Reporter's Guide to **Multiple Myeloma**

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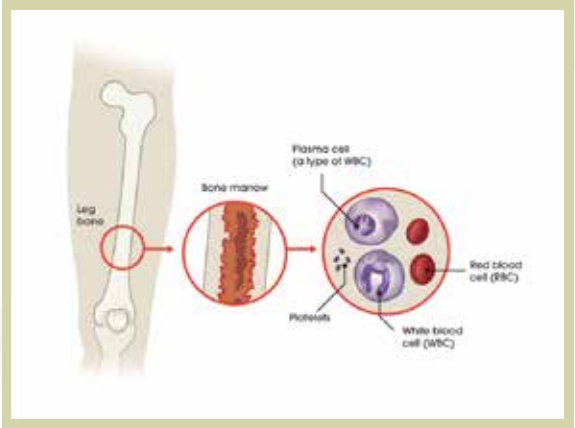
What is **multiple myeloma?**

Multiple myeloma is a relatively rare form of blood cancer that accounts for roughly 1.8% of all cancers and roughly 2% of all deaths from cancer.[1]

Multiple myeloma starts in the plasma cells of the bone marrow, the soft tissue part of the bones.[2] It is characterized by an uncontrolled growth of cancerous plasma cells.[3] This results in the formation of a tumor in the solid bone.

Normal plasma cells produce antibodies that help fight infection and disease. In myeloma, these plasma cells become abnormal, multiply uncontrollably and release only one type of antibody – known as 'M' proteins or paraproteins – which has no useful function. It is often through the measurement of 'M' proteins that myeloma is diagnosed and monitored.[3]



Myeloma can develop wherever there are plasma cells and often affects multiple places in the body, hence the name 'multiple myeloma'.[4]

Globally, it is estimated that 124,225 people were diagnosed and 87,084 died from the disease in 2015.[5,6] In the U.S., approximately 30,330 new patients will be diagnosed with multiple myeloma and approximately 12,650 people will die from the disease in 2016.[7]

The incidence of multiple myeloma is expected to rise globally.[1]

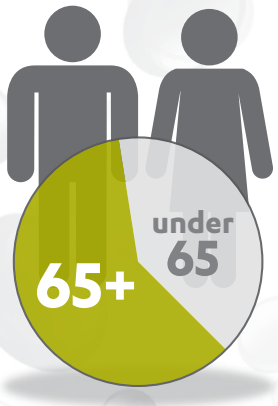
Globally, it is estimated that **124,225** people were diagnosed with **multiple myeloma** in **2015**.

What causes **multiple myeloma?**

It is not known exactly what causes multiple myeloma. However, exposure to certain chemicals, radiation, viruses, a weakened immune system and DNA mutations are thought to be potential causes or 'triggers'.[8,9]

Researchers have also identified certain factors that may increase the risk of developing multiple myeloma, including:

60% of cases occur in people over age 65.[1]



- **Age:** This is the most significant risk factor for multiple myeloma. In fact, more than 60% of cases occur in people over age 65.[1]
- **Gender:** Men have a slightly higher risk in developing multiple myeloma than women.[1]
- **Race:** African Americans are twice as likely to develop multiple myeloma as Caucasians, while Asians and American Indians have the lowest risk.[1,10]
- **Family history:** There is some evidence that close family members of someone with myeloma (parents, brothers and sisters) are at an increased risk, but the likelihood is very low, and no tests are currently available to predict this. Even when myeloma occurs more than once within a family, it may be due to a common exposure to environmental factors rather than an indication of a genetic trait.[11]
- **Obesity:** Studies have shown that overweight or obese people have an elevated risk of multiple myeloma.[12]
- **Other plasma cell diseases:** Monoclonal gammopathy of undetermined significance (MGUS) or single plasmacytoma tumors can be precursors to developing multiple myeloma.[12]

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What are the symptoms of **multiple myeloma?**

Multiple myeloma is difficult to diagnose as there are often no symptoms until it reaches an advanced stage. Rarely, it may be discovered during a routine blood test.

Symptoms, if present, may be vague and confused with those of other conditions.[13,14]

Most people will visit their doctor complaining of pain, often in the lower back or in the ribs. Pain is the most prominent symptom of myeloma.[14]

Other symptoms include:

- Bone pain or fractures[14]
- Fatigue, shortness of breath or weakness[14,15]
- Unusual bleeding or bruising more easily than normal[14]
- Swollen ankles[14]
- Thirst[14]
- Nausea[15]
- Low red blood cell count (anemia)[14]

How is **multiple myeloma** diagnosed and staged?

Multiple myeloma can be diagnosed through a number of tests, including:

- **Blood tests:** There are a number of different blood tests that can be done, each analyzing various chemicals and identifying indicators of multiple myeloma.[16]
- **Urine tests:** Various urine tests can be conducted as well, measuring abnormal immunoglobulins in the urine.[16]
- **Tissue tests:** Also called a biopsy, tissue or fluid is removed from the body for testing.[17]
- **Imaging tests:** Different types of imaging tests can reveal abnormalities and patterns in the bone marrow.[17]

Doctors will look at a number of factors holistically before diagnosing a patient with multiple myeloma, including:[17]

- Observed symptoms
- Physical exam results
- Results of blood/urine and x-ray tests
- Results of biopsy tests
- Imaging tests

Once diagnosed, doctors also use a series of tests to 'stage' the cancer so that prognostic estimates can be made. There are currently two staging systems used for multiple myeloma:

- The **Durie-Salmon Staging System** has historically been the most widely used system. Lately, its use has been limited due to newer diagnostic methods, however.[18] It is based on a number of different criteria, including the level and type of monoclonal protein, hemoglobin levels, the amount of calcium in the blood and number of bone lesions.
- **The International Staging System**, a more cost effective, and sensitive system, looks at the results of two blood tests - ß2-microglobulin (ß2-M) and albumin - as part of staging.[19]

Both staging systems are useful for estimating prognosis but not for choosing therapy and both have limitations.

The disease can also be staged as **asymptomatic (smoldering/indolent) myeloma**, which is characterized by a slightly increased number of plasma cells and increased M-protein in the bone marrow and lack of symptoms.[20]

Relapsed and refractory myeloma is defined as the progression of therapy in patients who achieve a minor response (MR) or better, or who progress within 60 days of their last therapy.[21] Unfortunately, because there is no cure, relapsed myeloma, also known as recurrent myeloma, is likely to occur in many patients.[22]

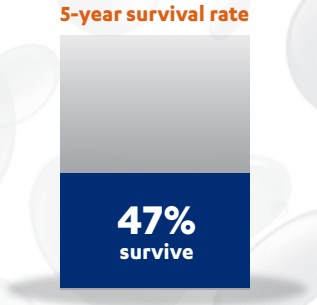
Primary refractory in myeloma is defined as patients who do not achieve an MR or better to initial therapy and progress while on therapy.[21]

What is the prognosis for **multiple myeloma?**

Although multiple myeloma is **incurable**, the prognosis will depend on the extent or stage of the disease at the time of diagnosis.[23]

The five-year **survival rate** of people with multiple myeloma is approximately 47%. However, a patient's age and overall health can impact these survival rates.[24]

Treatment is usually aimed at **preventing** or **addressing** symptoms and complications, **destroying** abnormal plasma cells and **slowing progression** of the disease.[17]



How is **multiple myeloma** treated?

There is currently **no cure** for multiple myeloma so the primary goal of **treatment** is to **prolong survival** and **manage symptoms** such as bone fractures and lesions, kidney damage, infections and anemia.[23]

The choice of treatment is influenced by the **age** and **general health** of a patient, the number and types of **previous treatments** they've been given and the **complications** of their disease.[25] Common treatment options include:

- Chemotherapy[23]
- Corticosteroids[23]
- Proteasome inhibitors (PIs)[26]
- Immunomodulating agents (IMiDs)[26]
- Radiation[23]
- Surgery[23]
- Biologic therapy[23]
- Stem cell transplant[23]
- Supportive therapy,[27] including biphosphonates

Often, these treatments are combined and are more effective than any single therapy.[26]

The number of multiple myeloma treatment options have **increased significantly** over the **last 10 years** and has resulted in **improved survival rates**.[1] In fact, in the last ten years, **survival rates** for multiple myeloma have nearly **doubled**.[28] However, many patients relapse soon after the completion of initial therapy or do not respond to therapy.[29]

An emerging class of monoclonal antibodies (mAbs) – such as anti-CD38 and anti-CS1 mAbs – may offer a new approach to treating multiple myeloma patients who are relapsed or refractory for whom there is a high unmet need.[30]

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How do we know if a **multiple myeloma** treatment is working?

As the number of available treatments for multiple myeloma continue to increase , the approach to measuring the success of a treatment has needed to evolve as well.[1]

A traditional criteria of response is **progression-free survival (PFS)**, which is the length of time during and after treatment in which a patient is living with a disease that does not get worse.[31] Another commonly used criteria is **complete response (CR)**, a treatment outcome where there are ≥ 5% plasma cells in the bone marrow and no evidence of myeloma proteins in the serum or urine.[31]

In light of increasingly higher rates of CR and improvements in PFS seen with novel treatments, new response categories have been defined that can identify even deeper responses, such as Minimal Residual Disease (MRD).[32] MRD refers to counting the number of multiple myeloma cells that remain in a patient after a course of therapy is completed.[31]

Additional **resources**

International Myeloma Foundation
www.myeloma.org

Multiple Myeloma Research Foundation
www.themmrf.org

Leukemia & Lymphoma Society
www.lls.org

American Cancer Society
www.cancer.org

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