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 education, awareness, access and research.

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This resource has been designed for:

1. Someone who has been newly diagnosed with myeloma and is wondering what myeloma is and what the future will bring.

2. Those who have been living with myeloma for some time, but would like to refresh their understanding of the disease.

3. A person who is a family member, friend or loved one of someone with myeloma, and who wants to gain a better understanding of the disease and treatment options.

The goal of this resource is simple: to educate myeloma patients and their loved ones so they can become more active partners in their care.

If you have been searching for information on myeloma, you know how complicated it can be. This resource will attempt to give you accurate, reliable and clear information on myeloma, its causes and effects, and how it is diagnosed, staged and treated in Canada.

There is a lot of information in this Handbook and the more times you refer to it, the easier it will be for you to understand it. Don’t be afraid to ask members of your healthcare team to explain any term you don’t understand. Over time, you will better understand your disease, your treatment options and what you can do to optimize your quality of life. As you read through this Handbook, some of the more technical or unusual words that might be new to you appear in bold the first time they are used. These terms are explained in the glossary on page 67.

Disclaimer

The information in this Handbook is not meant to replace the advice of your medical team. They are the best people to ask if you have questions about your individual situation.
Myeloma Canada

Myeloma Canada is a registered non-profit organization created by, and for, people living with 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, government agencies and local support groups across Canada, Myeloma Canada seeks to strengthen the voice of the Canadian myeloma community and improve the quality of life for myeloma patients, their caregivers and families through education, awareness, advocacy and research.

Myeloma Canada’s goals are to:

- Provide educational resources and support to patients, their families and caregivers
- Increase awareness of the disease and its effects on the lives of patients and families
- Promote clinical research and access to new drug trials in Canada
- Facilitate access to new therapies, treatment options and healthcare resources

This Handbook is dedicated to the patients and their families who are living with myeloma and to the dedicated healthcare professionals and researchers who are working towards more effective treatments and a cure.
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In this chapter, we’ll define what is meant by “multiple myeloma” and its underlying disease process. Some of this information may appear intimidating or complex at first. Don’t worry – over time you will understand more and more. Refer to this resource frequently and don’t be afraid to ask your healthcare team for explanations.

As early as possible, start collecting and organizing key information about your condition and your care. This should include contact information for members of your healthcare team, copies of your lab results, your medication regimens and side effects. You’ll find information on these and other issues later in this resource (Chapter 9 – How to be Your Own Advocate). In Chapter 7 (Your Healthcare Team), we’ll also discuss how to optimize communications with the main partners in your treatment – your healthcare team.

Bone Marrow and Plasma Cells

You have probably heard the terms “multiple myeloma” and “myeloma”. The word “multiple” is often used because the cancerous (malignant) cells usually affect multiple areas of the bone marrow. In this resource, we’ll use the term “myeloma” to keep things simple.

Myeloma is a cancer of the plasma cells. A plasma cell is a type of immune cell that produces antibodies to fight infection. Plasma cells are found in the bone marrow, the “blood factory” found within the hollow area of bones. As plasma cells are found in the blood, myeloma is referred to as a hematologic or blood cancer. It may also be referred to as a cancer of the immune cells.
Myeloma vs. Melanoma

Myeloma is often confused with melanoma. Myeloma is a cancer of the plasma cells, a type of immune cell, in the bone marrow. Melanoma refers to a form of cancer that usually occurs in the skin, but can also occur in the eye and mucous membranes.

Three types of plasma/blood cells are made in the bone marrow:

1. **Red blood cells (RBCs; erythrocytes)** that carry oxygen.
2. **Platelet cells (thrombocytes)** that help the blood to clot whenever you cut yourself.
3. A variety of **white blood cells (WBCs; leukocytes)**, including **lymphocytes** that play important roles in the functioning of the immune system. There are two types of lymphocytes: T cells and B cells. Another variety of white blood cell you may hear of is the neutrophil. This type of cell plays an important role in protection from infection. If you have a low neutrophil level you are more susceptible to infection.

With regard to lymphocytes:

- “T”, in T cell (or T lymphocyte), stands for thymus – the principal organ for their development.
- B cells (or B lymphocytes) are found in the bone marrow. As they mature, B cells turn into plasma cells.

When plasma cells are exposed to foreign substances (antigens), they produce different antibodies. These antibodies are called **immunoglobulins** (the short form is Ig).

Immunoglobulins are proteins made up of two types of chains:

- Heavy chains (G, A, M, D or E type)
- Light chains (kappa [κ], or lambda, [λ])

Normally, the most common immunoglobulin in the blood is **IgG**, followed by **IgA** and **IgM**. **IgD** and **IgE** are usually present in the blood in very small amounts.
What is Multiple Myeloma?

In myeloma, the B lymphocyte (the cell that matures into a plasma cell) is damaged. It begins to reproduce plasma cells uncontrollably. We commonly refer to this “good cell gone bad” as being malignant.

When plasma cells reproduce uncontrollably, two things happen.

- Too many plasma cells are produced. In healthy people, plasma cells make up 2-3% of the cells in the bone marrow. In someone who has myeloma, plasma cells make up at least 10% of the cells – or even more. The abnormally high number of plasma cells can “crowd” out other types of cells you need to be healthy, such as red blood cells or platelets.

- Too much of the same immunoglobulin is produced, such as too much IgG or IgA. This is referred to as the monoclonal protein (M-protein), monoclonal spike (M-spike), monoclonal peak (M-peak), or paraprotein. All these terms are interchangeable. For more information about the M-protein and the different types of myeloma, please refer to Chapter 2 – Types of Myeloma.

As myeloma cells multiply in the bone marrow, the attached to other structural cells of the bone marrow known as stromal cells. Once attached to stromal cells, interactions occur that stimulate the myeloma cells to continue reproducing.

- Chemical messengers called cytokines are produced and stimulate the growth of myeloma cells and prevent them from dying naturally. Interleukin 6 (IL-6) is one of these chemical messengers.

- Myeloma cells secrete chemicals called growth factors that promote the creation of new blood vessels that usually accompanies the growth of malignant cells (a process called angiogenesis). One of the most important of these growth factors is vascular endothelial growth factor (VEGF).

- As more and more myeloma cells grow and multiply within the bone marrow, little space is left for your healthy immune cells to grow, and the immune system begins to weaken. Ordinarily your immune system would try to clear out or stop the growth of abnormal cells. But as the immune system weakens, it is unable to battle the abnormal cells.

As the myeloma cells invade the bone, they may cause multiple areas of damage that weaken the bone. These areas are known as osteolytic lesions, or lytic bone lesions for short.

Sometimes, myeloma cells collect in a single bone and form a tumour called a plasmacytoma. Occasionally, a plasmacytoma can affect areas of soft tissue outside of the bone (extramedullary plasmacytoma).
History of Myeloma Research

The first medical descriptions of myeloma date back to the 1840s. By the early 1900s, the role of plasma cells in the development of myeloma had been described and X-rays were used to find areas of bone damage (lytic lesions). It was not until 1962 that the first modern treatment of myeloma emerged. The use of melphalan (Alkeran®), a chemotherapy drug, in combination with prednisone, a corticosteroid (steroid), was first described by Dr. Daniel Bergsagel from the University of Toronto. For many years, melphalan and prednisone, the “MP” regimen, was the only available treatment for myeloma.

In the 1970s, various combinations of chemotherapy agents were developed, such as VAD (vincristine, adriamycin and dexamethasone). High-dose therapy (chemotherapy) and stem cell transplantation (also known as bone marrow transplantation) for myeloma patients began in the 1980s. It was not until 1996, however, that a randomized phase III controlled trial (see Chapter 8 – Development, Approval and Reimbursement of New and Emerging Therapies) was able to show a clear benefit for high-dose therapy.

Over the past 15 years, there has been increasing use of novel therapies such as thalidomide (Thalomid®), bortezomib (Velcade®), lenalidomide (Revlimid®) and most recently pomalidomide (Pomalyst®), carfilzomib (Kyprolis®), daratumumab (Darzalex®) and ixazomib (Ninlaro®). This has resulted in new treatment combinations that have extended the lives of many myeloma patients.

Research has been able to increase our understanding of the genetics of myeloma and the underlying disease process. This has resulted in the development of new approaches for diagnosing and treating myeloma.

Although there is still no absolute “cure” for myeloma, a growing number of patients with active myeloma are living ten or more years after their diagnosis. Moreover, improvements in the treatment of complications associated with myeloma have resulted in the best and longest possible quality of life for patients living with the disease.
**Incidence and Prevalence in Canada**

There are approximately 8,000 Canadians living with myeloma. According to the 2017 Canadian Cancer Statistics report by the Canadian Cancer Society and Statistics Canada, 2,900 new cases of myeloma are diagnosed annually in Canada, with the age-standardized estimate being about 7 per 100,000 people. Myeloma represents 1.6% of new cases of cancer in men and 1.2% of new cases in women. It was estimated there would be 1,450 deaths from myeloma in 2017: approximately 800 men and 650 women. Myeloma accounts for 1.8% of all cancer deaths during that year.

Myeloma is fairly rare before age 40, and most people are in their 60s when they are diagnosed. Given that the population is ageing and patients are living longer, the prevalence of myeloma is increasing. The Canadian Cancer Society has estimated that between 2003-07 and 2028-32, the number of new cases per year will increase by approximately 125%. From 1999-2009, 7,460 Canadians were diagnosed with the disease, and this number will continue to increase. Despite the growing prevalence, myeloma remains a relatively unknown cancer.

We know that the incidence of myeloma varies from country to country, from less than one per 100,000 people in China to about five per 100,000 in most Western industrialized countries. In the United States, myeloma is more common in African Americans than Caucasians.

Factors that may be associated with an increased risk of myeloma include exposure to toxic chemicals, radiation and obesity. There is still much to learn about what causes myeloma.

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**Is myeloma an inherited cancer?**

Studies have shown that there are some genetic variations that can increase the likelihood that a person will develop myeloma. These genetic variations are inherited; however, their effect is very small. This means that individuals may inherit a certain combination of genetic variations that puts them at higher risk of developing myeloma, but the inherited factors are only a small part of the puzzle. It is certain that other genetic and environmental factors are needed before myeloma develops.

Population studies have shown that immediate family members have approximately double the risk of developing myeloma compared to people with no family connection. This might sound alarming but it’s important to understand what this actually means: instead of a 5 in 100,000 risk of developing myeloma (within the general population), an immediate family member will have a 10 in 100,000 risk. The risk in real numbers is therefore very small.

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**Incidence vs. Prevalence**

Incidence refers to the total number of new myeloma cases diagnosed in a given year.

Prevalence describes the total number of people living with myeloma at a specific time.

* Source: 2016 Canadian Cancer Society cancer statistics
Myeloma is not one disease. In this chapter we will look at the different types of myeloma. A table that summarizes the different criteria for each type of myeloma can be found at the end of this chapter.

## Monoclonal Gammopathy of Undetermined Significance (MGUS)

MGUS is a **benign** condition where monoclonal protein (M-protein), monoclonal spike (M-spike), monoclonal peak (M-peak), or paraprotein is present but there is no underlying disease. MGUS can, however, be a precursor of myeloma. In someone with MGUS:

- There may be more plasma cells than normal in the bone marrow, but it is still less than 10% of all blood cells (part of the definition of myeloma includes 10% or more plasma cells).
- M-protein level in the blood is usually less than 30 g/L.
- There is no anemia (low blood hemoglobin), renal insufficiency (kidney disease), hypercalcemia (high levels of calcium in the blood) or bone damage (lytic lesions).

MGUS is one of the most common premalignant disorders in Western countries, with a prevalence of 3.2% in the general population 50 years of age or older.

Why is MGUS important? People with MGUS have approximately 1% chance per year of developing active myeloma. Currently, there is no clear way to predict who will progress to active myeloma. MGUS is usually monitored but not treated.
Asymptomatic or Smouldering Myeloma

In some patients, there is a transitional state called asymptomatic myeloma (also known as smouldering or indolent myeloma) that lies between MGUS and symptomatic or active myeloma.

In asymptomatic myeloma, 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 anemia, renal failure, hypercalcemia, bone lesions or myeloma-defining events. Because the disease is not yet active, asymptomatic myeloma is usually observed but not treated. Clinical trials are presently studying whether patients with high-risk asymptomatic myeloma should be treated before the onset of active myeloma.

Symptomatic or Active Myeloma

Symptomatic myeloma is characterized by the presence of myeloma protein in the blood or urine and an increased number of plasma cells in the bone marrow. Another possible sign of symptomatic myeloma is the growth of a plasmacytoma or tumour in the bone or soft tissue.

People with symptomatic or active myeloma can develop complications such as anemia (low blood hemoglobin), renal insufficiency (kidney disease), or excessive levels of calcium (hypercalcemia) in the blood. Soft spots (lytic lesions) can appear on X-rays of the bone. These lesions weaken the bone, causing pain and increasing the risk of fractures. People with symptomatic or active myeloma require treatment.

Myeloma is often referred to by the type of heavy chain immunoglobulin (M-protein) or light chain (kappa $\kappa$ or lambda $\lambda$) that is over-produced by the cancerous plasma cells.

Definition of Active Myeloma – SLiM CRAB

The International Myeloma Working Group recently expanded the definition of active myeloma, to include any one of the following myeloma-defining events (SLiM criteria) to confirm the diagnosis of myeloma:

[S] Sixty (60) percent or greater clonal plasma cells on bone marrow examination

[Li] Serum involved/uninvolved free LIGHT CHAIN (FLC) ratio of 100 or greater, provided the absolute level of involved light chain is at least 100 mg/L

[M] More than one focal lesion (5 mm or greater) found by MRI (magnetic resonance imaging)

Traditionally, the diagnosis of myeloma was based on the presence of one or more of the following CRAB criteria:

[C] Elevated serum (blood) CALCIUM

[R] RENAL insufficiency (reduced kidney function)

[A] ANEMIA (low hemoglobin)

[B] Lytic BONE lesions or osteoporosis (one or more lesions on skeletal survey [full-body X-ray], computerized axial tomography [CAT or CT scan] or positron emission tomography [PET scan])
**M-protein**

In the previous chapter, we saw that immunoglobulins can be defined by the type of heavy chain they contain (G, A, M, D or E). About 60-65% of all myeloma cases involve the overproduction of IgG. In about 20% of cases, it is the IgA protein that is involved. Myeloma can also involve IgM, IgD or IgE, but these forms occur less frequently. Uncontrolled production of IgM can also be a rare form of plasma cell cancer known as *Waldenström macroglobulinemia*.

**Light Chain Myeloma**

Although a high level of M-protein in the blood is a hallmark of myeloma, about 15-20% of patients produce only the light chain portion of the immunoglobulin. These are referred to as free light chains because they lack the heavy chain portion of the immunoglobulin. Light chain protein is also referred to as Bence-Jones protein, after the physician who discovered them in the urine of myeloma patients.

When free light chain protein is in the urine, they can accumulate in the kidney and damage it. A 24-hour urine collection is usually required to measure and monitor light chain protein. Some laboratories, however, use *serum free light chain assays (Freelite®)* to detect and measure free light chains.

Approximately 30% of patients produce light chains in the urine as well as heavy and light chains in the blood.

**Oligosecretory Myeloma**

When very small amounts of M-protein are produced by malignant plasma cells, it is called oligosecretory myeloma. Oligosecretory means that only small amounts of protein can be measured in the blood or urine – much less than would be expected based on the level of abnormal (myeloma) plasma cells in the bone marrow. Sensitive measurement of the M-protein with Freelite® testing may be available in some centres and can be useful in monitoring this type of myeloma.

**Nonsecretory Myeloma**

Less than 5% of all patients with myeloma have nonsecretory myeloma. Nonsecretory myeloma means myeloma cells are present in the bone marrow but the level of M-protein (either heavy or light chain) in the blood or urine is so low that it is hard to measure. The disease cannot be diagnosed or tracked by the usual blood and urine tests; it can, however, be detected in the bone marrow or upon *biopsy* of bone lesions. Patients with nonsecretory myeloma are treated in the same fashion as active myeloma. Kidney problems associated with myeloma are much less common in patients with nonsecretory myeloma.

**Genetic Sub-Types**

It is now known that there are multiple different genetic (DNA) abnormalities associated with myeloma. Having one of these genetic abnormalities affects how your disease will respond to different treatments. In the future, genetic profiling will play an increasingly important role in the customization of myeloma treatments.

**Amyloidosis**

About 10–15% of people with myeloma will have or develop amyloidosis. In amyloidosis, a specific protein called amyloid can collect and cause damage in one or more organs, such as the kidneys or the heart.
<table>
<thead>
<tr>
<th>Type of Myeloma</th>
<th>Criteria</th>
</tr>
</thead>
</table>
| **MGUS** *(Monoclonal Gammopathy of Undetermined Significance)* | **Non-IgM MGUS:**<br>1. Serum monoclonal protein less than 30 g/L<br>2. Monoclonal bone marrow plasma cells less than 10%
3. Absence of end-organ damage (none of the CRAB criteria)<br>**IgM MGUS:**<br>1. Serum IgM monoclonal protein less than 30 g/L<br>2. No evidence of anemia, constitutional symptoms (fatigue, fever, night sweats, or weight loss), thickening of the blood (*hyperviscosity*), disease of the lymph nodes (lymphadenopathy), swelling of the liver and spleen (hepatosplenomegaly), or other end-organ damage attributable to the growth of monoclonal plasma cells<br>**Light chain MGUS:**<br>1. Abnormal FLC (free light chain) ratio of less than 0.26 or greater than 1.65<br>2. Increased level of kappa (κ) FLC in patients with a ratio greater than 1.65 and increased lambda (λ) FLC in patients with a ratio less than 0.26<br>3. No immunoglobulin heavy chain expression found in **immunofixation** testing<br>4. Absence of end-organ damage (none of the CRAB criteria)<br>5. Clonal bone marrow plasma cells less than 10%
6. Urinary monoclonal protein less than 500 mg/24 hours |
| **Asymptomatic or Smouldering Myeloma**             | **Both of the following must be present:**<br>1. Serum monoclonal protein (IgG or IgA) equal to or greater than 30 g/L or urinary monoclonal protein equal to or greater than 500 mg per 24 hours, and/or clonal bone marrow plasma cells between 10-60%
2. Absence of myeloma-defining events of amyloidosis (none of the CRAB criteria) |
| **Symptomatic or Active Myeloma**                   | 1. Monoclonal plasma cells in the bone marrow is equal to or greater than 10% and/or the presence of biopsy-proven bone or extramedullary plasmacytoma<br>2. Myeloma-defining events (1 or more of the following **SLiM** criteria):<br>• [S] Sixty (60) percent or greater clonal plasma cells on bone marrow examination<br>• [Li] Serum involved/uninvolved free **LIGHT CHAIN** (FLC) ratio of 100 or greater, provided the absolute level of involved light chain is at least 100 mg/L<br>• [M] More than one focal lesion (5 mm or greater) found by **MRI** (magnetic resonance imaging)<br>3. Myeloma-related organ dysfunction (1 or more of the following **CRAB** criteria):<br>• [C] Elevated serum (blood) **CALCIUM**<br>• [R] **RENAL** insufficiency (reduced kidney function)<br>• [A] **ANEMIA** (low hemoglobin)<br>• [B] Lytic **BONE** lesions or osteoporosis (one or more lesions on skeletal survey [full-body X-ray], computerized axial tomography [CAT or CT scan] or positron emission tomography [PET scan]) |
During the early stages of myeloma, there may be no symptoms. Most people first go to their doctor because of vague symptoms that can be difficult to diagnose, such as fatigue, recurrent infections or back pain.

Common symptoms of myeloma can include any of the following:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Why It Occurs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain in the lower back, ribs or sternum</td>
<td>Osteolytic lesions (lytic bone lesions) weaken the bone, resulting in tiny fractures or the collapse of a vertebra in the spine. About 70% of myeloma patients seek medical attention because of pain related to bone lesions.</td>
</tr>
<tr>
<td>Fatigue</td>
<td>The increased number of myeloma cells can decrease the production of red blood cells in the bone marrow, leading to anemia.</td>
</tr>
<tr>
<td>Recurrent infections</td>
<td>Due to crowding in the bone marrow, the production of a variety of infection-fighting white blood cells is reduced. The immune system is therefore unable to fight off infections and illnesses.</td>
</tr>
<tr>
<td>Tiredness accompanied by other symptoms such as thirst, frequent urination, nausea or muscle weakness</td>
<td>The breakdown of bone releases excess amounts of calcium into the blood (hypercalcemia). Hypercalcemia can result in a number of symptoms, such as loss of appetite, fatigue, muscle weakness, restlessness, difficulty in thinking, confusion, constipation, increased thirst, increased urine production, and nausea and vomiting.</td>
</tr>
<tr>
<td>Kidney problems</td>
<td>Excessive protein in the blood (which is filtered through the kidneys), excessive light chains in the urine or high levels of calcium in the blood can cause kidney damage.</td>
</tr>
</tbody>
</table>
How Myeloma is Diagnosed

Diagnostic or prognostic, lab tests for myeloma involve testing the blood, urine and bone. The condition is diagnosed through (diagnostic) lab tests that help:

- Establish whether monoclonal protein (M-protein) is present in the blood or urine.
- Confirm the presence of abnormal numbers of cancerous (malignant) plasma cells in the bone marrow.
- Determine whether or not there is organ damage as a result of the myeloma (for example, bone damage or kidney dysfunction)

Prognostic lab tests help determine the best course of treatment by:

- Determining tumour burden (severity of the disease)
- Suggesting how aggressive the cancer is

Some prognostic tests can even characterize genetic abnormalities of the cancerous (malignant) plasma cell.

During treatment, there is no “one schedule fits all” for testing – everyone’s condition is assessed individually. Some may undergo testing on a weekly or monthly basis, or as deemed necessary by your doctor depending on:

- The specific treatment regimen
- The symptoms being experienced
- How rapidly the myeloma is progressing/advancing

Blood Tests

A complete blood count (CBC) measures the number of white and red blood cells in your blood as well as the number of platelets. When studying the results of a CBC, your doctor will look for decreased levels of:

- Hemoglobin (an indication of anemia)
- Platelets (referred to as thrombocytopenia)
- White blood cells that causes the immune system to weaken (referred to as granulocytopenia)

Although values can vary, normal CBC results are summarized in the following table. Values that are significantly outside of the normal range will raise questions and may lead to other tests.

To find out more about your blood, please read the Myeloma Canada InfoGuide, *Understanding Your Blood and Blood Tests*. 
<table>
<thead>
<tr>
<th>Count</th>
<th>Definition</th>
<th>SI Units*</th>
<th>Traditional Units*</th>
</tr>
</thead>
</table>
| **Erythrocytes** (red blood cells, RBCs) | Red blood cells or erythrocytes transport oxygen and carbon dioxide between the lungs and all the tissues of the body. Circulating erythrocytes act as small containers for holding hemoglobin. Low numbers of red blood cells or low hemoglobin or hematocrit is called anemia, which can cause physical and mental fatigue. | **F:** 4.2 – 5.4 x 10^{12}/L  
**M:** 4.6 – 6.2 x 10^{12}/L | **F:** 4.2 – 5.4 million/mm³  
**M:** 4.6 – 6.2 million/mm³ |
| **Hemoglobin** (Hb or Hgb) | Hemoglobin is an iron-containing protein in red blood cells that binds oxygen and carbon dioxide. | **F:** 120 - 160 g/L  
**M:** 140 - 180 g/L | **F:** 12.0 – 16.0 g/dL  
**M:** 14.0 – 18.0 g/dL |
| **Hematocrit** (HCT) | Measures of the proportion of the blood volume that is occupied by red blood cells. | **F:** 0.37 – 0.47  
**M:** 0.40 – 0.54 | **F:** 37 – 47%  
**M:** 40 – 54% |
| **Leukocytes** (white blood cells, WBCs) | White blood cells or leukocytes are cells of the immune system that defend the body against both infectious disease and foreign materials. A low number of white cells can increase the possibility of infection. Neutrophils defend against bacterial infection and other very small inflammatory processes and are usually first responders to bacterial infection. Lymphocytes are responsible for immune responses. There are two main types of lymphocytes: B cells and T cells. Monocytes are large white blood cells that ingest microbes or other cells and foreign particles. **Basophils** are involved in immediate hypersensitivity reactions, such as allergic reactions or wasp stings, and are also involved in some delayed hypersensitivity reactions. Eosinophils are responsible for combatting infection by parasites; they also control mechanisms associated with allergy and asthma. | **Total WBC:**  
3.5 – 12.0 x 10⁹/L  
Neutrophils: 3,000 – 5,800 x 10⁶/L  
Lymphocytes: 1,500 – 3,000 x 10⁶/L  
Monocytes: 300 – 500 x 10⁶/L  
Basophils: 50 – 250 x 10⁶/L  
Eosinophils: 15 – 50 x 10⁶/L | **Total WBC:**  
3,500 – 12,000/mm³  
Neutrophils: 3,000 – 5,800/mm³  
Lymphocytes: 1,500 – 3,000/mm³  
Monocytes: 300 – 500/mm³  
Basophils: 50 – 250/mm³  
Eosinophils: 15 – 50/mm³ |
| **Platelets** | Platelets (or thrombocytes) are involved in the formation of blood clots. Low levels of platelets can cause bleeding problems, while high levels may increase the risk of clotting (thrombosis). | 150 – 400 x 10⁹/L | 150,000 – 400,000/mm³ |

*Please note that normal values may vary from lab to lab. The ranges are for reference only.*
A blood chemistry panel will also be conducted. These tests look for indications of:

- Increased levels of total protein in the blood
- Poor kidney function (renal dysfunction). Indicators include:
  - Abnormal blood urea
  - Increased creatinine
  - Decreased albumin
  - An elevated level of lactate dehydrogenase (LD or LDH)

- More bone breakdown than normal. Indicators are:
  - Hypercalcemia - an elevated calcium level in the blood that occurs when calcium is released from the bone
  - In some cases, there may be elevated levels of alkaline phosphatase (ALP); in other cases, lytic lesions can occur without any increase in ALP levels

Other tests that may be performed include measuring the level of:

- **Beta-2 microglobulin (β2-M)**, an indicator to help evaluate the severity and prognosis of the myeloma
- C-reactive protein (CRP), an indicator for interleukin-6 (IL-6), a growth factor for myeloma cells

Once the diagnosis of myeloma is made, even more specialized blood tests may be ordered to confirm the diagnosis and determine what type of myeloma you have.

- Serum protein electrophoresis (SPE or SPEP) gives a picture of the level of various proteins in the blood. SPE shows if there is a monoclonal peak or abnormal level of a particular immunoglobulin, as well as kappa (κ) and lambda (λ) free light chains.

- Urine protein electrophoresis (UPE or UPEP) checks for the presence of monoclonal protein (M-protein) or paraprotein in the urine.

- Immunofixation is a specialized type of electrophoresis that can identify the type of monoclonal paraprotein that makes up the M-spike seen by SPE. This immuno-electrophoresis test can be done on the blood (serum) or the urine.

- A quantitative immunoglobulin (QIG) test measures the levels of different types of immunoglobulins or antibodies in the blood (IgG, IgA and IgM).

- Serum free light chain assays (Freelite®) can be used to measure the level of free light chains in the blood (M-protein). The International Myeloma Working Group recommends that this test be used for screening at diagnosis in combination with serum immunoelectrophoresis and SPE. **Baseline** values of the serum free light chain ratio can be helpful in developing a prognosis for monoclonal gammopathy of undetermined significance (MGUS) and asymptomatic (smouldering or indolent) and symptomatic (active) myeloma, as well as solitary plasmacytoma tumour in the bone and amyloidosis. It may also be used to assess response to treatment, particularly for those with nonsecretory myeloma or amyloidosis.
Urine Tests (Urinalysis)

When myeloma is suspected, urine tests may be ordered. Urine tests can be used to:

- Measure the amount of M-protein in the urine
- Look for free light chains (kappa [κ] or lambda [λ])
- Test for creatinine, a waste product excreted by the kidneys
- Look for bilirubin, a breakdown product of hemoglobin

A 24-hour urine test may be conducted to measure the amount of protein in the urine over one day. Urine protein electrophoresis (UPE or UPEP) may be done to look for free light chains in the urine and to assess kidney function. If they are present, your doctor may follow up with urine immunofixation or blood tests.

These tests can help to determine what stage of disease you are in and how the disease is responding to treatment.

Bone Tests

Samples of the bone marrow may be taken to check the number of plasma cells. There are two bone marrow sampling techniques. In both cases, samples are usually taken from the hip bone (aspiration only).

- **Bone marrow aspiration** — a needle with a syringe attached is used to draw a sample of liquid bone marrow. As well as examining the sample under a microscope, the cytogenetics (genetics) of the plasma cells can be studied.
- **Bone marrow biopsy** — a biopsy needle is inserted into the bone and rotated to force a tiny sample of solid bone tissue into the needle. A biopsy is usually performed when you are first diagnosed and may not need to be repeated.

A variety of imaging techniques can be used to look for bone damage from myeloma or monitor the course of bone damage.

- X-rays can be used to check for changes in the bone structure and to determine if there are weak spots (osteolytic or lytic lesions). A skeletal survey (full-body X-ray) consists of a series of X-rays of the skull, spine, arms, ribs, pelvis and legs. Although X-ray is a tried and true technology, it does have some limitations. For example, some areas may be difficult to visualize and it has been estimated that 10-20% of lesions or abnormalities may be missed. It is not optimal for showing response to treatment.
- Computerized tomography (CT) scans can detect small osteolytic lesions and is faster than a standard bone survey. The major drawback to CT scanning is that the dose of radiation can be between 1.3 and 3 times higher than that delivered during standard X-rays.
- Magnetic resonance imaging (MRI) provides very detailed and accurate pictures. It is capable of showing myeloma cell infiltration before bone destruction becomes visible on X-rays, as well as amyloid/light chain deposits in the heart and other sites. As a result, some advanced centres may use MRI to assess disease status in MGUS, asymptomatic myeloma and solitary bone plasmacytoma or to monitor response to treatment. However, not all centres can provide ready access to MRI.
- Nuclear medicine imaging techniques such as positron emission tomography (PET scanning).
- Not all techniques are available at all centres and each has its strengths and limitations. Talk to your healthcare team about all of the imaging options available to you.
Cytogenetics is the study of the structure of chromosomes (the ribbons of DNA that make up our genes). It is used to identify errors such as translocation (a part of a chromosome has broken off and attached to another chromosome) or deletion (when a chromosome is missing). The two techniques most commonly used in the cytogenetics of myeloma are karyotyping and fluorescence in situ hybridization (FISH).

- **Karyotyping** – a means of looking at the chromosomes of an individual cell arranged in pairs and sorted by size. This test can detect large genetic changes, such as the existence of an extra chromosome.

- **FISH** – a powerful molecular technique that uses a fluorescent-labelled probe to determine the presence or absence of a particular segment of DNA. It can detect small changes, such as the translocation or rearrangement of chromosome segments. FISH can be conducted by using either a sample of blood or bone marrow.

Genome sequencing is a powerful scientific tool that can be used to better understand the mechanisms underlying the development of myeloma. In genome sequencing, the makeup of a patient’s genetic information can be determined. By comparing the genomic sequence of a healthy cell to the sequence of a cancerous (malignant) cell, different mutations can be identified and studied.
In Chapter 3 (Diagnosing Myeloma), we discussed how some tests are considered “prognostic”. Prognostic tests are not conducted in order to tell you whether or not you have active myeloma, but to learn more about the disease and how advanced it is (known as its “stage”). Prognostic testing will help to determine the appropriate level of care for you.

There are two main systems used to “stage” active myeloma: the revised International Staging System (R-ISS) and the Durie-Salmon staging system.

R-ISS is based on the following measurements:

- **Beta-2 microglobulin (\(\beta_2M\))** — \(\beta_2M\) is a protein that is normally found on the surface of cells. A higher-than-normal level of this protein indicates inflammation somewhere in the body. It may also indicate some types of white blood cell (lymphocyte) disorders. A normal level of \(\beta_2M\) in the blood is usually less than 2.5 \(\mu\text{g/mL}\), **depending on the laboratory**.

- **Albumin** — The most common protein in the blood is albumin. The normal range for albumin is 35-50 g/L. Lower levels may be an indicator of kidney dysfunction.

- **Chromosomal abnormality** — Chromosomal abnormalities can be detected by using a test called **fluorescent in situ hybridization (FISH)** on a sample of purified plasma cells. Certain chromosomal abnormalities are called “high risk” because they are associated with more aggressive or harder to treat myeloma. Such abnormalities include del(17p) (a deletion of the short arm of chromosome 17) and/or t(4;14) (translocation of chromosomes 4 and 14) and/or t(14;16) (translocation of chromosomes 14 and 16).

- **Serum lactate dehydrogenase** — Lactate dehydrogenase (LD or LDH) is an **enzyme** found in almost all cells. High levels of LDH are an indicator that cells have been damaged or destroyed. A blood test showing LDH levels above the upper limit of normal is has been associated with a poorer outlook for some forms of cancer.
The Durie-Salmon staging system requires a number of other blood tests:

- **Hemoglobin (Hb or Hgb)** — A protein in red blood cells that carries and releases oxygen. Normal hemoglobin levels are 120-160 g/L for adult women and 140-180 g/L for men. Abnormally low values may indicate anemia.

- **Serum calcium** — Although calcium is an important electrolyte in the body, too much calcium in the blood can be an indicator of bone disease. The normal value range may vary slightly among different laboratories but is usually 2.10-2.50 mmol/L.

- **Serum monoclonal protein** — This refers to the level of individual M-protein, such as IgG, IgA, etc., or free light chains (kappa [κ] or lambda [λ]).

- **Serum creatinine** — Creatinine is a byproduct produced when creatinine phosphate is broken down, an important part of muscle. If kidney function is abnormal, blood creatinine levels may be elevated. Because they typically have more muscle mass, men usually have higher creatinine levels than women. A normal creatinine value is usually 50-110 μmol/L.
### Staging Systems for Symptomatic Myeloma
The following table summarizes the R-ISS and Durie-Salmon systems.

<table>
<thead>
<tr>
<th>Stage</th>
<th>ISS Conditions</th>
<th>Durie-Salmon Conditions</th>
</tr>
</thead>
</table>
| I     | $\beta_2$ microglobulin is less than 3.5 $\mu$g/mL AND Albumin is equal to or greater than 35 g/L AND No high-risk chromosomal abnormalities AND Normal LDH level | **All** of the following must be present:  
  a. Hemoglobin is greater than or equal to 100 g/L  
  b. Normal serum calcium (less than 2.88 mmol/L)  
  c. Low levels of monoclonal protein:  
     - IgG less than 50 g/L  
     - IgA less than 30 g/L  
     - Urine light chain less than 4 g per 24 hours  
  d. No areas of bone damage on skeletal survey (full-body X-ray) or one solitary bone plasmacytoma (tumour in the bone) |
| II    | Includes all possible combinations of Stage I and Stage III | Fitting neither Stage I nor Stage III |
| III   | $\beta_2$ microglobulin is equal to or greater than 5.5 $\mu$g/mL AND Presence of high-risk chromosomal abnormalities OR High LDH level | One or more of the following abnormalities must be present:  
  a. Hemoglobin less than 85 g/L  
  b. Elevated serum calcium (greater than 2.88 mmol/L)  
  c. High levels of monoclonal protein:  
     - IgG greater than 70 g/L  
     - IgA greater than 50 g/L  
     - Urine light chain is greater than 12 g per 24 hours  
  d. Advanced lytic bone lesions on skeletal survey (full-body X-ray)  
  
  **Subclassification:**  
  a. Relatively normal renal function  
     (serum creatinine less than 180 $\mu$mol/L)  
  b. Abnormal renal function  
     (serum creatinine equal to or greater than 180 $\mu$mol/L) |
Other Factors

A number of factors can affect your prognosis. Some of the most commonly recognized factors are summarized in the following chart. In general, higher or abnormal test results indicate more active myeloma and possibly less likelihood of having a long response with treatment.

<table>
<thead>
<tr>
<th>Test</th>
<th>Significance</th>
</tr>
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<tbody>
<tr>
<td>$\beta_2$ microglobulin</td>
<td>The higher (greater than 3 $\mu$g/mL) the level the more advanced the stage</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>The lower (less than &gt; 35 g/L) the level the higher the stage</td>
</tr>
<tr>
<td>Lactate dehydrogenase (LD or LDH)</td>
<td>Increased with active disease</td>
</tr>
<tr>
<td>Abnormal chromosomes on bone marrow cytogenetics and FISH (FISH)</td>
<td>Several chromosome deletions or translocations can be associated with shorter duration of remission</td>
</tr>
</tbody>
</table>
How your myeloma is treated depends on a number of factors:

- Physical examination and diagnostic test (blood, urine, bone) results
- The stage (severity) of your disease
- Presence of prognostic indicators (eg, chromosome mutation and which type)
- Your age and general state of health
- Symptoms you are experiencing (eg, bone pain or fractures)
- Complications you are experiencing (eg, kidney disease, anemia or infections)
- Previous treatments and how your myeloma responded to them
- New treatments that are becoming available, such as those accessed through clinical trials

Each patient is assessed individually. What works for one patient may not work for someone else. Regardless of the treatment you are given, the goals of therapy are similar:

- Stop the production of abnormal (myeloma) plasma cells
- Strengthen bones and prevent fractures
- Increase hemoglobin count and reduce fatigue
- Reduce the risk of infections
- Promote your well-being and quality of life
Response to Treatment

When reading about myeloma – particularly myeloma research – you may hear terms such as “Complete Response” (CR) or “Partial Response” (PR). Different studies may use different definitions, so check the study for what it is using. The International Myeloma Working Group response categories are:

**sCR (Stringent Complete Response):** Complete Response (see description below) plus normal free light chain \( \kappa/\lambda \) ratio (\( \leq 4:1 \) or \( \geq 1:2 \) for \( \kappa \) and \( \lambda \) patients, respectively) and an absence of clonal cells in the bone marrow by immunohistochemistry.

**CR (Complete Response):** No detectable monoclonal protein (M-protein) in the serum and urine by immunofixation, disappearance of any soft tissue plasmacytomas (extramedullary tumours) and 5% or less of (cancerous) plasma cells in the bone marrow.

**VGPR (Very Good Partial Response):** Serum and urine M-protein detectable by immunofixation but not on electrophoresis or 90% or greater reduction in serum M-protein plus urine M-protein less than 100 mg per 24 hours.

**PR (Partial Response):** 50% or greater reduction in serum M-protein and a reduction in 24-hour urinary M-protein of 90% or more, or to less than 200 mg per 24 hours. If serum and urine M-protein are unmeasurable, PR is defined as a 50% or greater decrease in the difference between involved and uninvolved free light chains. If free light chains are unmeasurable, PR is defined as a 50% or greater reduction in (cancerous) bone marrow plasma cells, provided that the baseline percentage was 30% or more. If a soft tissue plasmacytoma (extramedullary tumour) was present at baseline, a 50% or greater reduction in its size is also required.

**MR (Minimal Response):** A reduction between 25-49% (inclusive) of serum M-protein and reduction in 24-hour urine M-protein by 50–89%. In addition to these criteria, if present at baseline, a reduction of 50% or greater in the size of the soft tissue plasmacytomas (extramedullary tumours) is also required.

**SD (Stable Disease):** Not meeting the criteria for CR, VGPR, PR, MR, or progressive disease. SD is not recommended for use as an indicator of response, as the stability of disease is best described by estimating the time-to-progression.

**PD (Progressive Disease):** Requires a 25% increase of one or more of the following:

- Serum M-protein (absolute increase of 0.5 g/dL or more; increase of 1 g/dL or more if the lowest M component was greater than 5 g/dL)
- Urine M-protein (absolute increase of 200 mg/24 hours or more)
- If serum and urine M-protein levels are unmeasurable, the difference between involved and uninvolved FLC levels (absolute increase greater than 10 mg/dL)
- If free light chains are unmeasurable, bone marrow plasma-cell percentage (absolute increase of 10% or greater)
- Development of a new lesion(s), increase of at least 50% in more than 1 lesion, or an increase of at least 50% in the longest diameter of a previous lesion greater than 1 cm in short axis
- If this is the only measure of disease, an increase of 50% or greater in circulating plasma cells (minimum of 200 cells per \( \mu L \))

Since relapse is common in myeloma, you and your healthcare team must think about the your immediate needs, as well as how to keep your future treatment options as open as possible.

Unfortunately, despite achieving a complete response, the vast majority of patients relapse because of the persistence of residual myeloma cells – so called minimal residual disease (MRD). MRD is the term used to describe the myeloma cells that remain in the bone marrow after treatment. They are present at such low levels that they cannot be detected by traditional blood or bone marrow testing.

MRD is potentially a very important measurement to determine exactly how well treatment has worked. However, more sensitive and standardized tests are needed before it can become a routine clinical measurement.
The Three Rs: Remission, Relapse and Refractory

**Remission:** Complete or partial disappearance of the signs and symptoms of myeloma.

**Relapse:** The reappearance of signs and symptoms of myeloma after a period of improvement.

**Refractory:** Myeloma that is unresponsive to a treatment.

Treatment for myeloma is increasingly being tailored to meet the needs of individual patients. It is important to discuss your specific treatment options with your healthcare provider.

At this point, the standard treatments for myeloma may include a combination of the following:

- **Observation**
- **Radiotherapy**
- Chemotherapy such as melphalan (Alkeran®) and cyclophosphamide (Cytoxan®)
- Corticosteroids such as dexamethasone (Decadron®) or prednisone, often in combination with chemotherapy medications
- **High-dose therapy and stem cell transplantation**
- Immunomodulatory agents (IMiDs®) such as thalidomide (Thalomid®), lenalidomide (Revlimid®) and pomalidomide (Pomalyst®)
- Proteasome inhibitors (PIs), such as bortezomib (Velcade®), carfilzomib (Kyprolis®) and ixazomib (Ninlaro®)
- **Monoclonal antibodies (MoAbs)** such as daratumumab (Darzalex®)

Treatments or drugs are commonly used in different combinations, such as lenalidomide and dexamethasone or melphalan and prednisone with bortezomib. A number of new and emerging treatment therapies are becoming available.

**Observation**

Sometimes, the best treatment is no treatment at all. If your myeloma is stable (that is to say, is not progressing or getting worse), a reasonable option may be to simply monitor your condition. Currently, there is no evidence that treatment is beneficial for people who have monoclonal gammopathy of undetermined significance (MGUS) or asymptomatic myeloma (smouldering or indolent myeloma).
First-line and Second-line Therapies

You may have heard these terms, but what do they mean? A first-line treatment is therapy that is used on people who have not had any previous treatment for their myeloma. If the myeloma does not respond (the disease is said to be refractory) or if it progresses after the first-line therapy has been completed (ie, there is a relapse), the subsequent therapy is referred to as second-line treatment.

Radiotherapy

High-energy radiation may be used to damage myeloma cells and prevent them from growing. Radiotherapy is typically used on specific parts of the body to treat bone pain and plasmacytomas (tumours in the bone or soft tissue), usually in combination with some form of chemotherapy.

Total body irradiation was used in the past in the preparation for high-dose therapy (chemotherapy) and stem cell transplantation (also known as bone marrow transplantation). Clinical trials have shown that radiotherapy does not improve outcomes in this setting and adds to side effects. It is usually not used in conjunction with autologous stem cell transplantation anymore.

Chemotherapy

The goal of chemotherapy is to reduce the number of plasma cells in the bone marrow and the M-protein they produce. Chemotherapy cannot “cure” myeloma but it may put the disease into remission (that is to say, stop it from progressing or getting worse). It must be tailored individually to each patient.

There are many forms and combinations of chemotherapy regimens. Some of the most common in Canada are:

<table>
<thead>
<tr>
<th>Agents</th>
<th>MP</th>
<th>CyBorD</th>
<th>CyBorP</th>
<th>CRd</th>
<th>VMP</th>
<th>MPT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemotherapy</strong></td>
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<tr>
<td>Cyclophosphamide (Cytoxan®)</td>
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<td>X</td>
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<tr>
<td>Melphalan (Alkeran®)</td>
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<tr>
<td><strong>Proteasome Inhibitor</strong></td>
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<tr>
<td>Bortezomib (Velcade®)</td>
<td>X</td>
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<tr>
<td><strong>Immunomodulatory Agents (IMiDs®)</strong></td>
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<tr>
<td>Thalidomide (Thalomid®)</td>
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<tr>
<td>Lenalidomide (Revlimid®)</td>
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<tr>
<td><strong>Corticosteroids (Steroids)</strong></td>
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<tr>
<td>Prednisone</td>
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<tr>
<td>Dexamethasone (Decadron®)</td>
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</table>
Central Lines

When you are receiving intravenous chemotherapy, you may be given a central line or catheter. You may hear it referred to as a Port-a-Cath®, PICC line or Hickman®. A central line is a long, hollow tube made from silicone rubber. It is inserted or tunneled under the skin of your chest and into a vein. The line can be left in for weeks or months and makes it possible for you to have your treatment without having to have needles inserted at each visit. When it is time for your chemotherapy, the nurse or doctor connects the line to a syringe or intravenous drip. When you no longer need chemotherapy, the line may be removed.

Corticosteroids

Corticosteroids (or steroids) are chemicals naturally produced by the adrenal gland to help prevent inflammation. The synthetic or man-made steroids most commonly used to treat myeloma are prednisone and dexamethasone. Steroids can be used alone or in combination with other drugs.
High-Dose Therapy and Stem Cell Transplantation

Stem cells are a class of cells that are able to divide and develop into specialized cell types. They are normally found in the bone marrow and in the blood and can be used to “repopulate” the bone marrow after a high-dose therapy treatment. There are several types of stem cell transplantation approaches that may be used to treat myeloma.

Autologous stem cell transplantation (ASCT) is the most common. It is referred to as an “autograft” because it uses your own stem cells. Stem cells can be obtained from blood (a peripheral blood stem cell or PBSCT) or bone marrow.

To prepare for the ASCT, the number of myeloma cells in your body needs to be reduced. This is done with induction therapy, most often using a bortezomib (Velcade®)-based combination such as CyBorD (cyclophosphamide, bortezomib and dexamethasone).

If the stem cells are being harvested from peripheral blood, drugs are used to “coax” or mobilize them out of the bone marrow and into the blood. By using a medication called a granulocyte-colony stimulating factor (G-CSF) (eg, Neupogen®) with or without chemotherapy, the bone marrow is stimulated to increase the number of stem cells in the blood. A process called pheresis is then used to collect the stem cells from the blood.

Prior to collection, be sure to talk to your physician about the number of stem cells that will be collected. By ensuring that enough stem cells are harvested and frozen to support two or more transplants, you can increase your treatment options for the future.

In situations where there is difficulty in collecting the required number of stem cells, another drug called plerixafor (Mozobil®) can be added to improve the release of stem cells.

After the collection of stem cells, SCT consists of the following steps:

1. The stem cells are frozen and stored until it is time for them to be reinfused following high-dose therapy.
2. You then undergo a conditioning regimen of high-dose therapy with melphalan (Alkeran®). This regimen will destroy the cancer cells in the bone marrow. In the process, it will also destroy the blood-producing cells in your bone marrow.
3. Shortly after completing the high-dose therapy, the stored stem cells are thawed and infused back into you. In time, the transplanted stem cells begin to produce new blood cells. You may or may not stay in the hospital following your transplant.

All treatments have both their risks and benefits. However, studies have shown that on average, people who undergo autologous SCT live longer than those who receive standard chemotherapy alone.
- **Allogeneic SCT** involves collecting stem cells from someone else, usually a brother or sister. The donor’s cells must match the recipient’s tissue type – note that this is different from blood type and requires special blood testing. The transplanted donor stem cells may also help attack any myeloma cells remaining in the patient’s bone marrow. This is referred to as the graft-versus-myeloma effect.

  Few patients are good candidates for allogeneic SCT. It is difficult to find good donor matches and the procedure has a greater risk of complications, including infections, graft-versus-host disease (GVHD, a potentially life-threatening condition in which the donor’s bone marrow attacks and destroys the patient’s own tissue) and death. For these reasons, allogeneic transplant is not a standard therapy for myeloma.

- A **syngeneic SCT** refers to a transplant using stem cells taken from an identical twin. The prognosis for syngeneic transplants is better than that of allogeneic transplants; however, this is an option for only a small number of patients.

- A **matched unrelated donor (MUD) SCT** refers to a transplant using stem cells taken from a donor who is not a relative but has the same tissue type.

- **Tandem (double) ASCTs** are performed in some centres. For a tandem transplant, the plan is to conduct a second transplant within six months of the first one. This approach may be beneficial for people who do not have a full response to the first transplant or who have “high risk” disease, as indicated by age or cytogenetics.

- An experimental approach is **ASCT followed by an allogeneic SCT**. With this approach, a patient first undergoes high-dose therapy to reduce the overall number of myeloma cells, followed by an autologous transplant. Next there is a second course of moderately high-dose therapy and an allogeneic transplant of donor stem cells. The second course of therapy – in combination with the help of the allogeneic transplant – should reduce the number of myeloma cells.

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**Maintenance and Consolidation Therapy**

Maintenance therapy is a prolonged, and often low-dose, form of treatment given to myeloma patients after their initial therapy. The goal of maintenance therapy is to prevent disease progression for as long as possible while maintaining a favourable quality of life.

Data from clinical trials suggest that maintenance therapy following high-dose therapy and stem cell transplant delays time to disease progression and improves overall survival.

Consolidation therapy is different from maintenance therapy since it usually involves a shorter course of treatment with the goal of deepening patients’ responses to the initial therapy. Clinical trials have demonstrated that some patients had a longer median progression-free survival than those who did not receive consolidation therapy after transplantation.
Is There an Age Cut-off for High-dose Therapy?

Many myeloma centres have a general rule that high-dose therapy is not routinely offered to people above a certain age, such as 65 or 70 years. These are not hard-and-fast rules. The important thing is not your chronological age but rather your biological age – how generally healthy you are. An otherwise healthy 72-year-old may be a good candidate for high-dose therapy, whereas a 66-year-old with multiple health problems may be a poor candidate.

Immunomodulatory Agents (IMiDs®)

Instead of destroying both myeloma and healthy cells (like chemotherapy drugs), IMiDs only attack myeloma cells and enhance the immune system cells that identify and fight cancerous (malignant) plasma cells. There are presently three IMiDs approved for the treatment of myeloma in Canada: thalidomide, lenalidomide and pomalidomide. Each of these drugs are taken orally.

- **Thalidomide (Thalomid®)**
  
  With the availability of newer IMiDs such as lenalidomide and pomalidomide, the use of thalidomide has decreased. In Canada, thalidomide is approved for use in combination with melphalan (Alkeran®) and prednisone (MPT) as a first-line treatment for patients who are not eligible for high-dose therapy and stem cell transplantation.

- **Lenalidomide (Revlimid®)**
  
  Lenalidomide is more potent and has a different side effect profile from thalidomide. Lenalidomide has multiple mechanisms of action that affect both the cancer cell and its microenvironment.

  Lenalidomide can be used as a:

  - First-line treatment in combination with dexamethasone for newly diagnosed patients that are not eligible for high-dose therapy (stem cell transplantation)
  
  - Second-line treatment in combination with low-dose dexamethasone (Rd) as a treatment for patients who have received at least one prior therapy

  Clinical trials have shown that lenalidomide taken continuously as a single agent is beneficial as a maintenance treatment following high-dose therapy and stem cell transplantation.

- **Pomalidomide (Pomalyst®)**

  Pomalidomide is a third-generation IMiD that is used in combination with dexamethasone for patients for whom both lenalidomide and bortezomib have failed and have received at least two prior treatment regimens and have demonstrated disease progression on their last treatment.
Proteasome Inhibitors (PIs)

Proteasome inhibitors are targeted drugs that block the activity of the proteasome, a substance in myeloma cells that breaks down protein. Blocking the proteasome causes myeloma cells to die.

In Canada, there are three PIs approved for use in myeloma: bortezomib, carfilzomib and ixazomib.

- **Bortezomib (Velcade®)**

  Bortezomib can be used as a first-line treatment for previously untreated myeloma patients who are not eligible for high-dose therapy and stem cell transplantation as part of a medically-recognized combination therapy such as CyBorD (cyclophosphamide, bortezomib and dexamethasone) or VMP (bortezomib, melphalan and prednisone).

  For previously untreated myeloma patients who are candidates for high-dose therapy and stem cell transplantation, bortezomib can used as part of a medically recognized combination therapy (e.g., in combination with cyclophosphamide and dexamethasone) for four to six cycles as an induction therapy.

  Patients who have relapsed after their first treatment may also be given bortezomib either alone or with other medications such as cyclophosphamide and dexamethasone.

  Bortezomib may be given intravenously or subcutaneously (under the skin), once or twice a week depending on the treatment schedule.

- **Carfilzomib (Kyprolis®)**

  Carfilzomib is approved for the treatment of people with relapsed myeloma who have received one to three prior therapies. Carfilzomib is used in combination with lenalidomide (Revlimid®) and dexamethasone (KRd). It is given intravenously twice a week.

- **Ixazomib (Ninlaro®)**

  Ixazomib is the first oral proteasome inhibitor approved for the treatment of myeloma. It is taken in the form of a once-weekly oral dose in combination with lenalidomide (Revlimid®) and dexamethasone (IRd). Ixazomib provides a treatment option for patients who have relapsed or whose condition has been non-responsive to at least one form of myeloma treatment.
Monoclonal Antibodies (MoAbs)

Monoclonal antibodies enlist the natural immune system functions to fight cancer. They are designed to bind to protein that are generally more numerous on the surface of cancer cells than healthy cells, thereby providing a more “targeted” approach to killing myeloma cells. In Canada, one monoclonal antibody has been approved for the treatment of myeloma: daratumumab.

- Daratumumab (Darzalex®)

Daratumumab targets a protein on the surface of myeloma cells known as CD-38 and works in multiple ways to kill the myeloma cells. It has been approved for the treatment of myeloma:

- In combination with lenalidomide (Revlimid®) and dexamethasone, or bortezomib (Velcade®) and dexamethasone, for those who have received at least one prior therapy
- As monotherapy (alone) for those who have received at least three previous types of therapy, including a proteasome inhibitor and an immunomodulatory agent or a combination of the two

New and Emerging Therapies

A number of new therapies are in development. At the time this Handbook was printed, among the new promising therapies being evaluated were a new proteasome inhibitor (oprozomib), an anti-CD38 monoclonal antibody (isatuximab), an XP01 inhibitor (selinexor), a histone deacetylase (HDAC) inhibitor (panobinostat or Farydak®), a programmed cell death (PD) protein 1 inhibitor (pembrolizumab or Keytruda®), a PD-L1 inhibitor (durvalumab), a B cell lymphoma (BCL)-2 inhibitor (venetoclax or Venclexta™) and other immunotherapeutic approaches such as B cell maturation antigen (BCMA), the measles vaccine and oncolytic viruses.

One of the most exciting aspects of current research is the insights that are being made into the genetics of the disease. In the future, knowing more about the genetics of myeloma will make it possible to more closely individualize and tailor treatment.

Another exciting area of research is the measurement of minimal residual disease (MRD) using very sensitive and sophisticated techniques to identify trace amounts of myeloma cells that remain after treatment. MRD will be an important tool in identifying possible curative approaches to treatment.

For more information about new and emerging therapies, please refer to the Myeloma Canada website (www.myeloma.ca), the Myeloma Matrix on the International Myeloma Foundation (IMF) website (www.myeloma.org), Cancer View Canada (www.canadiancancertrials.ca) and the US National Institutes of Health (www.clinicaltrials.gov).
The build-up of abnormal (myeloma) plasma cells in the bone marrow can cause a number of medical problems. It is important that such problems be identified, monitored and treated.

**Bone Complications**

Healthy bones are continually breaking down (referred to as resorption) so new bone can be laid down. There are two types of cells that are important for bone:

- **Osteoclasts** — Cells that break down old bone. If you are replacing the roof on your house, one of the first things you should do is tear off the old roof. Osteoclasts breaks down old bone so there is room for new bone.

- **Osteoblasts** — Cells that form new bone. These are the cells that follow osteoclasts and strengthen the bone by laying down fresh, new bone.

Myeloma cells send signals that speed up the bone breakdown activity of osteoclasts and also prevent osteoblasts from making new bone. This vicious cycle of bone loss can lead to:

- Areas of damage or “holes” in the bone, known as osteolytic or lytic lesions

- Progressive bone thinning, called osteoporosis

To learn more about bone complications, read the Myeloma Canada InfoGuide, *Myeloma Bone Disease*. 
When bone thins or there are lytic lesions:

- You are at increased risk of fractures. Sometimes, even everyday activities can cause bones to break. Myeloma patients with bone disease can experience fractures in the ribs or compression fractures of the vertebrae in the spine, which in turn can cause nerve damage and pain.

- You may experience bone pain. The majority of myeloma patients experience bone pain at some point. Words commonly used to describe bone pain in myeloma include “constant”, “aching”, “deep” and “sharp”. The pain is often localized and gets worse when you move or shift positions.

What is done for bone disease in myeloma?

- Skeletal survey (full-body X-ray) and bone density tests (a form of special X-ray) are used to monitor bone loss and to check for specific areas of damage.

- People with myeloma are routinely prescribed **bisphosphonate** drugs that strengthen the bone, such as clodronate (Bonefos®), pamidronate (Aredia®) or zoledronic acid (Zometa®).

- Radiotherapy (radiation therapy) can be used to treat specific lytic bone lesions and help relieve pain. Extensive radiation of the spine or the long bones should be avoided, as it can lead to prolonged suppression of the bone marrow.

- Fractures of the vertebrae in the spine have traditionally been treated by vertebroplasty, a procedure that consists of injecting bone cement into the affected vertebrae to stabilize it. A newer alternative is kyphoplasty. In kyphoplasty, a balloon is inserted into the compressed vertebra and inflated to raise the collapsed section. The cavity is then filled with a bone cement, stabilizing the vertebrae and preserving the reestablished height.

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**Is Exercise Safe?**

Unless there are reasons why you cannot exercise, mild to moderate exercise such as walking or swimming may be physically and emotionally beneficial. It is important to avoid contact sports or activities that could result in falls. Talk to a physical therapist or your healthcare team about activities that would be suitable for you.
Anemia

With abnormal (myeloma) plasma cells crowding the bone marrow, myeloma can result in a reduced red blood cell count. Red blood cells are important because they contain hemoglobin. Hemoglobin carries oxygen from the lungs to the cells of your body, giving you energy and stamina. If hemoglobin is less than 120 g/L in a woman or less than 140 g/L in a man, it is called anemia. Whether anemia requires treatment will depend on its level, how quickly the level is changing, and how well you are feeling and functioning.

Symptoms of anemia include:

- Feeling very tired even though you are getting enough rest
- Looking pale
- Shortness of breath after even mild exertion
- Difficulty with daily chores, concentration or remembering things
- Feeling lightheaded or dizzy

Different people react differently to having a low hemoglobin count. Some people also report headaches, leg pains or feeling cold.

Why treat anemia? Studies have shown that in people with cancer, treating anemia can help relieve fatigue, make it easier to perform everyday activities, reduce the need for blood transfusions, improve quality of daily life and increase their likelihood of completing cancer therapy.

There are a number of treatment options for anemia, and it is important to discuss all of them with your healthcare team.

- If your anemia is due to a change in your diet, eating healthier or taking iron, vitamin B12 or folic acid (folate) supplements may help. **Always check with your doctor or pharmacist before taking any non-prescription, over-the-counter iron or vitamin supplement, or any herbal remedy.** Some supplements or remedies can interact with prescription medications.
Blood transfusions can be used to treat severe anemia and can quickly increase hemoglobin levels on a short-term basis.

Medication that stimulates the body into making more red blood cells can be prescribed. Epoetin alfa (Eprex®) and darbepoetin alfa (Aranesp®) contain versions of the human hormone erythropoietin, which tells the bone marrow to make more red blood cells. Both drugs are given by subcutaneous injection (an injection just under the skin).

**Infections**

Myeloma and some of its treatments can affect the normal production of antibodies and reduce white blood cell counts. This can leave a person susceptible to repeated infections or illness, especially respiratory infections, or take a long time to recover from them.

Many infections cannot be prevented, so it is important that they be treated as soon as they develop. Fever or other signs of infection or disease should be reported promptly to your healthcare team. Antibiotics may be required.

It is important to have a complete dental examination before you begin any treatment. Because of the increased risk of infection, myeloma patients may require antibiotics before dental work.

**Reduce Your Risk**

To reduce the risk of infections and illnesses, remember to practice good hand-washing techniques. When in public places, wash your hands frequently or use a hand sanitizer (the small containers can easily fit into your pocket or purse). Avoid situations where you may come into contact with people who are ill.
**Kidney Damage**

M-protein produced by myeloma cells are cleared from the body in the kidneys. Over time, the elevated levels of abnormal M-protein in the blood and urine can damage the kidneys. This is why renal function is assessed regularly by creatinine testing of the blood.

The best way of preventing kidney damage (renal disease) is to treat the myeloma and keep M-protein levels as low as possible. Sometimes – but infrequently – if the renal dysfunction is severe, **dialysis** may be required.

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**Drink Up!**

Drinking lots of fluids can help to flush medications and toxins from your body, maintain normal blood volume and pressure, lubricate the joints, limit fatigue and help prevent kidney damage. The best single fluid to drink is water. Unless you are advised otherwise by your healthcare team, try to gradually increase your intake until you are drinking 6-8 glasses of water every day.

Try to limit drinks that contain caffeine, such as coffee, tea and soft drinks. Caffeine and alcohol increase your urine output and can lead to dehydration and fatigue.

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**High Blood Calcium**

Your bones are constantly being broken down and rebuilt. When old or damaged bone is broken down, the calcium in the bone is released into the bloodstream. Myeloma commonly causes excess bone breakdown and this can cause high levels of calcium in the blood (hypercalcemia). Symptoms can include constipation, increased frequency of urination, weakness and in extreme cases, confusion.

Hypercalcemia is treatable with bisphosphonates, drugs that help prevent bone breakdown that are used in the treatment of myeloma bone disease. With bisphosphonates, less calcium is released from the bones and hypercalcemia may be prevented or resolved.

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**Hold Off Taking Calcium Supplements**

In people without myeloma, calcium supplements are often recommended for bone health. But if you have myeloma, never take a calcium supplement without checking with your doctor. Too much calcium in the blood can be unhealthy.
Other Blood Complications

Myeloma can result in other complications of the blood, although most are relatively rare. If the number of platelets in the blood drops below a healthy level, normal clotting will be affected. This can lead to bruising or excessive bleeding.

When combined with steroids, some medications, such as thalidomide (Thalomid®) and lenalidomide (Revlimid®) can also increase the risk of blood clots in the veins, such as those in the legs. Known as deep vein thrombosis (DVT), this can be a potentially dangerous complication. Blood-thinning medications can be prescribed to reduce this risk.

In a small number of people, a high M-protein level can cause the blood to thicken (known as hyperviscosity). If this occurs, blood flow to the skin, fingers, toes, nose, kidneys or brain can be affected.

Bone Pain, Nerve Pain and Neuropathy

There are three main causes of pain for myeloma patients:

- Bone pain
- Nerve damage, often due to compression fractures
- Peripheral neuropathy

The treatment you require depends on the cause of the pain, its severity, and how you respond to different therapies. Other treatments may be helpful. For example, bone pain may be relieved by radiation (radiotherapy) or bisphosphonates, and nerve damage due to compression fractures by vertebroplasty or kyphoplasty.

Painkillers come in a variety of forms – tablets, injections and patches that allow medication to be absorbed through the skin. Although non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (Motrin® or Advil®), naproxen (Naprosyn® or Aleve®) and diclofenac (Voltaren®) are common and effective painkillers, people with myeloma should avoid them, particularly if they have kidney damage.

There are several categories of painkillers that can help with your pain:

- Painkillers for mild pain, such as over-the-counter medications like acetaminophen (Tylenol®)
- Prescription medications such as COX II inhibitors (Celebrex®)
- Various opioids (narcotics) can be prescribed, depending on the intensity of the pain
  - Opioids such as codeine, Percocet®/Percodan® and Oxycet®
  - Stronger opioids that come in either short-acting forms (meperidine or Demerol®), longer-acting forms (MS Contin®, Oxycontin®) or patches
  - Painkillers such as morphine and fentanyl (Duragesic®) for severe pain

You can work together with your doctor to find the right painkiller for you – no two people are alike, so it might take some trial and error. Your doctor will usually start you on a low-dose or milder painkiller and increase your dose or prescribe you another type of painkiller that controls your pain best and gives you the least number of side effects. You may find that you get the most relief from a combination of painkillers. If your usual combination of painkillers becomes less effective, contact your doctor or nurse.
It may take some time to find the right treatment for your pain. Extreme cases may require treatment by a pain specialist.

Peripheral neuropathy appears to be a side-effect of certain drugs used to treat myeloma, such as thalidomide (Thalomid®), bortezomib (Velcade®) and vincristine (Oncovin®). It usually occurs in the feet, legs, hands or arms and is very different from bone pain. Characteristics of neuropathic pain include:

- Painful sensitivity to touch (known as allodynia)
- Sensation of “electric jolts” or that the pain travels
- A burning, tight or pulling sensation
- Numbness or a “pins and needles” feeling
- Weakness or loss of reflexes

These sensations may come on spontaneously without movement or get worse at night. Symptoms such as weakness or loss of function may occur with or without pain.

Drug-induced neuropathy must be treated differently from bone pain or nerve damage resulting from spinal compression. First, in some cases it can be reversed by changing the frequency or dose of the drug that is causing the neuropathy. Sometimes, it may be necessary to stop the treatment. Second, the types of medication used for neuropathic pain are different and may include:

- Medications such as gabapentin (Neurontin®) or pregabalin (Lyrica®)
- Tricyclic antidepressants such as amitriptyline (Elavil®), nortriptyline (Aventyl®), imipramine (Tofranil®) or clomipramine (Anafranil®)
- Serotonin-norepinephrine reuptake inhibitors such as venlafaxine (Effexor®) or duloxetine (Cymbalta®)

If you’re prescribed any of these medications, be sure to talk to your doctor and pharmacist about how to take them and what side effects can occur.

A number of unconventional and alternative approaches have been proposed for treating neuropathy, but to date there is no evidence that they are effective. Some patients have reported that acupuncture has provided some relief from the pain of neuropathy.
Osteonecrosis of the Jaw (ONJ)

Dental health is very important for myeloma patients. Encourage your dentist to talk to your oncologist to discuss any special precautions you may require, especially when receiving treatment. Check to see if your cancer centre has a dental clinic. Before starting any therapy, have a complete dental examination.

ONJ is a relatively rare side-effect of long-term bisphosphonate (eg, pamidronate or zoledronic acid) use that causes abnormal death (necrosis) of the jaw bone. A review of patients at one of Canada’s largest myeloma centres, the Princess Margaret Cancer Centre in Toronto, found that 2% of patients taking pamidronate developed ONJ. It can occur spontaneously but appears to be more likely following particularly traumatic dental work such as extractions. The risk of ONJ appears to be higher among those taking zoledronic acid (Zometa®), compared to pamidronate (Aredia®).

If you think you may take bisphosphonates in the future, be sure to have a complete dental examination and all corrective work completed. Once you start taking bisphosphonates, it is recommended that you:

- Practice good oral hygiene to reduce the odds of needing dental care
- Visit your dentist regularly to catch problems when they are small
- Avoid extractions and peridontal surgery if possible
- Do not have dental implants

Restorative work such as fillings, bridges, crowns and root canals are probably safe, provided that the wounds are as small as possible and all the rough edges are carefully smoothened.

To reduce the risk of ONJ, many cancer centres have changed the way they prescribe bisphosphonates by reducing their dose or by shortening the length of time that they are taken.
Medication Side Effects

All prescription medications have intended effects and others that you may not want, commonly known as side effects. Your healthcare team, particularly your pharmacist and nurse educator, can explain what side effects you can expect from the medications you are prescribed, which ones to report right away, and what can be done to relieve them.

Common side effects of chemotherapy are:

- **Nausea and vomiting** — Anti-nausea (anti-emetic) drugs can help to prevent and control nausea and vomiting. Avoiding strong smells and getting lots of fresh air may also help. Vomiting can dehydrate you, so it is important to try and keep taking sips of cool drinks.

- **Hair loss (alopecia)** is common with some – but not all – kinds of chemotherapy, such as melphalan (Alkeran®). If it occurs, remember that your hair will grow back once your treatment has finished.

- **Changes in the mouth** — Depending on the type of chemotherapy you are receiving, you may experience mouth sores, or a sore or dry mouth. Medicines or a special mouthwash can help to prevent or treat mouth ulcers. When undergoing high-dose therapy (eg, with melphalan), sucking on ice chips may help to prevent mouth sores. Keep your teeth clean by regularly using a soft toothbrush, and try to avoid things that might irritate your mouth, such as spicy, salty or tangy foods. If you have a sore or dry mouth, avoid foods that stick to the roof of your mouth (eg, peanut butter or chocolate) and mouthwashes that contain alcohol. Moisten your food with gravy or sauces and try drinking through a straw or sucking ice cubes or frozen treats.

- **Loss of appetite** — At times over the course of your treatment, you may have no appetite or feel you cannot face food. To avoid losing weight, try to eat small amounts of food – particularly fresh fruits and vegetables – frequently throughout the day. Or if you feel hungry at some parts of the day and not at others, eat your larger meal when you are hungry. No matter what you eat, be sure to always drink plenty of fluids.
Corticosteroids (steroids) such as dexamethasone are frequently used to treat myeloma. Side effects can include:

- Fluid retention and swelling, particularly if you also have congestive heart failure
- An increase in blood sugar, which is of concern to people with diabetes or at risk of diabetes
- Insomnia
- Increased appetite
- Indigestion or heartburn – speak to your physician about medication to prevent this problem
- Hiccups
- Blurred vision – it may be short-term (acute) or long-term if due to cataracts
- Mood or emotional changes, such as depression, mood swings, agitation, anxiety, or even psychosis

Other effects than can develop after long-term use of high-dose steroids include the Cushingoid appearance (weight gain with a “moon face”), osteoporosis or bone loss, and muscle weakness and/or wasting. Fatigue and depression are other potential side effects.

**Coping with “‘Roid Rage”**

Dealing with the diagnosis of cancer is hard – for you and your loved ones. The mood changes brought about by steroids can add to that burden. It is important that you talk to your loved ones and explain the effects steroids can have on your mood and activity levels. Give them a “heads up” when you will be going on and off your medication. Family members and friends can help by being supportive and understanding that sometimes “it’s the ‘roids talking”.
Depression

Some studies suggest that up to 40% of cancer patients experience depression or anxiety. As you deal with your disease, periods of feeling “blue” or “down” are not unusual. After all, you are going through a lot of changes. You may sometimes feel that you are no longer the person you used to be. Physical and mental changes may threaten your sense of self-worth and self-esteem.

If depression lasts for many weeks without relief or is severe enough that it interferes with everyday life, you may need some help. Talk about your feelings with your doctor, nurse or counsellor. Sometimes just talking with someone is enough to help. In other cases, medication can be prescribed to help relieve depression.

Speak to a healthcare professional if you experience five or more of the following symptoms for more than two weeks:

- Feeling sad, anxious, irritable, nervous and/or guilty
- Feelings of worthlessness or hopelessness
- Changes in your usual sleep patterns (either having trouble sleeping or sleeping more than normal)
- Changes in your appetite; gaining or losing weight without trying
- Loss of interest in activities you used to enjoy
- Restless or slowed behaviour
- Persistent or recurring headaches, digestive disorders, or chronic pain
- Difficulty concentrating, remembering or making decisions
- Fatigue, loss of energy
- Change in work style or productivity
- Thoughts of suicide – if these occur, seek immediate professional help
When you were diagnosed with myeloma, you may have felt like you were alone in the battle of your life. But in reality, there is a whole team of dedicated professionals who are behind you and ready to help you. They are the members of your healthcare team. In this section, we’ll begin by looking at the roles played by the different members of your team. Then we’ll discuss how you can optimize communication with your team members and become a more informed and active participant in your care.

**Family Doctor**

When you first became ill, the first person you probably saw was your family doctor. Your family doctor helped narrow down the possibilities of what might be wrong and provided referrals to specialists. Most family doctors see only a few, if any, myeloma patients in their practices.

**Oncologist**

A medical oncologist is a physician who specializes in the diagnosis and treatment of cancer. This doctor may be the key member of your healthcare team. He or she will determine your exact diagnosis and, in consultation with you and other specialists, design your treatment plan.

**Nurse Practitioner**

A nurse practitioner is a nurse who has undergone advanced training and has the authority, under specific circumstances, to diagnosis and treat patients. This can include prescribing certain medications. In some areas, for example, a primary care practice may be led by a nurse practitioner.
**Hematologist**

Because myeloma is a cancer of the blood, you may be referred to a hematologist. A hematologist is a physician who studies, diagnoses and treats diseases and disorders of the blood. Some hematologists specialize in blood cancers, whereas others may specialize in other blood problems such as clotting disorders. This doctor may be the key member of your healthcare team.

**Radiation Oncologist**

If you require radiotherapy, you will be referred to a radiation oncologist. As the name implies, a radiation oncologist is a physician who specializes in treating cancer with radiotherapy.

**Surgical Oncologist**

A surgical oncologist is a surgeon who specializes in cancer operations. For example, if a tumour must be removed, you may be referred to a surgical oncologist.

**Nurse**

Nurses may fill several important roles in your healthcare team. An oncology nurse is a specially-trained nurse who works closely with your medical oncologist, hematologist or radiation oncologist to coordinate your care, oversee your therapy and keep your physicians informed of any problems you may encounter. Other nurses may specialize as cancer educators. Nurses are invaluable sources of information and support.

**Orthopedic Surgeon**

If you require surgery on your bones, muscle or joints, you may be referred to an orthopedic surgeon.
**Pharmacist**

Your treatment for myeloma will involve many medications, some of which may be oral and others which may be delivered through an intravenous line. Whether working in the hospital or the community, pharmacists are valuable sources of information for patients and care providers. Pharmacists can help you to understand what different medications are designed to do, how to take them, what effects and side effects to expect, and what to do if side effects occur.

**Dentist**

Your dentist is an important but often overlooked member of your healthcare team. Good oral health is important at all times, and even more so when you are undergoing myeloma treatment. Infections from the teeth can drain into the lymph glands in the neck, and if your teeth and gums are not kept clean large quantities and varieties of bacteria can colonize the gums. These types of infections are an important and preventable source of problems.

If possible, it is best to identify and treat dental problems before you start chemotherapy, undergo stem cell transplant, or start taking bisphosphonates. Generally, the best time to be treated is when your hemoglobin count is 100 g/L or more, platelet count is 80 x 10⁹/L or more, and your neutrophil count is 2,000 x 10⁶/L or more. Special precautions such as prophylactic antibiotics are probably required if you have a central line or catheter in place.

Dentists who work at cancer centres are familiar with the special requirements of myeloma patients, but some community dentists may not be. Speak to your dentist and clearly outline what drugs you are taking (including intravenous therapies), where you are in your therapy and what the plans may be for the future. Encourage him or her to talk to a cancer centre specialist.
Registered Dietitian/Nutritionist

Cancer and cancer treatment can make eating difficult. You may find it difficult to eat enough – or to eat the right kinds of food – to keep your strength up. Or some medications can increase your appetite, making it difficult to avoid overeating. A dietitian can help you maintain the healthiest diet possible throughout the different stages of your treatment. If you are struggling with nausea, vomiting, anorexia (loss of appetite) or a dry or sore mouth, your dietitian can suggest foods or drinks to help.

Psychiatrist or Psychologist

A psychiatrist is a physician trained in the diagnosis and management of mental illness. A psychologist is not a physician, but someone who has advanced training in counselling and human psychology. Both psychiatrists and psychologists can be very helpful in dealing with the psychological, emotional or behavioural problems you may encounter. In addition to “talk therapy”, psychiatrists are licensed to prescribe medication, such as anti-depressants, if required.

Social Worker or Counsellor

Like a psychologist, a social worker or counsellor can help you deal with the many emotional changes being diagnosed with myeloma can bring. In addition, a social worker may be able to help you deal with some of the practical issues that arise, such as finding out more about your healthcare coverage.

Clergy or Spiritual Advisor

Some people find that talking with their clergy or spiritual advisor can be very helpful.
Optimizing Communication

As a patient, you have rights and responsibilities when interacting with the members of your healthcare team.

Rights:
- To be treated with respect and courtesy
- To be your own advocate or to bring an advocate with you
- To be kept fully informed and to have things explained to you in language you can understand
- To be informed of all possible treatment options available at your centre or other facilities, including clinical trials
- To be allowed, and even helped, to obtain a second opinion if you want one
- To be given the opportunity to participate in treatment decision-making, including the right to refuse any treatment you do not want
- When you ask, to receive copies of your records, such as lab results, X-rays, and test results, at a reasonable cost (e.g., for the cost of copying)

Responsibilities:
- To tell the whole truth and nothing but the truth
- To speak up if you aren’t happy or don’t understand (it helps to be tactful when doing so)
- To try and learn about your condition and treatments so you can participate in decision making
- To comply with any mutually acceptable treatment plan
- To treat the members of your healthcare team with respect and courtesy
As you probably know only too well, most healthcare professionals are very busy. Their time to talk is often limited. And most healthcare professionals are so used to the medical terms they use that they may forget that other people do not understand them. Here are some tips for optimizing your communications with your healthcare team.

- Write down any questions you have as well as any side-effects or symptoms you are experiencing. Bring these lists or documents with you to your appointment. Give the list to your doctor at the beginning of your consultation. Don't wait until the end, when the doctor is out of time.

- Take notes during your consultation of what your doctor says. Or bring someone with you to take notes for you. Some patients bring tape recorders to their appointments so that they can easily refer back to what was discussed.

- Ask your doctor if he or she has an assistant or nurse that you can talk to whenever you have questions.

- Ask if there are any brochures or other educational material you can take home with you.

- Keep your own records of your medical history and treatment. Many patients find it helpful to keep a binder in which they write down all of their appointments and treatments, who treated them, what medications they received, and their test results. In Canada, patients by law must be given access to their medical information if they request it (a reasonable fee may be charged to cover copying costs). Creating and maintaining your own binder of information will give you a better understanding of your condition, and may be helpful when dealing with healthcare professionals who are not familiar with your condition.

Not certain of what to ask? Below are some sample questions for different members of your healthcare team.

For your oncologist, hematologist or radiation oncologist:

- Who should I contact if I have problems, especially after hours or on weekends? Ask for names and telephone numbers.

- What are the results of my tests and what do they mean?

- What are all my treatment options, which one do you recommend and why do you feel this is the best approach?

- Are there clinical trials available at this centre or other centres that I could consider?

- What should I expect when undergoing treatment?

- How will we know if the treatment is working?

- Are there any warning signs or side effects that I should watch out for, and if they occur, whom should I report them to? Which ones do I need to report immediately?

- Are there foods, vitamins, supplements or herbal therapies that I should avoid?

- How often will I require testing or follow-up care?
For your **surgical oncologist** or **orthopedic surgeon**:

- Can you explain my surgical procedure in detail?
- What should I expect before, during and after surgery? What will my recovery be like?
- When do I need to come back for a follow-up visit?

For your **oncology nurse** or **educator**:

- What is your role in my cancer care? Are you the person I should contact if I have a problem or question?
- Can you help me find reliable and accurate information on myeloma?
- What advice can you give me at this stage of my cancer treatment?
- What activities can you suggest so I can stay as active as possible? Which activities should I avoid?

For your **pharmacist**:

- What is the purpose of this medication? What side effects are likely to occur and which ones should I report immediately?
- Are there vitamins, supplements or herbal remedies that I should avoid while taking this drug?
- Can you help me set up a system, such as daily pill boxes or blister packs, to ensure I take all of my medications as prescribed?

For your **dentist**:

- Are there any infections or dental problems that should be taken care of before I begin my myeloma treatment?
- Are you familiar with the requirements for treating someone with myeloma and/or with a central line in place?
- What can I do to reduce the risk of requiring extractions or other traumatic dental work while undergoing treatment?
For your **dietitian:**

- I’m finding it difficult to eat. Is there anything you can recommend to help me?
- I’m going to start a new therapy soon. What do we know about this treatment’s effect on appetite, digestion, etc.? Is there anything you can recommend to reduce its effects?
- Steroids have increased my appetite and I’m finding it difficult to control my eating. What should I do?

For your **psychiatrist, psychologist, counsellor or spiritual advisor:**

- Can you help me better deal with the emotional effects of my diagnosis?
- My family and loved ones are very upset about my illness. What can I do to help them?

For your **social worker:**

- Can you help me and my family to learn ways of coping with the changes brought by my disease?
- Can you help me figure out what healthcare or other benefits I may be eligible for, such as short or long-term disability leaves?
For decades, only a very small number of therapies were available for myeloma. Today, the treatment of myeloma has entered a new and exciting phase. Research into the underlying cellular and biochemical processes of the disease is making a variety of innovative therapies possible. In this chapter, we’ll look at how new therapies are developed and the approval process they must undergo. We’ll also look at how new therapies are paid for.

Development of New Therapies

Developing new therapies is a long and very expensive process. A number of phases or types of studies are required.

1. Pre-clinical Research

The research that eventually leads to a new drugs or treatments typically begins in a laboratory. Using study results of the basic genetic, cellular or biochemical processes that can lead to myeloma, scientists test different molecules or substances. This research may begin by using cells in a test tube (in vitro) and if promising, proceed to testing in small animals such as rats or mice (in vivo). Repeated animal trials are required to establish that a new agent is safe before it can be tested in any humans. Many molecules may be studied, but only the most promising will make the leap from pre-clinical to clinical trials.
2. Clinical Trials

Clinical trials are research studies that involve people; therefore, all clinical trials must be: 1) reviewed by Health Canada; 2) shown to be safe; and 3) approved by Ethics Committees of all the participating hospitals. These rigorous review processes are in place to protect the safety of participants and only studies that are approved are allowed to recruit patients.

There are four phases or types of clinical trials, and each phase is designed to answer specific questions.

- **Phase I**

The primary question of a Phase I trial is: “What is the best and safest way to administer the new therapy?” A Phase I trial usually involves a small number of volunteers. The testing establishes the optimal dose for the new agent (enough that it is effective but not so much that it has toxic side effects), and perhaps the best way to administer it (eg, orally or intravenously). A Phase I trial is an essential safety check for the new agent. Only those agents that are shown to be safe can proceed to the next phase of testing.

- **Phase II**

The primary question of a Phase II trial is: “Does the new agent work in a selected group of patients?” A Phase II trial typically involves a larger group of volunteers than a Phase I trial. Volunteers are usually chosen to reflect a particular type or stage of the disease. The goal is to evaluate how effective the new therapy is in treating the disease in this type of patient. Possible side effects are also monitored.
Phase III

Only therapies that are effective, safe and have tolerable side effects can proceed to Phase III testing. Phase III trials are usually the largest, and can involve hundreds or even thousands of patients at cancer centres around the world. Patients in a Phase III trial are usually assigned randomly to either the new therapy (often referred to as the “treatment group”) or the existing therapy (“usual care” or “control” group). If there is no existing therapy, the new agent may be compared to a placebo (“sugar pill”) but this is seldom necessary in myeloma research. The term “randomized controlled trial” is derived from the random way that people are allocated to either the treatment or control group.

The primary question answered by a Phase III trial is: “Is the new agent effective, particularly in comparison to the best available existing treatment?”

To ensure expectations don’t affect the assignment of people into groups or the interpretation of the data, Phase III trials are often “blinded”. “Blinded” means the patients do not know which agent they are getting. “Double blinding” is sometimes used so that neither the patient nor the researcher knows who is getting the new agent until the study is completed.

Phase IV

A Phase IV trial is sometimes referred to as “post-marketing research”. It is research on a drug that has already been approved and is being used widely. Phase IV trials may be conducted to determine if the drug works as well in the “real world” as it did under the controlled conditions of a Phase III clinical trial. It may also be conducted to see if there are any significant long-term effects of the therapy or whether the drug could be used for other indications.

Myeloma Canada Research Network (MCRN)

One of Myeloma Canada’s goals is to promote clinical research and access to new drug trials in Canada. To this end, MCRN was established to bring together Canada’s leading myeloma researchers and transform the research and treatment landscape in Canada through collaboration, knowledge-sharing and leveraging of expertise. MCRN’s mission is to:

- Conduct innovative clinical and translational research in a collaborative manner to improve patient outcomes in myeloma
- Publish evidence-based and peer-reviewed consensus statements on the diagnosis and treatment of myeloma
- Develop a nationwide myeloma patient database
As the first and only national myeloma research group, MCRN brings together Canada’s leading myeloma researchers from over 20 hospitals across the country under the umbrella of Myeloma Canada. MCRN develops made-in-Canada clinical trials that incorporate promising new treatments and makes them available through its member hospitals located in both large cities and smaller communities across the country. This means that more patients will benefit by having greater access to more promising new therapies in more locations across Canada.

The dedicated scientists, investigators and clinicians who are MCRN members all share a common vision: to work together to accelerate Canadian myeloma research, improve patient care and move closer to a world where myeloma is no longer a fatal disease.

To learn more about the trials that are underway in Canada, go to the following websites:

- Myeloma Canada (www.myeloma.ca)
- Cancer View Canada (www.canadiancancertrials.ca)
- International Myeloma Foundation (www.myeloma.org)
- US National Institutes of Health (www.clinicaltrials.gov)

**You can Contribute to Myeloma Research**

As a myeloma patient, you may be able to make an invaluable contribution to myeloma research and the development of new therapies. Perhaps you can donate marrow for laboratory research, or can volunteer for a clinical trial. Speak to your doctor or your healthcare team.

There are both advantages and disadvantages to participating in clinical trials. The advantages are that you:

- May gain access to a new therapy that is not available outside of the trial. If the agent is effective, you will be among one of the first patients to benefit from it.
- Will be monitored even more closely and frequently than you would ordinarily
- Will be helping other patients, now and in the future
Among the disadvantages to consider:

- The new treatment may not turn out to be as effective as the existing therapy or there may be unexpected side effects
- You may need to be tested more frequently than you would ordinarily

It is important that you understand all of the potential risks and benefits before you agree to join a clinical trial. People who are asked to participate in a clinical trial provide their informed consent. To do so, the clinical trial coordinator must give you a written document that explains, in plain language, the study protocol or written plan, as well as all potential risks, benefits and requirements.

If you are considering a clinical trial, don’t be afraid to ask a lot of questions. The more you know about a study, the more informed your decision will be. Some questions you may want to ask include:

- What is the purpose of this study?
- Is it a Phase I, Phase II, Phase III or Phase IV study?
- Has the treatment or therapy been tested before? If so, what were the results? Were there side effects that I should know about?
- Who has reviewed and approved this clinical trial?
- How long will the study last? How long will I be involved?
- Who will be in charge of my care? Will I be cared for by my own doctor?
- Where will my treatment take place?
- How will my safety be monitored during the study?
- What treatments, tests or procedures should I expect? How do they compare with what I would receive if I didn’t participate?
- What are the possible short- and long-term risks, side effects and benefits for me? How do these risks, side effects and benefits compare to those of the usual treatment?
- If the study requires other medications – either as part of the treatment or for side effects – will they be supplied by the study? If not, will they be covered by my private or public drug plan?
- How might being in the trial affect my daily life? Is there anything my family should know about the treatment?
The Drug Approval Process in Canada

Just because a new therapy has been shown to be effective in a Phase III trial doesn’t mean that it is automatically available in Canadian hospitals, clinics or pharmacies. Before a drug can be used in Canada, it must go through a rigorous approval process by Health Canada. Health Canada does not look solely at whether a new agent is safe, but at the balance between risks and benefits.

If the drug company’s submission is approved, Health Canada will issue a Notice of Compliance (NOC) and give the drug a Drug Identification Number (DIN). This means the company is now allowed to market the new drug in Canada. In some cases, Health Canada may award a Notice of Compliance with Conditions (NOC/c). A drug awarded with a NOC/c is given a DIN but the sponsoring company must agree to special conditions or requirements, such as research or professional and patient education.

Once a new cancer drug is approved for use in Canada, the manufacturer must make a submission to the Canadian Agency for Drugs and Technologies in Health (CADTH) pan-Canadian Oncology Drug Review (pCODR) for evaluation. The pan-Canadian Oncology Drug Review was set up by the provincial and territorial Ministers of Health to make recommendations as to whether new drugs should be covered under provincial formularies – the list of medications they will pay for. The hope is that pCODR will streamline the drug review process and help encourage greater consistency in cancer drug funding across the country. For more information, visit www.cadth.ca/pcodr/

The pan-Canadian Pharmaceutical Alliance (pCPA) conducts joint price negotiations with the drug manufacturers on behalf of the federal, provincial and territorial governments for new drugs in Canada. All new drugs coming forward for public funding through pCODR are now considered for negotiation through the pCPA.

Despite the national review processes that are in place, most publically-funded drug plans continue to make their own decisions as to which medications they will or will not list. As a result, the coverage of new treatments often varies across the country. In some cases, even when a new drug is added to a formulary, the decision as to whether to pay for it is made on a case-by-case basis. This special authorization process requires your physician to write a letter to the drug plan, explaining why you require this particular medication.
Reimbursement of New Therapies

There are basically four ways of paying for cancer drugs:

- You are a member of a government health insurance drug plan that the medication is approved and listed on (either as a general benefit or through a special authorization process)
- You have a private drug plan that will pay for the drug (many private plans have formularies or lists of drugs covered)
- You pay for the drug yourself
- If you meet certain financial eligibility criteria, assistance may be provided by the drug manufacturer

It may take some research to ensure you have optimal access to new prescription medications – and to minimize your own out-of-pocket costs. Here are some tips to help you:

- Know your health insurance coverage. Some provinces only provide drug coverage for people who are 65 and older or on social assistance. Others may have a variety of plans, such as special coverage for those facing substantive prescription drug costs. Drugs provided through cancer care centres can also vary from province to province. Talk to your cancer team social worker or pharmacist, or call your provincial Ministry of Health to learn about all your options.

- If you have private health insurance or a drug plan at work, sit down and carefully review your benefits. If you are employed, meet with your Human Resources department or union representative to help you better understand your benefits. Ask your doctor what drugs you may need in the future and check to see if your plan covers them. Try to coordinate the benefits so any portion of a drug cost that is not paid for by one plan is applied to the next.

- Some private insurance plans require that you pay up-front and then apply for reimbursement. If this is a problem for you (e.g., you need a very expensive drug), ask your insurance company to allow your pharmacy to send the bill directly to them.
- Don’t be afraid to advocate for yourself. For instance, if your employee health plan does not cover a certain drug, ask your employer or human resources manager if the company can make an exception in your case. Or ask your employer if they would waive the cap on your drug coverage.

- Find someone to work with you to advocate for the drug coverage you need. This person (family member, friend, etc.) can help continue to advocate for you even when you cannot.

- If you are refused coverage of a medication you need, appeal the decision. Sometimes the refusal may be the result of nothing more than faulty paperwork. Insurance companies will sometimes change their mind if you appeal.

- Some pharmaceutical companies have free services that will help you search for coverage of specific drugs or even supply you with the drug you require. Talk to your cancer care team or search online to see if you may be eligible for such a program.
Chapter 9

How To Be Your Own Advocate

Being diagnosed with cancer can be overwhelming as you are facing a number of major life changes. One of the most important things you can do to help yourself is to become your own advocate.

1. Document your experience

It is important that people with myeloma keep a binder or log with detailed information on their treatments, test results and consultations. It can help you to better understand your condition and support your efforts to act as your own advocate.

The information you may want to collect includes:

- Name and contact information for all the professionals involved in your care
- Dates of all appointments, reasons for the appointments and any outcomes or decisions that were made
- Copies of all test results (blood and urine tests and X-rays)
- Dates and details of all treatments you undergo
- Details of all medications you are prescribed (dose, how and when you are supposed to take them, and side affects you should report)
- Daily reports of any side effects or symptoms you experience during treatments or while taking medications
If you are experiencing fatigue, try recording your energy level on a scale of 0 (absolutely exhausted) to 10 (full of energy) at different times during the day. Keeping a log can help identify when you have the most and the least energy, so you can plan your activities accordingly.

A pain log can be extremely helpful in identifying the type of pain you are experiencing and how it should be treated. At different times during the day, write down how severe your pain is on a scale ranging from 0 (pain-free) to 10 (the most excruciating pain possible). You might also want to describe the type of pain, where it is and whether it moves or changes throughout the day.

2. **Sort out the information or services you need and identify the appropriate person to address each one**

During your treatment for myeloma, you will have a number of different needs. Sorting out what these needs are will help you identify the most appropriate person or organization to address them. For example, your medical needs are best addressed by your healthcare team; emotional or spiritual needs by a social worker, counsellor, clergy or spiritual advisor; personal issues such as housekeeping and transportation by your family; or job-related and/or financial issues by your employer, accountant or lawyer.
3. Prepare for each appointment

We prepare for all the important events of our life, such as job interviews, presentations, weddings and celebrations. Your medical appointments are equally important, so be sure to prepare for them too.

Keeping important records of your myeloma will be a big help in preparing for your medical appointments. A quick review may help clarify the questions you should ask.

During most medical appointments, things happen so quickly that it can be difficult to remember what you meant to ask. Don’t take chances – come with your list of questions and give it to the healthcare professional at the beginning of your appointment. If there isn’t enough time to cover all of the questions on your list, ask if you can book another appointment so you can address them or if there is someone else on your cancer care team who can talk to you.

4. Take, review and store notes of your visits

During appointments and treatments you will probably be given a lot of information. Don’t expect that you will be able to accurately remember everything. Bring a notepad with you and take notes during your appointment and as you talk to different members of your healthcare team. You may also bring a tape recorder and record the appointment. Don’t be afraid to ask questions, especially if someone uses unfamiliar terms. If you want, bring someone with you to take notes for you or to help you make a record of your visit. Review these notes when you get home and call your healthcare team contact if anything is unclear to you. Add these notes to your permanent record or binder.
5. Educate yourself

While it may be overwhelming at the beginning, it is important to educate yourself about myeloma and about your own condition. Ask your healthcare team for literature and brochures to read. Consult reputable web sites, such as those we describe at the end of this chapter.

6. Involve others

Support is essential when you are living with myeloma. There are various ways that different people can help. Some may be able to offer emotional support. Others may give practical support, such as running errands or driving you when you are not feeling well.

When you feel too tired or ill to act as your advocate, it can be very helpful to have someone who can step in and take over this role for you. Whether going with you to your appointment, taking notes, or asking questions, having someone to advocate for you can be extremely helpful.

7. Find a support group in your area

Patient support groups can be valuable sources of information and support. Many arrange for talks by healthcare providers, or can give you access to resources such as brochures or booklets. Ask at your hospital or cancer centre if there is a myeloma patient support group in your area, or check the Myeloma Canada website. If there is no group in your area, consider forming one. Myeloma Canada will give you information and support on how to start a patient group in your area.
Let’s begin with a resource that is unique to Canada, and therefore most pertinent to Canadians. On the internet, your first stop should be Myeloma Canada. This bilingual website gives you:

- Information about myeloma and living with myeloma
- Publications you can download
- Links to listings of clinical trials currently underway in Canada, as well as the U.S. and elsewhere
- Calendar of upcoming events and meetings
- Information on support groups in communities across Canada, so you can meet with others facing the same challenges and experiences
- Links to other Canadian and international resources

Joining an existing support group is an excellent way of learning more about myeloma. When you meet with other myeloma patients, you not only benefit from their support and experiences – but you help others. If there is no support group in your area, contact Myeloma Canada for information on how to start one.
International Myeloma Foundation

(www.myeloma.org)

The International Myeloma Foundation is a U.S.-based organization that provides information for patients and healthcare professionals, and funds myeloma research. Its website will give you access to a wealth of information, including a world-wide listing of support groups. When consulting this site remember that units of measurement and some drug names may vary from those used in Canada.

Myeloma UK

(www.myeloma.org.uk)

Established in 1997, Myeloma UK is the only organization in the United Kingdom dealing exclusively with myeloma.
In this Handbook, we have covered a lot of material. Don’t expect to be able to understand or remember all of it. Focus your attention on the parts that are most relevant to your current situation. Come back whenever you have questions, are unclear about something or want to learn more.

Hundreds of years ago, explorers set sail, uncertain of where they would end up or what they would encounter. Being diagnosed with a disease such as myeloma is similar in many ways. The life and world you have known has changed, and you are embarking on a journey in a new and often unfamiliar world. Sometimes it may seem overwhelming and frightening; however, there are people to help and support you. Some of them are in your home and community; others are at your hospital, cancer centre or place of worship.

The journey you are facing is challenging and the outcome is uncertain. Remember that you are never alone. Around the world, patient groups, healthcare professionals and researchers are working hard to improve the outlook for myeloma patients everywhere.
**Albumin**: Simple water-soluble protein that is found in the blood.

**Amyloidosis**: A condition in which myeloma light chains (M-protein) are deposited in tissues and organs throughout the body. This occurs more commonly with lambda (λ) versus kappa (κ) M-protein. In patients with amyloidosis, light chain protein binds to certain tissues such as heart, nerves and kidney rather than being excreted out of the body through the kidneys.

**Anemia**: A decrease in the normal number of red blood cells. Myeloma in the bone marrow blocks red blood cell production, causing shortness of breath, weakness, and tiredness.

**Angiogenesis**: Blood vessel formation, which usually accompanies the growth of malignant tissue, including myeloma.

**Antibodies**: Protein that are produced by certain white blood cells (plasma cells) to fight infection and disease in the form of antigens such as bacteria, viruses, toxins or tumours. Each antibody can bind only to a specific antigen. The purpose of this binding is to help destroy the antigen. 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 white blood cells.

**Antigen**: Any foreign substance (such as a bacteria, virus, toxin or tumour) that, when introduced into or arising in the body, causes the immune system to produce natural antibodies.

**Aspiration**: The process of removing fluid or tissue, or both, from a specific area.

**B cells**: White blood cells that develop into plasma cells in the bone marrow and are the source of antibodies. Also known as B lymphocytes.

**Baseline**: Observations or values that represent the initial level of a measure. Values that are taken after a medical intervention are compared to the initial (baseline) values in order to measure the response to treatment.

**Basophil**: A type of white blood cell. Basophils are granulocytes.

**Bence-Jones 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.

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

**Beta-2 microglobulin (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. For these patients, β2M testing cannot be used to monitor the disease. At the time of relapse, β2M can increase before there is any change in the myeloma protein level. Therefore, 90% of the time, β2M is very useful for determining disease activity.

**Biopsy**: The removal of a sample of tissue for microscopic examination to aid in diagnosis.
Bisphosphonate: A type of drug that binds to the surface of bone where it is being resorbed (or destroyed) and protects against osteoclast activity.

Blood cells: Minute structures produced in the bone marrow; they include red blood cells, white blood cells and platelets.

Bone marrow: The soft, spongy tissue in the centre of bones that produces white blood cells, red blood cells and platelets.

Bone marrow 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: A mineral found mainly in the hard part of bone matrix.

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.

Catheter: A tube that is placed in a blood vessel to provide a pathway for drugs or nutrients. The catheter allows medications, fluids, or blood products to be given and blood samples to be taken.

Chemotherapy: The treatment of cancer with one or more drugs that kill all rapidly-dividing cells.


Chronic: Persisting over a long period of time.

Clinical trial: A research study of new treatment that involves patients. Each study is designed to find better ways to prevent, detect, diagnose or treat cancer and to answer scientific questions.

- Control group – The arm of a randomized clinical trial that gets the standard treatment.
- End point – What a clinical trial is trying to measure or find out; the goal of the trial. Typical end points include measurements of toxicity, response rate and survival.
- Treatment group – The arm of a randomized trial that gets the new treatment.
- Randomized controlled trial – A research study in which subjects are randomly assigned to receive a particular treatment.

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.

Corticosteroids (steroids): Chemicals that are naturally produced by the adrenal gland to help prevent inflammation. Steroids are often given to patients along with one or more anticancer drugs and appear to help to control the effects of the disease on the body.

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

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 use in myeloma: karyotyping and fluorescence in situ hybridization (FISH).

Cytokine: A substance secreted by cells of the immune system that stimulates growth/activity in a particular type of cell. Cytokines are produced locally (ie, in the bone marrow) and circulate in the bloodstream.

Diagnosis: The process of identifying a disease by its signs and symptoms.

Dialysis: The process of removing waste products and excess fluid from the blood. It is necessary when a patient’s kidneys are unable to adequately filter their blood.
**DNA:** The substance of heredity; a large molecule that carries the genetic information that cells need to replicate and to produce protein.

**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. There are two types of electrophoresis:

- Serum protein electrophoresis (SPE or SPEP)
- Urine electrophoresis (UPE or UPEP)

**Enzyme:** A substance that affects the rate at which chemical changes take place in the body.

**Erythrocytes:** Cells in the blood that contain hemoglobin and deliver oxygen to and take carbon dioxide from all parts of the body. Also called red blood cells (RBCs).

**Erythropoietin:** A hormone produced by the kidneys. Myeloma patients with damaged kidneys don’t produce enough erythropoietin and can become anemic. Injections with synthetic erythropoietin can be helpful. Blood transfusion is another alternative, especially in an emergency.

**Extramedullary plasmacytoma:** A collection of plasma cells found outside the central cavity (medulla) of the bone.

**Free light chain:** A portion of the monoclonal protein of light molecular weight that can be measured in a sensitive test, the Freelite® assay.

**Gene:** A specific sequence of DNA or RNA; the biological unit of heredity located in a specific place on a chromosome and found in all cells in the body. When genes are missing or damaged, cancer may occur.

**Genetic:** Inherited; having to do with information that is passed from parents to children through DNA in the genes.

**Granulocyte:** A type of white blood cell that kills bacteria. Neutrophils, eosinophils, and basophils are granulocytes.

**Hemoglobin (Hb or Hgb):** The substance in the red blood cell that contains iron and transports oxygen.

**Hematologic:** Originating in the blood, or disseminated by the circulation or through the bloodstream.

**High-dose therapy and stem cell transplantation:** High-dose therapy is an intensive drug treatment that kills cancer cells, destroys the bone marrow and can cause severe side effects. Following high-dose therapy, stem cells are used to "rescue" or rebuild the bone marrow and its blood-forming potential.

**Hormones:** Chemicals produced by various glands of the body that regulate the actions of certain cells or organs.

**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.

**Hyperviscosity:** A syndrome that results in blood that is thicker (less liquid) usually due to increased numbers of immunoglobulins.

**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 of immunoglobulins are IgA, IgG, IgM, IgD and IgE.

**IgG, IgA:** The two most common types of myeloma. The G and the A refer to the type of protein produced by the myeloma cells. The myeloma protein, which is an immunoglobulin, consists of two heavy chains, (for example of a G type) combined with two light chains, which are either kappa (κ) or lambda (λ). Therefore, the two most common subtypes of myeloma have identical heavy chains (ie, IgG kappa and IgG lambda). The terms heavy and light refer to the size or molecular weight of the protein, with the heavy chains being larger than the light chains. Since the light chains are smaller, they are more likely to leak out into the urine, resulting in Bence-Jones protein.
IgD, IgE: Two types of myeloma that occur less frequently.

IgM: Usually associated with Waldenström macroglobulemia. In rare cases can be a type of myeloma.

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

Immunofixation: A specialized type of electrophoresis that can identify the type of monoclonal paraprotein or M-protein that makes up an M-spike (ie, whether it is IgG, IgA, kappa (κ) or lambda (λ)). This immunoelectrophoresis test can be conducted on the blood (serum) or the urine.

Induction therapy: The initial therapeutic measure in a series of treatments given in an effort to achieve remission of a disease. When used by itself, induction therapy is accepted as the best (first-line) treatment. If it doesn’t cure the disease or it causes severe side effects, other treatments may be added or used instead.

Informed consent: The process requiring a doctor to give a patient enough information about a proposed procedure for the patient to make an informed decision about whether or not to undergo it. The doctor must, in addition to explaining all procedures, address the issues of risks, benefits, alternatives and potential costs.

Interleukin: A naturally produced chemical released by the body or a substance used in biological therapy. Interleukins stimulate the growth and activities of certain kinds of white blood cells. Interleukin-2 (IL-2) is a type of biological response modifier that stimulates the growth of certain blood cells in the immune system that can fight some types of cancer. Interleukin-6 (IL-6) is a cytokine which is a potent stimulus to osteoclast and plasma cell activities.

Lactate dehydrogenase (LD or LDH): An enzyme (protein) that helps the process of turning sugar into energy for your cells to use. It may be used to monitor myeloma activity.

Lesion: An area of abnormal tissue change. A lump or abscess that may be caused by injury or disease, such as cancer. In myeloma, “lesion” can refer to a plasmacytoma or a hole in the bone.

Leukocytes: Cells that help the body fight infections and other diseases. Also called white blood cells (WBCs).

Lymphocytes: A type of white blood cell (leukocyte) that fights infection and disease.

Lytic bone lesions: The damaged area of a bone that shows up as a dark spot on an X-ray when enough of the healthy bone in any one area is eaten away. Lytic lesions look like holes in the bone and are evidence that the bone is being weakened.

Melanoma: A cancer of the pigment-forming cells of the skin or the retina of the eye. Not associated with myeloma despite the similar-sounding name.

Minimal residual disease (MRD): Myeloma cancer cells that are resistant to treatment can be found in patients in remission with no symptoms of the disease. Measuring the level of MRD may help to detect potential relapses as quickly as possible. Until recently none of the tests used to assess or detect myeloma have been sensitive enough to detect MRD. However, now M-protein levels in the blood may be used to establish MRD.

Monoclonal: A clone or duplicate of a single cell. Myeloma develops from a single malignant plasma cell (monoclonal). 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 (M-protein) is that it shows up as a sharp spike (M spike) in the serum electrophoresis test.

Monoclonal antibodies (MoAbs): Artificially manufactured antibodies specifically designed to find and bind to cancer cells for diagnostic or treatment purposes. They can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to tumour cells.

Monoclonal protein (M-protein): Also known as monoclonal spike (M-spike), monoclonal peak (M-peak), paraprotein or 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 when an M-protein is present (see “monoclonal”).
**Magnetic resonance imaging (MRI):** A diagnostic test that uses magnetic energy, rather than X-ray energy, to produce detailed two- or three-dimensional images of organs and structures inside the body. Gives very fine resolution of soft tissues, especially encroachments on the spinal cord, but is less accurate for bone lesions.

The presence of at least one of these three markers will be considered sufficient for a diagnosis of myeloma, regardless of the presence or absence of CRAB features or symptoms.

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

**Osteoblast:** The cell that produces osteoid, which becomes mineralized with calcium to form new hard bone.

**Osteoclast:** A cell found in the bone marrow at the junction between the bone marrow and the bone that resorbs or breaks down old bone. In myeloma, the osteoclasts are over-stimulated while osteoblast activity is blocked. The combination of accelerated bone resorption and blocked new bone formation results in lytic lesions.

**Osteonecrosis of the jaw (ONJ):** A previously rare jaw problem now being observed in a small percentage of patients taking bisphosphonates. The condition produces pain, swelling, and bone damage around the tooth sockets in the jaws. There is bone necrosis or loss of bone which can lead to loose teeth, sharp edges of exposed bone, bone spurs and the breaking loose of small bone spicules or dead bone. A case definition is ≥3 months with non-healing exposed bone. Symptoms may not be obvious at first, or may include pain, swelling, numbness or a “heavy jaw” feeling, or loosening of a tooth.

**Osteoporosis:** Reduction in bone density typically associated with old age. Diffuse involvement of bones with myeloma produces what looks like osteoporosis on X-ray and bone density measurement.

**Pheresis:** A procedure that separates and filters the blood into its components.

**Placebo:** An inert (inactive) substance often used in clinical trials for comparison with an experimental drug.

**Plasma:** The liquid part of the blood in which red blood cells, white blood cells and platelets are suspended.

**Plasma cells:** Special white blood cells that produce antibodies. The malignant cell in myeloma. Normal plasma cells produce antibodies to fight infection. In myeloma, malignant plasma cells produce large amounts of abnormal antibodies that lack the capability to fight infection. The abnormal antibodies are the monoclonal protein, or M protein. Plasma cells also produce other chemicals that can cause organ and tissue damage (ie, anemia, kidney damage and nerve damage).

**Plasmacytoma:** A collection of plasma cells found in a single location rather than diffusely throughout the bone marrow, soft tissue, or bone.

**Platelet cells (thrombocytes):** One of the three major blood elements, others being the red blood cells and white blood cells. Platelets are the major defense against bleeding.

**Positron Emission Tomography (PET scan):** A diagnostic test that uses a sophisticated camera and computer to produce images of the body. PET scans show the difference between healthy and abnormally functioning tissues.

**Prognosis:** The projected outcome or course of a disease; the chance of recovery; the life expectancy.

**Progression-free survival:** The time period during which the patient survives and the cancer does not become worse. The improved survival of a patient that can be directly attributed to the treatment given for the myeloma. This term identifies myeloma patients who are in complete remission versus those who have had an episode of relapse or progression.

**Protocol:** A detailed plan of treatment including the dose and schedule of any drugs used.

**Radiotherapy:** Treatment with X-rays, gamma rays, or electrons to damage or kill malignant cells. The radiation may come from outside the body (external radiation) or from radioactive materials placed directly in the tumour (implant radiation).

**Red blood cells (RBCs) or erythrocytes:** Cells in the blood that contain hemoglobin and deliver oxygen to and take carbon dioxide from all parts of the body. Red cell production is stimulated by a hormone (erythropoietin) produced by the kidneys. Myeloma patients with damaged kidneys don’t produce enough erythropoietin and can become anemic. Injections with synthetic erythropoietin can be helpful. Blood transfusion is another alternative, especially in an emergency.

**Relapse:** The reappearance of signs and symptoms of a disease after a period of improvement or remission.

**Remission:** A temporary or permanent disappearance of the signs and symptoms of cancer.
Serum free light chain assays (Freelite®): A test that can be used to measure the level of free light chains in the blood.

Side effects (also known as adverse events, AEs): Problems that occur due to drugs used for disease treatment. Common side effects of cancer chemotherapy are fatigue, nausea, vomiting, decreased blood cell counts, hair loss and mouth sores.

Skeletal survey (full-body X-ray): A series of plain X-rays of the skull, spine, ribs, pelvis and long bones to look for lytic lesions and/or osteoporosis.

Stem cell: An immature cell from which all blood cells develop. A normal stem cell can develop into normal blood components such as red cells, white cells and platelets. Stem cells are normally located in the bone marrow and can be harvested for transplant.

Thrombocyte: See “Platelet”

Tumour: An abnormal mass of tissue that results from excessive cell division. Tumours perform no useful body function. They may either be benign or malignant.

Vaccine: A preparation of killed microorganisms, living attenuated organisms, or living fully virulent organisms that is administered to produce or artificially increase immunity to a particular disease.

Waldenström macroglobulemia: 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 (WBCs) or leukocytes: 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.

X-ray: A quick test that uses high-energy electromagnetic radiation in low doses to produce images of the structures inside your body (i.e., your bones).
Every year, Myeloma Canada provides information to thousands of people with myeloma and their families and caregivers, and helps many more by providing programs and services such as the annual Myeloma Canada National Conference, Patient and Family InfoSessions, the *Myeloma Matters* newsletter and webinars.

That is why we need your help. We depend on support and generous donations from people like you to provide support to myeloma patients, their families and their caregivers. All donations are greatly appreciated and allow us to continue our vital work.

**Ways You Can Help**

**Donate**

You can make your donation online at [www.myeloma.ca](http://www.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 Trans-Canada Highway, Suite 160  
Dorval, QC H9P 2V4

**Fundraise**

There are other 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 myeloma.

Contact the fundraising team toll-free at 1-888-798-5771 for more information, or visit [www.myeloma.ca](http://www.myeloma.ca).
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The mission of the Myeloma Canada Research Network is to conduct clinical and translational research in a collaborative manner to improve patient outcomes in multiple myeloma, and to provide scientifically valid and peer-reviewed consensus opinions on the diagnosis and treatment of multiple myeloma.
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Myeloma Canada publications are extensively reviewed by patients and healthcare professionals prior to publication.

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