Understanding MGUS and Smoldering Multiple Myeloma

A publication of the International Myeloma Foundation
About the International Myeloma Foundation

Founded in 1990, the International Myeloma Foundation (IMF) is the oldest and largest myeloma-specific charity in the world. With more than 350,000 members in 140 countries, the IMF serves myeloma patients, family members, and the medical community. The IMF provides a wide range of programs in the areas of Research, Education, Support, and Advocacy:

**RESEARCH** The IMF is the leader in globally collaborative myeloma research. The IMF supports lab-based research and has awarded over 100 grants to top junior and senior researchers since 1995. In addition, the IMF brings together the world’s leading experts in the most successful and unique way through the International Myeloma Working Group (IMWG), which is publishing in prestigious medical journals, charting the course to a cure, mentoring the next generation of innovative investigators, and improving lives through better care.

**EDUCATION** The IMF’s educational Patient & Family Seminars, Medical Center Workshops, and Regional Community Workshops are held around the world. These meetings provide up-to-date information presented by leading myeloma specialists and researchers directly to myeloma patients and their families. Our library of more than 100 publications, for patients and caregivers as well as for healthcare professionals, is updated annually and available free of charge. Publications are available in more than 20 languages.

**SUPPORT** Our toll-free InfoLine at 800-452-CURE (2873) is staffed by coordinators who answer questions and provide support and information via phone and email to thousands of families each year. The IMF sustains a network of more than 150 support groups and offers training for the hundreds of dedicated patients, caregivers, and nurses who volunteer to lead these groups in their communities.

**ADVOCACY** The IMF Advocacy program trains and supports concerned individuals to advocate on health issues that affect the myeloma community. Working both at the state and federal level, the IMF leads two coalitions to advocate for parity in insurance coverage. Thousands of IMF-trained advocates make a positive impact each year on issues critical to the myeloma community.

Learn more about the way the IMF is helping to improve the quality of life of myeloma patients while working toward prevention and a cure. Contact us at 800-452-CURE (2873) or 818-487-7455, or visit myeloma.org.

Improving Lives Finding the Cure®
What you will learn from this booklet

The IMF’s Understanding series of booklets is designed to acquaint you with treatments and supportive care measures for multiple myeloma (which we refer to simply as “myeloma”). Words in bold type are explained in the “Terms and definitions” section at the end of this booklet, as well as in a more complete compendium of myeloma-related vocabulary, the IMF’s Glossary of Myeloma Terms and Definitions, located at glossary.myeloma.org.

Myeloma is a disease that is not known to most patients at the time of diagnosis. To be empowered to play an active role in your own medical care and to make good decisions about your care with your doctor, it is vital for you to learn as much as possible about myeloma and its treatments. The information in this booklet will help you in discussions with your healthcare team.

From this booklet, you will learn about monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM). MGUS is not cancer or a disease. SMM is not active myeloma. However, both MGUS and SMM may be precursors to active disease, and it is therefore important to understand if, when, and how active myeloma might evolve and which monitoring or interventions are appropriate.

Monoclonal Gammopathy of Undetermined Significance

What is MGUS?

MGUS (pronounced “EM-gus”) is a term coined in 1978 by Professor Emeritus Robert A. Kyle of the Mayo Clinic in Rochester, Minnesota. The term MGUS describes a benign and asymptomatic condition that is characterized by an excess of monoclonal protein (M-protein), a type of blood protein made by immune system cells called plasma cells. MGUS is not cancer or a disease.

What are plasma cells?

Plasma cells develop from white blood cells called B-cells (B-lymphocytes) and are a key part of the immune system. Plasma cells make antibodies to proteins or molecules that the body recognizes as foreign (not part of the body). In medical language, the particular foreign protein that reacts with or binds to the antibody is called an antigen (a word coined from the two words “antibody” and “generator”). Examples of antibody-generating foreign materials (antigens) are bacteria, viruses, parasites, fungi, and toxins.

In the normal immune response, B-cells mature into plasma cells in the bone marrow, where they produce antibodies (or in medical language, immunoglobulins or “Ig”) to fight the invading antigen. There are five types of heavy chain immunoglobulins: IgG, IgA, IgD, IgE, and IgM. There are two types of immunoglobulin light chains, kappa (κ) and lambda (λ).

![Figure 1. Structure of an immunoglobulin (antibody)](image)

Under normal circumstances, these antibodies attach to specific invader antigens and, together with other immune system cells, disable and destroy the antigen and/or associated infectious agent or cell. Antibodies that arise from plasma cells in a normal immune response are called “polyclonal,” because they derive from many different plasma cells and are capable of attacking a wide range of antigens.

What is monoclonal protein?

MGUS represents the expansion and persistence of a single clone of abnormal plasma cells producing an antibody against a single antigen. The single type of antibody secreted by the clone of identical plasma cells is known as a monoclonal antibody or monoclonal protein. M-protein is abnormal and is not usually a fully functional antibody. However, sometimes such antibodies do react with and bind to normal body antigens to become “auto-antibodies.” Many autoimmune diseases, such as lupus, psoriasis, and diabetes type 1, are caused by auto-antibodies.

How is MGUS detected?

MGUS may be detected during a routine physical exam. If there is an increased level of protein in the blood or urine, tests should be ordered to determine the cause of this increase. Serum protein electrophoresis (SPEP) and/or urine protein electrophoresis (UPEP) and immunofixation electrophoresis (IFE) tests indicate the presence of M-protein. For more information about the tests used to identify and quantify M-protein, see the IMF publication Understanding Your Test Results.

Is there more than one type of MGUS?

MGUS can arise from either lymphoid cells or plasma cells, and these two cell types of MGUS are biologically different. The lymphoid type produces only IgM-type M-protein and accounts for about 15% of all MGUS. This type of MGUS, should it progress, becomes Waldenström’s macroglobulinemia (WM) or lymphoma. The plasma cell type of MGUS can progress to become myeloma or other related plasma cell disorders (including amyloidosis and light chain deposition disease). This booklet focuses on the plasma cell type of MGUS, which comprises 85% of all MGUS cases.

What is the incidence of MGUS?

MGUS occurs in 3%–4% of the population over the age of 50; incidence increases with age. It is highly likely that many people have MGUS and never know it. Current data demonstrate that myeloma is consistently preceded by MGUS, although only one-fifth of cases of MGUS actually develop into a malignancy.

What are the diagnostic criteria for MGUS?

The diagnostic criteria for MGUS are:

- Less than 3 grams/deciliter (g/dL) of M-protein in the serum (the liquid part of the blood),
- Fewer than 10% monoclonal plasma cells in the bone marrow, and
- No CRAB criteria, which define active myeloma: elevated Calcium, Renal (kidney) damage, Anemia, or Bone disease.
What is the risk that MGUS will progress to active myeloma?

The risk of progression of MGUS to active malignancy was studied at great length by Dr. Kyle, who determined that it occurs at a rate of only 1% per year, and that only 20% of people with MGUS ever develop myeloma or another malignant condition.

The 2010 publication by the International Myeloma Working Group (IMWG), Monoclonal Gammopathy of Undetermined Significance (MGUS) and Smoldering (Asymptomatic) Multiple Myeloma: IMWG Consensus Perspectives – Risk Factors for Progression and Guidelines for Monitoring and Management, establishes criteria for MGUS that is at low, intermediate, and high risk of progression to myeloma.

The three criteria for low-risk MGUS are:
- M-protein less than 1.5 g/dL (or 15 g/L).
- IgG-type M-protein.
- Normal free light chain (FLC) ratio (number of kappa chains divided by the number of lambda chains; the result should be close to 1.65).

Low-intermediate-risk MGUS is defined as having one of the risk factors, that is, more than 1.5 g/dL of M-protein, a type of M-protein other than IgG, or an abnormal FLC ratio.

High-intermediate-risk MGUS is defined as having two of the risk criteria.

MGUS at high risk of progression has all three of the risk criteria.

For more information about free light chains and the test used to quantify them, see the IMF publication Understanding Freelite® and Hevylite® Tests.

Researchers have developed some understanding of the biologic events that take place when MGUS develops into myeloma, but they do not yet know what triggers the progression in certain patients and not in others or how to prevent it. Researchers continue to seek answers to these questions. Although only one-fifth of patients with MGUS will develop myeloma or another malignancy, all cases of myeloma are preceded by MGUS.

What is the diagnostic process for MGUS?

■ All newly diagnosed MGUS
The IMWG consensus on management of a patient newly diagnosed with MGUS is that a complete history and physical exam should be performed to check for symptoms that may suggest myeloma or amyloidosis. Lab tests should include complete blood count (CBC), serum calcium and creatinine levels, and a test to identify if urine protein is present. If protein in the urine (proteinuria) is found, UPEP and IFE tests are indicated.

■ Low-risk MGUS
Patients with low-risk MGUS do not require a baseline bone marrow biopsy or a skeletal X-ray survey (or other bone imaging study) if the clinical exam, CBC, serum creatinine, and calcium values suggest MGUS. SPEP should be repeated 3–6 months after the MGUS is discovered. Time is an important factor in the diagnosis of MGUS: Your hematologist/oncologist must evaluate the status of your health and of your protein level in the months after diagnosis to see if there is any change.

A bone marrow biopsy is always required if the patient has unexplained anemia, evidence of kidney dysfunction, hypercalcemia, bone lesions, or a suspicion of AL amyloidosis. Patients should be followed with a repeat SPEP within 3–6 months and, if stable, can be followed at intervals of 1–2 years at the doctor’s discretion, barring any change in health or any suggestion of symptoms.

■ Intermediate-risk or high-risk MGUS
Patients with intermediate- or high-risk MGUS should have a bone marrow aspirate and biopsy at baseline, and genetic studies should be done on the bone marrow sample.

If the patient has IgM-type M-protein, a computerized axial tomography (CAT or CT) scan of the abdomen should be performed to check for lymph node enlargement. Lactate dehydrogenase (LDH), beta-2 microglobulin (β2M), and C-reactive protein (CRP) levels should be determined if there is evidence of myeloma or WM. If these tests are within normal ranges, patients can be followed with SPEP and CBC in 6 months, and then annually for life or until any changes occur when more frequent and/or additional testing may be required.

Is there treatment for MGUS?

In rare cases, if an MGUS patient has an underlying, pre-existing infection, treating the infection may cause the MGUS to remit, but this is not typical. In general, MGUS patients are not treated outside the context of clinical trials, which have included interventions with supplements such as green tea extract, omega-3 fatty acids, and curcumin (a component of the spice turmeric), and with such medications as zoledronic acid (a bisphosphonate used to prevent skeletal breakdown), anakinra (an interleukin-1 antagonist), and celecoxib (a nonsteroidal anti-inflammatory drug). None of these trials demonstrated success in preventing the progression of MGUS to myeloma. As of the date of this writing, currently open MGUS clinical trials include both non-interventional measures such as genetic studies, registries, and observational studies as well as two interventional studies. Because a relationship between obesity and myeloma has been established, one of the interventional studies treats patients with high levels of epicardial fat (fat deposits around the heart) with a drug that is given for weight loss, liraglutide. The other interventional study for high-risk MGUS and low-risk SMM uses an approved myeloma therapy, Darzalex® (daratumumab), to see if early intervention can prevent patients from developing active myeloma.

Possible complications of MGUS

■ Peripheral neuropathy
MGUS, though defined as asymptomatic, does sometimes cause medical problems. In approximately 10% of patients, the low-level M-protein can cause peripheral neuropathy (PN), a feeling of numbness, tingling, or burning in the hands, feet, and sometimes the lower legs. IgM-type MGUS is the most common type of monoclonal gammopathy associated with PN, but IgA and IgG monoclonal gammopathies can also cause PN. If you are experiencing any feelings of numbness or tingling in your extremities, be sure to report this to your
Skeletal complications
Patients with MGUS and SMM are at a higher risk for osteoporosis and for fractures of the hip and vertebrae than the general population. These patients should be aware of the potential risk to bone health and should inform their primary care physicians and other specialists they see that they have been diagnosed with MGUS.

Infections
MGUS patients are more than twice as likely as the general population to develop bacterial or viral infections because they have reduced production of polyclonal (normal) immunoglobulins, and therefore have diminished immune response. Patients who have an M-protein level of more than 2.5 g/dL have the highest risk of infection, although the risk is increased even among MGUS patients with less than 0.5 g/dL of M-protein. MGUS patients should take logical precautions to reduce the risk of infection, such as careful hand hygiene, annual flu vaccination, and avoidance of contact with friends and family members who have contagious illnesses.

Smoldering Multiple Myeloma
What is SMM?
Smoldering multiple myeloma (SMM), a term coined in 1980 by Professor Emeritus Philip Greipp of the Mayo Clinic, describes an asymptomatic intermediate stage between MGUS and active myeloma. It reflects a higher level of plasma cells in the bone marrow and a higher level of M-protein in the blood than does MGUS. Like MGUS, SMM causes no damage to the kidneys, red blood cells, or bones. In other words, it causes no CRAB criteria, defined as high calcium level in the blood due to bone loss (“C”), renal or kidney insufficiency (“R”), anemia (“A”), and bone damage (“B”).

How is SMM detected?
SMM may be picked up “by accident” during a medical exam or may be diagnosed in an asymptomatic patient who has been followed for MGUS. The amount of M-protein in the blood and/or urine and of plasma cells in the bone marrow may increase to the point that they are in the range of SMM rather than MGUS.

Is there more than one type of SMM?
SMM is not a single entity but rather a spectrum of different stages of disease, including at least three distinct possibilities:
1. MGUS with an increased but stable number of tumor cells.
2. Minimally progressive myeloma without damage to the bones, red blood cells, or kidneys (also called “end-organ” damage).
3. Moderately progressive myeloma, but with end-organ damage that is not yet detectable.

This new understanding of the biology and behavior of SMM enables doctors to avoid treating patients who do not need to be treated, but to intervene promptly in the case of patients who are at very high risk of progression to myeloma.

What are the diagnostic criteria for SMM?
The IMWG definition of SMM is:
- M-protein greater than or equal to 3 g/dL, and/or
- Greater than or equal to 10% monoclonal plasma cells in the bone marrow, and
- Absence of CRAB criteria.

As with MGUS, the hematologist’s judgment and experience are crucial in making this diagnosis, and in differentiating SMM from MGUS on the one hand, and from active myeloma on the other. A second opinion with a myeloma specialist is recommended.

What is the risk that SMM will progress to cancer?
Dr. Kyle’s research established that the risk of progression of SMM to MM is 10% per year for the first five years, 3% per year for the next five years, and then 1% per year for the next decade. A substantial proportion of SMM patients remain free of progression for long periods of time (50% do not progress in the first five years after diagnosis, and approximately 30% are free of progression after 10 years).

Risk factors for progression of SMM include the amount of M-protein, the presence and number of focal lesions seen on magnetic resonance imaging (MRI), the number of plasma cells in the bone marrow, and the ratio of involved (monoclonal) to uninvolved (normal, or polyclonal) light chains.

New diagnostic criteria have been established for active myeloma to include “ultra-high-risk SMM” that is at 80% or greater risk of progression to active myeloma within two years. This new, broader definition of myeloma is set forth in the “International Myeloma Working Group Updated Criteria for the Diagnosis of Multiple Myeloma,” published in 2014 in Lancet. The IMWG determined that it was imperative to develop these new criteria, called myeloma-defining events, “to prevent patients with very early disease from developing end-organ damage.” The criteria that determine if a patient with early disease should be treated or not can be established with three widely available tests (bone marrow biopsy, Freelite® assay, and MRI), and are:
- Bone marrow that is 60% or more monoclonal plasma cells,
- A ratio of involved to uninvolved free light chains of 100 or higher,
- Two or more focal lesions seen on MRI.

If an asymptomatic patient has any one of these three criteria, he or she should be treated for active myeloma.

What is the diagnostic process for SMM?
For an asymptomatic patient with M-protein of at least 3 g/dL, the diagnostic process includes SPEP, CBC, and measurement of calcium and creatinine values. Twenty-four-hour urine collection for electrophoresis and immunofixation should be performed at diagnosis and in 2 to 3 months after the initial recognition of SMM. A baseline bone marrow biopsy and skeletal survey are mandatory. MRI of the spine and pelvis are highly
Is there treatment for SMM?
The IMF's Black Swan Research Initiative® funded a project known as iStopMM® (Iceland Screens, Treats, Or Prevents Multiple Myeloma). This large population study and clinical trial was launched in November 2016. iStopMM is designed to screen approximately 140,000 residents of Iceland who are over 40 years of age for evidence of previously undetected MGUS, SMM, or active myeloma. As of early 2018, blood and bone marrow samples have been collected from more than 80,000 study participants, and 1,000 new cases of MGUS have been identified. This is the largest population-based screening study for myeloma and its earlier disease precursors that has ever been conducted. Not only will iStopMM allow researchers to observe patterns of occurrence, but they will be able to better understand disease biology and to identify the genes that drive disease progression. Moreover, monitoring patients with MGUS for many years will demonstrate which prognostic tests are most reliable as indicators of disease progression and which patients benefit most from early intervention. Patients with high-risk SMM will be invited to participate in a treatment trial.

Also with the support of the IMF’s Black Swan Research Initiative, two clinical trials – one in Spain with two years of data and one that is about to open in the US – are being conducted to attempt to cure patients with high-risk smoldering myeloma. Data from the Spanish trial, dubbed CESAR, were presented at the 2017 American Society of Hematology meeting, and demonstrate that at 13 months’ median follow-up, 99% of the patients are alive and free of progression after treatment with carfilzomib (Kyprolis®), lenalidomide (Revlimid®), and dexamethasone (KRd) induction, followed by high-dose therapy with autologous stem cell transplant (HDT-ASCT), consolidation with KRd, and maintenance with Rd.

The US trial, called ASCENT, combines KRd with the monoclonal antibody Darzalex® (daratumumab) as induction therapy followed by either autologous stem cell transplant or four more cycles of KRd + Darzalex. All patients then will receive consolidation therapy with another four cycles of KRd + Darzalex and two years of maintenance therapy with Kyprolis and Darzalex. We will keep you updated on the progress of this trial, which will open in the first quarter of 2018.

There are many other clinical trials for patients with both standard-risk and high-risk smoldering myeloma offering a wide range of treatments, but outside of clinical trials, there are no current standardized treatment options for SMM. “Ultra-high-risk” SMM is now considered early active myeloma and should be treated as newly diagnosed myeloma.

If you are interested in pursuing a clinical trial for SMM, you should discuss this option with your doctor and weigh the pros and cons carefully. You and your doctor must have a good understanding of the relative risk of progression in your case and of the potential risks and benefits of treatment, including the psychological aspects of treatment versus observation.

Possible complications of SMM
Complications of SMM are the same as those of MGUS. Please see the “Possible complications of MGUS” section.

In closing
While a diagnosis of cancer is something you cannot control, gaining knowledge that will improve your interaction with your doctors and nurses is something you can control, and it will have a significant impact on how well you do throughout the disease course.

This booklet is not meant to replace the advice of your doctors and nurses who are best able to answer questions about your specific healthcare management plan. The IMF intends only to provide you with information that will guide you in discussions with your healthcare team. To help ensure effective treatment with good quality of life, you must play an active role in your own medical care.

We encourage you to visit myeloma.org for more information about myeloma and to contact the IMF InfoLine with your myeloma-related questions and concerns. The IMF InfoLine consistently provides callers with the most up-to-date and accurate information about myeloma in a caring and compassionate manner. IMF InfoLine specialists can be reached at InfoLine@myeloma.org or 818-487-7455 or 800-452-CURE (2873).

Terms and definitions
Amyloid light-chain amyloidosis (AL amyloidosis): A condition in which myeloma light chains cross-link with each other in a beta-pleated fashion and then are deposited in tissues and organs throughout the body, such as the heart, nerves, and kidneys, rather than being excreted through the kidneys. This condition is also known as primary amyloidosis.

Amyloidosis: A general term for a group of diseases characterized by cross-linked...
light chains. The light chains form rigid fibrils that are insoluble and that are deposited in various organs or tissues. Different types of amyloidoses have different signs and symptoms depending on where and in which organs the amyloid proteins are deposited.

Anemia: A decrease in hemoglobin contained in red blood cells that carry oxygen to the body’s tissues and organs. Anemia is usually defined as hemoglobin below 10 g/dL, with over 13–14 g/dL considered normal, and/or a decrease of ≥ 2 g/dL from the normal level for an individual.

Antibody: A protein produced by white blood cells called plasma cells that helps fight infection and disease.

Antigen: Any foreign substance (such as bacteria, a virus, toxin, or tumor) that causes the immune system to produce natural antibodies.

Asymptomatic myeloma: Myeloma that presents no signs or symptoms of disease; early-stage myeloma. Also called “Smoldering multiple myeloma (SMM).”

Autoimmune disease: A condition that occurs when the immune system abnormally creates antibodies to a normal body part. Common autoimmune diseases include diabetes type 1, celiac disease, inflammatory bowel disease, multiple sclerosis, psoriasis, and rheumatoid arthritis.

B-cells (B-lymphocytes): White blood cells that are part of the natural immune system. Some B-cells develop into plasma cells in the bone marrow and are the source of antibodies.

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body. MGUS is a benign condition.

Beta-2 microglobulin (also called β2-microglobulin, β2M, or β2M): A small protein found in the blood. High levels occur in patients with active myeloma. Low or normal levels occur in patients with early myeloma and/or inactive disease. Approximately 10% of patients have myeloma that does not produce β2M. At the time of relapse, β2M can increase before there is any change in the myeloma protein level. Factors such as viral infection can sometimes produce elevated serum β2M levels.

Bisphosphonate: A type of drug that protects against osteoclast activity (bone breakdown) and binds to the surface of bone where it is being resorbed or destroyed.

Bone marrow: The soft, spongy tissue in the center of bones that produces white blood cells, red blood cells, and platelets. This is the tissue within which abnormal plasma cells build up to cause myeloma.

C-reactive protein (CRP): A protein made in the liver that rises when there is inflammation throughout the body.

Calcium: A mineral found mainly in the hard part of bone matrix or hydroxyapatite. If produced or released in excess, it can build up in the bloodstream. See “Hypercalcemia.”

Cancer: A term for diseases in which malignant cells divide without control. Cancer cells can invade nearby tissues and spread through the bloodstream and lymphatic system to other parts of the body.

Cell: The basic unit of any living organism. Millions of microscopic cells comprise each organ and tissue in the body.

Computerized axial tomography (CAT or CT) scan: A test using computerized X-rays to create three-dimensional images of organs and structures inside the body, used to detect small areas of bone damage or soft tissue involvement.

CRAB criteria: An elevated level of Calcium in the blood, Renal damage, Anemia or low red blood cell count, and Bone damage.

Creatinine: A small chemical compound normally excreted by the kidneys into the urine. If the kidneys are damaged, the serum level of creatinine builds up, resulting in an elevated serum creatinine. The serum creatinine test is used to measure kidney function.

Electrophoresis: A laboratory test in which a patient’s serum (blood) or urine molecules are subjected to separation according to their size and electrical charge. For myeloma patients, electrophoresis of the blood or urine allows both the calculation of the amount of myeloma protein (M-protein) as well as the identification of the specific M-spike characteristic for each patient. Electrophoresis is used as a tool both for diagnosis and for monitoring.

Focal lesion: An area of irregular cells seen in the bone marrow on MRI (magnetic resonance imaging) study. In order to be considered diagnostic of myeloma, there must be more than one focal lesion that is ≥ 5 mm in size.

Free light chain: A portion of the monoclonal protein that is of low molecular weight. It may be bound to a heavy chain or it may be unbound, or free. Free light chains can be measured in a sensitive assay called the Freelite® test.

Hypercalcemia: A higher than normal level of calcium in the blood. In myeloma patients, it usually results from bone breakdown with release of calcium from the bone into the bloodstream. This condition can cause a number of symptoms, including loss of appetite, nausea, thirst, fatigue, muscle weakness, restlessness, and confusion. See “Calcium.”

IgD, IgE: Two types of myeloma that occur less frequently. See “IgG, IgA.”

IgM: Usually associated with Waldenström’s macroglobulinemia. In rare cases, IgM can be a type of myeloma.

Immune system: The complex group of organs and cells that produces antibodies, cellular responses to defend the body against foreign substances such as bacteria, viruses, toxins, and cancers.

Immunofixation electrophoresis (IFE): An immunologic test of the serum or urine used to identify proteins. For myeloma patients, it enables the doctor to identify the M-protein type (IgG, IgA, kappa, or lambda). The most sensitive routine immunostaining technique, it identifies the exact heavy- and light-chain type of M-protein.

Immunoglobulin (Ig): A protein produced by plasma cells; an essential part of the body’s immune system. Immunoglobulins attach to foreign substances (antigens) and assist in destroying them. The classes (also called isotypes) of immunoglobulins are IgG, IgA, IgD, IgE, and IgM. The non-medical word for immunoglobulin is “antibody.”

Incidence: The number of new cases of a disease diagnosed each year.
Lactate dehydrogenase (LDH): An energy-producing enzyme that is present in almost all of the tissues in the body. LDH levels in the bloodstream rise in response to cell damage. LDH may be used to monitor myeloma activity.

Light chain deposition disease: A type of monoclonal gammapathy that is characterized by deposition of immunoglobulin light chains in various organs, most frequently in the kidneys.

Magnetic resonance imaging (MRI): A diagnostic imaging test that uses magnetic fields and radio waves, not ionizing radiation, to produce detailed two- or three-dimensional images of organs and structures inside the body. MRI gives very fine resolution of soft tissues, especially encroachments on the spinal cord, but is less accurate for bone lesions.

Monoclonal: A clone or duplicate of a single cell. Myeloma develops from a single malignant plasma cell (monoclon). The type of myeloma protein produced is also monoclonal; a single form rather than many forms (polyclonal). The important practical aspect of a monoclonal protein is that it shows up as a sharp spike (M-spike) in the serum electrophoresis test.

Monoclonal protein (M-protein, M-spike): An abnormal protein produced by myeloma cells that accumulates in and damages bone and bone marrow. Antibodies or parts of antibodies found in unusually large amounts in the blood or urine of myeloma patients. A monoclonal spike (M-Spike), the sharp pattern that occurs on protein electrophoresis, is the telltale indicator of M-protein in the blood, a marker for the activity of myeloma cells. See “Monoclonal.”

Multiple myeloma: A cancer arising from the plasma cells in the bone marrow. The cancerous plasma cells are called myeloma cells.

Nonsteroidal anti-inflammatory drug (NSAID): A drug used to reduce fever, swelling, pain, and redness.

Oncologist: A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer.

Osteopetrosis: A progressive bone disease that is characterized by a decrease in bone mass and density, leading to an increased risk of fracture. Diffuse involvement of bones with myeloma produces what looks like osteoporosis on X-ray and bone density measurement.

Plasma cells: Special white blood cells that produce antibodies (immunoglobulins). Myeloma is a cancer of the plasma cells. Malignant plasma cells are called myeloma cells. In myeloma, malignant plasma cells produce large amounts of abnormal antibodies that lack the capability to fight infection. These abnormal antibodies are the monoclonal protein, or M-protein, that functions as a tumor marker for myeloma. Plasma cells also produce other chemicals that can cause organ and tissue damage (i.e., anemia, kidney damage, and nerve damage).

Tumor: An abnormal mass of tissue that results from excessive cell division.

Waldenström’s macroglobulinemia (WM): A rare type of indolent lymphoma that affects plasma cells. Excessive amounts of IgM protein are produced. Not a type of myeloma.

White blood cells (WBC): General term for a variety of cells responsible for fighting invading germs, infection, and allergy-causing agents. These cells begin their development in the bone marrow and then travel to other parts of the body. Specific white blood cells include neutrophils, granulocytes, lymphocytes, and monocytes.