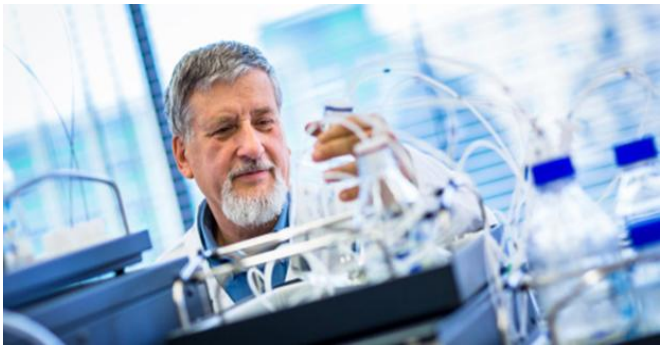
Multiple Myeloma



WHAT IS MULTIPLE MYELOMA?

Multiple myeloma is a cancer formed by malignant plasma cells. Normal plasma cells are found in the bone marrow and are an important part of the immune system.

The immune system is made up of several types of cells that work together to fight infections and other diseases. Lymphocytes (lymph cells) are the main cell type of the immune system. The major types of lymphocytes are T cells and B cells.

When B cells respond to an infection, they mature and change into plasma cells. Plasma cells make the antibodies (also called *immunoglobulins*) that help the body attack and kill germs. Lymphocytes are in many areas of the body, such as lymph nodes, the bone marrow, the intestines, and the bloodstream. Plasma cells, however, are mainly found in the bone marrow. Bone marrow is the soft tissue inside some hollow bones. In addition to plasma cells, normal bone marrow has cells that make the different normal blood cells.

When plasma cells become cancerous and grow out of control, they can produce a tumor called a *plasmacytoma.* These tumors generally develop in a bone, but they are also rarely found in other tissues. If someone has only a single plasma cell tumor, the disease is called an *isolated* (or *solitary*) *plasmacytoma*. If someone has more than one plasmacytoma, they have *multiple myeloma*.

Multiple myeloma is characterized by several features, including:

Low blood counts

In multiple myeloma, the overgrowth of plasma cells in the bone marrow can crowd out normal blood-forming cells, leading to low blood counts. This can cause anemia – a shortage of red blood cells. People with anemia become pale, weak, and fatigued. Multiple myeloma can also cause the level of platelets in the blood to become low (called*thrombocytopenia*). This can lead to increased bleeding and bruising. Another condition that can develop is *leukopenia*– a shortage of normal white blood cells. This can lead to problems fighting infections.

Bone and calcium problems

Myeloma cells also interfere with cells that help keep the bones strong. Bones are constantly being remade to keep them strong. Two major kinds of bone cells normally work together to keep bones

healthy and strong. The cells that lay down new bone are called *osteoblasts*. The cells that break down old bone are called *osteoclasts*. Myeloma cells make a substance that tells the osteoclasts to speed up dissolving the bone. Since the osteoblasts do not get a signal to put down new bone, old bone is broken down without new bone to replace it. This makes the bones weak and they break easily. Fractured bones are a major problem in people with myeloma. This increase in bone break-down can also raise calcium levels in the blood. (Problems caused by high calcium levels are discussed in the section "How is multiple myeloma diagnosed?")

Infections

Abnormal plasma cells do not protect the body from infections. As mentioned before, normal plasma cells produce antibodies that attack germs. For example, if you developed pneumonia, normal plasma cells would produce antibodies aimed at the specific bacteria that were causing the illness. These antibodies help the body attack and kill the bacteria. In multiple myeloma, the myeloma cells crowd out the normal plasma cells, so that antibodies to fight the infection can't be made. The antibody made by the myeloma cells does not help fight infections. That's because the myeloma cells are just many copies of the same plasma cell – all making copies of the same exact (or monoclonal) antibody.

Kidney problems

The antibody made by myeloma cells can harm the kidneys. This can lead to kidney damage and even kidney failure.

Monoclonal gammopathy

Having many copies of the same antibody is known as a *monoclonal gammopathy*. This condition can be found with a blood test. Although people with multiple myeloma have a monoclonal gammopathy, not everyone with monoclonal gammopathy has multiple myeloma. It can also occur in other diseases, such as Waldenstrom macroglobulinemia and some lymphomas. It can also occur in a disorder known as *monoclonal gammopathy of undetermined significance (MGUS),* which does not cause problems like multiple myeloma does. However, some people with MGUS will eventually go on to develop multiple myeloma or other diseases.

Light chain amyloidosis

Antibodies are made up of protein chains joined together – 2 short light chains and 2 longer heavy chains. In light chain amyloidosis, abnormal plasma cells make too many light chains. These light chains can deposit in tissues, where they build up. This accumulation of light chains can lead to an abnormal protein in tissues known as amyloid. The buildup of amyloid in certain organs can lead them to enlarge and not work well. For example, when amyloid builds up in the heart, it can cause an irregular heart beat and cause the heart to enlarge and get weaker. A weak heart can lead to a condition called *congestive heart failure*, with symptoms like shortness of breath and swelling in the legs. Amyloid in the kidneys can cause them to work poorly. This may not cause symptoms early on, but the poor kidney function may be found on blood tests. If it gets worse, amyloid in the kidney can lead to kidney failure. See the section "Signs and symptoms of multiple myeloma" for more information about the signs and symptoms of light chain amyloidosis.

Other names for light chain amyloidosis include *AL* and *primary amyloidosis*. This is sometimes considered a separate disease from multiple myeloma, but because treatment is often similar to that of myeloma, we will discuss it in this document.

Light chain amyloidosis is only one of the diseases where amyloid builds ups and causes problems. Amyloidosis can also be caused by a genetic (hereditary) disease called *familial amyloidosis*. Long-standing (chronic) infection and/or inflammation can also cause amyloidosis. This is known as *secondary* or *AA amyloidosis*. This document does not talk about these other kinds of amyloidosis.

Monoclonal gammopathy of undetermined significance

In monoclonal gammopathy of undetermined significance (MGUS), abnormal plasma cells produce many copies of the same antibody (a monoclonal antibody protein). However, these plasma cells do not form an actual tumor or mass and do not cause any of the other problems seen in multiple myeloma. MGUS usually does not affect a person's health. In particular, it doesn't cause weak bones, high calcium levels, kidney problems, or low blood counts. It's most often found when a routine blood test finds a high level of protein in the blood and further testing shows the protein is a monoclonal antibody. In MGUS, the number of plasma cells may be increased, but they still make up less than 10% of the cells in the bone marrow.

Some people with MGUS will eventually develop multiple myeloma, lymphoma, or amyloidosis. Each year, about 1% of people with MGUS develops one of these diseases. The risk is higher in people whose protein levels are particularly high. Patients with MGUS don't need treatment, but they are watched closely to see if they get a disease that does need to be treated, such as multiple myeloma.

Recently, scientists have studied the genes of the plasma cells in patients with MGUS. They found that the genetic make-up of these plasma cells resembles myeloma plasma cells more than it resembles that of normal plasma cells. This suggests that these cells are truly malignant, not just slow growing. Because people with MGUS are generally elderly, they may not live long enough for it to transform into myeloma.

Solitary plasmacytomas

This is another type of abnormal plasma cell growth. Rather than many tumors in different locations as in multiple myeloma, there is only one tumor, hence the name *solitary* plasmacytoma.

Most often, a solitary plasmacytoma develops in a bone, where it may be called an *isolated plasmacytoma of bone*. When a plasmacytoma starts in other tissues (such as the lungs or other organs), it is called an *extramedullary plasmacytoma*. Solitary plasmacytomas are most often treated with radiation therapy. Sometimes surgery may be used for a single extramedullary plasmacytoma. As long as no other plasmacytomas are found later on, the patient's outlook is usually excellent. However, since many people with a solitary plasmacytoma will develop multiple myeloma, these people are watched closely for signs of this disease.

CAUSES, RISK FACTORS, AND PREVENTION

What are the risk factors for multiple myeloma?

A *risk factor* is anything that changes a person's chance of getting a disease such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for lung cancer and many other cancers. But risk factors don't

tell us everything. People who have no risk factors can still get the disease. Also, having a risk factor, or even several, does not mean that a person will get the disease.

Scientists have found few risk factors that may affect someone's chance of getting multiple myeloma.

Age

The risk of multiple myeloma goes up as people age. Less than 1% of cases are diagnosed in people younger than 35. Most people diagnosed with this cancer are at least 65 years old.

Gender

Men are slightly more likely to develop multiple myeloma than women.

Race

Multiple myeloma is more than twice as common in African Americans than in white Americans. The reason is not known.

Radiation

People who were exposed to radiation from an atomic bomb blast had a higher risk of multiple myeloma. Exposure to lower levels of radiation may also increase the risk of multiple myeloma. At most, this accounts for a very small number of cases.

Family history

Multiple myeloma seems to run in some families. Someone who has a sibling or parent with myeloma is 4 times more likely to get it than would be expected. Still, most patients have no affected relatives, so this accounts for only a small number of cases.

Workplace exposures

Studies looking at workplace exposures and multiple myeloma risk have found no clear links.

Obesity

A study by the American Cancer Society has found that being overweight or obese increases a person's risk of developing myeloma.

Having other plasma cell diseases

Many people with monoclonal gammopathy of undetermined significance (MGUS) or solitary plasmacytoma will eventually develop multiple myeloma.

EARLY DETECTION, DIAGNOSIS, AND STAGING

Can multiple myeloma be found early?

It's difficult to diagnose multiple myeloma early. Often, multiple myeloma causes no symptoms until it reaches an advanced stage. Sometimes, it might cause vague symptoms that at first seem to be caused by other diseases. Rarely, multiple myeloma is found early when a routine blood test shows an abnormally high amount of protein in the blood.

TREATING MULTIPLE MYELOMA

How is multiple myeloma treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

After multiple myeloma is found and staged, your cancer care team will discuss treatment options with you. The treatment for multiple myeloma may include:

- Chemotherapy and other drugs
- Bisphosphonates
- Radiation
- Surgery
- Biologic therapy
- Stem cell transplant
- Plasmapheresis

It is important to discuss all of your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. It's also very important to ask questions if you're not sure about something. You can find some good questions to ask in the section "What should you ask your doctor about multiple myeloma?"

For information about some of the most common approaches used based on the extent of the disease, see the section "Treatment of multiple myeloma, by stage."

You should take a reasonable amount of time to think about all of the choices. Getting a second opinion can provide more information and help you feel more confident about the chosen treatment plan. Some insurance companies require a second opinion before they will agree to pay for certain treatments.

TALKING WITH YOUR DOCTOR

What should you ask your doctor about multiple myeloma?

As you deal with your cancer and the process of treatment, you need to have frank, open discussions with your cancer care team. They want to answer all of your questions, no matter how minor they might seem. You should ask any question you have. Among the questions you might want to ask are:

- What's my stage of multiple myeloma? What does that mean?

- What are my treatment choices?
- Based on what you've learned about my cancer, how long do you think I'll survive?
- What side effects can I expect from treatment?
- How long will it take me to recover from treatment?
- When can I go back to work or resume other activities after treatment?
- What are the chances that the cancer will come back after treatment (recur)?
- Does one type of treatment reduce the risk of recurrence more than another?
- What should I do to be ready for treatment?
- Should I get a second opinion?

You will no doubt have other questions about your personal situation. Be sure to write down your questions so that you remember to ask them during each visit with your cancer care team. Also keep in mind that doctors are not the only ones who can give you information. Other health care professionals, such as nurses and social workers, may have the answers you seek.

AFTER TREATMENT

What happens after treatment for multiple myeloma?

For most people, multiple myeloma never goes away completely. These people may get regular treatments withchemotherapy and other drugs, radiation therapy, or other therapies to try to help keep the cancer in check. Although there may be a time when they stop treatment for a time, most patients never really finish treatment. Follow up is needed for the doctor to know when to start treatment again. This can help prevent problems that can interfere with daily life.

Learning to live with cancer that does not go away can be difficult and very stressful. Our document *When Cancer Doesn't Go Away*, talks more about this.

Follow-up care

During and after treatment, it's very important to go to all follow-up appointments. During these visits, your doctors will ask about symptoms, examine you, and order blood tests or imaging studies such as CT scans or x-rays. Follow-up is needed to see if more treatment is needed and to check for any side effects. This is the time for you to talk to your cancer care team about any changes or problems you notice and any questions or concerns you have.

Almost any cancer treatment can have side effects. Some last for a few weeks to several months, but others can be permanent. Don't hesitate to tell your cancer care team about any symptoms or side effects that bother you so they can help you manage them.

It's also important to keep your medical insurance. Myeloma is rarely curable at this time. It may go away for a while, but the disease is likely to come back again. When that happens, the last thing you want is to have to worry about paying for treatment. The American Cancer Society document *When Your Cancer Comes Back: Cancer Recurrence*gives you information on how to manage and cope with this phase of your treatment.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know anything about your medical history. It's important that you be able to give your new doctor the details of your diagnosis and treatment. Gathering these details soon after treatment may be easier than trying to get them at some point in the future. Make sure you have this information handy:

- A copy of your pathology report(s) from any biopsies or surgeries
- Copies of imaging tests (CT or MRI scans, etc.), which can usually be stored on a CD, DVD, etc.
- Copies of your lab results
- If you had surgery, a copy of your operative report(s)
- If you were in the hospital, a copy of the discharge summary that doctors prepare when patients are sent home
- If you had drug treatment (such as chemotherapy or immunotherapy), a list of the drugs, drug doses, and when you took them
- If you had radiation, a copy of the treatment summary

The doctor may want copies of this information for his records, but always keep copies for yourself.

WHAT`S NEW IN MULTIPLE MYELOMA RESEARCH?

What's new in multiple myeloma research and treatment?

Important research into multiple myeloma is being done in many university hospitals, medical centers, and other institutions around the world. Each year, scientists find out more about what causes the disease and how to improve treatment. Many new drugs are being tested.

Researchers have found that bone marrow-support tissues and bone cells produce growth factors that increase the growth of myeloma cells. In turn, the myeloma cells produce substances that cause bone cells to undergo changes that weaken the bones. These discoveries are helping the researchers develop new drugs to block these growth factors, slow down the cancer, and reduce bone destruction. For example, bone marrow support (*stromal)* cells produce interleukin-6 (IL-6). Because IL-6 is a strong growth factor for multiple myeloma cells and eventually destroys bone, some current research efforts are focused on developing ways to block IL-6 function.

A form of arsenic, arsenic trioxide, is used to treat a certain kind of leukemia, and is also being tested to treat myeloma.

Drugs that act differently than the ones in use are being studied. For example, a drug called panobinostat is a histone deacetylase (HDAC) inhibitor, which means it affects the proteins in chromosomes. It has shown promising results when used in combination with bortezomib (Velcade) and dexamethasone, and it is now approved for use along with these drugs.

A test called *gene expression profiling* has been studied in recent years in multiple myeloma. This test looks to see what genes are active in cancer cells, and may be able to tell if and when a patient

with multiple myeloma will need to have chemotherapy. Much more work lies ahead though, before this test can be used routinely.

Source: