



Understanding multiple myeloma and its treatment

Information for people with multiple myeloma

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janssen  Oncology

JANE KIELT
Mystic Seaport

Cover artwork by a person
living with multiple myeloma.

Janssen Oncology has produced this text with the greatest care in July 2023.

All the photographs of people in this booklet are models and are included just to illustrate the publication.

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Introduction

When someone is first diagnosed with multiple myeloma, it can often lead to feelings of anxiety, a sense of being overwhelmed, and even anger at the situation. Building knowledge can help you tackle the disease and deal with it every day. It's the first step towards effective treatment.

The information in this booklet is intended to give you an overview of multiple myeloma and provide answers to some of the most commonly asked questions we hear from other multiple myeloma patients.

Remember, though, that your haematologist should be the first person you talk to about more specific queries.

What is multiple myeloma?

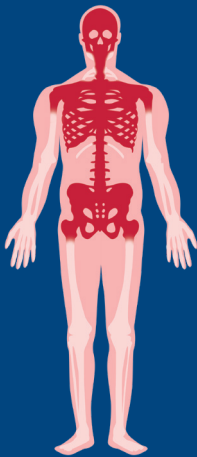
Each healthy cell in the body follows certain rules, it:

- multiplies only when needed
- changes when necessary
- dies when the body requires it¹

Unfortunately, a cancer cell does not follow these rules, it:

- multiplies at the wrong time
- multiplies in the wrong place
- does not develop in the way needed to perform its proper function¹

Multiple myeloma is a cancer of plasma cells – a type of white blood cell in the bone marrow that makes antibodies. A cancerous or malignant plasma cell is called a myeloma cell.^{2,3} Multiple myeloma can appear as a tumour, an area of bone damage, or both. Bone damage is referred to as 'lesions'. Multiple myeloma affects the places where bone marrow is active in an adult.^{2,3}



Myeloma is called 'multiple' because there are often multiple areas in the body where it grows.^{2,4}

Myeloma most often grows in the marrow of bones located in the:^{2,4}

- spine
- skull
- pelvis
- rib cage
- areas around the shoulders and hips

Usually, the bones of the hands, feet and the lower portions of the arms and legs are unaffected.⁴

The accumulation of myeloma cells in the bone marrow results in the following medical issues:



The release of calcium from damaged bone into the bloodstream can result in:

- thirst
- nausea
- vomiting
- confusion
- constipation^{2,4}



The overproduction of an abnormal antibody called M-protein can slow blood circulation and damage the kidneys.^{2,3}



An imbalance in the body's bone-forming and bone-destroying cells (osteoblasts and osteoclasts) can lead to the bones becoming weak and damaged.³



A decrease in the number of red blood cells produced can cause anaemia, resulting in weakness and tiredness.^{2,3}



A decrease in the number of white blood cells can leave patients susceptible to infection and delay their recovery from infections.^{2,3}

Diagnosis and tests

There are a few ways to test for multiple myeloma. Your condition may have been diagnosed through one or a combination of the following:

Blood test²⁻⁴

Multiple myeloma is often discovered from a blood test. The main test for the condition is a type of analysis called 'protein electrophoresis'. This is done on the proteins in the blood. It can show whether or not there is too much immunoglobulin (antibodies) in the blood, called M proteins. Higher than normal levels of M proteins suggest a sign of multiple myeloma, but this needs to be confirmed using bone marrow samples.

A blood test can also be used to find out:

- what level of anaemia you have
- if your blood platelets are 'deficient' (do not clot normally)
- if your kidneys are working normally
- what your calcium levels are

All these things help to confirm a diagnosis and suggest the best course of treatment.

Urine test^{3,4}

Electrophoresis can also test your urine. This is because a part of the immunoglobulin can often be found there.

Imaging techniques^{2,4}

An X-ray of the bone can help identify changes in the bone and if there are cavities in the bone (called bone lesions). The most frequent parts of the body X-rayed are the:

- skull
- spine
- humerus bones in the arms
- the thigh bones

Other, more sensitive imaging techniques may also be used to detect any tumours outside the bone marrow, like:

- magnetic resonance imaging (MRI)
- a CT (computerised/computed tomography) scan
- a PET (positron emission tomography) scan

Bone marrow analysis²⁻⁴

Bone marrow can be analysed by:

- drawing a small amount of bone marrow fluid (aspiration)
- surgically removing a small amount of tissue (biopsy)

These tests can determine the presence and extent of cancerous cells in the bone marrow.

The samples can also undergo cytogenetic testing, which may show genetic changes that would suggest a more aggressive disease requiring specific treatment.

Classification and staging

You may have heard myeloma referred to as having different **classifications** and different **stages**.

It's important to note that these are two different things, although both help determine the most appropriate treatment for you.

Classification refers to the type of myeloma you have.

Staging reflects the extent of the disease.

Both classification and staging help to determine the most appropriate treatment.

Classification

Monoclonal gammopathy of unknown significance (MGUS)^{4,5}

If you have MGUS it means that there is a very low level of M-protein in your bone marrow, but it has not caused you any symptoms or damaged any of your organs. MGUS is a benign condition – it doesn't actually mean that you have cancer, but it is an early indicator; 20% of people with MGUS will progress to active myeloma. If you have MGUS, your condition will be monitored but you won't receive treatment for it.

Solitary plasmacytoma^{3,6}

In rare cases, a single lesion (group of malignant myeloma cells) is seen. This is often in the bone and without signs of bone marrow abnormalities. Various treatments are possible, but radiotherapy is often preferred.

Asymptomatic or smouldering/indolent myeloma^{4,5}

Asymptomatic, smouldering/indolent myeloma is when either low levels of M-protein are found in your blood or there are more than 10% plasmocytes (white blood cells responsible for producing antibodies) in your bone marrow.

With this condition there is no sign of damage to the organs, no anaemia, no bone lesions, no hypercalcaemia, and adequate kidney function.

In most cases, patients with asymptomatic smouldering/indolent myeloma do not require any treatment. However, it is essential that you are monitored to make sure it does not progress. Sometimes, additional tests show that you are at an increased risk of quickly developing active myeloma. In that case, your doctor can consider starting treatment immediately if you start showing symptoms.

Active or symptomatic myeloma³

Active or symptomatic myeloma means that as well as abnormal proteins and malignant plasma cells that are present in your bone marrow, you have damage to your bones and various organs, for example the kidneys. If you have active or symptomatic myeloma, you will likely already be receiving one or more treatments that your doctor will have discussed with you.

Myeloma staging^{2,3}

Staging is essential to set up appropriate treatment. The most common way to stage myeloma is by using the Revised International Staging System (R-ISS). It looks at the levels of specific blood proteins and takes into account individual genetic traits to classify myeloma at Stage 1, Stage 2 or Stage 3.

Remember though, that your haematologist should be the first person you talk to about more specific queries.

Making the most of your appointments

Before your appointments:

- Write down any questions you have as you think of them and take them with you to your appointment
- Make sure you share your questions with your doctor at the start of your appointment. Don't wait until the end, when the doctor has run out of time
- You could ask a family member or friend to come with you to your next appointment. Perhaps they can take notes while you talk to the doctor

During your appointments:

- It can often be difficult to remember everything that is said during an appointment. You might want to write down what your doctor says so you can refer to your notes afterwards, or even record the appointment (with your doctor's permission)
- You might not know all of the medical terms mentioned during your consultation or treatment. If there's a word you have not heard of before, ask the doctor or nurse to explain it

Getting familiar with your healthcare team

When you were diagnosed with multiple myeloma, you might have felt like you were alone, but apart from your family and friends, there is a team of healthcare professionals who are with you every step of the way, in addition to patient advocacy groups who are always here to help.

Your multiple myeloma care team is known as 'multidisciplinary' because it includes specialists from different areas of medicine working together for your wellbeing. Understanding their roles and responsibilities may help you prepare specific questions you might want to ask during your treatment visits.



Here is a list of health and care professionals you're likely to speak with at some stage in your treatment journey and their roles.

Primary care physician – your General Practitioner (GP)

Your GP was probably the first person you saw when you became ill. Even after your treatment gets under way, your GP may still be the first person you contact for any healthcare issues.

Oncologist and haematologist

Your GP will have referred you to a specialist in multiple myeloma who is either a medical oncologist or a haematologist. Oncologists are trained in the diagnosis and treatment of cancer, while haematologists are experts in diseases that affect the blood.

Radiation oncologist

You may be referred to a radiation oncologist. This is a physician who specialises in treating cancer with radiation therapy.

Orthopaedic surgeon

An orthopaedic surgeon is an expert in bone surgery and will be there to address any orthopaedic (bone-related) problems that you may have during treatment.

Oncology nurse

An oncology nurse is specially trained to work closely with your haematologist or oncologist to coordinate your care and give treatments.

Social worker

Social workers can help you with emotional, physical or financial problems. They can also advise you about any practical support services that may be available.

Psychiatrists and psychologists

Living with multiple myeloma can be tough and some might find it challenging at an emotional level.⁴ You may benefit from speaking with a professional counsellor, like a psychiatrist or a psychologist.

What is the difference between a psychiatrist and a psychologist?

A psychiatrist is a medical doctor trained to diagnose and manage mental illness. Psychiatrists can prescribe medication, such as antidepressants, if you need them.

A psychologist is not a medical doctor, but someone who is well trained in counselling and human psychology. They cannot prescribe medication.

Dietitians and nutritionists

Multiple myeloma and its treatment can make eating difficult. A registered dietitian can help you to maintain the healthiest diet possible throughout treatment.⁴ Your dietitian will be able to suggest foods or drinks to help if you are experiencing:

- nausea
- vomiting
- loss of appetite
- a dry or sore mouth

Pharmacist

As well as dispensing medications, your pharmacist is a valuable source of information. They can answer questions about:

- when and how to take medicines
- what side effects to expect
- what to do if you have side effects

Dentist

Since myeloma affects your bones, your jaw and teeth may be affected too.⁴

If your dentist is not already familiar with the special needs of people with multiple myeloma, you should tell them about your medication or pass on the details of your specialist so that any necessary treatments can be planned properly.

Treating multiple myeloma

Although we are still working towards a cure for multiple myeloma, treatments are more effective than they have ever been.^{2,4}

The goal of multiple myeloma treatment is three-fold:^{2,4}

- To stop or slow the progression of myeloma.
- To encourage and prolong the periods where symptoms partially or completely disappear – known as remissions.
- To improve your quality of life – for example by relieving symptoms.



Available treatments

There are a number of treatment options available for multiple myeloma, detailed below. Depending on the myeloma you have, your general health and fitness, and the stage you're at in your myeloma journey, you will receive some or all of these options. Often, more than one of these options are combined to achieve maximum effect.²

Research into multiple myeloma treatment options is still ongoing, and so it's worth noting that there may be additional kinds of treatment under development to those detailed below.

Your healthcare team may have prescribed one, or a combination of some of the below treatments.

When you are prescribed a treatment or treatments, you may also receive additional information from your healthcare team. You should also read any patient information leaflets that may accompany your medicine.

Anti-myeloma medicines

These medications can be divided into seven major categories:

Proteasome inhibitors (PIs)⁷

In a normal cell, proteins are broken down by a small structure known as a 'proteasome'. This acts like a waste bin where used proteins are recycled.

Cancer cells, which have increased metabolism, use these proteasomes very intensively to keep functioning, and by inhibiting its function this will eventually lead to myeloma cell death.

Immunomodulators (IMiDs)⁷

These drugs have a direct effect on cancer cells, and they also regulate certain parts of the immune system. They can activate certain immune cells and prevent certain types of growth signals for cancer cells.

By 'modulating' the immune system in this way, they use the body's own defense mechanisms against the cancer.

Monoclonal antibodies (mAbs)⁷

These antibodies are used as immunotherapy to activate the body's own immune system to eliminate cancer cells. These antibodies are highly targeted, attaching to particular proteins located on the wall of the tumour cells. As a result, the immune system recognises these cells and they are attacked. Some of the mAbs may also exert direct anti-myeloma cell activities, killing the malignant cells.

Steroids^{7,8}

These have long been used in myeloma treatment due to their ability to kill myeloma cells in high doses. They may be used in combination with other anti-myeloma medicines.

Histone deacetylase (HDAC) inhibitors⁷

These kill cells by interfering with specific enzymes, weakening the genetic structures of cancer cells.

Antibody-drug conjugates⁹

Antibodies that are attached to an anti-cancer drug or a therapeutic agent, with a linker, are used to search for and enter cancer cells. Once inside these cancer cells, the anti-cancer drug is released where it can prevent their growth and can also cause cell death. In addition, the antibodies themselves can activate the body's immune system to further help eliminate cancer cells.

Selective inhibitor of nuclear export (SINE)^{10,11}

Overexpression of a protein called exportin 1 (XPO1) has an important role in helping cancer cells survive – it is also associated with poorer treatment outcomes. SINEs block the activity of the XPO1 protein, which can prevent growth of cancer cells and can also lead to cancer cell death.

Standard chemotherapy

These medicines are administered either orally or intravenously (through a drip). They aim to kill cancer cells.^{7,12} A key drug used in this context is melphalan, which is given orally and is generally tolerated quite well.¹² Melphalan is also used as part of autologous transplantation, but in this context it is administered at a high dose intravenously.¹³

Allogenic transplantation¹³

In this type of transplantation, the stem cells come from another person: a compatible donor – usually a brother or sister. Allogenic transplants aim to use the immune system of the donor to help fight the patient's myeloma.

However, these transplants are associated with risks. The most significant are that you will get an infection or that your body tissues will react badly to the transplanted cells from the donor.

Autologous stem cell transplantation (ASCT)^{13,14}

One issue with chemotherapy is that when given in high doses it destroys stem cells in the bone marrow. These are the cells that go on to develop into blood cells, and are therefore essential for maintaining good health. A solution is to collect a sample of stem cells from a patient before high-dose chemotherapy, so that they can be given back to them afterwards. Because it's the patient's own cells being given back to them, it is called an 'autologous' stem cell transplant.

See the booklet 'Autologous stem cell transplantation: Understanding your journey' for more information, if your healthcare team has said you are eligible for this treatment.

Chimeric Antigen Receptor T (CAR-T)¹⁵⁻¹⁷

CAR-T cell therapy is a type of immunotherapy that helps the immune system to fight cancer including multiple myeloma. T cells are a type of white blood cell and part of the immune system responsible for attacking foreign cells in the body. During CAR-T therapy, some of the body's own T cells will be collected and then reprogrammed in a lab to become CAR-T cells. The CAR-T cells are then reintroduced into the patient's body through an infusion so they can recognise and attack the multiple myeloma cells.

Follow-up

During your treatment

You will have regular check-ups where you can report anything that you are worried about.⁴ Do not hesitate to mention any symptoms even if you think they are minor, for example, gradual loss of feeling in your feet or hands. These symptoms often indicate peripheral neuropathy (nerve damage). In that case, the healthcare team need to adjust your treatment schedule.

Alongside the regular contact with your carers, you must contact your healthcare team to report any rise in temperature or any new bleeding. These symptoms need urgent treatment.

At the end of your treatment^{2,4}

Your healthcare team will assess your treatment again based on:

- the abnormal proteins in your blood and urine
- an analysis of the bone marrow
- a magnetic resonance imaging scan of the bone, possibly supplemented by a PET scan and X-rays

These examinations will show how complete your remission is. The more complete the remission, the longer it is likely to last. Based on these test results, your doctor will let you know how often you will have to return for checks.

After your treatment

On the basis of your test results (blood and urine), your doctor will let you know how often you will have to return for checks. **It is important that you consult the doctor outside of these planned visits if you have any worrying symptoms, particularly a rise in temperature and pain. Do not wait until your next appointment.**

Your notes

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This information is intended for patients with multiple myeloma and is intended to inform patients about the clinical characteristics and treatment of their condition. You are receiving this information through the doctor treating you.