care focused on providing relief from symptoms and the stresses of a serious illness. The goal of supportive care is to improve the patient's quality of life and to relieve discomfort as much as possible. Supportive care is an important part of myeloma treatment that helps relieve the symptoms of myeloma and the side effects of myeloma treatment. It does not treat the disease itself. Supportive care is important regardless of other treatments for myeloma. Supportive care for myeloma should be given whenever a person has symptoms or side effects that need to be controlled. Supportive care may include treatment for bone damage, pain and low blood cell counts. For more information on supportive care, see *Complications, Side Effects and Supportive Care* on page 37.

**Radiation Therapy.** This treatment uses high-energy radiation (x-rays) to kill cancer cells. In myeloma, radiation therapy can be used to treat a solitary plasmacytoma. The type of radiation therapy used to treat a solitary plasmacytoma is called external beam radiation therapy. The radiation is aimed at the cancer from a machine outside the body. Radiation therapy is similar to an x-ray except that each treatment lasts longer, and the treatment may take several weeks. Radiation therapy can also be used to treat a painful area of bone damage.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view **External Beam Radiation Therapy**.

**Induction.** Induction is the first treatment for active myeloma. It is also called frontline treatment. Induction typically consists of four (or sometimes three) drugs given over three to six cycles. Quadruplet therapy (four-drug regimens) generally includes an immunomodulatory drug, a proteasome inhibitor, a monoclonal antibody and a corticosteroid. Triplet therapy (three-drug regimens) generally includes an immunomodulatory drug, a proteasome inhibitor and a steroid. People who are unable to tolerate a three-drug or four-drug combination may start with two medications. See **Table 3** below for *Some Drug Combinations for Newly Diagnosed Myeloma*; **Table 5**, *Drug Classes and Drug Mechanisms* on page 50; and **Table 6**, *Some Drugs Used in the Treatment of Myeloma* on page 52.

### **Table 3. Some Drug Combinations for Newly Diagnosed Myeloma**

- **Dara-VRd:** daratumumab, bortezomib, lenalidomide, dexamethasone
- **Isa-VRd:** isatuximab, bortezomib, lenalidomide, dexamethasone
- **Dara-KRd:** daratumumab, carfilzomib, lenalidomide, dexamethasone
- **Dara-CyBorD:** daratumumab, cyclophosphamide, bortezomib, dexamethasone
- **Dara-Rd:** daratumumab, lenalidomide, dexamethasone
- **VRd:** bortezomib, lenalidomide, dexamethasone
- **KRd:** carfilzomib, lenalidomide, dexamethasone

New treatments may have been approved since this booklet was printed. Check [www.LLS.org/DrugUpdates](http://www.LLS.org/DrugUpdates) or call (800) 955-4572.

Treatment for myeloma may or may not include autologous stem cell transplantation. Patients who are not eligible for a transplant typically continue with the same drugs used during induction for another two to four cycles. The goal is to deepen the gains made with the initial cycles of therapy before starting maintenance therapy.

After induction, patients who are eligible for autologous stem cell transplant will have their stem cells harvested (removed). When possible, enough stem cells should be collected for two transplants in case there is a second transplant at a later date. For more information on stem cell transplantation see page 29.

**Assessing Treatment Response.** During myeloma treatment, patients will be tested to see how well their treatment is working. The doctor will check for disease remission. Myeloma is in remission when the signs and symptoms go away. See **Table 4** on page 27 for possible responses to treatment. Treatment response should be evaluated after one or two cycles of therapy, continuing after every subsequent cycle.

**Table 4. Some Terms Used to Describe Myeloma Treatment Responses**

- **Remission**
  - No detectable disease
  - The terms “complete remission” and “partial remission” (or “complete response” and “partial response”) are sometimes used.
- **Stringent complete response**
  - No detectable disease based on serum or urine immunofixation
  - Normal kappa (k) lambda (λ) light chain reaction
  - No detectable disease based on bone marrow flow cytometry
- **Complete response**
  - No sign of monoclonal protein (M protein) using standard tests
  - Disappearance of any soft tissue plasmacytomas
  - Less than 5% plasma cells in bone marrow aspirates
- **Very good partial response**
  - A 90% or greater decrease in M protein level in the blood
  - Urine monoclonal (M) protein level <100 mg in 24-hour urine collection
- **Partial response**
  - A 50% or greater decrease of M protein level in the blood
  - A 90% reduction in M protein level or <200 mg in 24-hour urine collection
  - A 50% or greater reduction in the size of soft tissue plasmacytoma (if present at diagnosis)
- **Minimal response**
  - A reduction between 25% and 50% in M protein level in the blood
  - A reduction between 50% and 89% in M protein level in 24-hour urine collection
  - A 50% or greater reduction in the size of soft tissue plasmacytoma (if present at diagnosis)
- **Stable disease**
  - Not meeting criteria for a complete remission, very good partial response, partial response, minimal response or progressive disease
- **Progressive disease**
  - At least a 25% increase in M protein level in the blood and urine
  - Appearance of new bone lesions, or 50% or greater increase in the size of previous lesions
  - If associated with symptoms, such as a new lytic bone lesion, usually indicates the need to start therapy or to change therapies if the patient is already receiving treatment
  - A biochemical relapse indicates that a patient has signs of relapse on blood and/or urine, but without evidence of worsening organ function

Most of the same tests used to diagnose myeloma are also used to monitor treatment response. These may include:

- Imaging tests, such as whole-body low-dose CT scan, PET/CT scan or MRI to see if treatment is reducing bone lesions. Depending on the number and location of the lesions, a targeted therapy, such as focal radiotherapy, may be used as treatment.
- Blood tests to measure blood cell counts, M protein, calcium and creatinine levels, and levels of free light chains.
- Urine tests to check for the presence of M protein, or a free light chains test for patients with non-secretory myeloma.
- Bone marrow aspiration and biopsy to measure the percentage of plasma cells in the bone marrow.

How well your myeloma responds to induction can determine your next step of treatment. It may indicate that you can proceed with stem cell transplantation or maintenance therapy. If you do not respond to induction, your myeloma is defined as “refractory.” In this situation, you may be treated with regimens designed for refractory disease. See *Treatment Options for Relapsed and Refractory Disease* on page 32.

**Measurable Residual Disease (MRD).** Even when a complete remission is achieved, myeloma cells that cannot be seen with a microscope may remain in the bone marrow. The presence of these cells is referred to as measurable residual disease (MRD). When a patient tests positive for MRD, it means that residual cancer cells were found. When a patient tests negative for MRD, no residual cancer cells were found.

The tests most often used to detect MRD are flow cytometry and next-generation sequencing. clonoSEQ® is an FDA-cleared test for measuring MRD in people with myeloma. They use a bone marrow sample to test for MRD. These tests are much more sensitive than standard tests that examine bone marrow samples under a microscope. The International Myeloma Working Group (IMWG) defined the presence of MRD in myeloma as having one myeloma cell in at least 100,000 cells in a bone marrow biopsy sample. At present, researchers are trying to determine exactly when MRD testing should be done.

In general, clinical trials have shown that patients with MRD-negative status (no detectable residual disease) have better outcomes than those with MRD-positive status (detectable residual disease). However, some myeloma patients may have MRD-positive disease for years (or their whole lives) after treatment without ever having a myeloma relapse. For older or more frail patients, the goal of treatment may not be MRD negativity. Instead, the goal of treatment may be controlling the disease while maintaining the best quality of life and prolonging survival.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Measurable Residual Disease (MRD)*.

**Stem Cell Transplantation.** High-dose chemotherapy and stem cell transplantation are important parts of treatment plans for eligible, recently diagnosed patients with active myeloma. The process typically involves administering intensive chemotherapy followed by an infusion of healthy stem cells. Intensive chemotherapy is given to destroy the myeloma cells in the bone marrow. Healthy bone marrow cells are also destroyed in the process. Without healthy stem cells, the bone marrow is not able to grow new blood cells. Stem cell transplantation restores healthy stem cells after intensive therapy. There are two main types of stem cell transplantation:

- Autologous. A patient's own stem cells are collected, stored and then given back to the patient after the patient completes a course of chemotherapy.
- Allogeneic. A patient receives stem cells from a matched or partially matched donor, either related or unrelated to the patient.

Allogeneic transplantation is not commonly used to treat people with myeloma, but it may be a treatment option for patients participating in a clinical trial.

**Autologous Stem Cell Transplantation.** Autologous stem cell transplantation is a common treatment for myeloma. It offers a good possibility for a long-lasting response.

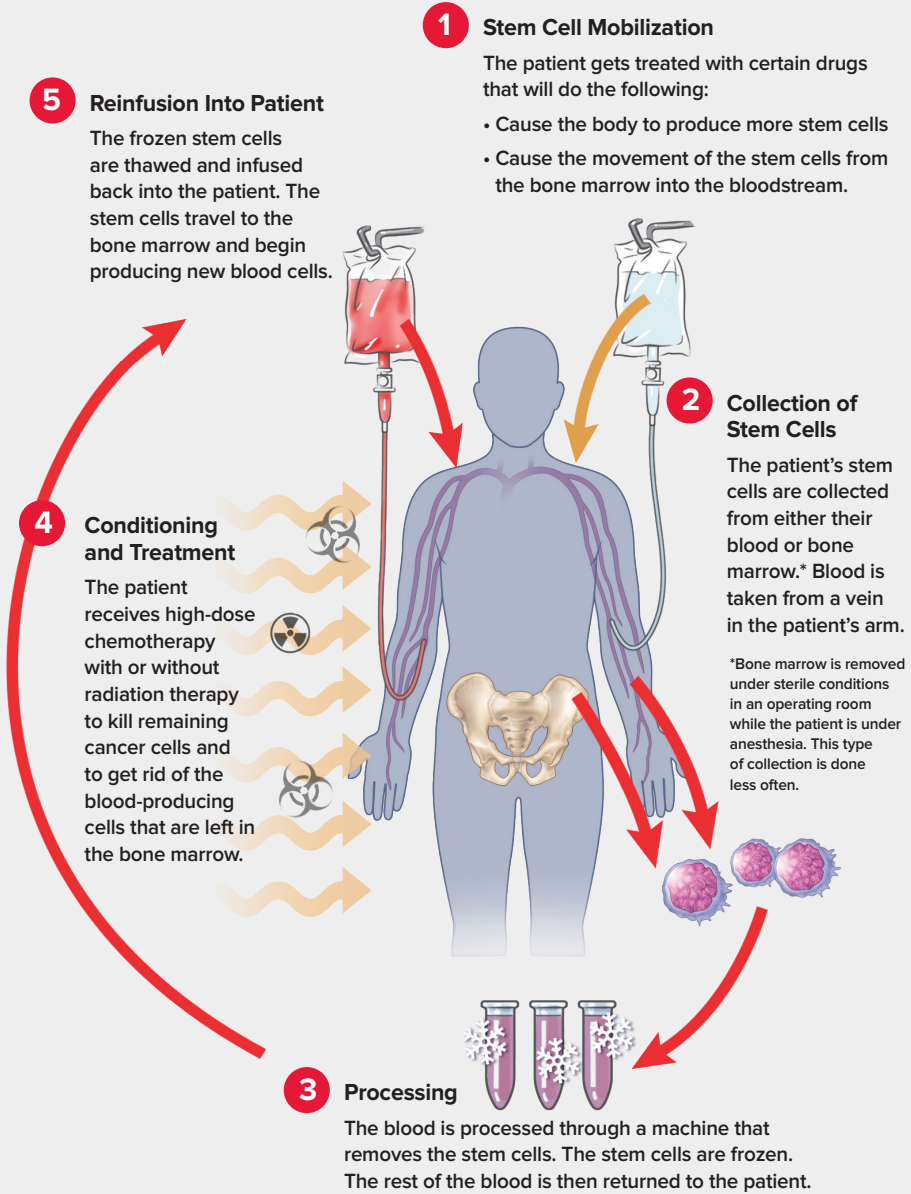
After induction (initial therapy), your own stem cells are collected and frozen. See **Figure 5** on page 30. A few sessions may be needed to obtain enough stem cells for transplantation. Stem cells are often taken from the bloodstream. You may be given medication to help increase the number of stem cells in your bloodstream and bone marrow.

The next step is treatment with high doses of chemotherapy, typically melphalan. This is called conditioning. The high-dose chemotherapy kills many more myeloma cells, but it also kills the blood-producing stem cells that are left in the bone marrow. Certain conditioning regimens may cause difficult side effects, and members of your transplant team will discuss these with you before you begin the conditioning therapy.

After chemotherapy, the stem cells that were collected are returned to your bloodstream by intravenous (IV) infusion (similar to a blood transfusion). The stem cells will travel in the bloodstream to the bone marrow. Once in the bone marrow, these stem cells begin to divide and make new blood cells in a process called engraftment. Engraftment usually happens within the first 14 days after transplantation.

**Figure 5. Autologous Stem Cell Transplantation**

## Autologous Stem Cell Transplantation





**Tandem Autologous Stem Cell Transplantation.** This term refers to a planned second course of high-dose chemotherapy and stem cell transplant within 6 months of the first transplant. Tandem autologous stem cell transplantation is now rarely done as frontline treatment for myeloma in the United States.

However, the National Comprehensive Cancer Network (NCCN) guidelines recommend collecting enough hematopoietic stem cells for at least one transplant in all eligible patients, and for two transplants in the case of younger patients. Historically this was done to have enough cells for a tandem or second transplantation in the future. However, collecting extra stem cells may be helpful even in patients who are not planning to do a second transplantation; for example, new studies suggest that stored stem cells may sometimes help with complications after chimeric antigen receptor (CAR) T-cell therapy (see page 34 for information on CAR T-cell therapy).



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Blood and Marrow Stem Cell Transplantation*.

**Maintenance Therapy.** After induction or induction with autologous stem cell transplantation, your doctor will likely recommend maintenance therapy. Maintenance therapy is medication that is given to help maintain the response obtained with induction therapy or stem cell transplantation. During maintenance therapy, medications are given at lower doses or with less frequency. Some studies have shown that maintenance is beneficial at improving survival, but maintenance therapy is not appropriate for every patient. Talk with your doctor about the risks and benefits of taking maintenance therapy.

For standard-risk patients, lenalidomide is the preferred medication for post-transplant maintenance, based on the results of several clinical trials. It does not produce the neurotoxicity of other immunomodulatory drugs. Based on recent trials, your doctor may add daratumumab to lenalidomide as well. However, lenalidomide appears to increase the risk for developing a secondary cancer during maintenance therapy, especially after transplantation or after therapy with a regimen that contains melphalan.

In some circumstances, maintenance therapy may also include bortezomib or carfilzomib. Your doctor may also discuss clinical trials that are studying the best type of maintenance therapy.

Maintenance therapy is intended to be continued over the long term. Studies remain ongoing to determine the optimal maintenance regimen and duration of maintenance therapy.

## Questions to Ask Your Doctor About Maintenance Therapy

- Will I need maintenance therapy?
- What is my risk of disease relapse without maintenance therapy?
- How long will this therapy last?
- What are the long-term side effects of maintenance therapy?
- Will my insurance cover this phase of treatment?
- What would happen if maintenance therapy is discontinued?

## Treatment Options for Relapsed and Refractory Disease

Some patients have myeloma that returns after remission. This is referred to as a “relapse” of the disease. In other patients, the cancer does not respond to treatment, and there is no remission. In those cases, the disease is referred to as “refractory.”

Almost all myeloma patients will experience relapse, and/or the disease will become refractory. The choice of a treatment regimen after relapse depends on a series of patient-, disease- and treatment-related factors, including:

- Previous therapy. If a previous therapy worked and was well tolerated, it can be considered for use again, along with stem cell transplantation.
- Rate of relapse. Patients with rapidly progressing myeloma should be treated with more aggressive combinations of drugs. In contrast, patients with slowly progressing myeloma may be treated with a milder combination therapy.
- Patient health and comorbidities. These are key factors for choosing a treatment regimen, since most patients with relapsed myeloma are older than 70. The general health of the patient and the presence of other health conditions help to determine the type of therapy and the dosage that will be used.
- Genetic abnormalities. There is increasing evidence that, in high-risk patients in particular, the disease may progress if additional cytogenetic abnormalities develop over time. These abnormalities will be considered by the treatment team when deciding whether to use previous treatments (to which the patient may have become resistant) or if different and/or more aggressive treatment options need to be considered.

Treatment for relapsed or refractory myeloma may include a clinical trial, medications that have not been used before, autologous stem cell transplantation and chimeric antigen receptor (CAR) T-cell therapy.

**Clinical Trial.** Treatment in a clinical trial should be considered for patients with refractory or relapsed myeloma. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. For more information see *Clinical Trials for Blood Cancers* on page 35.

**New Drug Regimen.** For many patients diagnosed with myeloma, treatments stop working. This is commonly known as drug resistance. When drug resistance happens, a different medication, or a different combination of medications can be tried. For example, in some patients, myeloma can become resistant to bortezomib. In that case, patients who receive the triplet therapy bortezomib, lenalidomide and dexamethasone may have their treatment changed to daratumumab, lenalidomide and dexamethasone.

Below are some treatments commonly used in the treatment of relapsed/refractory myeloma in the United States. Additionally, CAR-T therapy, a bispecific antibody or in some cases a second autologous stem cell transplantation can be used as well (see page 34).

- **KPd:** carfilzomib, pomalidomide, dexamethasone
- **Dara-Kd:** daratumumab, carfilzomib, dexamethasone
- **Dara-Pd:** daratumumab, pomalidomide, dexamethasone
- **Elranatamab** (a bispecific antibody, see page 34)
- **Elo-Pd:** Elotuzumab, pomalidomide, dexamethasone
- **Isa-Pd:** Isatuximab, pomalidomide, dexamethasone
- **Isa-Kd:** Isatuximab, carfilzomib, dexamethasone
- **Seli-Vd:** Selinexor, bortezomib, dexamethasone
- **Talquetamab** (a bispecific antibody, see page 34)
- **Teclistamab** (a bispecific antibody, see page 34)
- **Venetoclax:** This is used in certain cases that your doctor may discuss

For more information on these drugs, see **Table 5, Drug Classes and Drug Mechanisms** on page 50; and **Table 6, Some Drugs Used in the Treatment of Myeloma** on page 52.

Talk to your doctor about which drug regimens are available to you. Your doctor can explain the reasons for choosing a particular drug combination and the side effects that may occur.

**Autologous Stem Cell Transplantation.** The use of high-dose chemotherapy followed by autologous stem cell transplantation may also be an option for some patients with relapsed or refractory myeloma—those who have either not been treated with a transplant or who have had a good, durable response to a prior transplant. See page 29 for more information on stem cell transplantation.

**Chimeric Antigen Receptor (CAR) T-Cell Therapy.** CAR T-cell therapy is a type of immunotherapy that uses a patient’s own immune cells called “T cells” (white blood cells that help the body fight infection and cancer) to identify and then attack cancer cells. Each dose of CAR T-cell therapy is made for a specific patient. The T cells are collected from the patient and then genetically modified in a laboratory to add new genes called “chimeric antigen receptors (CARs)” that can recognize and bind to a specific target found on the myeloma cells. Currently approved CAR T-cell immunotherapy for myeloma targets the B-cell maturation antigen (BCMA). BCMA is considered an ideal target because it is expressed on the surface of plasma cells but not on stem cells in the bone marrow.

Idecabtagene vicleucel and ciltacabtagene autoleucel are FDA approved for the treatment of adult patients with relapsed or refractory multiple myeloma after they have undergone multiple prior lines of therapy. See **Table 5, Drug Classes and Drug Mechanisms** on page 50; and **Table 6, Some Drugs Used in the Treatment of Myeloma** on page 52 for more information.

While CAR T-cell therapy can be an effective treatment, it can also be associated with serious complications. These include cytokine release syndrome (CRS), which involves fevers and inflammation as the CAR T-cells attack the myeloma cells all at once. As a result, this therapy can only be given at specialized centers where doctors have expertise in delivering this type of treatment. Some patients may also require therapy to bridge the waiting time (up to 6 to 8 weeks) that it takes to produce the CAR T-cells.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view **Chimeric Antigen Receptor (CAR) T-Cell Therapy**.

**Bispecific Antibodies.** These drugs are similar in some ways to CAR-T therapy as discussed above because they also help T cells to attack myeloma cells. However, instead of genetically modifying a patient’s T cells in the lab, these antibodies are infused into the patient to redirect temporarily normal T cells to attack myeloma cells. One side effect of bispecific antibodies is cytokine release syndrome with fevers as can happen with CAR T-cell therapy. As such, bispecific antibodies can only be given at specialized centers where doctors have expertise in delivering this type of treatment. Unlike CAR T-cell therapy, bispecific antibodies do not require a waiting period. However, based on the studies that are available so far, bispecific antibodies are generally dosed every 1 to 4 weeks for years even if patients achieve remission. FDA-approved bispecific antibodies for myeloma include teclistamab, elranatamab and talquetamab.

See **Table 5, Drug Classes and Drug Mechanisms** on page 50; and **Table 6, Some Drugs Used in the Treatment of Myeloma** on page 52 for more information.

## Clinical Trials for Blood Cancers

Every new cancer drug goes through a series of carefully controlled research studies before it can become part of standard cancer care. These research studies are called “clinical trials.” Researchers use them to find better ways to care for and treat people with cancer. In the United States, the FDA requires that all new drugs and other treatments be tested in clinical trials before they can be used. At any given time, there are thousands of cancer clinical trials taking place. Doctors and researchers are always looking for new and better ways to treat cancer. Researchers use cancer clinical trials to study new ways to

- Treat cancer using:
  - A new drug
  - An approved drug to treat a different kind of cancer
  - A new combination of drugs
  - A new way of giving a drug (by mouth, intravenously (IV), etc.)
- Manage cancer symptoms and treat side effects
- Find and diagnose cancer
- Keep cancer from coming back after treatment
- Manage long-term treatment side effects

By taking part in a clinical trial, patients can see doctors who are experts in their disease, gain access to new, cutting-edge therapies and provide helpful information for future patients. The treatments and information we have today are due in large part to patients who have been willing to join clinical trials. Anyone interested in participating in a clinical trial should talk to their hematologist-oncologist about whether a clinical trial might be right for them. During this conversation it may help to:

- Have a list of questions to ask about the risks and benefits of each trial (visit [www.LLS.org/WhatToAsk](http://www.LLS.org/WhatToAsk) for lists of suggested questions)
- Ask a family member or friend to go with you to your doctor visit—both for support and to take notes

Clinical trials can be difficult to navigate and figure out, but The Leukemia & Lymphoma Society is here to help. Patients and caregivers can work with **Clinical Trial Nurse Navigators** who will help find potential clinical trials, overcome the barriers to enrollment and provide support throughout the entire clinical-trial process.

Our Clinical Trial Nurse Navigators are registered nurses who are experts in adult and pediatric blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about your treatment goals
- Help you to understand the clinical-trial process, including your rights as a patient
- Ask you for details about your diagnosis (such as past treatments, treatment responses, and your cancer genetic profile), your current health and your medical history. This information is taken into account and may factor into your eligibility to participate in certain clinical trials
- Help you to understand how your finances, insurance coverage, and support network, as well as your ability and willingness to travel, might impact your choice of a clinical trial
- Guide you and help you in your efforts to find and enroll in a clinical trial, including connecting you with trial sites
- Help deal with any problems you might have as you participate in a trial
- Support you throughout the clinical-trial process



**Call an LLS Information Specialist at (800) 955-4572 or visit [www.LLS.org/CTSC](http://www.LLS.org/CTSC) for more information about clinical trials and the Clinical Trial Support Center at LLS.**



**Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Understanding Clinical Trials for Blood Cancers*.**

**The Promise Study (Research Study on Myeloma).** This study seeks to identify, screen and track individuals who are at high risk of developing myeloma. The goal of the Promise Study is to increase early detection of myeloma precursor conditions in order to develop new therapies that prevent disease progression and improve survival. Study participants are individuals from 45 to 75 years of age who are African American, and/or individuals with a first-degree relative with a plasma cell disorder such as myeloma. All participation is online or by mail. Call, send an email or visit the study's website to learn more.

- Call: (617) 582-8544
- Email: [promisestudy@partners.org](mailto:promisestudy@partners.org)
- Website: [promisestudy.org](http://promisestudy.org)

# Complications, Side Effects and Supportive Care

Supportive care helps manage the complications of myeloma and the side effects of the drugs used for treatment. People with myeloma may receive supportive care at any time from the point of diagnosis, throughout treatment and beyond. It is an important part of your overall care.

**For more information on on drugs listed in this section, see the package insert and/or the full prescribing information for each medication (available on the internet).**

**Reducing Bone Damage and Bone Pain.** Myeloma often weakens and destroys bones. This can lead to bone pain, fractures and compression of the spine. Treatment is available to help strengthen bones and reduce bone pain. Treatment options include the following:

- **Bisphosphonates.** Bisphosphonates are a class of medications that help treat osteoporosis. Osteoporosis is a condition that weakens bones and increases the risk for bone fractures. Bisphosphonates reduce bone pain and help slow the destruction of bone caused by myeloma cells. They can also help correct and prevent hypercalcemia (elevated level of calcium in the blood). The bisphosphonates commonly used for treating bone problems in people with myeloma are pamidronate (Aredia®) and zoledronic acid (Zometa®). These drugs are given intravenously. Most patients are treated with these drugs once a month at first, but the doctor may eventually reduce the frequency of these infusions if the patients are doing better. In the United States, these medications are normally stopped after 2 years.

Bisphosphonates can have a rare but serious side effect called osteonecrosis of the jaw (ONJ). This condition may develop when the jaw fails to heal after a minor procedure, such as a tooth extraction, that results in bone exposure. Symptoms include pain, swelling, poor healing or infection of the gums, loosening of teeth or numbness (or a feeling of heaviness) in the jaw. Before beginning therapy with bisphosphonates, it is important to have a dental examination performed by an experienced dentist who has seen and understands ONJ. Dental treatments and procedures that require bone healing should be completed before intravenous bisphosphonate therapy is started. Patients should receive and follow instructions for maintaining good oral hygiene and should have regular dental checkups before and during treatment with bisphosphonates.

- **Monoclonal Antibody.** Denosumab (Xgeva®) is a monoclonal antibody approved by the FDA to prevent bone fractures in myeloma patients. It is also an osteoporosis medication. Denosumab is administered through subcutaneous injection every 4 weeks. This medication is recommended

when bisphosphonates cannot be prescribed due to potential damage to the kidneys. Denosumab can also cause the rare but serious side effect of ONJ (see page 37).

- **Vertebroplasty and Kyphoplasty.** These surgical techniques are used to treat compression fractures in the vertebrae. A compression fracture is a type of break in a vertebra caused by pressure in which the bone collapses. In vertebroplasty, chemical cement is inserted into the damaged or broken vertebrae through a catheter. Kyphoplasty involves inserting and inflating a balloon into the vertebra, to get it into its normal position before stabilizing the area with the chemical cement. These procedures relieve bone compression and may alleviate pain, as well as reduce the amount of pain medication that the patient needs. In some cases, height lost through vertebral collapse is restored. The usefulness of either of these procedures in specific cases of back pain is a matter that should be carefully discussed between patients and their doctors. These techniques tend to relieve pain caused by recent fractures more effectively than they do in cases involving older fractures.
- **Radiation Therapy.** This type of therapy uses high-energy radiation to kill masses of myeloma cells in the bone marrow. When the myeloma cells die, new bone replaces the tissue that had cancer. Bones hurt less and become stronger.
- **Physical Therapy or Rehabilitation.** In some cases, back pain in myeloma can be caused by the paraspinal muscles (the muscles around the vertebral bones) being out of alignment after prior lytic lesions or fractures. Physical therapy (PT) or rehabilitation can sometimes help patients to both feel stronger and have less pain.

Successful treatment of myeloma and its complications may relieve bone pain, but many patients may require medications to relieve the pain, including narcotics. Narcotic pain medications can cause constipation, and any patient on narcotics should make sure they are on stool softeners or a high-fiber diet. Note: nonsteroidal drugs such as ibuprofen should be avoided in patients with myeloma, given the increased risk of kidney failure.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Pain Management Facts*.

Your cancer doctor may also refer you to palliative care providers who specialize in pain management. Then, your cancer doctor can focus on controlling the myeloma at the same time that the palliative care provider focuses on controlling your pain (you do not have to choose between the two). Note: “Hospice” and “palliative care” are not interchangeable terms. Hospice is only one type of specialized palliative care for end-of-life. Palliative care is for anyone with a serious illness, regardless of age, stage or prognosis.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Palliative Care*.



**Low Blood Cell Counts.** Bone marrow is constantly producing red blood cells, white blood cells and platelets. Myelosuppression is a condition in which bone marrow activity is decreased, resulting in low red blood cell, white blood cell and/or platelet counts. Myeloma and myeloma treatments often cause drops in blood cell counts. Chemotherapy agents, immunomodulatory drugs such as lenalidomide, and proteasome inhibitors such as bortezomib can cause myelosuppression. If not managed effectively, myelosuppression can be life threatening and interfere with treatment and quality of life.

**Anemia.** A reduction in the number of red blood cells can result in anemia, which can make patients feel extremely tired and experience shortness of breath. Anemia can be treated with red blood cell transfusions. Some patients with severe anemia caused by chemotherapy or kidney disease may be treated with erythropoietin therapy. Erythropoietin (EPO) is a hormone needed for normal production of red blood cells. It is made primarily by the kidneys and is released into the blood in response to decreased blood oxygen levels. Drugs with synthetic EPO, such as epoetin alfa (Procrit®) and darbepoetin alfa (Aransep®), are available to help stimulate the bone marrow to make red blood cells. These drugs may alleviate anemia and decrease the need for blood transfusions. However, some studies suggest that treating anemia too aggressively may increase the risk for blood clots. Also, in some forms of cancer, the use of synthetic EPO may be associated with a worse outcome, although this may not be the case in myeloma. Patients should discuss the risks and benefits of EPO therapy with their doctors.

**Neutropenia.** When there is a decrease in the number of white blood cells called “neutrophils,” which are important in fighting infections, a condition called “neutropenia” occurs. Neutropenia can lead to serious infections that require antibiotic therapy and possibly hospitalization. Drugs known as white blood cell growth factors may be given to stimulate the bone marrow to make new white blood cells and to reduce the chance of serious infections. Certain drugs, such as filgrastim (Neupogen® or Zarxio®), pegfilgrastim (Neulasta® or Fulphila®) or sargramostim (Leukine®), may be prescribed to treat neutropenia.

**Thrombocytopenia.** When myelosuppression causes low platelet counts in the blood, a condition called “thrombocytopenia” occurs. Patients who have low platelet counts may experience excessive bleeding from cuts or injuries and may need platelet transfusions.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Side Effect Management: Managing Low Blood Cell Counts*.

**Infections.** Infections are not just a troublesome medical problem for patients with myeloma; they can be life-threatening. Patients with myeloma may have decreased ability to fight infections effectively. Myeloma cells may crowd out blood cells in the bone marrow, which can reduce the number of healthy white

blood cells. Some medications to treat myeloma can also decrease the number of white blood cells, which further contributes to the risk of infection. To prevent infections:

- Intravenous immunoglobulin therapy should be considered for patients with low levels of immunoglobulins, especially if they are having infections. Immunoglobulin therapy can help prevent frequent and life-threatening infections.
- The risk of infection can be reduced with vaccines for pneumonia, flu and shingles—infections people with myeloma often get. COVID-19 vaccinations are also recommended for people with myeloma. Talk to your doctor to get more information.
- Treatment to prevent against *Pneumocystis pneumonia* (PCP), herpes and fungal infections is sometimes recommended if a high-dose drug regimen has been given.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Side Effect Management: Reducing Your Risk of Infection*.

**Fatigue.** Fatigue is extreme tiredness and lack of energy that can interfere with a person’s daily activities. A person with fatigue may feel weak, worn out, heavy, slow or run down. Fatigue is a common problem for people with myeloma. It can be caused by many factors, including disease-related anemia, treatment side effects, physical immobility, sleep disturbances, nutritional deficits, depression, stress and anxiety or another medical problem. Patients with fatigue should talk with their doctor for help in managing their fatigue.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Cancer-Related Fatigue and the Side Effect Management series* (filter by “**Side Effect Management**”).

**Kidney Impairment.** Myeloma patients may have serious problems with kidney function for two main reasons. One reason is the excretion of large amounts of monoclonal proteins into the urine. This excess protein can damage the kidney filtration apparatus and the channels or tubules that are important in urine formation. Another reason is that patients with myeloma often have hypercalcemia (high levels of calcium) in the blood. When bones are damaged, calcium is released into the blood. A high level of calcium in the blood can damage the kidneys. Timely, adequate treatment of myeloma can improve kidney function and, in most cases, potentially even return it to normal. When this is not the case, some patients may need dialysis.

In rare cases, a procedure known as “plasmapheresis and exchange” may be helpful in limiting kidney damage. It may be used for patients who have very recent or acute kidney failure due to high levels of antibody proteins in the blood. However, this approach is controversial. It provides temporary removal of proteins from the blood; however, they will accumulate again if the source of

the problem (the myeloma) is not eliminated. The most important and successful treatment for kidney failure secondary to myeloma is to treat the myeloma itself without delay. Drinking adequate amounts of water and other healthy fluids can flush the kidneys and help them filter impurities from the blood. To prevent further kidney damage, it is essential to avoid use of nonsteroidal anti-inflammatory drugs (NSAIDs), iodinated IV contrast and aminoglycoside antibiotics.

**Peripheral Neuropathy.** This term refers to nerve damage in the peripheral nervous system, which transmits information from the brain and spinal cord to every other part of the body and vice versa. There are several possible causes for this condition. It can be a result of myeloma or a side effect of certain anticancer drugs, most commonly bortezomib. Other problems that can either cause or contribute to neuropathy include diabetes, nerve compression caused by vertebral fractures, amyloidosis and vitamin deficiencies (particularly folate or vitamin B-12). Symptoms may include either temporary or ongoing numbness, tingling, burning, coldness or weakness in the arms or legs. Patients who develop neuropathy while receiving chemotherapy should tell their healthcare providers as soon as the symptoms appear. Often, reducing the dosage of the drugs being used, or stopping them altogether, can alleviate these symptoms or even allow them to resolve completely.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Side Effect Management: Managing Peripheral Neuropathy (Nerve Damage)*.

**Thrombosis and Embolism.** The term “deep vein thrombosis” (DVT) refers to the condition caused by a blood clot that forms in the deep veins of the body, usually in the legs. Patients who receive myeloma treatments that are associated with DVT risk are usually prescribed medication to reduce the likelihood of developing this condition. It is important for patients to discuss DVT risk with their doctors and ask which of the options to reduce this risk is best for them. A DVT can cause blood flow obstruction, pain and swelling.

Pulmonary embolism is a sudden blockage in a lung artery. In most cases, it happens when a blood clot breaks loose, travels through the bloodstream and lodges in the arteries of the lungs. Depending on the size and number of clots that reach the pulmonary arteries, a patient may experience chest pain, shortness of breath and other potentially severe or even life-threatening effects.

Lenalidomide and pomalidomide are associated with an increased incidence of DVT and pulmonary embolism, even when they are used by themselves. The incidence is particularly increased when these drugs are combined with carfilzomib. Other factors that can increase the risk of DVT include the presence of a central line (central venous catheter), decreased mobility, recent surgery, pregnancy, smoking, a prior history of DVT or a family history of blood-clotting problems. Your doctor may put you on aspirin or another blood thinner to lower this risk.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Side Effect Management: Managing Blood Clots and Deep Vein Thrombosis*.

**Hyperviscosity Syndrome.** Rarely, in some myeloma patients, the monoclonal protein level is so high that it makes the blood “viscous” (thick). This condition, called “hyperviscosity syndrome,” interferes with the blood flow and delivery of oxygen to the tissues. The circulation of the oxygen-carrying red blood cells slows down, as the heart works harder to pump viscous blood throughout the body. This complication can lead to headaches, dizziness, weakness, fatigue, sleepiness, vision problems and damage to kidneys and other organs. Hyperviscosity syndrome is considered a medical emergency and requires urgent treatment with plasmapheresis. This treatment filters blood through a machine to remove the M proteins from the blood.

**Other Cancers.** Myeloma patients have an increased risk of developing other types of blood cancers, including myelodysplastic syndromes and acute myeloid leukemia. This is rare and only occurs in a small number of patients.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Myelodysplastic Syndromes and Acute Myeloid Leukemia*.

**Nutrition and Cancer.** Eating well is important for patients receiving treatment for blood cancer. Proper nutrition plays a key role in keeping the body strong, supporting the immune system and reducing the risk for diseases. Patients who eat well and maintain a healthy weight usually manage treatment and its side effects better. It is also important for patients with weakened immune systems to follow all food safety guidelines to reduce the risk of foodborne illness. Speak to your healthcare team about food and nutrition and for a referral to an oncology registered dietitian (RD) for specific nutrition advice and guidance.



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Food and Nutrition During Cancer Treatment and Nutrition Handbook: Feeding your family from meal planning to meal time*.



LLS registered dietitians have expertise in oncology nutrition and provide patients, parents and caregivers with free nutrition consultations by phone. Call 877-467-1936 or visit [www.LLS.org/nutrition](http://www.LLS.org/nutrition) to schedule a consult.

# Financial Concerns

Myeloma patients are living longer, primarily because of the development of new and effective drugs. It is estimated that the average myeloma patient will live more than 10 years from the time of diagnosis, and perhaps longer. While this progress is exciting, the financial costs associated with new treatments can become an obstacle to treatment. Paying for healthcare is a major concern for many people who are living with blood cancer. The high cost of cancer can lead to significant financial and emotional stress for both patients and their families.

Even if you have health insurance, cancer can still take a toll on your finances. You may have new expenses such as co-payments or travel for treatment. You may also have less income if you need to take time off from work.

Speak with your healthcare team if you have any concerns about being able to afford your treatment. They may be able to provide information and resources that can help. Health insurance plans may not cover all the costs of cancer care, but there are many resources available to help with prescription drug payment. In addition, several major drug manufacturers currently provide patient assistance or prescription assistance programs. These programs can provide both insured and uninsured patients free or reduced-cost medications.



**LLS offers financial assistance programs for eligible patients. Other organizations also offer financial assistance programs. You can call an LLS Information Specialist at (800) 955-4572 for more information about our financial assistance programs.**



**Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Cancer and Your Finances*.**

# Follow-Up Care

Follow-up care for myeloma varies from patient to patient. People with myeloma require regular follow-up visits with their hematologist-oncologist. You should see a primary care doctor for a general health examination at least once a year and you should also be examined regularly by your hematologist-oncologist.

Regular medical check-ups may include blood work as well as other tests to look for signs of a relapse. The tests also check how well your organs are working. This is important because myeloma and its treatment can cause organ damage.

If you have been treated for myeloma, you are encouraged to:

- Maintain regular follow-up appointments with your hematologist-oncologist. Your doctor will monitor you for signs of relapse and also inquire about any

side effects from treatment or the onset of any other medical problems.

- Keep a record of your cancer diagnosis, treatment and follow-up care needs. This is often called a “survivorship care plan.” Ask your doctor for a written survivorship care plan. Share this information with any new healthcare providers you see. The survivorship care plan should include the following information:
  - A list of all healthcare providers
  - A diagnosis summary with specifics such as subtype and/or genetic markers
  - A treatment summary with specifics such as the names, dates and dosages of chemotherapy or other drugs, site of radiation treatment, surgery and/or transplantation information, response to treatment, and side effects
  - Maintenance treatment information, if applicable
  - A list of possible late effects
  - A schedule for ongoing monitoring with recommended tests, frequency and coordinating provider
  - Health and wellness recommendations such as nutrition, exercise or other disease screenings
  - Vaccination history
- Have regular screenings for cancer. Myeloma is associated with an increased risk of developing acute myeloid leukemia, especially after receiving treatment with certain chemotherapy drugs.
- Seek medical and psychosocial support for fatigue, depression and other long-term effects, if needed.
- Consider cancer risk-reduction strategies, such as smoking cessation, skin protection against prolonged sun exposure, healthy eating and exercise.



**Visit [www.LLS.org/SurvivorshipWorkbook](http://www.LLS.org/SurvivorshipWorkbook) to view or order the free survivorship workbook, *Navigating Life During and After a Blood Cancer Diagnosis*, with versions for adults, young adults and children and adolescents.**

## Related Diseases

**Waldenström Macroglobulinemia (WM).** This is also called lymphoplasmacytic lymphoma (LPL) in most cases. WM has some features in common with myeloma. It is a malignancy of B lymphocytes that produce a monoclonal immunoglobulin (IgM) that can be measured in the blood. The malignant B lymphocytes replace the normal bone marrow cells and may cause anemia and other blood cell deficiencies by preventing the normal marrow cells from making blood cells efficiently. The IgM produced by the malignant B lymphocyte is a very large type of IgM, referred to as a “macroglobulin” (large globulin).



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Waldenström Macroglobulinemia*.

**Monoclonal Gammopathy of Renal Significance (MGRS).** This is a group of conditions that cause kidney damage. The damage is caused by plasma cells or B cells that make M proteins that can build up in the kidneys and damage them. MGRS is not cancer and does not meet the criteria for active myeloma, but nonetheless requires treatment because of the effects of the M proteins on kidney function. Both a bone marrow and a kidney biopsy are usually required to make the diagnosis. Typically, treatment for patients with this condition is similar to the treatment for patients with active myeloma. AL amyloidosis (see below) is a type of MGRS.

**AL Amyloidosis.** AL amyloidosis (amyloid light chain or primary amyloidosis) involves clumps of the light chain produced by myeloma cells that are called amyloid fibrils and can deposit in organs. Symptoms include nerve damage, kidney damage or heart damage. AL amyloidosis can occur in patients who also have active multiple myeloma, but it is more often diagnosed in patients who otherwise only have MGUS or smoldering myeloma. In other words, AL amyloidosis is often diagnosed because the proteins (light chain clumps called amyloid fibrils) are causing symptoms, not because the cells (pre-cancerous myeloma cells that are not themselves causing bone damage) are causing symptoms.

Many of the drugs that work against myeloma are also effective against amyloidosis, including corticosteroids, melphalan, bortezomib and daratumumab. In contrast, lenalidomide should be used with caution particularly in patients who have heart issues (shortness of breath) or gut issues (constipation) related to their underlying amyloidosis.

The goal of amyloidosis treatment is to normalize the light chains to prevent any further amyloid fibril (clump) deposition in the organs; after that, the body can slowly clear out the clumps on its own. For patients whose light chains normalize with treatment, autologous stem cell transplantation can be considered but is no longer required (unlike in multiple myeloma, where it is generally still recommended).



Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to view *Amyloidosis*.

**Plasma Cell Leukemia (PCL).** This rare plasma cell disease may be primary (diagnosed at the same time as multiple myeloma) or secondary (evolving from an existing diagnosis of multiple myeloma). In this disorder, patients have a high level of plasma cells (greater than 5 percent) circulating in the blood, often creating plasmacytomas throughout the body. This disease is treated like myeloma. However, patients frequently require more aggressive therapy because PCL is more aggressive than myeloma.

**POEMS Syndrome.** POEMS is a very uncommon disorder similar to AL amyloidosis. Patients also have abnormal plasma cells (typically not meeting criteria for active multiple myeloma) and nerve issues. Instead of the light chains forming clumps in the nerves, however, in POEMS syndrome the abnormal immunoglobulin prevents the nerves from functioning properly. Doctors are not sure exactly how this nerve dysfunction happens, but a protein called vascular endothelial growth factor (VEGF) is quite elevated in patients with POEMS syndrome and may play a role.

POEMS is an acronym; the letters represent the five most common features of the syndrome:

**P** for peripheral neuropathy

**O** for organ enlargement

**E** for endocrine gland dysfunction

**M** for monoclonal plasma cells and monoclonal immunoglobulin

**S** for skin changes

Peripheral neuropathy is often the most disabling feature of the syndrome and can include progressive weakness of the arms or legs. Liver or spleen enlargement is less common. The bone alterations related to the accumulation of plasma cells in the marrow are different from bone alterations in classic myeloma (the bone marrow looks denser than normal, rather than less dense). Thyroid or sex hormone deficiencies caused by endocrine gland dysfunction may require hormone replacement therapy. Other features not included in the POEMS acronym are high red blood cell or platelet counts, extravascular volume overload (swelling) and lung disease. Patients can benefit from radiation or standard myeloma treatment and, in some cases, from autologous stem cell transplantation.



## Treatment Outcomes

With advances in treatment and supportive care, survival rates for myeloma patients have improved significantly in the last decade. It is not unusual for transplant-eligible myeloma patients to live for 10 years or longer after diagnosis. Among patients older than 75, overall survival is lower and is approximately 5 to 10 years.

It is important to know that outcome data show how groups of people with myeloma responded to treatment in the past. These numbers, however, likely underestimate current survival since they predate the arrival of monoclonal antibodies and other new treatments that have been introduced in the last five years.

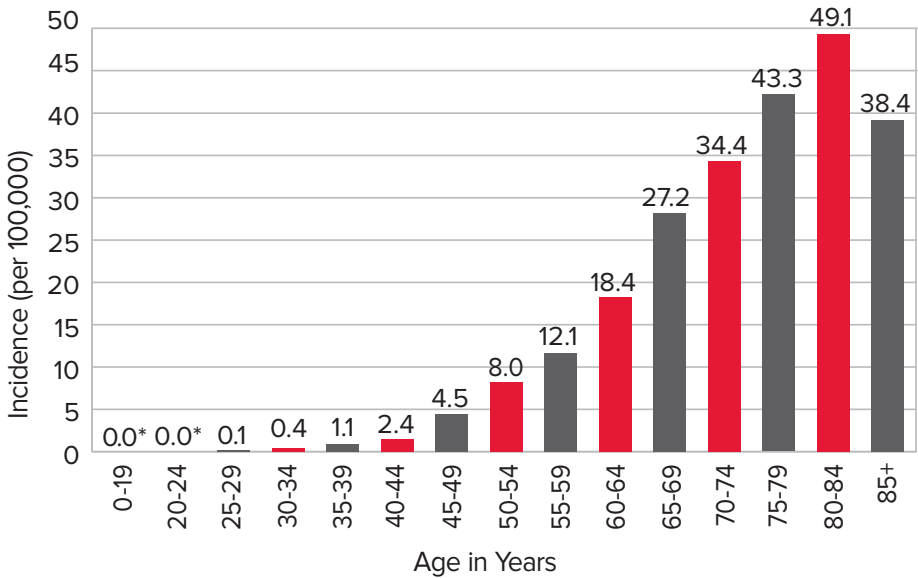
Survival statistics cannot always determine how a particular person will respond. They are only estimates based on large groups of people, and every person's experience is unique. You should discuss your potential outcome with your doctor.

## Incidence, Causes and Risk Factors

**Incidence.** While myeloma is a rare disease, it is the second-most common type of blood cancer. In the United States, approximately 35,780 new cases of myeloma were diagnosed in 2024. As of 2020, an estimated 168,234 people were living with myeloma.

Myeloma is seldom diagnosed in people younger than 40 years (see **Figure 6** on page 48). The median age at diagnosis is 69 years.

**Figure 6. Age-Specific Incidence Rates for Myeloma, 2016-2020**



Source: SEER\*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute; 2023 Apr 19.[updated: 2023 Nov 16; cited 2024 Feb 21]. Available from: <https://seer.cancer.gov/statistics-network/explorer/>. Data source(s): SEER Incidence Data, November 2022 Submission (1975-2020), SEER 22 registries.

\* Estimates based on fewer than 16 cases are suppressed and not shown.

**Causes and Risk Factors.** In most cases, it is not clear what causes the genetic changes that lead to myeloma. Researchers are trying to understand why these changes occur and how they cause myeloma to develop. Not all people with myeloma have the same genetic changes, and some changes are more common than others. The genetic changes associated with myeloma are not usually inherited from a parent; more often they occur during a person’s lifetime.

Although the cause of myeloma is unknown, there are some known risk factors associated with myeloma. A “risk factor” is anything that increases a person’s chance of developing a disease. Having a risk factor, however, does not mean that a person will develop the disease. Some people with several risk factors for a disease may never develop it, while others with no known risk factors do develop it.

Some of the following factors may increase the risk of developing myeloma:

- **Age.** The risk of developing myeloma increases with age. Most people who develop myeloma are older than 50 years.
- **Sex.** Males are more likely than females to develop myeloma.
- **Race.** Non-Hispanic Blacks have more than twice the age-adjusted incidence rate (14.4 per 100,000 population) of myeloma than non-Hispanic Whites (6.4 per 100,000 population).

- **Familial Risk/Germline Predisposition.** Having a sibling or parent with myeloma increases the risk of the disease.
- **Medical History.** The incidence is higher in people with a history of monoclonal gammopathy of unknown significance (MGUS). For more information about MGUS, see page 7.
- **Environmental Factors.** Some studies are investigating a link between the development of myeloma and exposure to
  - Radiation
  - Certain kinds of chemicals, such as pesticides, fertilizers and Agent Orange
  - Certain metals, such as cadmium, antimony and lead
- **Firefighting.** Some studies indicate that firefighters have a statistically significant higher risk for multiple types of cancer than the general population. It is estimated that firefighters in the United States are at a 1.53 times higher risk of developing myeloma, compared to the risk for members of the general public.

Two recent studies examined whether exposure to the wreckage of the World Trade Center (WTC) disaster after the 9/11 attacks increased firefighters' risk of developing cancer. One study indicated that the exposure of firefighters involved in the WTC rescue and recovery efforts to chemicals and environmental carcinogens may be linked to the increased incidence of monoclonal gammopathy of undetermined significance (MGUS) in this population. MGUS is considered a precursor to myeloma. The other study estimated that more WTC firefighters will continue to develop certain types of cancer than would be expected if they had not been exposed to the area of the disaster.



**Visit [www.LLS.org/booklets](http://www.LLS.org/booklets) to order the free Firefighters and Cancer Risk awareness postcards.**

**For information on the World Trade Center Health Program, see page 58.**

# Drug Information

**Table 5. Drug Classes and Drug Mechanisms**

<b>Alkylating Agents (DNA-Damaging Drugs)</b>	Chemotherapy that works by stopping or slowing the growth of cancer cells
<b>Antitumor Antibiotics</b>	Chemotherapy that prevents cell division by either binding to DNA to prevent the cells from duplicating or inhibiting RNA synthesis.
<b>BCL-2 Inhibitors</b>	These drugs inhibit the production of a protein that controls whether a cell lives or dies.
<b>Bispecific Antibodies</b>	Bispecific antibodies are designed to seek two targets. These drugs attach to both myeloma cells and T cells, bringing them together so the T cells can attack the myeloma cells.
<b>Chimeric Antigen Receptor (CAR) T-Cell Therapy</b>	This is a type of cellular immunotherapy that consists of modifying a patient's own immune cells to recognize and attack cancer cells.
<b>Corticosteroids</b>	Certain hormones (corticosteroids) can kill lymphocytes. They are believed to work by blocking cell metabolism through their effect on specific genes. In high doses, these synthetic hormones—relatives of the natural hormone cortisol—can kill malignant lymphocytes.
<b>Immunomodulatory Drugs (IMiDs)</b>	Immunomodulatory drugs act in multiple ways to kill myeloma cells and affect other cells, including immune system cells and structural cells. These drugs induce a cancer suppressor response directed by the immune system.

**Table 5. Drug Classes and Drug Mechanisms (continued)**

<b>Monoclonal Antibodies</b>	Monoclonal antibodies are laboratory-produced proteins that target specific antigens on the cancer cell's surface to interfere with the cell's function and destroy it. Once the antibody finds and attaches to its target, it can "recruit" (harness) other parts of the immune system to destroy cells that contain the antigen. Some monoclonal antibodies work by themselves and are therefore known as "naked antibodies." Some monoclonal antibodies are combined with a toxin or radioactive substance.
<b>Proteasome Inhibitors (PIs)</b>	These drugs block the function of the proteasome, leading to the accumulation of proteins in the cancer cells and thereby causing their destruction.
<b>Selective Inhibitors of Nuclear Export (SINE)</b>	SINE compounds block the export of tumor suppressor proteins so that they stay in the nucleus and stop tumor growth, leading to cell death.

**Table 6. Some Drugs Used in the Treatment of Myeloma**

**For more information, see the package insert and/or the full prescribing information for each medication (available on the internet).**

Some medications are dosed subcutaneously (sub-Q or SC) into the skin, others are dosed as an intravenous (IV) drip into a vein, and others are oral (pills).

Drug Name Administration Type of Drug	When the Drug Is Commonly Used	
	Newly Diagnosed Myeloma	Relapsed / Refractory Myeloma
<b>Bortezomib (Velcade®, Boruzu®)</b> Subcutaneous (sub-Q or SC) or Intravenous (IV) Proteasome Inhibitor	✓	✓
<b>Carfilzomib (Kyprolis®)</b> Intravenous (IV) Proteasome Inhibitor	✓	✓
<b>Ciltacabtagene autoleucel (Carvykti®)</b> Intravenous (IV) CAR T-Cell Therapy		✓
<b>Cyclophosphamide (Cytoxan®)</b> Intravenous (IV) or oral Alkylating Agent (Chemotherapy)	✓	✓
<b>Daratumumab and hyaluronidase-fihj (Darzalex Faspro®)</b> Subcutaneous (sub-Q or SC) [In some low-resource centers, intravenous daratumumab is still used] Monoclonal Antibody	✓  Also approved for newly diagnosed light chain (AL) amyloidosis	✓

**Table 6. Some Drugs Used in the Treatment of Myeloma (continued)**

Drug Name Administration Type of Drug	When the Drug Is Commonly Used	
	Newly Diagnosed Myeloma	Relapsed / Refractory Myeloma
<b>Dexamethasone (Decadron)</b> Intravenous (IV) or oral Corticosteroid	✓	✓
<b>Elotuzumab (Empliciti®)</b> Intravenous (IV) Monoclonal Antibody		✓
<b>Elranatamab (Elrexfio™)</b> Subcutaneous Injection (sub-Q or SC) Bispecific antibody		✓
<b>Idecabtagene vicleucel (Abecma®)</b> Intravenous (IV) CAR T-Cell therapy		✓
<b>Isatuximab-irfc (Sarclisa®)</b> Intravenous (IV) Monoclonal Antibody	✓ (in certain settings)	✓
<b>Ixazomib (Ninlaro®)</b> Oral Proteasome Inhibitor		✓
<b>Lenalidomide (Revlimid®)</b> Oral Immunomodulatory Drug (IMiD)	✓	✓
	Also approved as maintenance following autologous hematopoietic stem cells transplantation.	

**Table 6. Some Drugs Used in the Treatment of Myeloma (continued)**

<b>Drug Name</b> <b>Administration</b> <b>Type of Drug</b>	<b>When the Drug Is Commonly Used</b>	
	Newly Diagnosed Myeloma	Relapsed / Refractory Myeloma
<b>Linvoseltamab (REGN5458)</b> Intravenous (IV) Bispecific Antibody		✓
<b>Melphalan hydrochloride (Evomela®)</b> Intravenous (IV) Alkylating Agent (Chemotherapy)	Approved for use as a high-dose conditioning treatment prior to hematopoietic progenitor (stem) cell transplantation in patients with multiple myeloma.	
<b>Pomalidomide (Pomalyst®)</b> Oral Immunomodulatory Drug (IMiD)		✓
<b>Selinexor (Xpovio®)</b> Oral Selective Inhibitor of Nuclear Export (SINE)		✓
<b>Talquetamab-tgvs (Talvey™)</b> Subcutaneous Injection(sub-Q or SC) Bispecific Antibody		✓
<b>Venetoclax (Venclexta®)</b> Oral BCL-2 Inhibitor		✓



# Normal Blood and Bone Marrow

**Blood.** Blood is the liquid that flows through a person's arteries and veins. It carries oxygen and nutrients throughout the body. It also carries away waste products. Blood is composed of plasma and cells.

**Plasma.** Plasma is largely made up of water in which many chemicals are dissolved. These chemicals each have a special role. They include:

- Proteins
  - Albumin. This is the most common blood protein.
  - Blood-clotting proteins (coagulation factors). They are made by the liver.
  - Erythropoietin. It is made by the kidneys and stimulates red blood cell production.
  - Immunoglobulins. These are cells that fight infection.
- Hormones, such as thyroid hormones and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin B-12
- Electrolytes, such as calcium, potassium and sodium

**Blood Cells.** Blood cells are formed in the bone marrow, a spongy tissue where blood cells grow and develop. Blood cells start as stem cells. The process of stem cells maturing into blood cells is called "hematopoiesis" (see **Figure 7** on page 57). The blood cells are suspended in the plasma.

Once the blood cell is created, it will develop into one of the three types of blood cells.

These are:

1. Red blood cells are the cells that carry oxygen; they
  - Make up a little less than half of the body's total blood volume
  - Are filled with hemoglobin, the protein that picks up oxygen from the lungs and takes it around the body. It binds with carbon dioxide (CO<sub>2</sub>) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the CO<sub>2</sub> is removed from the lungs.
2. Platelets are cells that help blood clot; they
  - Are small cells (one-tenth the size of red blood cells)
  - Help stop bleeding from an injury or cut

- Stick to the torn surface of the vessel, clump together and plug up the bleeding site. They form a clot, with the help of proteins, such as fibrin, and electrolytes, such as calcium.
3. White blood cells (WBCs) are cells that fight infections. The several types of WBCs include:
- Neutrophils and monocytes. These are “phagocytes” (eating cells) that ingest and destroy bacteria and fungi. Unlike red blood cells and platelets, monocytes can leave the bloodstream and enter tissues to attack invading organisms and fight off infection.
  - Eosinophils and basophils. These WBCs respond to allergens or parasites.
  - Lymphocytes. WBCs found mostly in the lymph nodes, spleen and lymphatic channels, lymphocytes are a key part of the immune system. Some enter the bloodstream. There are three major types of lymphocytes:
    - T lymphocytes (T cells)
    - B lymphocytes (B cells)
    - Natural killer (NK cells)

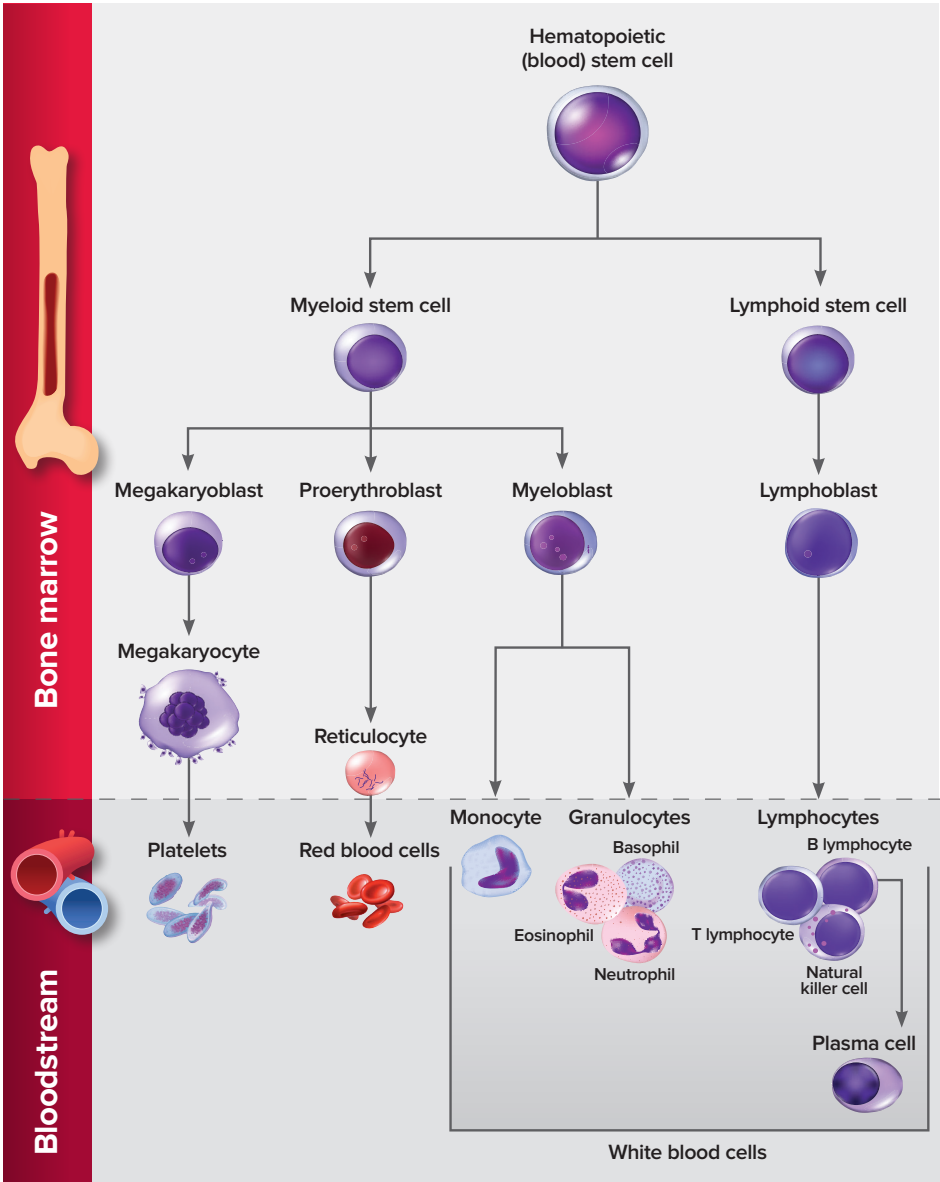
In healthy people, stem cells in the bone marrow produce new blood cells continuously. When blood cells are fully developed, they enter the bloodstream as it passes through the bone marrow and then circulates throughout the body.

In babies, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms and legs no longer have blood-forming marrow. In adults, bone marrow is only found in the spine (vertebrae), hip and shoulder bones, ribs, breastbone and skull.

Hematopoietic stem cells are found in the bone marrow. These stem cells are important because they can be transplanted. Some stem cells enter the bloodstream and circulate; there are not enough of them to be counted in standard blood tests. Doctors know how to stimulate the growth of these cells in the bone marrow and have them migrate into the bloodstream. Then a special technique called “apheresis” is used to separate them from the circulating blood so they can be collected and stored. Stem cells from the placenta and the umbilical cord of a newborn infant can also be collected and stored for future use in transplantation.

## Figure 7. Blood Cell and Lymphocyte Development

Most blood cells start as hematopoietic (blood) stem cells in the bone marrow. Hematopoietic stem cells are the most immature blood-forming cells. They must mature (go through many stages) to become a red blood cell, white blood cell or platelet. Some blood cells mature in the bone marrow. Other blood cells leave the bone marrow and travel to other parts of the body to develop into mature blood cells.



## Additional Resources

**Other Helpful Organizations.** LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. For more information, visit [www.LLS.org/ResourceDirectory](http://www.LLS.org/ResourceDirectory) to view the directory.

**Language Services.** Let members of your healthcare team know if you need translation or interpreting services because English is not your native language, or if you need other assistance, such as a sign language interpreter. Often these services are free.

**Information for Veterans.** Veterans who were exposed to Agent Orange while serving in Vietnam; to airborne hazards and burn pits while serving in Iraq, Afghanistan and other areas of Southwest Asia; to contaminated water at Camp Lejeune between 1953 and 1987; or to ionizing radiation during service may be able to get help from the United States Department of Veterans Affairs. For more information, please

- Call: the VA (800) 749-8387
- Visit: <https://www.va.gov/disability/eligibility/hazardous-materials-exposure/>

**Information for Firefighters.** Firefighters are at an increased risk of developing cancer. There are steps that firefighters can take to reduce the risk. Please visit [www.LLS.org/FireFighters](http://www.LLS.org/FireFighters) for resources and information.

**World Trade Center Health Program.** People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be able to get help from the World Trade Center (WTC) Health Program. People eligible for help include:

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were in the NYC disaster area and those who lived, worked or were in school in that area
- Responders to the Pentagon and the Shanksville, PA, crashes

For more information, please

- Call: WTC Health Program at (888) 982-4748
- Visit: [www.cdc.gov/wtc/faq.html](http://www.cdc.gov/wtc/faq.html)

**Mental Health.** Caring for your mental health has benefits if you are a cancer patient. Seek medical advice if you are struggling. For more information, please:

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at [www.nimh.nih.gov](http://www.nimh.nih.gov)

If you or your loved is experiencing a mental health crisis, call 988 to talk to a trained mental health professional. The 988 Suicide and Crisis Lifeline is free, confidential and always available. For the Crisis Text Line, text HOME to 741741.

## Health Terms

**Albumin.** A major protein in the blood that plays a role in fighting infections and building or repairing muscle tissue. The normal reference range for albumin is 3.5 to 5.5 g/dL (grams per deciliter). The optimal level is 4 g/dL. Test results can vary slightly between laboratories and may be affected by the method the laboratory uses to process the blood sample.

**Amyloidosis.** A health condition in which proteins called amyloids build up in and damage certain organs throughout the body.

**Anemia.** A decrease in the number of red blood cells and, therefore, in the hemoglobin concentration of the blood. This results in a diminished ability of the blood to carry oxygen. If severe, anemia can cause a pale complexion, weakness, dizziness, fatigue and shortness of breath.

**Antibody.** A protein made by plasma cells (a type of white blood cell) in response to an antigen (a substance that caused the body to make a specific immune response). Each antibody can bind to only one specific antigen. The purpose of this binding is to help destroy the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen. An antibody is a type of immunoglobulin.

**Antigen.** A foreign substance, usually a protein, that stimulates an immune response when it is ingested, inhaled or comes into contact with the skin or mucous membranes. Examples of antigens are bacteria, viruses and allergens. Antigens stimulate plasma cells to produce antibodies.

**Autologous Stem Cell Transplantation.** A procedure in which a patient's healthy blood-forming stem cells are collected from the blood or bone marrow before treatment, stored and then given back to the patient after

treatment. An autologous stem cell transplant replaces a patient's stem cells that were destroyed by treatment with high doses of chemotherapy or radiation. **See the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.**

**Basophil.** A type of white blood cell that participates in certain allergic reactions.

**Bence Jones Protein.** An abnormal protein (light chain), made by malignant plasma (myeloma) cells, that enters the blood and is excreted rapidly in the urine. This protein can cause injury to the kidneys or kidney failure when excreted in large amounts.

**Beta 2 ( $\beta$ 2)-Microglobulin.** A cell protein found in the blood. A high level of  $\beta$ 2-microglobulin molecules may be a sign of faster-growing myeloma. Levels of this protein, together with levels of albumin, are significant when staging myeloma.

**Biomarker.** A biological molecule found in blood, other body fluids or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition. Also called molecular marker.

**Bispecific Antibody.** A type of drug that temporarily redirects T cells (immune cells) to attack cancer cells.

**Bisphosphonate.** A drug that helps improve bone strength and prevent bone loss.

**Bone Marrow.** The soft, spongy tissue that is found in the center of most bones, where blood cells form. It contains blood stem cells that can become red blood cells, white blood cells or platelets.

**Bone Marrow Aspiration.** A procedure in which a liquid sample of bone marrow is removed for examination. After the patient is given a numbing agent, a special wide needle is pushed into the bone, usually the back of the patient's hip bone. This procedure may be done at the same time as a bone marrow biopsy.

**Bone Marrow Biopsy.** A procedure in which a sample of bone with bone marrow is removed for examination. After medication is given to numb the skin and tissue, a special biopsy needle is used to remove a core of bone containing bone marrow from the back of the patient's hip bone.

The bone marrow sample is sent to a laboratory to be looked at under a microscope. The procedure may be done at the same time as a bone marrow aspiration.

**Chemotherapy.** Treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing.

**Chimeric Antigen Receptor (CAR) T-Cell Therapy.** Treatment that uses a patient's own T cells (a type of white blood cell) to identify and attack cancer cells. The T cells are taken from the patient's blood and sent to a laboratory, where they are genetically modified to attack cancer cells. The engineered T cells are then multiplied and re-infused into the patient's bloodstream. **See the free LLS fact sheet, *Chimeric Antigen Receptor (CAR) T-Cell Therapy*.**

**Computed Tomography (CT) Scan.** A procedure that uses a computer linked to an x-ray machine to make a series of detailed pictures of areas inside the body. The pictures are taken from different angles and are used to create 3-dimensional views of tissues and organs.

**Creatinine.** A waste compound that is filtered out of blood into urine by the kidneys. Creatine levels are measured to monitor kidney function. High levels of creatinine in the blood may be a sign of kidney damage.

**Cytogenetic Analysis.** The process of analyzing cells in a sample of tissue, blood or bone marrow to look for changes in chromosomes. Changes in certain chromosomes may be a sign of some types of cancer. Cytogenetic analysis may be used to help diagnose disease, plan treatment or find out how well treatment is working

**DNA.** The molecule inside cells that contains the genetic instructions for making and controlling cells. Also called "deoxyribonucleic acid." **For more information, see the free LLS booklet, *Understanding Genetics*.**

**Eosinophil.** A type of white blood cell that participates in allergic reactions and helps fight certain parasitic infections.

**Extramedullary Plasmacytoma.** A tumor of abnormal plasma cells that grows in soft tissue, not in the bones.

**Fluorescence In Situ Hybridization (FISH).** A laboratory method used to look at genes and chromosomes in cells and tissues. FISH can be used to identify where a specific gene is located on a chromosome, how many copies of the gene are present, and any chromosomal abnormalities. It is used to help diagnose disease, such as cancer, and help plan treatment.

**Focal.** In terms of cancer, limited to a specific area.

**Heavy Chain.** Any of the large protein chains that are part of an antibody.

**Hematologist.** A doctor who specializes in treating blood diseases.

**Hematopathologist.** See Pathologist.

**Hemoglobin.** A protein inside red blood cells that carries oxygen from the lungs to tissues and organs in the body and carries carbon dioxide back to the lungs. Measuring hemoglobin in the blood is usually part of a complete blood count (CBC) test.

**Hypercalcemia.** Higher than normal levels of calcium in the blood.

**Imaging Test.** A type of test that makes detailed pictures of areas inside the body. Imaging tests use different forms of energy, such as x-rays, ultrasound and radio waves.

**Immune System.** A complex network of cells, tissues and organs, and the substances they make, that helps the body fight infections and other diseases. The immune system includes white blood cells and organs and tissues of the lymph system, such as the thymus, spleen, tonsils, lymph nodes, lymph vessels and bone marrow.

**Immunoglobulin (Ig).** A protein that helps the body fight infection. Normal plasma cells produce one of five types of antibodies (polyclonal immunoglobulins): IgG, IgA, IgM, IgE or IgD. Low levels of immunoglobulin may be a cause of repeated infections in some patients.

**Immunophenotyping.** Use of flow cytometry to identify each individual type of cell in a sample (for example, cells in a marrow aspirate). This is done using antibodies that recognize different cell surface proteins that are characteristic of each cell type and are therefore different for B cells, T cells and plasma cells, among others.

**Immunotherapy.** Any of several treatment approaches that harness the body's immune system to treat diseases. These therapies include monoclonal antibody therapy, radioimmunotherapy and vaccine therapy.

**Kidney.** One of a pair of organs in the abdomen. The kidneys remove waste and extra water from the blood (as urine) and help keep chemicals (such as sodium, potassium and calcium) balanced in the body.

**Light Chain.** Either of the two small protein chains that, when linked



to heavy chains, make up the antibody molecule of an immunoglobulin. There are two types of light chains, referred to as kappa (k) and lambda ( $\lambda$ ).

**Lymphocyte.** A type of white blood cell that is essential to the body's immune system. There are three major types of lymphocytes: 1) B lymphocytes (B cells), which produce antibodies to help combat infectious agents, such as bacteria, viruses and fungi; 2) T lymphocytes (T cells), which have several functions, including assisting B lymphocytes to make antibodies; and 3) natural killer cells, which can attack virus-infected cells or tumor cells.

**Lytic Lesion.** Destruction of an area of bone due to a disease process, such as cancer. Also known as "osteolytic lesions."

**Magnetic Resonance Imaging (MRI) Scan.** A procedure that uses radio waves, a powerful magnet and a computer to make a series of detailed pictures of areas inside the body. MRI may be used to help diagnose disease, plan treatment or find out how well treatment is working.

**Measurable Residual Disease (MRD).** The small amount of cancer cells that may remain in the body after treatment. These residual cancer cells can only be identified by very sensitive tests. **See the free LLS fact sheet, *Measurable Residual Disease*.**

**MGUS.** See monoclonal gammopathy of undetermined significance.

**Monoclonal Antibody Therapy.** Therapy using proteins (antibodies) made in the laboratory that either react with or attach to antigens on the cancer cells they are targeted against.

**Monoclonal Gammopathy of Undetermined Significance (MGUS).** A benign condition in which there is a higher-than-normal level of a protein called M protein in the blood. Patients with MGUS are at an increased risk of developing cancer.

**Monocyte/Macrophage.** A type of white blood cell that makes up about 5 to 10 percent of the cells in normal human blood. When monocytes leave the blood and enter the tissues, they are converted into macrophages. Macrophages surround and kill microorganisms, ingest foreign material, remove dead cells and boost immune responses.

**M Protein.** An antibody found in unusually large amounts in the blood or urine of people with myeloma and other types of other plasma cell disorders.

**Mutation.** Any change in the DNA sequence of a cell. Mutations may be caused by mistakes during cell division, or by exposure to DNA-damaging agents in the environment. **See the free LLS booklet, *Understanding Genetics*.**

**Neurotoxicity.** The tendency of some treatments to cause damage to the nervous system.

**Neutrophil.** A type of white blood cell that is an important part of the immune system and helps the body fight infection.

**Osteoporosis.** A condition in which there is a decrease in the amount and thickness of bone tissue. This causes the bones to become weak and break more easily.

**Pathologist.** A doctor who identifies diseases by studying tissues under a microscope. A hematopathologist is a type of pathologist who studies diseases of blood cells by examining blood, bone marrow, lymph node and other tissue samples.

**PET Scan.** See Positron Emission Tomography (PET) Scan.

**Plasma.** Liquid that remains when clotting of the blood is prevented.

**Plasma Cell.** A type of white blood cell that makes large amounts of a specific antibody. Plasma cells develop from B cells that have been activated.

**Plasmacytoma.** A localized tumor of malignant plasma cells, either in a bone or in another tissue of the body.

**Platelet.** A tiny, disc-shaped piece of cell that is found in the blood and spleen. Platelets are pieces of very large cells in the bone marrow called megakaryocytes. They help form blood clots to slow or stop bleeding and to help wounds heal.

**Positron Emission Tomography (PET) Scan.** An imaging test used to detect cancer sites in the body. It uses glucose (a type of sugar), which is marked with a positron particle that emits a radioisotope, such as fluorine-18. Cancer cells use more sugar than normal tissues, so the isotope becomes concentrated in areas where cancerous cells are present. To establish the precise location of cancer cells, PET is combined with computed tomography (CT) in a procedure called “PET-CT.”

**Radiation Therapy.** The use of x-rays and other forms of radiation to kill cancer cells and shrink tumors.

**Red Blood Cell.** A type of blood cell that contains a protein called hemoglobin. Hemoglobin carries oxygen from the lungs to the tissues of the body. Red blood cells make up about 40 to 45 percent of blood in volume in healthy people. Also called an “erythrocyte.”

**Refractory.** The term used to describe a disease that is progressing despite ongoing treatment, does not respond at all to treatment, or starts to progress significantly within 60 days of stopping treatment.

**Relapse.** The term used to describe a disease that initially responds to therapy but then begins to progress. Usually, the disease must begin to progress 60 days or more after treatment ends for it to be considered relapsed.

**Remission.** The disappearance of evidence of a disease, usually after treatment. The terms “complete remission” (“complete response”) and “partial remission” (“partial response”) are used to further classify the remission.

**RNA.** One of two types of nucleic acid made by cells. RNA contains information that has been copied from DNA. Cells make several different forms of RNA, and each form has a specific job in the cell. Many forms of RNA have functions related to making proteins. Also called ribonucleic acid.

**Serum.** The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed.

**Serum Free Light Chain Test.** A diagnostic test that measures the amount of free light chains (protein components) in blood samples.

**Serum Immunofixation Electrophoresis (SIFE).** A laboratory test that can identify the type of M protein (myeloma protein) being produced by myeloma cells in the blood.

**Serum Protein Electrophoresis (SPEP).** A laboratory test that identifies the presence of abnormal proteins and the absence of normal proteins, as well as increases and decreases of different groups of proteins.

**Skeletal Bone Survey.** Head-to-toe x-ray study of the body undertaken to detect lytic bone lesions, compression fractures and osteoporosis (thinning of the bones), which can result from myeloma. This test is no longer recommended in the US.

**Stem Cell.** A cell from which other types of cells develop. In the bone marrow, blood-forming stem cells mature into red blood cells, white blood cells and platelets. Stem cells can be collected, preserved and used for stem cell therapy.

**Translocation.** A genetic change in which a piece of one chromosome breaks off and attaches to another chromosome. Sometimes pieces from two different chromosomes trade places with each other. **For more information, see the free LLS booklet, *Understanding Genetics*.**

**Urine Immunofixation Electrophoresis (UIFE).** A laboratory urine test that can identify the type of M protein (monoclonal protein) being produced by myeloma cells.

**Urine Protein Electrophoresis (UPEP).** A laboratory test that uses a urine sample to identify the presence of abnormal proteins and to determine increases and decreases of different groups of proteins in urine.

**White Blood Cell.** A blood cell that is part of the body's immune system. The five major types of white blood cells are: neutrophils, eosinophils, basophils, monocytes and lymphocytes. Also called "leukocyte."

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## A six-word narrative about living with blood cancer from patients in our LLS Community

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Stay strong and keep moving forward. Find the positive in every day. Be your own best patient advocate. Changed my life for the better. Accept, learn and focus on present. Learning to live a different life. Sudden and life changing—be positive. Waiting, worrying, anxiousness/happy I'm alive! Embrace a new normal each day. 5 years, 41 infusions, constant fatigue. Patience, positive attitude, hope and faith. Test to test, I will survive! Treatment, fatigue, treatment, fatigue and survival. Love life, live better every day. I don't look back only forward. So far, so good, live life. Meditation, mindfulness, wellness, faith and optimism. Finding joy while living with uncertainty. Watch, wait, treat, regroup, rest, re-energize. Blessed to be doing so well! Eye opening needed learning and healing. Feel great: uncertain travel plans annoying. Renewed faith, meditation, diet, mindfulness, gratitude. Watchful waiting can be watchful worrying. Scary, expensive, grateful, blessings, hope, faith. Thank god for stem cell transplants! Do not know what to expect. Extraordinarily grateful, I love my life. Diagnosed; frightened; tested; treating; waiting; hoping. I'm more generous, impatient less often. Embrace your treatment day after day. Live today, accept tomorrow, forget yesterday. Strength you never realized you had. Challenging to our hearts and minds. Life is what we make it. Live life in a beautiful way.



Discover what thousands already have at  
[www.LLS.org/Community](http://www.LLS.org/Community)

Join our online social network for people who are living with or supporting someone who has a blood cancer. Members will find:

- Thousands of patients and caregivers sharing experiences and information, with support from knowledgeable staff
- Accurate and cutting-edge disease updates
- The opportunity to participate in surveys that will help improve care



For more information, please  
contact our Information Specialists  
**800.955.4572** (Language interpreters  
available upon request.)

**The Leukemia & Lymphoma Society Mail Center** 1201 15th Street N.W., Suite 410, Washington, D.C. 20005

The mission of The Leukemia & Lymphoma Society (LLS) is to cure blood cancer and improve the quality of life of all patients and their families. Find out more at [www.LLS.org](http://www.LLS.org).