



Myeloma Canada
InfoGuide Series

MGUS and Smouldering Multiple Myeloma



MYELOMA CANADA

MAKING MYELOMA MATTER

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The information in this InfoGuide is not meant to replace the advice of a medical professional.
They are the best people to ask if you have questions about your specific medical/social situation.



Introduction

Myeloma Canada's *MGUS and Smouldering Multiple Myeloma InfoGuide* has been created specifically for people diagnosed with monoclonal gammopathy of undetermined significance (MGUS) or smouldering multiple myeloma (SMM) – also known as indolent or asymptomatic multiple myeloma (MM) – and their family and friends.

The InfoGuide is intended to help you understand what these two conditions are, how they are diagnosed and how they may be managed by your healthcare team. Not all people with MGUS or SMM experience the same symptoms or carry the same risks of developing another related condition. It's important to understand your condition, the impact it can have on your day-to-day life and on your overall well-being.

Among the information you'll find in this InfoGuide:

- what are MGUS and SMM;
- how are MGUS and SMM diagnosed;
- what are some of the symptoms you may experience;
- the similarities and differences between MGUS, SMM, and MM;
- the potential risk of progression from MGUS or SMM to MM;
- how MGUS and SMM are monitored and managed.

Some of the more technical or unusual words in this InfoGuide appear in ***bold italics*** the first time they're used and are explained in the Glossary starting on page 28. As you read through the InfoGuide, refer to the "More Information" and "Did You Know?" boxes to learn more about selected topics. Moreover, don't be afraid to ask members of your, or your loved one's healthcare team to explain any terms or concepts you may have trouble understanding.

Throughout your journey with MGUS or SMM, your healthcare team will provide you with a large amount of information. Early identification, assessment and diagnosis is key. You may find it helpful to write down any questions that you have along the way and share these with your healthcare team regularly. They are the best people to help you understand what is happening and guide you to make informed decisions.

Be an informed and cautious information consumer

Be cautious of information that comes your way. While books and the internet offer a wealth of information, not all of it is correct, it may not apply to your unique situation, and it may be confusing or misleading. Well-intended people may also try to offer you health advice without knowing the details of your condition and its treatment.

Certain online support groups may also be helpful, but again be wary of possible misinformation. It's important to know that your source is reputable and to discuss what you read with your healthcare team. Never make any change to your treatment plan without checking with them first for any symptom you're experiencing. Be sure to visit myeloma.ca for reliable, up-to-date resources, support group information and more.

Drug Access Navigator

Over the past 15 years, thanks to advances in research, new molecules and targeted therapies to treat myeloma are being developed at an impressive rate, with more options available than ever before. In Canada, access to, and coverage for, these new treatments varies across provinces and territories, making it often confusing and overwhelming to get the information you need.

To simplify the process of finding which drugs are available and covered within your province or territory, Myeloma Canada has created an easy-to-use, interactive online tool called the **Myeloma Drug Access Navigator**.





About Myeloma Canada

Myeloma Canada is a registered non-profit organization created by, and for, people impacted by multiple myeloma. As the only national organization exclusively devoted to the Canadian myeloma community, Myeloma Canada has been making myeloma matter since its founding in 2005.

Working with leading myeloma researchers and clinicians as well as other cancer organizations and local support groups across Canada and internationally, Myeloma Canada seeks to strengthen the voice of the Canadian myeloma community and improve quality of life for those impacted by myeloma through awareness, education, advocacy, fostering an empowered community and supporting clinical research to find a cure.

Myeloma Canada's goals:

- **Increase awareness** of the disease and its effects on the lives of patients and their families
- **Educate** patients, families and caregivers
- **Advocate** for access to new therapies, treatment options and healthcare resources
- **Empower** patients and caregivers through community engagement
- **Advance** clinical research and promote access to new drug trials in Canada

Myeloma Canada educational publications

For more detailed information about myeloma and living with the disease, visit **myeloma.ca** and click on "Resources". From here, you can download Myeloma Canada's educational publications, watch educational videos, find a local support group and so much more.

Whether you're downloading a copy or requesting a printed version, all Myeloma Canada publications are free of charge. To order your printed copies of the materials below, email us at contact@myeloma.ca, or call us toll-free at 1-888-798-5771.

- *Multiple Myeloma Patient Handbook*
- *Multiple Myeloma Caregiver Handbook*
- *Managing Pain & Fatigue InfoGuide*
- *High-dose Therapy and Autologous Stem Cell Transplantation InfoGuide*
- *Myeloma Bone Disease InfoGuide*
- *Understanding Your Blood and Blood Tests InfoGuide*
- *Myeloma and the Kidney InfoGuide*
- *Clinical Trials as a Treatment Option InfoGuide*





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Introduction to Plasma Cell Disorders

What are Plasma Cell Disorders?

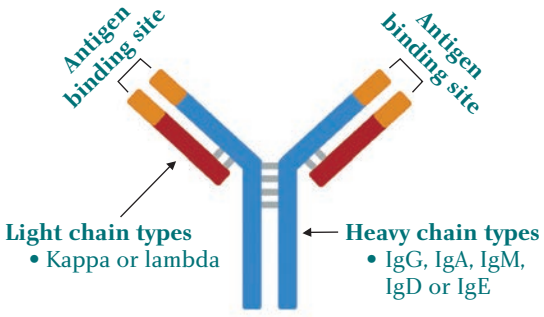
Monoclonal gammopathy of undetermined significant (MGUS), smouldering multiple myeloma (SMM) and ***multiple myeloma*** (referred to as myeloma throughout this InfoGuide) are a group of conditions and diseases that fall under the category of plasma cell disorders. As the name suggests, plasma cell disorders affect plasma cells – a type of ***white blood cell (WBC)*** produced in the ***bone marrow.***

Plasma cells are critical to the body's immune response to infection as they produce ***antibodies*** (proteins known as ***immunoglobulins,*** abbreviated as ***Ig***) that identify and kill harmful substances in the body (e.g., bacteria, viruses, fungi, parasites, and chemicals).

Under a specialized microscope, antibodies look Y-shaped (Figure 1) and are made up of heavy chains and light chains:

- five types of heavy chains: G, A, M, D or E
- two types of light chains: kappa or lambda

Figure 1: Structure of an antibody (immunoglobulin)



The most common type of antibody found in the blood is immunoglobulin G (IgG), followed by immunoglobin A (IgA) and immunoglobin M (IgM). Under normal circumstances, when an antibody recognizes a molecule (called an ***antigen*** – i.e., virus, bacteria) on the surface of a harmful cell, it is able to bind to it and destroy it, protecting against disease and infection.

In otherwise healthy people, aged or damaged plasma cells die and new plasma cells are produced to replace them. In people with MGUS, SMM and myeloma, plasma cells go rogue, leading to the uncontrolled growth of abnormal plasma cells, called ***myeloma cells*** (Figure 2).

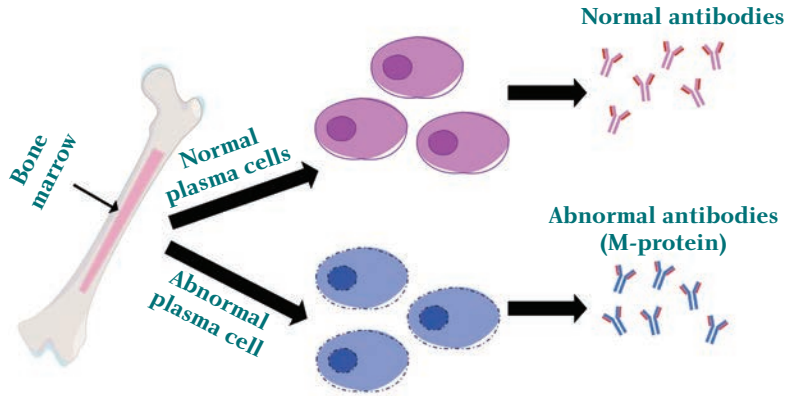
Instead of producing a variety of healthy antibodies that can fight infection, myeloma cells produce abnormal non-functional clones of one type of antibody – known as ***monoclonal antibodies*** – and lead to a weakened immune system. Monoclonal antibodies are also commonly referred to as ***M-protein, monoclonal protein, paraprotein, myeloma protein*** or ***M-spike***.

Myeloma cells can also overcrowd and take up a larger than normal amount of space in the bone marrow. This can lead to the decreased production of other types of blood cells such as ***red blood cells (RBCs)*** in the bone marrow, causing more health complications and further weakening the immune system.

Did You Know?

Bone marrow is the spongy tissue that is found inside your bones. It is soft, fatty and full of blood vessels. Your bone marrow is where most of the blood cells in your body are made.

Figure 2: Production of plasma cells, myeloma cells, and antibodies



The Chain of Progression

MGUS and SMM

MGUS is the earliest state of myeloma and is often referred to as a pre-cursor condition. However, only a small proportion of people diagnosed with MGUS will actually go on to develop myeloma (individual patient risk of approximately 1% per year). In the majority of cases, MGUS does not cause symptoms ***(asymptomatic)*** and does not require treatment.

SMM is the intermediate state between MGUS and myeloma. Compared to MGUS, SMM carries a higher risk of progression to myeloma – with an individual patient risk of approximately 10% per year for the first five years. As with MGUS, SMM is typically an asymptomatic condition without the organ damage ***(end-organ disease)*** that is characteristic of myeloma.

The distinction between MGUS and SMM is based on the percentage of myeloma cells in the bone marrow and the amount of M-protein produced by myeloma cells.

It is important to note that not all people diagnosed with MGUS will progress to SMM, and not all persons diagnosed with SMM will develop myeloma. This will be discussed further in the InfoGuide, under each specific MGUS and SMM section.

Did You Know?

In Canada, approximately 3,300 cases of myeloma were reported in 2019. Of these cases, approximately 1,950 were men and 1,400 were women. The annual incidence of myeloma is 9.6 per 100,000 for men and 6.0 per 100,000 for women.

Myeloma

During the MGUS and SMM stages, abnormal M-protein produced by the myeloma cells may begin to build up in different areas of the body. The myeloma cells also take up a lot of space within the bone marrow, restricting space that's available for other healthy cells. In some people, this process advances, leading to symptoms caused by damage to organs (end-organ disease), like the kidneys. This is characteristic of active myeloma and means that the condition has progressed.

Symptoms associated with the overproduction of myeloma cells and M-protein are commonly evaluated using the **"CRAB"** criteria below:

- ***HyperCalcemia*** – elevated calcium in the blood
- ***Renal insufficiency*** – kidney damage
- ***Anemia*** – low levels of hemoglobin in red blood cells (RBCs)
- ***Lytic Bone lesions*** – pain in the bones and/or fractures

Other general symptoms include frequent or recurring infections and fatigue/weakness.

You may also hear the term **"SLiM"** in relation to myeloma. SLiM refers to a newer, more in-depth diagnostic criteria that better identifies people requiring active myeloma treatment even if they are not experiencing CRAB symptoms.

SLiM criteria include the following three ***myeloma defining events (MDEs):***

- **S**ixty percent (60%) or more myeloma cells in the bone marrow;
- **Li**ght chains: Involved/uninvolved ***serum free light chain (sFLC)*** ratio of 100 or greater;
- ***M*agnetic resonance imaging (MRI):** More than 1 bone lesion of at least 5 mm in size.

The concept of CRAB and SLiM MDEs are discussed further in the InfoGuide. Although the cure for myeloma has not yet been found, the prognosis today is much better than ever before. Over the past 15 years there have been an extraordinary amount of myeloma treatment breakthroughs and significant advances in our understanding of the disease.

More Information

For more information on the different types of myeloma, symptoms, diagnosis, management and treatment, please refer to Myeloma Canada's *Multiple Myeloma Patient Handbook.* Designed to provide educational support to patients, caregivers, families, and friends, this Handbook gives accurate, reliable, and clear information on myeloma. Topics covered include the causes and effects of myeloma, how it is diagnosed, as well as treatment options available in Canada.

Visit the Resources section on myeloma.ca to download your free Handbook. For a hard copy, email us at contact@myeloma.ca or call, toll-free 1-888-798-5771.





Common Diagnostic Tests for MGUS and SMM

This section will introduce you to the types of tests your healthcare team may recommend in order to diagnose MGUS, SMM, or a related disorder. Please note that not all of the following tests are necessary for all patients; the blood and urine tests are part of routine testing and follow-up assessments, but whether or not you require a ***bone marrow biopsy,*** additional imaging scans or ***fluorescence in-situ hybridization (FISH)*** will depend on the results of other tests and your individual symptoms.

Blood and Urine Tests

Samples of your blood and urine are analyzed to determine:

- the number of different types of cells in your blood;
- the level of ***calcium*** and ***albumin*** in your blood;
- your kidney and liver function;
- the level of protein and the amounts of different antibodies in both, your blood and urine.

All of these results are looked at to determine whether further testing is required or if a diagnosis can be made. Table 1 highlights tests that are run on blood and urine samples, as well as those that measure general kidney and liver function. Additional tests may be recommended depending on your initial results.

Table 1: Blood and urine tests for diagnosing plasma cell disorders

Sample	Test	Purpose of test
Blood	***Complete blood count (CBC)***	Measures the numbers of different blood cells such as ***red blood cells (RBCs), white blood cells (WBCs), platelets***, as well as your ***hemoglobin*** level.
Blood	WBC differential count	Determines the percentages of different WBCs.
Blood	Peripheral blood smear	Blood viewed using a microscope to look at the appearance of the cells and detect any abnormalities.
Blood	Serum ***creatinine***	Measures the levels of creatinine in your blood. If your creatinine level is higher than normal, it may indicate that your kidney function is decreased. An ***estimated glomerular filtration rate (eGFR)*** may also be calculated at the same time.
Blood & urine	***Creatinine clearance***	Measures the amount of blood per minute the kidneys can make that is creatinine-free.
Blood	Serum **calcium**	Measures the level of calcium in your blood. High levels of calcium (hypercalcemia) can indicate bone disease.
Blood	Total serum protein	Measures how much protein there is in the blood. This test measures ***albumin*** and ***globulin.*** M-protein will increase the level of globulin leading to a higher amount of protein in the blood. An elevated protein test will require further investigation.
Blood	Quantitative immunoglobulins	Measures the amount of each primary antibody present in the blood (IgG, IgM and IgA). This test also assesses the levels of other normal antibodies and ***monoclonal antibodies*** (myeloma-related).
Blood	***Serum protein electrophoresis (SPEP)*** with ***immunofixation electrophoresis (IFE)***	SPEP measures the amount of M-protein being made by myeloma cells. This gives a clear spike on the test, hence the term "M-spike". IFE identifies what type of antibody is being overproduced (i.e., IgG, IgA, IgM, IgD or IgE) but not the amount.
Blood	sFLC test & ratio	Normally, heavy chains and light chains are joined and are intact. However, myeloma cells produce excess light chains that circulate freely in the blood, not bound to a heavy chain. These are known as ***serum free light chains (sFLCs)***. Some people's myeloma cells produce heavy chains only, some produce light chains only, and some produce both. The sFLC test is for people who produce light chains. It measures the amount of sFLCs in the blood. The sFLC ratio (involved:uninvolved) may be calculated using sFLC test results: either the ratio of kappa-to-lambda or of lambda-to-kappa, depending on which light chain (kappa or lambda) is present in larger quantities (involved).
Blood	24-hour total ***urine protein with electrophoresis (UPEP)*** and IFE	UPEP measures the amount of light chains in your urine. A high level of light chains in your urine can indicate a plasma cell disorder. It is possible to have light chain protein in the urine, as well as heavy chain protein in the blood. Some people produce only light chains. The IFE identifies what type of antibody is being overproduced but not the amount.

Bone Marrow Biopsy

In some cases, your healthcare team may advise that a sample of your bone marrow (bone marrow biopsy) should be collected for analysis. The biopsy is usually performed on the back pelvic bone. Less commonly, other large bones such as the breastbone may be used. A local ***anesthetic*** will be applied to numb the area; you may also be given a short-acting sedative to minimize discomfort during the procedure. While you are lying on your side, the doctor or nurse will insert a needle through your skin, into the bone, and extract a sample of liquid marrow into the needle's syringe. This is called a ***bone marrow aspirate***. After this, a small core of marrow will be taken from the bone. This is the bone marrow biopsy. The procedure may leave you feeling bruised and you may ache for a few days afterwards, but generally this can be managed with mild painkillers. The bone marrow biopsy is usually an outpatient procedure and takes approximately 15–20 minutes.

Imaging

Different types of imaging analyses may be necessary, depending on the results of your other tests. Listed below is an explanation of the various types of imaging tests that may or may not be performed:

- **Skeletal survey:** Series of ***X-rays*** allowing the limbs, spine, skull, ribs and pelvis (skeleton) bones to be seen. This typically takes 30–45 minutes and is a painless procedure, though some positions may be uncomfortable.
- **Whole-body low-dose computerized tomography (WBLDCT):** Scan that takes cross-section images of the body using low doses of radiation. This method is more sensitive than X-rays, painless, and takes approximately 10–30 minutes to complete. This is also often referred to as a whole-body CT scan.
- **Positron emission tomography (PET):** Imaging test that requires an injection of a liquid sugar with a radioactive label (myeloma cells absorb sugar faster than healthy cells). A specialized camera is then able to see where the dye has been absorbed more. PET scans are often combined with computerized tomography (CT) scans.
- **Magnetic resonance imaging (MRI):** Uses magnetic fields and radio waves to produce 2-dimensional or 3-dimensional images of organs or structures in the body. MRIs obtain detailed and accurate images of the inside of our body, including organs and tissues. MRIs can show where myeloma cells have infiltrated before any bone damage would be visible by X-ray. MRIs can also identify ***amyloid/light chain deposits*** in the heart. An MRI scan requires you to lie very still for approximately one hour. While the MRI is painless, some people may feel uncomfortable in the machine's confined space. It is important to let your team know if this is something you may find difficult beforehand.

Cardiac Testing

Your healthcare team may recommend additional tests if your blood sFLC results are abnormal or if your urine analysis indicates ***albuminuria;*** albumin in your urine may be an indication of kidney disease and/or heart failure. Other tests may include checking your ***cardiac biomarkers*** to help identify whether your heart is under additional strain. This could indicate an alternative diagnosis of cardiac ***amyloid light-chain (AL) amyloidosis***.

FISH Analysis

If your test results indicate that you do have myeloma, SMM or intermediate-to-high risk MGUS (i.e., with 10% or more myeloma cells present in your bone marrow), your healthcare team may recommend that a sample of your bone marrow be sent for analysis by ***FISH.***

FISH is a laboratory-based method of analyzing the ***cytogenetics*** of your condition. This analysis allows scientists to look at the genetic make-up of your myeloma cells, identify specific changes, and provide detailed information about your condition to your healthcare team. Some cytogenetic features are associated with a higher risk that your condition may progress to myeloma. In the event that your condition does progress to myeloma, this cytogenetic information can be helpful for your healthcare team to better understand the characteristics and behavior of your particular disease.

Some ***cytogenetic abnormalities*** common in myeloma and plasma cell disorders are below. These are examples of alterations and changes that can happen to the ***genes*** within your plasma cell:

- ***translocations*** – i.e., t(4;14);
- ***deletions*** – i.e., del(17p);
- ***gains*** – i.e., gain(1q).

Did You Know?

There are many exciting clinical trials of new medicines and therapies for people living with myeloma. Research indicates that some of these may having varying levels of effectiveness in patients with different cytogenetics as well.

What this means is that in the future, treatments may be personalized to your individual disease (personalized medicine). This is not yet routine practice as more data is required, but it could represent an incredible breakthrough for those living with blood disorders.





Similarities and Differences Between MGUS, SMM and Myeloma

Both MGUS and SMM tend to be asymptomatic in most people, meaning you will generally not experience any obvious signs of illness. Most commonly, MGUS and SMM are diagnosed as a result of routine tests or by a chance finding following an investigation for a different reason. On the other hand, people with myeloma will often experience one or more CRAB symptoms and therefore will likely self-report to their healthcare professional.

People with MGUS have approximately a 1% risk of progression to myeloma per year; this is not cumulative, it remains at 1% per year. SMM however carries a higher risk of progression to myeloma (Table 2). The ***standard of care*** treatment for both MGUS and SMM is observation and monitoring. The frequency of your follow-up observation and monitoring visits will depend on your individual risk of progression (see below):

Table 2: Similarities and differences between MGUS, SMM and myeloma

	MGUS	SMM	Myeloma
Symptoms	Generally asymptomatic	Generally asymptomatic	Symptomatic - CRAB or SLiM
Myeloma cells in bone marrow	Lower number of myeloma cells than SMM	Higher number of myeloma cells than MGUS	Usually a higher number of myeloma cells than SMM
Risk of progression	To myeloma: Approximately 1% per year *(not cumulative risk)*	To myeloma: **First 5 years:** Approximately 10% per year **Next 5 years:** Approximately 3% per year **Each year thereafter:** Approximately 1% per year *(cumulative risk)*	Not applicable
Treatment	Observation and monitoring	Observation and monitoring	Treatment required

Most people living with myeloma require active treatment for their disease. The SLiM criteria described on page 5 are used to identify individuals who are advised to treat their active myeloma.

The key differences in diagnostic criteria between MGUS, SMM and myeloma are shown below in Table 3. This will also be discussed in more detail later in this InfoGuide.

Table 3: Key differences in diagnostic criteria for MGUS, SMM and myeloma

Diagnostic criteria	MGUS	SMM	Myeloma
% of myeloma cells in the bone marrow	Less than 10%	10–60% *and/or* meeting the M-protein criteria below	60% or greater *or* at least 10% plus one or more of the following MDEs: • CRAB symptoms • Involved/uninvolved sFLC ratio of 100 or greater • More than 1 ***focal lesion*** of at least 5mm in size by MRI
M-protein (blood)	**Blood:** Less than 30 g/L	**Blood:** At least 30 g/L *and/or* **Urine:** 500 mg/24 hours	• Levels can vary • May not be present/detectable
CRAB symptoms (end-organ disease)	No	No	• High calcium levels (serum calcium greater than 2.75 mmol/L) • Kidney damage (creatinine clearance less than 40 mL/min) or blood creatinine greater than 177 µmol/L) • Anemia (hemoglobin less than 100 g/L) • Bone lesions (one or more as shown by imaging)





Introduction to MGUS

In this section, we will explore the different types of monoclonal gammopathy of undetermined significant, more commonly referred to as MGUS. Among topics covered are the different types of MGUS, how the condition is diagnosed, symptoms you may experience, how to tell if your condition might progress to SMM and/or myeloma, and how to monitor and manage your condition.

What is MGUS?

MGUS, a condition that may progress to SMM and/or myeloma, affects the production of normal plasma cells in the bone marrow. Abnormal plasma cells – myeloma cells – are produced instead, leading to the overproduction of abnormal clones of one type of antibody called a ***monoclonal antibody*** or ***M-protein*** (also referred to as ***paraprotein, myeloma protein*** or ***M-spike***).

In most people, MGUS is asymptomatic, meaning that you will not experience any symptoms and no treatment is required. There is a small risk, approximately 1% per year, that MGUS could progress to a disease that would require active treatment.

Different types of MGUS

There are three main types of MGUS which are categorized by the type of antibody involved:

1. **Non-IgM MGUS:** an antibody other than IgM is affected. This is the most common type of MGUS, and the heavy chain part of the antibody is usually IgG or IgA;
2. **IgM-MGUS:** the heavy chain part of the affected antibody is IgM;
3. **Light chain MGUS:** the light chain part of the antibody (kappa or lambda) is affected instead of the heavy chain.

Knowing what type of MGUS you have can help identify your potential risk of progression and help you manage your condition most effectively.

Does MGUS Always Progress to Myeloma?

MGUS does not always progress to myeloma and the risk of progression is not cumulative; it remains at 1% each year, even after more than 25 years of observation. In fact most people living with MGUS are in good general health and remain in stable condition.

There are, however, a minority of people who may experience progression to another related blood disorder such as AL amyloidosis, ***Waldenström macroglobulinemia,*** or ***lymphoma.***

The diseases that MGUS can potentially progress to are related to the type of MGUS you have, as shown in Figures 3, 4 and 5. Again, this does not mean that your MGUS will progress to any of these.

Figure 3. Potential diseases arising from non-IgM MGUS (IgA, IgD or IgG)

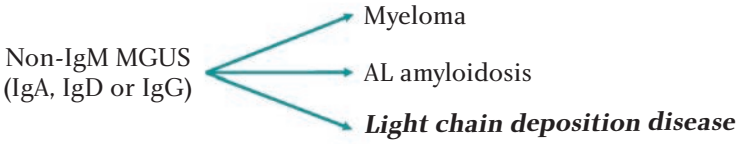


Figure 4. Potential diseases arising from IgM MGUS

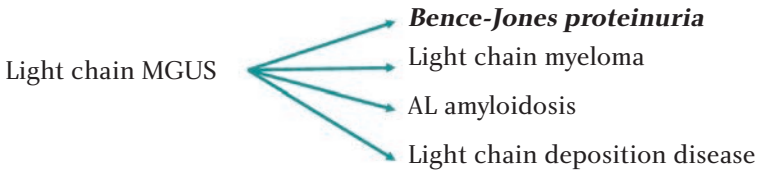
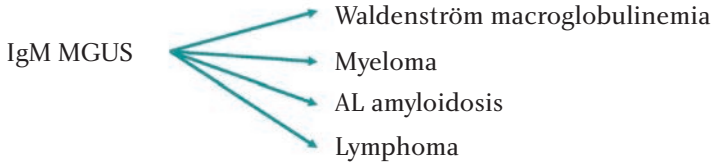


Figure 5. Potential diseases arising from light chain MGUS



Did You Know?

MGUS is present in approximately 5% of the general population aged 50 years or older, and its ***prevalence*** increases with age.

Causes of MGUS and Risk Factors

While the specific causes of MGUS are still unknown, we have made encouraging progress in recent years regarding our understanding of some of the factors involved. We know that complex genetic changes occur within plasma cells, and that environmental factors may also play a part in causing the genetic changes. For more on risk factors, please refer to the **"Risk of MGUS Progression"** subsection on page 17.

Among known factors associated with the prevalence of MGUS:

- **Age:** MGUS occurs more commonly in older people. The average age at diagnosis is 70 years.
- **Pre-existing conditions:** People with immune system disorders such as rheumatoid arthritis and chronic infections like hepatitis C are more commonly diagnosed with MGUS than those who do not have these conditions.
- **Race:** People of African descent are more likely to develop MGUS than those from other racial backgrounds.
- **Gender:** MGUS is more common in men than women.
- **Family history:** Family history of a plasma cell disorder can indicate a higher chance that you may develop MGUS.

Symptoms of MGUS

Most people living with MGUS do not experience any obvious signs or symptoms; they usually aren't even aware that they have the condition until a more serious diagnosis, such as myeloma, is made. Some people with MGUS may experience a rash or nerve problems, like numbness or tingling in the hands and feet ***(peripheral neuropathy)***, or problems with balance. These are likely due to the accumulation of abnormal myeloma cells in the bone marrow that restrict the space available for healthy cells.

Complications of MGUS

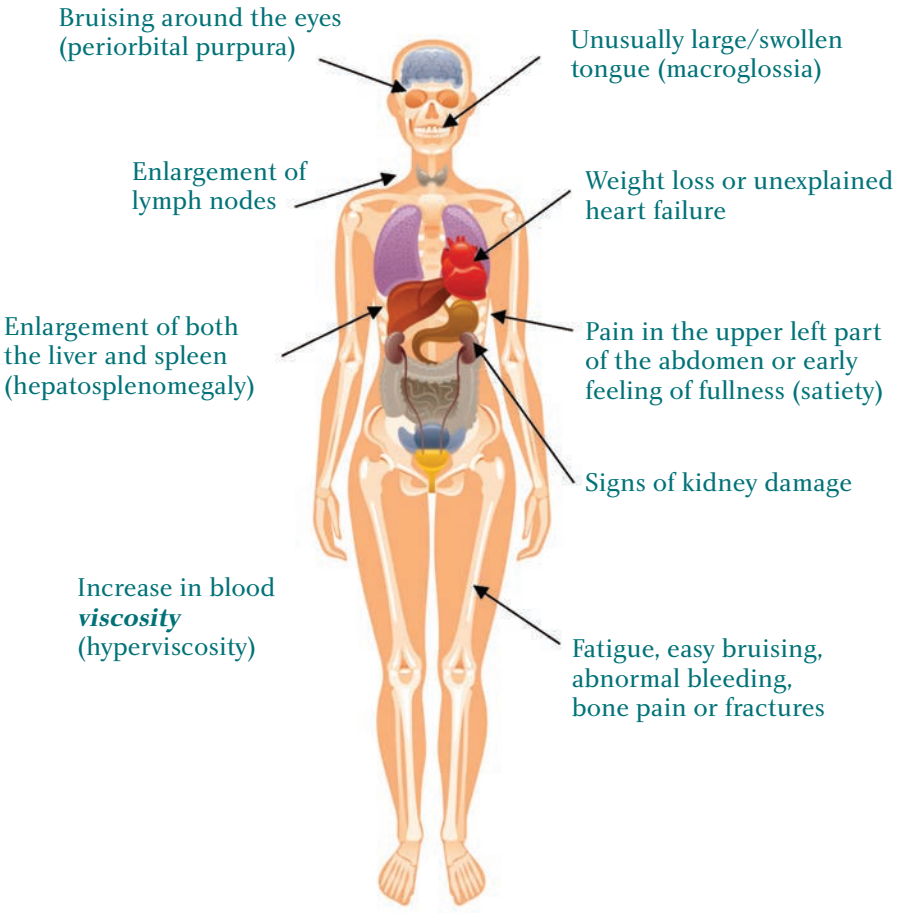
Although MGUS is predominantly asymptomatic, there are some known complications that some people with MGUS may experience. These include:

1. **Skeletal conditions** such as ***osteoporosis:*** Cells in the bone marrow are compromised by the high number of abnormal myeloma cells and some bones become weaker, are more prone to fractures, and may cause bone pain.
2. **Infections:** People with MGUS have reduced levels of normal antibodies and are twice as likely to develop bacterial or viral infections. As such, it's recommended that you be extra cautious with hygiene measures like regular hand washing and avoiding close contact with family and friends who are unwell.
3. **Peripheral neuropathy:** Typically associated with IgM-type MGUS, you may experience numbness or tingling in your hands and feet.

What Else Could It Be?

When considering a diagnosis of MGUS, your healthcare team will make sure to exclude other conditions. Figure 6 shows some common symptoms that may suggest a diagnosis other than MGUS alone.

Figure 6. Symptoms that may be associated with a condition other than MGUS alone



Some of these symptoms are indicative of other related disorders such as AL amyloidosis, Waldenström macroglobulinemia, lymphoma, ***plasma cell leukemia, solitary plasmacytoma, POEMS syndrome***, or other monoclonal gammopathies that can affect specific organs (i.e., the kidneys). If you are experiencing any of these symptoms, be sure to let your healthcare provider know so they can further investigate to determine the cause.

Solitary Plasmacytoma

Solitary plasmacytomas account for approximately 2-5% of all plasma cell disorders. Here, myeloma cells collect in the bone with minimal or no bone marrow involvement and form a single tumour called a solitary plasmacytoma of the bone (SPB). A plasmacytoma can also affect areas of soft tissue (e.g., fat, muscle, nerves, blood vessels, skin) outside of the bone and bone marrow – called an extramedullary plasmacytoma (EMP).

Both SPB and EMP are characterized by no additional bone lesions and no other signs or symptoms of myeloma. Solitary plasmacytomas can develop in the spine as well as in other areas of the body such as the pelvis, ribs, arms, thigh, breast bone, and skull, among others.

Both types of plasmacytoma are most often treated with radiation therapy. The majority of people with EMP have localized disease that is potentially curable with this approach. However, a large percentage of those with SPB do eventually progress to myeloma, and therefore require close follow-up and monitoring.

Diagnosing MGUS

As stated earlier, MGUS is usually asymptomatic in the majority of people. Most are not even aware they have the condition until their increased level of M-protein (associated with MGUS) is discovered by chance, e.g., following routine pre-operative blood tests or those for other conditions.

MGUS is often termed "a diagnosis of exclusion". What this means is that the presence of M-protein in your blood is not sufficient alone to diagnose MGUS. As such, your healthcare team will seek to rule out other causes of your test results or any symptoms you may be experiencing. As previously mentioned, there are other related conditions that can present similarly to MGUS such as SMM, myeloma, AL amyloidosis, Waldenström macroglobulinemia and lymphoma, so it is important to investigate these.

Depending on where you live, tests to diagnose MGUS will either be arranged by your family doctor, or you'll be referred to a ***hematologist***. To learn more about the types of tests that are recommended for diagnosing MGUS, please refer to the **"Common Diagnostic Tests for MGUS and SMM"** section on pages 6-9 of this InfoGuide.

Criteria for diagnosing MGUS vary slightly between the 3 different forms (non-IgM, to IgM to light chain MGUS). The main criteria for diagnosing MGUS are:

- **less than 10%** myeloma cells in the bone marrow;
- **M-protein in the blood** (IgM or non-IgM) that is less than 30 g/L;
- **urine M-protein** less than 500 mg/24 hours;
- **no CRAB symptoms/criteria.**

Further Investigation of Test Results

Depending on the results of your first set of tests and your symptoms, your healthcare team may want to conduct additional tests. These will not only help them to make an accurate diagnosis, but will ensure that you receive the most appropriate care.

Imaging

Current recommendations for imaging are dependent on your individual risk of progression (further discussed in the next section – **"Risk of MGUS Progression"**).

- Low-to-intermediate, intermediate-to-high and high risk:
  - If one or more risk factors is present, whole-body low-dose computed tomography (WBLDCT) imaging is typically recommended. If this isn't available at your healthcare site, your team may use conventional radiography or magnetic resonance imaging (MRI) instead.
- Low risk:
  - Even if you have low or even no risk factors, your healthcare team may still consider imaging such as a skeletal survey, WBLDCT, MRI or PET/CT scanning.

Risk of MGUS Progression

Will My MGUS Develop into SMM and/or Myeloma?

Unfortunately, there is no definitive way to tell if your MGUS will develop into SMM and/or myeloma, or any other related condition. This is understandably difficult for many people to cope with because of the large element of uncertainty. To best understand your personal risk and situation, please read through this section and be sure to speak with your healthcare team.

On the whole, chances of your MGUS progressing to another condition or disease is very low. While there is no concrete way to determine if your condition will progress or not, there are some factors that will indicate to your healthcare team whether your specific condition puts you at a higher risk of progression.

Progression Factors

Factors that are known to influence the progression of MGUS include:

- **the size and shape of M-protein** - people with IgM MGUS have a higher risk of progression over 20 years compared to people with non-IgM MGUS;
- **the amount of serum free light chain (sFLC) protein**.

Risk Factors

Health professionals have identified certain factors that have been shown to affect a person's risk of progression and developed a ***risk stratification*** system. This risk stratification will help determine how often your team will monitor and evaluate your condition.

There are three main risk factors for progression that are used to classify an individual's risk of MGUS progression:

- M-protein in the blood greater than 15 g/L;
- non-IgG type MGUS (IgA or IgM);
- abnormal sFLC ratio (kappa-to-lambda ratio less than 0.26 or greater than 1.65).

Based on the presence of these risk factors, your MGUS will be classified as low risk (no risk factors), low-to-intermediate risk (1 of these risk factors), intermediate-to-high risk (2 risk factors) or high risk (all 3 risk factors). The risk of progression for each of these risk groups is set out in Table 4.

Table 4. MGUS risk groups and risk of progression[1]

Number of Risk Factors	MGUS risk classification	Approx. % of patients affected	Absolute risk of progression (20 years)
0	Low	39%	5%
1	Low-to-intermediate	37%	21%
2	Intermediate-to-high	20%	37%
3	High	4%	58%

[1] Rajkumar SV et al. *Blood.* 2005;106:812-817.

What Causes MGUS to Progress?

MGUS typically remains stable for many years without progression. While it is not known for certain why some MGUS progresses into SMM, myeloma or any one of the other related conditions, we do know that there are many complex genetic events that occur at the cellular level. It is also thought that environmental factors may play a part, as well as the interactions between cells of the immune system, bone cells and other cells in the bone marrow.

Environmental factors that may influence the development and progression of MGUS include vitamin D deficiency, exposure to radiation, asbestos, fertilizers, mineral oils or pesticides.

There is extensive ongoing research in this area. We are continuously increasing our understanding of these complex genetic disease processes, as well as identifying individuals who are at the greatest risk of progression so that we may improve potential treatment options.

Managing and Monitoring MGUS

Treatment for MGUS

The current standard of care treatment for asymptomatic MGUS is observation. Your healthcare team will monitor your condition by conducting regular blood and urine tests. They may request bone marrow biopsies, imaging scans or additional tests depending on the results and if you develop any symptoms.

Frequency of MGUS Monitoring

The frequency of testing and the types of tests you undergo may vary depending on your individual risk. In general, repeat testing is recommended at 6 months after diagnosis, and, if stable, can decrease to annually thereafter. It is also advised that all people living with MGUS are periodically monitored for osteoporosis. The recommended frequency of monitoring is shown in Table 5.

Table 5. Recommended monitoring based on MGUS risk group[2]

MGUS risk level	Low	Low-to-intermediate, intermediate-to-high and high risk
Number of risk factors	0	At least 1
Complete blood count, calcium with albumin, SPEP, sFLC and creatinine	Repeat 6 months after diagnosis and if stable, repeat annually	Repeat 6 months after diagnosis and if stable, repeat annually
Bone marrow examination, imaging and more frequent monitoring	Not required unless (additional) symptoms develop	May be advised if your healthcare team suspects your condition is progressing
Osteoporosis assessments	Periodic assessment is recommended	Periodic assessment is recommended

[2] Bergstrom DJ, et al. *Clin Lymphoma Myeloma Leuk.* 2020;20(7):e352-e367.

Fluctuations of M-protein Over Time & the Importance of MGUS Monitoring

It's normal for M-protein levels to increase and decrease in people living with MGUS. However, steady increases in M-protein or the development of any new symptoms may indicate that further testing should be done. It is therefore very important to notify your healthcare team if there are any changes to your symptoms and let them know if you develop any new ones.

Frequent monitoring is important because although the risk of progression to another condition or disease is relatively small, keeping an eye on your MGUS will mean that any changes are identified as soon as possible. This can lead to earlier diagnosis and treatment, and a better outcome for you. Earlier treatment, if required, can reduce or prevent potentially irreversible organ damage that may otherwise occur.

Why is MGUS Treatment Not Currently Recommended?

Currently, there is no evidence to suggest that actively treating MGUS is beneficial. Several medicines have been tested in people with MGUS, but none have shown to prevent MGUS from progressing into myeloma or a related condition.

Since the risk of progression is low and MGUS is typically asymptomatic, treating MGUS with medications would likely lead to more treatment-related side effects than the condition itself causes. This means that many patients would receive treatment that is ultimately not necessary and could cause more harm than good. Treatment is therefore only recommended if and when MGUS progresses to a more serious condition.





Introduction to SMM

This section will explore the topic of smouldering multiple myeloma (SMM), how it is diagnosed, the symptoms you may experience, your individual risk of progression, and how your SMM may be monitored and managed.

What is SMM?

SMM is a second intermediate stage between MGUS and myeloma. As with MGUS, most people with SMM are asymptomatic. The main difference between MGUS and SMM is the number of myeloma cells in the bone marrow. In people with SMM, this is between 10% and 60%. Individuals living with SMM do not have CRAB symptoms.

The risk of progression from SMM to myeloma is approximately 10% per year for the first five years. Due to this higher risk of progression, most people spend less time in the SMM stage (compared to MGUS) and present to their healthcare team when either symptoms begin to become apparent or when activity is picked up during routine blood tests.

Symptoms of SMM

As with MGUS, most people living with SMM do not experience any symptoms. There are those that may have rash or nerve problems like numbness or tingling in the hands and feet (peripheral neuropathy), or problems with balance. This is likely due to the accumulation of abnormal myeloma cells in the bone marrow that restrict the space available for healthy cells.

Potential Complications of SMM

Much like with MGUS, SMM can cause complications in the bones (e.g., osteoporosis), make you more prone to infections, and cause peripheral neuropathy. If you are concerned about any of these, or are experiencing any difficulties, you must tell your healthcare team as soon as possible.

Did You Know?

The risk of progression from SMM to myeloma is approximately 10% per year for the first five years. Approximately half of newly diagnosed people will progress to myeloma within the first 5 years. One-third of newly diagnosed people will not progress in the first 10 years following their diagnosis.

Diagnosing SMM

Since SMM is generally asymptomatic, it is usually found and diagnosed after a routine test, or based on the results from a test used to check for other health conditions. Depending on where you live, tests to diagnose SMM can be arranged by your family doctor, or you may be referred to a hematologist. Please refer to the section **"Common Diagnostic Tests for MGUS and SMM"** on pages 6-9 for an overview of the types of tests typically recommended for diagnosing SMM.

Below are some main criteria used to reach a SMM diagnosis:

- **Percentage of myeloma cells in the bone marrow:** 10–60% without CRAB symptoms, MDEs, and AL amyloidosis (AL amyloidosis should be ruled out);
- **M-protein in the blood:** IgG or IgA of 30 g/L or greater;
- **Urine M-protein:** 500 mg per 24 hours, or greater.

Depending on your symptoms, and in order to rule out any other related conditions, your healthcare team may recommend additional tests to be performed.

Risk of SMM Progression

Will My SMM Develop into Myeloma?

Since not everyone with SMM will ultimately progress to, or be diagnosed with myeloma, it's important to find ways to identify people who are at a higher risk of progression. While it's not possible to say for certain whether you will progress from SMM to myeloma, your individual risk can be estimated using a certain set of criteria.

In Canada, the current definition of high-risk SMM is based on a combination of models used by the Mayo Clinic in the United States, the International Myeloma Working Group (IMWG), as well as from other criteria.

Mayo Clinic

The Mayo Clinic has developed a well-established model that classifies SMM into 3 risk groups. The criteria looks at the amount of M-protein in the blood as well as the percentage of myeloma cells in the bone marrow (Table 6).

Table 6. Mayo Clinic SMM progression risk model[3]

Risk group	M-protein in the blood marrow		Myeloma cells in the bone
1	At least 30 g/L	**and**	At least 10%
2	Less than 30 g/L	**and**	At least 10%
3	At least 30 g/L	**and**	Less than 10%

[3] Kyle RA, et al. *N Engl J Med.* 2007;356(25):2582-2590.

By applying the Mayo Clinic model in clinical trials and analyses, it was found that the three groups of people experienced different risks of progression; patients in the first risk group had an 87% chance of their SMM progressing to myeloma within 15 years compared to 70% and 39% for those in the second and third risk groups, respectively.

International Myeloma Working Group

The IMWG model looks at three factors when predicting risk progression: the percentage of myeloma cells in the bone marrow, the sFLC ratio, and the level of M-protein in the blood. In this model, the risk factors that indicate a high risk of progression are:

- more than 20% of myeloma cells in the bone marrow;
- an involved/uninvolved sFLC ratio greater than 20;
- more than 20 g/L of M-protein in the blood.

People with none of these risk factors are considered to be low risk; people with one risk factor are considered intermediate risk, and people with two or more are considered to be at high risk of progression to myeloma.

Why Does SMM Progress to Myeloma?

The reasons for why some cases of SMM progress into myeloma and others do not are unfortunately not fully understood. However, research scientists are working extensively to try and better grasp the mechanisms involved and their effect on the risk of progression.

As with MGUS, we know that in people with SMM, there are complex genetic changes that happen within the bone marrow plasma cells. These changes may be affected by environmental factors such as exposure to certain chemicals, pesticides, and radiation.

Managing and Monitoring SMM

Treatment for SMM

Currently the recommended standard of care for SMM is observation. The frequency of observation and monitoring will depend upon your risk level (as determined by the factors listed above).

Frequency of SMM Monitoring

How frequently your SMM will be monitored will depend on your risk of progression. As summarized in Table 7, people identified as being at a high risk of progression will have more frequent monitoring and testing than those at a low or intermediate risk.

Table 7. Recommended monitoring based on SMM risk group[2]

Follow-up	Low and intermediate risk	High risk
Investigations in the first year after diagnosis (baseline)	Every 3–4 months	Every 2–3 months
Subsequent follow-up testing	If findings are stable: • Every 6 months for 5 years (or unless myeloma progression occurs)	If findings are stable: • Every 4–6 months for 5 years (or unless myeloma progression occurs) • May decrease to every 6 months
Repeat imaging	Not usually required unless symptoms develop or another condition is suspected	Not usually required unless to rule out asymptomatic myeloma progression
Osteoporosis assessment	All patients are recommended to have periodic assessments for osteoporosis	

[2] Bergstrom DJ, et al. *Clin Lymphoma Myeloma Leuk*. 2020;20(7):e352-e367.

Investigatory Treatments

At the time of publication, there are ongoing clinical trials for people diagnosed with SMM. These trials test different drugs as an early intervention strategy in people with SMM who are at high risk of progressing to myeloma. Some examples of medications that have been/are being investigated include lenalidomide (Revlimid), daratumumab (Darzalex), and carfilzomib (Kyprolis). Researchers are looking at whether using one or more of these agents can prevent people with high risk SMM from developing into myeloma. Currently, the data from these trials is not sufficient to change the current standard of care – observation – in Canada.

Why is Treatment Not Currently Recommended?

The reason why healthcare professionals are cautious to systematically treat SMM is simply because not all cases of SMM progress to active myeloma. Treating everyone living with SMM could result in unpleasant or even harmful side effects from a treatment that ultimately may not have been necessary. In these cases, the side effects of treatment could potentially be more damaging than the asymptomatic condition itself. Treatment is only recommended if and when the SMM progresses to a more serious condition.





What If My Condition Progresses into Myeloma?

If your tests indicate that your MGUS or SMM has progressed into myeloma, your healthcare team will advise you of the next steps to be taken. Results from your previous and new tests will be used to identify the best treatment option for you and your myeloma. Given that your team was aware of your previous condition and you were being monitored regularly, the positive news is that you should be able to start treatment as soon as possible, minimizing or preventing potential organ damage.

Resources for Managing a Diagnosis of Myeloma

Myeloma Canada has a wide range of resources to help you and your loved ones navigate your myeloma diagnosis. If you have just been diagnosed with myeloma, remember that you are not alone in your myeloma journey. It's so important to be an active and informed participant in the important decision-making surrounding your healthcare.

The section that follows features a brief guide to some questions that you may want to consider asking your healthcare team. We hope you will find this empowering and informative so that you feel more confident in understanding and managing your myeloma.

More Information

Resources that can help you understand, manage and navigate your diagnosis

There is a vast array of educational videos and publications from Myeloma Canada that can help demystify your diagnosis. Please visit the Resources section on our website at myeloma.ca to learn more. All publications are offered to you free-of-charge. **You can download them at myeloma.ca, or order printed copies by e-mailing us at contact@myeloma.ca or by calling, toll-free 1-888-798-5771.**

The *Multiple Myeloma Patient Handbook* is an excellent resource for those who are newly diagnosed, as well as their family and loved ones. Designed to provide educational support to patients, caregivers, families and friends, this Handbook gives accurate, reliable, and clear information on myeloma. Some of the topics covered include the causes and effects of myeloma, how it's diagnosed, and treatment options available in Canada.

Be sure to visit Myeloma Canada's YouTube channel (www.youtube.com/myelomacanada) which features over 100 educational videos, webinars, and inspiring patient journey videos that you can watch at your own pace and leisure.

Making Decisions About Treatment

There is so much to digest when you're first diagnosed - new information, treatment options, etc. - it can all feel very overwhelming. It's important to take a step back, make sure you feel like an active partner in your treatment plan and are empowered to make informed decisions on what's best for you.

When your healthcare team first discusses treatment options with you, some questions that may help guide your decision might include:

- What are the current goals of my treatment?
- What are my treatment options? What treatment do you recommend and why? What are the side effects of the treatment you are recommending?
- Are there any clinical trials available that I should consider?
- When do you recommend starting treatment and why?
- How long will treatment last?
- What type of exams or follow-up tests will I need to do while on treatment?
- What if the treatment doesn't work?

You may also want to consider what factors are important to your decision-making:

- Understand how each treatment will affect your day-to-day life
- Talk to someone about their experience
- Understand what adaptations would be required to adjust to treatment
- Understand what side effects you might experience and how to identify them
- Find out about the support available (i.e., childcare, transport, insurance coverage)

In order to reach a conclusion that is right for you, we recommend you make a list of all the treatment options proposed by your healthcare team and consider the benefits/advantages and risks/disadvantages of each. You should also consider who else is involved in your decision and how it will affect them.

Thinking About the Future

When considering which treatment is right for you, some questions you may want to ask your healthcare team include:

- How long will I be on this treatment?
- Does this treatment choice affect my future treatment options, and if so, how?
- What are my future treatment options after this?





Beyond Family and Friends: Myeloma Patient Support Groups

Local Support Groups

Talking to people outside your immediate circle may be easier than talking to family and close friends. Meeting and speaking to others with shared experiences through support groups can truly provide you with invaluable information and support. Other patients may be, or have already been, in a similar situation to yours. They understand what you're going through and how to help from a different perspective. Sometimes relief can be found just by speaking to people that can personally identify and relate to you, your experiences and your feelings.

Visit **myeloma.ca** to find a support group near you. If a patient support group doesn't exist in your area, consider forming one yourself. Myeloma Canada can help you get started.

Virtual, Online Support Groups

You may also be able to meet and connect with other patients through an online support group. Myeloma Canada has created, and is the lead administrator of three online, virtual patient support groups on Facebook. These closed groups offer a safe environment for myeloma patients to connect and exchange experiences with others facing similar challenges. Thanks to the Facebook "translate" button, language barriers can be overcome, enabling you to communicate, in your mother tongue, with people nation-wide. Moreover, the information shared on the page is private and can't be viewed by the public. All members must request to join the group to gain access. To join, search for the **"Myeloma Canada Patient & Caregiver Support Group"**, **"Myeloma Canada Support Group for Young Patients and Caregivers"**, or **"Myeloma Canada Support Group for Caregivers"** on Facebook.



Glossary

Albumin: Simple water-soluble protein found in the blood that can be increased in people with myeloma.

Albuminuria: High levels of albumin in the urine.

Amyloid light-chain (AL) amyloidosis: Condition where light chains produced by myeloma cells link together and build-up in tissues and organs throughout the body such as the heart and kidney, causing damage.

Amyloid/light chain deposits: Group of light chains that have joined together and accumulated within a tissue or organ.

Anesthetic: Medicine given to cause a loss of feeling or awareness - can be local (to numb one area) or general (a loss of sensation throughout the body that leads to unconsciousness).

Anemia: Decreased blood hemoglobin level. Hemoglobin is found in red blood cells and carries oxygen around the body.

Antibodies (immunoglobulins): Y-shaped protein molecules that have heavy and light chains (portions). They are produced by plasma cells and attach to and fight infection and disease in the form of antigens (bacteria, viruses, toxins or tumours). Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies disable antigens directly; others make the antigen more vulnerable to destruction by other blood cells.

Antigen: Foreign substance that can be recognized by cells of the immune system leading to the production of protective antibodies.

Asymptomatic: Where a person does not experience any symptoms of their condition.

Bence-Jones proteinuria (or protein): A myeloma protein present in urine. The amount of Bence-Jones protein is expressed in terms of grams per 24 hours. Normally a very small amount of protein (less than 0.1 grams per 24 hours) can be present in the urine, but this is albumin rather than Bence-Jones protein. The presence of any Bence-Jones protein is abnormal.

Beta-2 microglobulin (b2M): 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 b2M. For these patients, b2M testing cannot be used to monitor the disease. At the time of relapse, b2M can increase before there is any change in the myeloma protein level. Therefore, 90% of the time, b2M is very useful for determining disease activity.

Bone marrow: Spongy tissue that is found inside your bones. It is soft, fatty and full of blood vessels. Your bone marrow is where most of the blood cells in your body are made.

Bone marrow aspirate or aspiration: The removal, by a needle, of a sample of fluid and cells from the bone marrow for examination under a microscope.

Bone marrow biopsy: The removal, by a needle, of a sample of tissue from the bone. The cells are checked to see whether they are cancerous. If cancerous plasma cells are found, the pathologist estimates how much of the bone marrow is affected. Bone marrow biopsy is usually done at the same time as bone marrow aspiration.

Calcium: Mineral found mainly in the hard part of bone.

Cardiac biomarkers: Tests that can indicate whether your heart is functioning normally.

Creatinine: Waste product produced by the body that is broken down in the kidneys.

Creatinine clearance: Test that measures how efficiently your kidneys are functioning by measuring how much blood per minute the kidneys can make creatinine-free.

Cytogenetics: The study of the structure of chromosomes that can help to identify genetic errors in myeloma cells. There are two main types of cytogenetics used in myeloma: karyotyping and fluorescence in situ hybridization (FISH).

Cytogenetic abnormalities: Changes to the genetics of a cell.

Deletions: Genetic change that can occur within a cell's genes causing part of the gene to be removed.

End-organ disease: Damage occurring in major organs due to uncontrolled disease.

Estimated glomerular filtration rate (eGFR): Test to determine how effectively the kidneys are able to filter out waste products.

Fluorescence in situ hybridization (FISH): Laboratory-based method of analyzing the cytogenetic profile of cells.

Focal lesion: Defined area of irregular cells seen in the bone marrow on imaging scans.

Gains: Type of genetic change that can occur within a cell's genes causing new genetic information to be inserted.

Genes: Specific sequence of DNA.

Globulin: Protein made in the liver that has a role in liver function, blood clotting and fighting infection.

Hematologist: Doctor specializing in conditions affecting the blood and bone marrow.

Hemoglobin (Hb or Hgb): Molecule found in red blood cells that contain iron and carries oxygen around the body.

Hypercalcemia: A higher-than-normal level of calcium in the blood. This condition can cause a number of symptoms, including loss of appetite, nausea, thirst, fatigue, muscle weakness, restlessness and confusion. Common in myeloma patients and usually resulting from bone destruction with release of calcium into the blood stream. Often associated with reduced kidney function since calcium can be toxic to the kidneys. For this reason, hypercalcemia is usually treated on an emergency basis using IV fluids combined with drugs to reduce bone destruction along with direct treatment for the myeloma.

Immunofixation electrophoresis (IFE): Test of blood or urine that identifies the different types of protein present.

Light chain deposition disease: Type of plasma cell disorder that is characterized by deposition of light chains in various organs, most frequently in the kidneys.

Lymphoma: Cancer of the lymph nodes.

Lytic bone lesions: Damaged area of a bone that appears as a dark spot on imaging scans. Lytic lesions look like holes in the bone and are evidence that the bone is being weakened.

Monoclonal antibody (MoAb): Antibody manufactured in the lab that is specifically designed to locate and bind to other cells for diagnostic or treatment purposes.

Monoclonal gammopathy of undetermined significance (MGUS): Condition whereby low levels of monoclonal protein are produced in the blood and/or urine.

M-protein (monoclonal protein, paraprotein, or M-spike): Also known as myeloma protein. These are antibodies or parts of antibodies found in unusually large amounts in the blood or urine of myeloma patients. M-spike refers to the sharp pattern that occurs on protein electrophoresis (blood test) when an M-protein is present.

Multiple myeloma: A cancer of the bone marrow plasma cells.

Myeloma cells: Plasma cells in the bone marrow that produce abnormal proteins.

Myeloma defining events (MDEs): Biologic markers that indicate that SMM has progressed to active myeloma.

Osteoporosis: Progressive condition characterized by a decrease in bone mass and density, and an increase in the risk of fracture.

Peripheral neuropathy: Damage to the nerves that make up the peripheral nervous system (i.e., hands, feet, arms or legs) causing pain, tingling and altered sensation.

Plasma cell leukemia: A rare and aggressive variant of myeloma characterized by high levels of myeloma cells circulating in the blood.

Platelets: Blood cells that are responsible for clotting.

POEMS syndrome: Blood disorder that damages the nerves and other parts of the body.

Prevalence: Total number of people living with a disease or condition at a specific time.

Red blood cells (RBCs): Type of cell found in the blood responsible for carrying oxygen around the body.

Renal insufficiency (damage): Reduction in kidney function.

Risk stratification: System of defining the risk of someone developing a condition or of the condition progressing.

Serum free light chain (sFLC): Light chain (kappa or lambda) portion of antibodies that are free to circulate in the blood.

Serum protein electrophoresis (SPEP): Test to determine the level of different proteins in the blood.

Smouldering multiple myeloma (SMM): Also known as indolent or asymptomatic myeloma. SMM is a generally asymptomatic precursor of myeloma where plasma cells may make up 10%-60% of the bone marrow, serum M-protein is greater than 30 g/L, and urinary M-protein is equal to or greater than 500 mg per 24 hours. However, there is still no CRAB symptoms of myeloma or MDEs.

Solitary plasmacytoma: Discreet, single mass (tumour) of monoclonal plasma cells either arising from the bone marrow (medullary) or soft tissues (extramedullary).

Standard of care: Treatment (medicine or procedure) or protocol that is accepted and widely used by doctors as an appropriate therapeutic approach for a certain type of disease or condition.

Translocation: Mutation caused by rearrangement of parts of different genes.

Urine protein with electrophoresis (UPEP): Test to evaluate the types of protein in the urine.

Viscosity: The property of resistance to flow by a fluid.

Waldenström macroglobulinemia: Condition affecting plasma cells where excessive amounts of IgM protein are produced. This is not a type of myeloma.

White blood cells (WBCs): 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 WBCs include neutrophils, granulocytes, lymphocytes, and monocytes.

X-rays: High-energy electromagnetic radiation used in low doses to view images of the bones in the body.





Make Myeloma Matter

Every year, Myeloma Canada provides information to thousands of people impacted by myeloma through programs and services such as the annual Myeloma Canada National Conference, InfoSessions, Meet & Greets, the Myeloma Matters online newsletter, webinars, videos, InfoGuides, and much more.

That's why we need your help. As the only national, charitable organization created by, and for, Canadians impacted by myeloma, we depend on your support and generous donations. Your contribution helps to improve the lives of those affected by myeloma by empowering the community through awareness, education and advocacy programs, and supporting research to find a cure. With your help, we've been making myeloma matter since we were founded in 2005.

Every donation is greatly appreciated and enables us to continue our vital work. There are many options for giving. Whether it's a one-time, a pre-arranged monthly, or a legacy gift, every donation brings us closer to finding a cure.

Ways You Can Help

Donate

We invite you to make your donation online at **myeloma.ca**, over the phone by calling toll-free at **1-888-798-5771**, or by mailing a cheque payable to Myeloma Canada to:

Myeloma Canada
1255 TransCanada, Suite 160
Dorval, QC H9P 2V4

Fundraise

There are many ways you can support Myeloma Canada, such as taking part in the annual Multiple Myeloma March held in cities across Canada, or by fundraising for Myeloma Canada in your local community. When so much about myeloma is beyond the control of the people that it affects - and those who care for them - fundraising can be a rewarding and fun way of doing something positive for yourself and for others affected by the disease.

Contact Myeloma Canada's fundraising team, toll-free, at 1-888-798-5771 for more information or visit www.myeloma.ca.



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Follow us on social media for the most up-to-date information and resources:

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MAKING MYELOMA MATTER

Myeloma Canada publications are extensively reviewed by patients and healthcare professionals prior to publication.

Sincere thanks to the fundraising efforts of the Canadian myeloma community who make myeloma matter by helping to advance Myeloma Canada's objectives of awareness, education, advocacy, community empowerment and support of clinical research so that a cure may be found.

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