MyelomaUK

Tests and investigations in myeloma

Treatments and tests Infoguide

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You will find a definition of the terms highlighted in **bold** throughout this publication in the 'Medical terms explained' section on page 37.

Disclaimer: The information in this Infoguide 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.

This publication is intended for a UK audience.
It therefore may not provide relevant or accurate information for a non-UK setting.

Myeloma – an overview

Myeloma is a type of cancer arising from plasma cells that are normally found in the bone marrow. Plasma cells are a type of white blood cell which form part of the immune system.

Normal **plasma cells** produce different types of **antibodies** to help fight infection. In myeloma, the plasma cells become cancerous (sometimes called **malignant**) and release a large amount of a single type of antibody, known as **paraprotein**, which has no useful function. It is often through the measurement of paraprotein that myeloma is diagnosed and monitored.

Myeloma affects multiple places in the body (hence why it is sometimes referred to as 'multiple myeloma') where **bone marrow** is normally active, such as the bones of the spine, pelvis, rib cage and the areas around the shoulders and hips.

Most of the complications and symptoms of myeloma are caused by a build-up of the abnormal plasma cells (often called myeloma cells) in the bone marrow and the presence of paraprotein in the body.

Common problems in myeloma include bone pain, bone fractures, fatigue, frequent or recurrent infection and kidney damage.

Myeloma is highly treatable in the majority of cases. Treatment is aimed at controlling the disease, relieving the complications and symptoms it causes, and extending and improving the **quality of life**.

Treatment for myeloma is often most effective when two or more drugs, with different but complementary mechanisms of action, are given together. Treatment is usually given over a number of weeks which may or may not be followed by a rest period. This pattern constitutes one cycle of treatment and a series of treatment cycles is referred to as a course or line of treatment.

While there are many effective treatments for myeloma, unfortunately it is currently incurable. This means that even after successful treatment has

provided a period of **remission** or stable disease, the myeloma will return. This is called a **relapse**.

The causes of myeloma are not fully understood but it is believed to be caused by an interaction of both genetic and environmental factors.

Key facts

- There are approximately 5,700 people diagnosed with myeloma every year in the UK
- There are approximately 17,600 people living with myeloma in the UK at any one time
- Myeloma accounts for 15% of blood cancers and 2% of cancers generally
- Myeloma mostly affects people aged 65 and over. However, it can also be diagnosed in younger people

Tests in myeloma – an overview

A range of different tests are done as part of the process of diagnosing myeloma, and later in the course of the disease.

Some of the tests done at the time of diagnosis are very general, and abnormal results may be due to causes other than myeloma. Other tests are fairly specific, but even so, the diagnosis of myeloma is based on a number of different tests, not just one.

The tests you may have as part of a diagnosis of myeloma will include some or all of:

- Blood tests
- Urine tests
- X-rays and/or scans (such as MRI)
- Bone marrow tests

Your doctor will look at the results of these tests alongside signs and symptoms you have which may suggest myeloma (such as bone pain, fatigue and repeated infections).

If you have already been diagnosed with myeloma, you will get some additional tests done. You may have tests to determine the genetic subtype of your myeloma, and blood tests to check the paraprotein type. These tests may contribute to an understanding of the likely course the disease will follow, and in a few cases will help with decisions about treatment, although the course of the disease can never be predicted with certainty.

You will also have tests to assess any complications of the myeloma that may need treatment. For example, you may have localised bone damage that needs surgery or radiotherapy.

You will have different tests at different stages in the course of your myeloma:

- Tests during treatment
- Follow-up tests during remission
- Tests to check for relapse

The different tests and investigations are explained in the following sections. You can read this Infoguide as a whole publication, but if you are a newly diagnosed patient, you may find the amount of information overwhelming – you may prefer to use the Infoguide as a reference tool to help you find out about specific tests you are undergoing. Not all patients receive all the tests and investigations described in this publication – it will depend on your individual situation.

Diagnosing myeloma

Anyone suspected of having myeloma will be referred to a haematologist (blood specialist) who will arrange for tests and investigations to be carried out.

You may be tested for myeloma because of a combination of symptoms that raised concern with your GP, such as bone pain, fatigue, signs of kidney problems, or persistent or repeated infections. The GP will arrange for blood tests, and depending on the results, will refer you to hospital.

For some patients, the trigger for myeloma testing may be that they were taken to hospital with more serious problems such as kidney failure, unexpected broken bones, or symptoms of compression of the spinal cord. If there is a suspicion of myeloma, the patient will be referred to the haematology department for relevant tests.

In a few cases, patients have not had any symptoms of myeloma, but blood or urine tests taken for other reasons have picked up the possibility of myeloma by chance.

It is important to remember that myeloma is a complex cancer and its diagnosis can involve a number of different tests. It is also a very individual cancer and therefore results from diagnostic tests may vary from patient to patient.

For more information see the **Infopack for newly diagnosed myeloma patients** from Myeloma UK

Waiting for test results

Waiting for test results can be a difficult and stressful time and you may feel quite anxious. The time taken for all your different test results to be ready can vary, so it may help while you are waiting to talk things through with your **key worker**/clinical nurse specialist or with a close friend or partner.

The **Myeloma Infoline** can provide a listening ear and emotional support at this time, as well as practical advice. **Call 0800 980 3332** to get in touch.

Tests at diagnosis

A number of tests may be done when someone is suspected of having myeloma, or when myeloma has just been diagnosed. The tests include blood and urine tests, bone marrow tests, imaging (X-rays or scans), and genetic tests.

The tests are done to confirm whether or not the patient has myeloma. However, many test results could have a variety of causes, so it is the combination of findings that is used to confirm the diagnosis of myeloma.

Tests may also be done at this time to:

- Find out more about the specific person's myeloma (for example using genetic tests)
- Investigate complications (such as bone damage and kidney problems)
- Assess any co-existing medical conditions
- Help decide what treatment is needed

The tests are explained in detail in the following sections. Less common types of myeloma (**light chain**, **oligosecretory**, and **non-secretory**), and the tests used for them, are also explained.

Blood tests

A number of different blood tests will be done at the time of diagnosis. To find out about normal ranges for blood tests, see Appendix 1 at the back of this Infoguide.

What does a blood test involve?

A needle is inserted into a vein, usually in your arm, and used to draw out a sample of blood into an attached container. You may feel a slight pricking or scratching sensation for a moment as the needle is inserted, but the needle should only be in the vein for a few moments. If you are having several blood samples taken for different blood tests, the container for each will be detached from the needle and a new one attached, for the next sample. The total amount of blood taken for blood tests is usually small (between one and three teaspoons depending on how many different blood tests are being done).

Full blood count

Why am I having these tests?

A full blood count measures the numbers of different cells in your blood. Blood cells have different functions in the body, and blood counts are done in many situations. Lowered blood counts can have many causes other than myeloma.

In myeloma, the myeloma cells affect the production of normal blood cells in the bone marrow, so the levels of these cells may be lower than normal.

Red blood cell count

Red blood cells carry oxygen round the body, and a low count indicates **anaemia**, one of the common effects of myeloma. Anaemia can cause symptoms like tiredness or dizziness.

Haemoglobin level

Haemoglobin is the chemical that red blood cells use to carry oxygen, and will be measured as part of a full blood count. A low level indicates anaemia.

White blood cell counts

White blood cells are involved in the **immune response**, the body's defence against infection.

Low counts of some or all of the different white blood cells means that you are at greater risk of infection. As well as the total white blood cell count, a 'differential white blood cell count' will be done. This counts the specific types of white blood cells such as neutrophils and lymphocytes.

Platelet count

Platelets help to clot the blood. A low count of platelets means that you are at increased risk of bleeding or bruising.

Blood chemistry

Why am I having these tests?

The blood contains a number of different chemicals, as well as blood cells (see previous section). Blood chemistry tests measure these chemicals, and are done to test for many different diseases that may alter the levels of one or more of them.

In testing for possible myeloma, there are several important blood chemistry tests which will be used as part of a diagnosis.

Creatinine and urea

Creatinine and urea are waste products that are normally filtered out by the kidneys and passed into the urine. If the levels of creatinine and urea are higher than normal in the blood, this can indicate that the kidneys are not working properly, which can be an effect of myeloma.

Albumin

Albumin normally makes up most of the protein found in the blood. In myeloma, the amount of albumin produced is less than normal. This is an effect of chemical messengers produced by myeloma cells.

Calcium

Calcium is a mineral which is normally found in bone. In patients with active **myeloma bone disease** (see page 18), calcium is released from bone which is being broken down, and goes into the blood, leading to higher than normal levels. This is called **hypercalcaemia**. The finding of hypercalcaemia can trigger testing for myeloma. Too

much calcium in the blood can also cause problems itself, so it is important that it is checked.

Beta 2 microglobulin (β2M)

β2M is a protein that is normally found on the surface of almost all cells in the body. It is shed by cells into the blood, especially by B cells (the type of cell from which myeloma cells develop) and by tumour cells in general. The level of β2M in the blood increases if cell turnover (rate of cell growth and death) is high, if the **immune system** is more active than normal, and if kidney problems mean that removal of β2M from the blood is reduced. These factors can all apply in myeloma. Therefore, measuring β2M in the blood is a useful test to indicate the amount of myeloma in the body. It is often used as part of the staging of myeloma (see page 34).

Erythroycte sedimentation rate (ESR)

ESR is a test which measures how fast red blood cells (erythrocytes) in a blood sample drop down a glass tube. The red cells fall more quickly if they are clumped together, and this increases the ESR result. This is not a specific test for any one disease, and an increased ESR can be caused by various conditions involving inflammation. It can be caused by myeloma, when the paraprotein causes the red blood cells to clump together.

Paraprotein tests

Why am I having these tests?

Paraprotein is the immunoglobulin produced by myeloma cells (see 'Myeloma – an overview' section on page 2). Presence of a large amount of paraprotein can be used to help to diagnose myeloma.

Immunoglobulin is made up of four parts forming a Y-shape (see Figure 1). The Y-shape consists of two longer parts called **heavy chains**, and two shorter parts called **light chains**. Paraprotein (or M-protein) consists of all four parts of the immunoglobulin. This is produced by the myeloma cells in about 80% of myeloma patients.

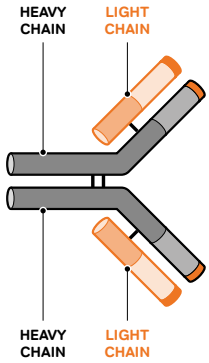

Figure 1. Immunoglobulin structure

Serum protein electrophoresis (SPE)

SPE detects the presence and amount of different proteins in the blood. It works by separating out all the proteins by their size. This can show whether there is a large amount of one identical protein (in this case, paraprotein) in the blood. This is shown in Figure 2.

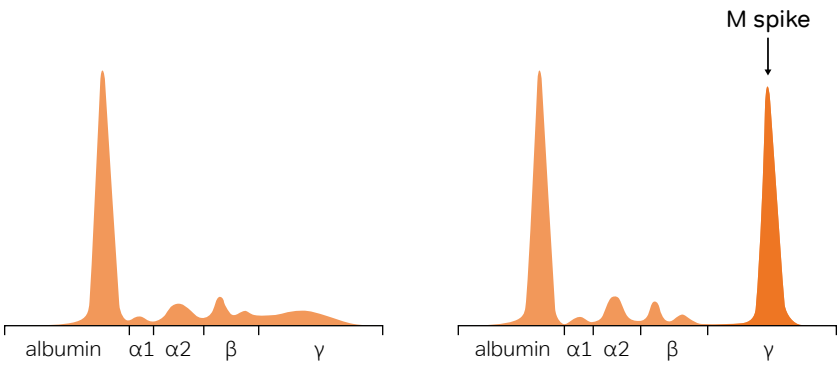

Figure 2. Serum protein electrophoresis result for a healthy person (left) and a myeloma patient (right), with blood proteins separated out by their size. The myeloma patient has a so-called 'M spike' which is the large amount of identical paraprotein (right-hand end of graph)

Immunofixation electrophoresis (IFE)

The IFE test gives more detailed information about the type of immunoglobulin being produced by myeloma cells. This information is helpful because the type of immunoglobulin can affect the way a person's myeloma develops. The IFE test is also very sensitive and can pick up small amounts of paraprotein if they are not detectable by SPE.

The types of immunoglobulin heavy chain are called IgG, IgA, IgM, IgD and IgE. The most common type in myeloma is IgG, followed by IgA. IgM, IgD and IgE myeloma are relatively rare.

The light chains in immunoglobulins also come in two types – kappa (κ) and lambda (λ). In people without myeloma, light chains are present in the blood, but the balance between kappa and lambda types (called the kappa to lambda ratio) will be fairly even. However, in myeloma, the myeloma cells produce either kappa or lambda light chains only, so the level of that type will be higher, and the kappa to lambda ratio will change. Kappa and lambda light chains can be detected by the IFE test, but only if the light chain levels are increased a lot.

Serum free light chain (sFLC) assay

What are free light chains?

Light chains are the smaller parts of the immunoglobulin (shown in Figure 1). Most myeloma cells produce separate light chains as well as those that are part of the whole paraprotein. These are called **free light chains** (FLCs) (or **Bence Jones proteins** when they are in the urine). Some patients produce only free light chains and no paraprotein at all – this is called light chain myeloma (see page 29).

The serum free light chain (sFLC) assay measures free light chains in the blood. Other names for the test are **Freelite®** or **Seralite®**. 'Serum' refers to the clear liquid part of the blood, and 'assay' is another word for a test.

Why am I having this test?

The sFLC assay is very sensitive, and picks up free light chains at low levels. The sFLC assay is now recommended as part of the diagnosis of myeloma, and is being used increasingly widely.

You may also have a sFLC assay done because no paraprotein was detected in your blood but your doctors suspect you may have myeloma. This might happen for example if you have light chain myeloma.

Hevylite® assay

The Hevylite assay is a relatively new test. It detects and measures the level of paraprotein in the blood, even when low paraprotein levels are present. It is not yet in routine use in the UK but may be done at some centres.

Recording your blood test results

It can be helpful for you to keep track of all your blood test results by noting them down in one place. The Myeloma UK Patient diary has space to record blood test results, as well as sections for recording your treatments, appointments, any side effects, and questions you want to ask your healthcare team.

Order your free **Patient diary** from Myeloma UK by calling **0800 980 3332** or visiting **myeloma.org.uk**

Appendix 1 gives an indication of normal ranges for blood tests, but what is normal for each person varies, so it can be useful to see your own pattern of results in the Patient diary.

Urine tests

Urine tests are done alongside blood tests at the time of myeloma diagnosis.

What do urine tests involve?

Urinalysis (or a 'urine test') is a set of tests done on a sample of your urine. For most urine tests, you will be asked to collect a 'mid-stream urine' sample. This involves collecting some of your urine into a labelled tube you will be given.

For some urine samples you will be asked for a 24 hour urine collection. This is done by collecting your urine in a special container over a full 24 hour period. The container must be kept cool until you take it in to the clinic.

You will be told how to carry out the urine collection by your healthcare team.

Urinalysis

Urinalysis tests are done in many different situations, including suspected myeloma. The urinalysis tests include some that indicate how well the kidneys are functioning. This is important because kidney problems often happen in myeloma.

For more information see the **Myeloma and the kidney Infoguide** from Myeloma UK

Protein tests on urine

Bence Jones test (urine protein electrophoresis or UPE)

Free light chains in the blood are filtered out by the kidneys (Bence Jones proteins) and removed from the body in the urine. They can be measured in the urine using the Bence Jones test, or urine protein electrophoresis. This test works in the same way as serum protein electrophoresis (see page 11), but uses a sample of urine from a 24 hour collection.

Immunofixation electrophoresis (IFE)

Immunofixation electrophoresis may be done on a urine sample to detect which of the two light chain types (kappa or lambda) is being produced by the myeloma cells. IFE is a sensitive test and can sometimes pick up light chains that are not detectable in the urine using UPE.

Bone marrow tests

People with myeloma have increased numbers of plasma cells in their bone marrow. The number and type of cells are looked at using bone marrow tests.

Why am I having these tests?

You will have bone marrow tests as part of the process of diagnosing whether you have myeloma. The bone marrow tests will also tell your healthcare team how many myeloma cells are present in your bone marrow (the **tumour burden**).

What do the tests measure?

There are two types of bone marrow tests.

A **bone marrow aspirate** is where a small amount of liquid bone marrow is removed. This test counts the percentage of myeloma cells compared with other cells in the bone marrow.

A **bone marrow biopsy** or **trephine biopsy** is where a small narrow core of solid tissue is taken from the bone marrow. This test makes it possible to see the myeloma cells in position in the bone marrow tissue itself.

What do the tests involve?

In most cases, patients have the two bone marrow tests done together. This is to avoid having to have the procedure done twice if the aspirate does not give enough information.

The bone marrow samples are usually taken from the pelvic bone (hip girdle). Before the procedure, the skin is cleaned and local anaesthetic is injected into the skin in the area. For the aspirate, a needle is passed through the skin and into the bone, and a sample of liquid bone marrow is drawn up through a syringe. For the trephine biopsy the aspirate needle is replaced with a slightly larger one, which is inserted into the bone, and turned while being inserted further into the bone marrow, until a core of bone marrow can be carefully removed. The procedures last only a few minutes.

You are likely to experience pain at points during these procedures, which may be a pulling and pushing sensation, or a sudden sharp pain. Depending on the circumstances, you may be offered sedation. There may be some discomfort and bruising for a few days after the biopsy, for which normal painkillers should help.

The bone marrow biopsy procedure is shown in Figure 3.

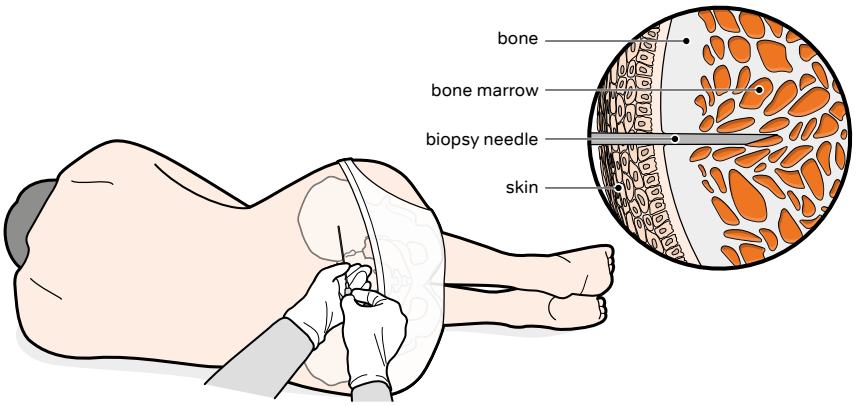

Figure 3. Bone marrow sample being taken from the pelvic bone

Imaging tests

Imaging tests (X-rays and scans) are used to investigate myeloma bone disease. They will be done as part of the diagnosis of myeloma. They may also be done after myeloma has been diagnosed, to give information about the extent of bone disease and complications it may be causing. Imaging tests will be used to locate any fractures which may need surgery, and to decide whether any treatment targeting particular areas of bone damage is needed.

Myeloma bone disease

Myeloma bone disease occurs when myeloma cells interfere with the normal process of bone maintenance, causing bone to be broken down faster than it can be repaired. This leads to complications including bone pain, bone thinning or holes, and fractures. Myeloma bone disease affects most myeloma patients, and is lessened once the myeloma is brought under control by treatment.

The bone thinning and holes are called **lytic lesions**, and these may be localised at particular points or scattered through the bones. Fractures can sometimes occur with only minor pressure or injury, for example in the ribs. Fractures of the vertebrae (spinal bones) can lead to their collapse, causing pain, loss of height and curvature of the spine (**kyphosis**). Myeloma bone disease can also lead to **spinal cord compression**, when damaged bones in the spine press on the spinal cord. This is a medical emergency and you should seek medical attention immediately if you have any symptoms of spinal cord compression (incontinence, limb weakness, limb numbness).

For more information see the **Myeloma bone disease and bisphosphonates Infoguide** and the **Vertebral compression fractures in myeloma Infoguide** from Myeloma UK

Skeletal survey

What is it?

A skeletal survey is a series of X-rays of the limb bones, spine, skull, ribs and pelvis.

Why am I having this test?

Most patients will be given X-rays as part of the diagnosis of myeloma. X-rays can examine large areas of the body and only expose patients to relatively small doses of radiation. X-rays can pick up areas where there is risk of fracture of a bone. However, one of the limitations of X-rays is that they only detect lytic lesions when 30–50% of the bone has been lost and this means that in 20% or more patients, bone damage is not detected by X-ray.

X-rays were for many years the main imaging test for detecting myeloma bone disease. In recent years, other imaging scans that can pick up smaller amounts of bone disease are increasingly being used. These include CT, MRI and PET scans (see following sections). However, the type of scans used will also depend on availability of scanning equipment. At many centres, X-rays are used as the main initial imaging method at the time of diagnosis of myeloma.

What happens during the test?

A skeletal survey will last about 30-45 minutes in total. Each X-ray will only last for a few moments. The X-ray procedure itself is painless, but you may be asked to lie in certain positions that may be uncomfortable or painful. It may help to take painkillers for a few hours before your X-ray appointment and to use pillows to make you more comfortable.

Magnetic resonance imaging (MRI)

What is it?

MRI uses a combination of radio-waves, a powerful magnetic field and a computer to generate images of the organs and tissues of the body.

Why am I having this test?

MRI (and CT) scans are the most sensitive ways to detect bone damage in myeloma. MRI scans can

provide an in-depth picture of how the myeloma is affecting the bones, and where it is occurring throughout the bone marrow.

UK guidelines recommend that MRI scanning of the whole body should be considered as first choice for diagnosing myeloma, if it is suitable for the patient. However, not all patients will have access to an MRI scanner at their local hospital. They may be referred to another hospital for the scan.

MRI is also used to detect suspected spinal cord compression. It can also be used when the healthcare team are deciding if you need any surgery or localised radiotherapy on areas of bone damage.

What happens before the test?

MRI scans involve a powerful magnet, so you will not be able to have an MRI if you have any metal in your body (such as a pacemaker, certain types of pins in bones, or metal fragments following an injury). Modern joint replacements are often safe in an MRI scanner – your doctor will be able to check this. You will be asked to remove any metal belongings such as jewellery.

You may be given an injection of dye into the arm. This is called a contrast medium, which can be used to increase the detail of the scan. Many myeloma patients will not have this dye, especially if they have kidney problems. If you do receive the dye, you may experience side effects just after it is injected (such as nausea or a metallic taste in your mouth).

What happens during the test?

During the scan you will lie on a flat bed. The operator will slide the bed into the large tube-shaped MRI machine. You will be asked to lie as still as possible, and the test will last for about an hour. You will have headphones to protect your ears from the noise of the machine. You will be able to hear the operator through the headphones and talk to them during the scan.

The confined space in the machine can make patients feel a little claustrophobic during the scan. If you think this may be a problem for you, speak to the department

in advance of the scan, so that they can make sure you are as comfortable as possible.

Figure 4 shows a typical MRI scanner.

Computerised tomography (CT) scan

What is it?

CT scans combine an X-ray procedure with a specialised computer to create detailed cross-section images of the body. CT scans are quicker to perform than skeletal surveys. A CT scan uses higher doses of radiation than a skeletal survey.

However, recently a scan called a whole-body low-dose CT (WBLDCT) scan has been developed, which uses a lower dose of radiation while still accurately assessing bone damage.

Figure 4. An MRI scanner

Why am I having this test?

Like MRI scans, CT scans are much more sensitive than standard X-rays and show areas of bone damage or areas of bone at risk of damage in greater detail. Because of this, they can show up smaller lytic lesions than ones that can be detected by X-rays. They can be used to detect lytic lesions in the vertebrae and other areas of the body that are harder to access with X-rays.

What happens before the test?

You will be asked not to eat or drink for several hours before the scan. You will also be asked to remove any metal belongings such as jewellery, as they can interfere with the images produced.

You may be given an injection of contrast medium, which can be used to increase the detail of the scan. Many myeloma patients will not have this dye, especially if they have

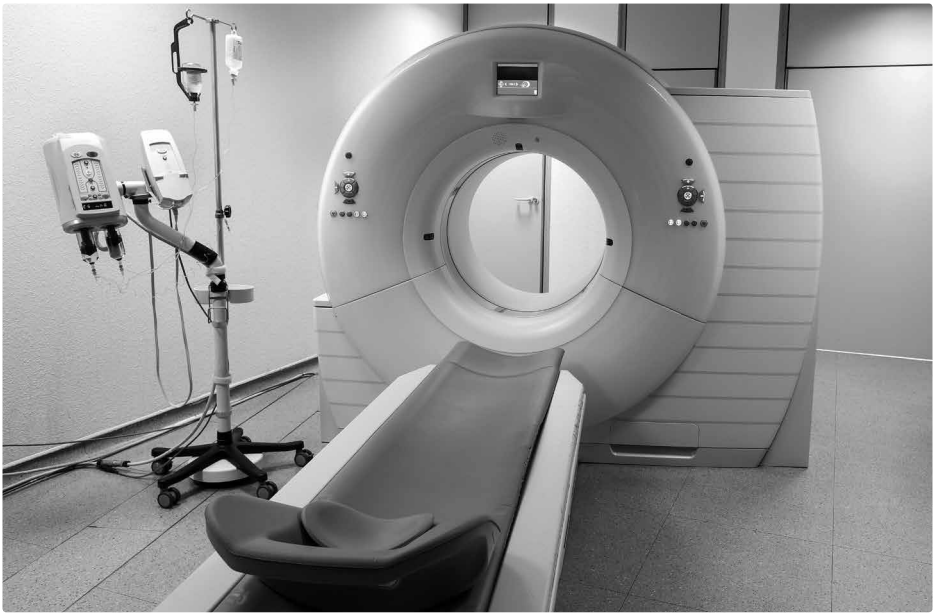

Figure 5. A CT scanner

kidney problems. If you do receive the dye, you may experience side effects just after it is injected (such as a feeling of warmth or a metallic taste in your mouth).

What happens during the test?

During the scan you will lie on a flat bed. The operator will slide the bed into the large doughnut-shaped CT machine. You will be asked to lie as still as possible, and the test will last about 10–30 minutes. You will be able to hear the operator and talk to them through an intercom during the scan.

Figure 5 shows a typical CT scanner.

Positron emission tomography (PET) scans

What is it?

In a PET scan, patients are given an injection of a form of liquid sugar to which a small amount of a radioactive label has been added. This is called a tracer. The sugar is taken up by cells in the body, and cells such as myeloma and other cancer cells which are actively multiplying take up sugar more quickly. A special camera detects where these cells are, and therefore can produce an image of the locations of the myeloma cells around the body.

In myeloma, PET scans are usually combined with CT scans (called PET-CT scans). PET scans can also be combined with MRI scans (PET-MRI scans). These combined scans help to provide a more detailed picture of a patient's myeloma.

Why am I having this test?

PET-CT and PET-MRI scans are not routinely used in myeloma. However, the sensitivity of the testing can be useful in some myeloma patients.

What happens before the test?

For most PET-CT and PET-MRI scans you will be asked not to eat for several hours beforehand. For both types of scan you will be asked to remove any metal jewellery etc. You will not be able to have a PET-MRI scan at all if you have any metal inside your body, such as a pacemaker (see 'Magnetic resonance imaging (MRI)' section on page 19). You will be given an

injection of the tracer liquid about an hour before the scan. You will be asked to rest while the tracer is spreading around your body. The amount of radioactivity is very small.

What happens during the test?

During the scan you will lie on a flat bed. The operator will slide the bed into the large tube-shaped PET-CT or PET-MRI machine. You will be asked to lie as still as possible, and the test will last for about 30 minutes. You will be able to hear the operator and talk to them during the scan.

The confined space in the machine can make patients feel a little claustrophobic during the scan. If you think this may be a problem for you, speak to the department in advance of the scan, so that they can make sure you are as comfortable as possible.

Deciding to start treatment

Once your doctor has the results for some or all of the tests described in the previous sections, and myeloma has been diagnosed, they will have a clear and in-depth picture of the pattern of your disease.

Results from the tests and investigations, together with your symptoms, will help decide when treatment should begin, and what that treatment should be. Your myeloma treatment may involve **high-dose therapy** and **stem cell transplantation**, and may include combinations of drugs. Drug treatments may be given for a number of cycles, until the myeloma has gone into remission, at which point there may be a rest period with no treatment.

For more information on specific myeloma treatments see the **Myeloma Treatment Guides** and the **High-dose therapy and autologous stem cell transplantation Infoguide** from Myeloma UK

Some patients having these tests will not be diagnosed with myeloma, but with a related condition, **smouldering myeloma** or **monoclonal gammopathy of undetermined significance (MGUS)**. Patients with MGUS, and most patients with smouldering myeloma, will not be given treatment. Instead, they will have ongoing monitoring to check for any signs that active myeloma is developing.

For more information see the **Smouldering myeloma Infosheet** and the **MGUS Infosheet** from Myeloma UK

Follow-up tests – during treatment

During your myeloma treatment, you will have regular tests. These will include tests to check how well the myeloma is responding to the treatment. Usually, paraprotein and/or free light chain tests will be used for this.

Other tests will also be done regularly (full blood count and blood biochemistry). These will be done to check the response of the myeloma to treatment, and also to monitor any complications you have, including side effects of your drug treatment.

Scans may be done to check how your bone lesions are responding to treatment.

Tests are generally done at least monthly during treatment, normally between treatment cycles.

Follow-up tests – during remission

Once you have finished your cycles of treatment and have no signs of active myeloma, you are in remission. You may be continuing longer-term treatment with one or more of your myeloma drugs during this time.

During remission you will continue to have a range of tests regularly. The tests will be similar to those done during treatment, but they are likely to be less often. You will have regular tests of paraprotein and/or free light chain, as well as routine blood tests.

How often you are tested during remission will depend on several factors, including how long you have been in remission, your age, and any other medical conditions you have.

Most patients in remission will be tested every two to three months initially.

Most patients will not have follow-up bone marrow tests or scans after the initial ones done at diagnosis. However, certain types of myeloma that cannot be monitored in other ways may require bone marrow tests or scans to be done more regularly (see the 'Different types of myeloma and how they are monitored' section on page 29).

In some patients, the paraprotein or light chain levels may still be measurable, but at a stable low level: this is known as a **plateau**. If you are in a plateau you will have similar testing to patients in remission, but they may be more frequent.

Follow-up tests – checking for relapse

During remission, regular monitoring is done to check for any signs of relapse. For most patients, this will entail regular blood tests for paraprotein and/or free light chain. Some patients who can't be monitored using paraprotein tests or sFLC assays may have more regular bone marrow biopsies or scans during remission.

A return of myeloma symptoms, or increases in paraprotein or free light chains, may indicate that you are going into a relapse. Relapse will be indicated by a trend towards higher paraprotein/free light chain readings, not just by a single higher reading.

A 'biochemical relapse' means that your paraprotein and/or free light chains are increasing, but you don't have any symptoms of myeloma.

A 'clinical relapse' means that as well as increasing paraprotein and/or free light chain levels, you also have symptoms and signs of myeloma (anaemia, raised calcium, bone pain, kidney problems) or a **plasmacytoma** (a localised build-up of myeloma cells).

Once a clinical relapse is occurring, you will have additional tests, such as blood tests for kidney problems and hypercalcaemia, and imaging if you experience new bone symptoms.

If your paraprotein level is increasing but you don't have any returning signs and symptoms of myeloma, there may be a period of "watch and wait", with more frequent clinic visits and blood tests, before treatment is restarted.

In rare cases, patients who have 'non-secretory' myeloma can relapse with new symptoms even though their paraprotein/light chain level has not increased. See the next section on page 29 for more detail about non-secretory myeloma.

Different types of myeloma and how they are monitored

Most commonly in myeloma, the myeloma cells produce whole immunoglobulin (paraprotein). In some less common types of myeloma, the cells produce only light chains, or they may produce little or no immunoglobulin of any type. These types of myeloma need to be diagnosed and monitored in different ways from standard myeloma.

Light chain myeloma

Light chain myeloma (also called Bence Jones myeloma), where the myeloma cells only produce light chains, occurs in about 20% of myeloma patients. The light chains can be measured in the blood using the sFLC assay (see page 12). The sFLC assay will be done regularly during treatment and in periods of remission.

Oligosecretory and non-secretory myeloma

For a very small number of myeloma patients (less than 1%), the myeloma cells produce very little or no abnormal immunoglobulin chains of any type (neither paraprotein nor light chains).

Oligosecretory myeloma patients have very low but measureable levels of abnormal protein in their blood or urine.

Non-secretory myeloma patients have no detectable levels of either paraprotein or light chains in their blood or urine.

The low or undetectable levels of paraprotein make it challenging for these types of myeloma to be diagnosed and monitored. The sFLC assay is able to detect very small amounts of light chains in the blood, making it easier to diagnose and monitor many oligosecretory patients. However, in some oligosecretory patients, the levels of free light chains are so low that even the sFLC assay will not be able to pick them up. These patients are likely to have more regular bone marrow biopsies during treatment and remission. Patients with non-secretory myeloma are also generally monitored using other tests (MRI/CT/PET scans or bone marrow biopsies).

In some patients, myeloma cells may produce paraprotein during earlier stages of their myeloma, but may eventually stop doing so. In these patients, methods of monitoring the disease other than paraprotein need to be used.

Screening tests for myeloma

Myeloma is not an inherited cancer in the sense of being caused by a single inherited gene.

For example, in cystic fibrosis a person has the disease if they inherit two faulty copies of a single gene, one from each parent. This is not the case with myeloma.

It has been found that there is a slightly higher risk (just over two times the risk) of developing myeloma amongst family members than in the general population. The risk in real numbers is still very small even for people with close family members with myeloma. Therefore, overall, people may inherit factors that increase their chances of developing myeloma, but their chances of developing it still remain very low, and other genetic and environmental factors are needed before it develops.

For these reasons, a screening test for myeloma does not currently exist. The very low overall risk of developing myeloma, and the fact the myeloma is not considered to be an inherited cancer, mean that setting up a screening programme would not be considered a cost-effective use of public health resources.

For more information see the **Is myeloma an inherited cancer? Infosheet** from Myeloma UK

Genetic testing in myeloma

There are a number of specific genetic mutations which can occur in myeloma, and some, though not all, myeloma patients may have genetic testing.

Genes and genetics

Genes are the sets of instructions that control how the body develops and how each cell in the body develops and grows. They are made up of a chemical called DNA and packaged into bundles called **chromosomes**. Genes instruct proteins to be made, which in turn control processes in the body. The **genetic code** is all the instructions contained in a person's genes.

We inherit our genes from both our parents. However, they can change over time in our cells. Changes, called **genetic mutations**, are mistakes in the genetic code in a cell. Genetic mutations can cause changes in the way a cell develops and multiplies. Sometimes a combination of several mutations causes the normal controls in a cell to be switched off or damped down and the cell becomes a cancer cell such as a myeloma cell.

Genetic changes in myeloma

There are a number of genetic mutations which frequently occur in myeloma. The mutations may involve part of a specific chromosome being removed, duplicated or moved (translocated). The mutations are given names which are codes for the specific change that has occurred, such as t(4;14) and del(17p). This is also known as the patient's **genetic subtype**.

Why is genetic testing done?

The different mutations may affect how myeloma cells develop, and how quickly or slowly the myeloma progresses. They may also affect how well patients respond to treatments. The genetic changes are referred to as high-risk or low-risk **prognostic markers** in myeloma.

Guidelines published by NICE (the National Institute for Health and Care Excellence) recommend that

patients should have genetic tests to identify whether they have lower or higher risk myeloma. In some cases, the genetic testing will also help to tailor treatment. In practice, however, genetic testing is not available to all patients. You may have genetic testing done if you are receiving treatment as part of a clinical trial.

Types of genetic tests

There are several different tests that detect different types of genetic changes in cells. The most common in myeloma are described below.

Karyotyping

This is a test of the overall appearance of the chromosomes. Cells from the patient's bone marrow are treated with a special stain, and the chromosomes are looked at under a microscope to pick up any abnormalities in their number or appearance.

Fluorescence in-situ hybridisation (FISH)

This is a test that is more sensitive than karyotyping, and can enable the laboratory to see specific DNA sequences on the chromosomes that are missing or in the wrong place. The chromosomes from bone marrow cells are stained with a fluorescent marker and looked at under a microscope. When stained, the chromosomes look like strings with light and dark bands. Small and subtle changes can be identified using the bands.

For more information see the **Genetics and myeloma Infoguide** from Myeloma UK

Staging myeloma

Once you have been diagnosed with myeloma, your myeloma will be staged.

Staging measures how much a patient's myeloma has developed (the tumour burden) and how much it has affected the body. Staging is also used to assess the prognosis (likely development) of the myeloma. Your myeloma will be staged at diagnosis, and possibly again once the myeloma relapses. Because staging does not usually affect treatment, your doctor may not discuss the staging results much.

The staging systems most commonly used are called the International Staging System (ISS) and the revised International Staging System (rISS). Your myeloma stage will be based on several different tests.

For the ISS the tests are:

- Beta 2 microglobulin in the blood – a higher level indicates more advanced myeloma (see page 10)
- Albumin in the blood – a lower level indicates more advanced myeloma (see page 9)

For the rISS there are two extra tests:

- Lactate dehydrogenase (LDH) – LDH is a protein that is found in almost all body cells, but very little is normally in the blood. More LDH is found in the blood when cells are being damaged or destroyed. LDH is used as an indicator in various different cancers, and increased levels in the blood are an indicator of a less good prognosis in myeloma
- Genetic changes – genetic changes measured by FISH testing may indicate a higher or lower risk of progression (see the 'Genetic testing in myeloma' section on page 32)

The stages of the ISS and rISS are shown in Table 1.

Stage	ISS	rISS
I	β2M < 3.5mg/L AND Albumin ≥ 35 g/L	β2M < 3.5mg/L AND Albumin ≥ 35 g/L AND Standard-risk genetics AND Normal LDH
II	Not ISS stage I or III	Not rISS stage I or III
III	β2M ≥ 5.5 mg/L	β2M ≥ 5.5 mg/L AND Either high LDH or high-risk genetics

Table 1. The International Staging System (ISS) and revised ISS (rISS) for myeloma

Future directions

Developments in newer and more precise DNA tests, and new scanning techniques, are progressing fast.

The newer methods of genetic testing can pick up smaller changes in the genes in myeloma cells. This information is being used to help develop treatments that target these changes.

Advanced genetic testing and imaging are also helping our understanding of how myeloma develops from precursor conditions, smouldering myeloma and MGUS.

Researchers are also trying to understand better how a patient's myeloma cells change over time. This is a process called clonal evolution. Modern scanning methods make it possible to look in detail at how this occurs, in the hope of improving the targeting of myeloma treatments. Researchers are using advanced scanning techniques and gene sequencing to map where different clones of myeloma cells are located in the body.

New tests are being used to pick up increasingly small amounts of residual myeloma cells present during remission. These residual cells are called **minimal residual disease (MRD)**. Detecting increasingly small amounts of MRD makes it possible to compare different treatments in clinical trials more accurately. It also helps provide information about likely prognosis.

Medical terms explained

Anaemia: A condition in which the amount of haemoglobin in the blood or the number of red blood cells is below the normal levels, causing shortness of breath, weakness and tiredness.

Antibodies (immunoglobulins): Proteins found in the blood produced by cells of the immune system, called plasma cells. Their function is to bind to substances in the body that are recognised as foreign, such as bacteria and viruses (known as antigens), enabling other cells of the immune system to destroy and remove them.

Bence Jones proteins: Free light chains that have been filtered from the blood by the kidneys and are found in the urine. The presence of any Bence Jones protein in urine is abnormal.

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

Bone marrow aspirate: A procedure to remove a sample of fluid and cells from the bone marrow for examination and testing.

Bone marrow biopsy (trephine biopsy): A procedure to remove a small sample of bone marrow tissue (for examination under a microscope).

Chromosomes: Structures in which the DNA is packaged within a cell.

Cytokine: Protein produced mainly by cells of the immune system that acts as a chemical messenger between cells. Cytokines can stimulate or inhibit the growth and activity of various types of cells.

Free light chain: A molecule which normally makes up part of an antibody. Called “free” light chain when it is not attached to the rest of the molecules that make up the antibody.

Freelite®: One of the brand names for the serum free light chain assay, a test used to detect and measure the type and amount of free light chains in the blood.

Genes: Strands of DNA which act as a set of instructions to make molecules called proteins. Together these make up the blueprint of life that determines how the body develops, grows and functions.

Genetic code: All the instructions contained in a person's genes.

Genetic mutation: Abnormal change or error in the genetic code.

Genetic subtype: A specific genetic mutation in a myeloma patient's DNA.

Heavy chain: The larger of two components that make up the structure of antibodies (immunoglobulins).

High-dose therapy: Treatment with high doses of chemotherapy given intravenously, usually via a central line (such as a HICKMAN® line), or a PICC line, prior to patients receiving healthy stem cells as part of the stem cell transplantation procedure. Also known as conditioning treatment.

Hypercalcaemia: A higher than normal level of calcium in the blood, which may cause loss of appetite, nausea, thirst, fatigue, muscle weakness, restlessness and confusion.

Immune response: The body's defence against infection or abnormal cells, which is generated by the immune system.

Immune system: The complex group of cells and organs that protect the body against infection and disease.

Key worker: A member of the multidisciplinary team (MDT), usually a clinical nurse specialist, who will be the patient's primary point of contact during treatment and care.

Kyphosis: An abnormal curvature of the spine.

Light chain: The smaller of two components that make up the structure of antibodies (or immunoglobulins). There are two types of light chain, kappa and lambda.

Light chain myeloma: A type of myeloma where only the light chain portion of the immunoglobulin is produced.

Lytic lesions: Damage to the bone caused by myeloma. They look like holes in the bone on an X-ray.

Malignant: Cancerous with the ability to spread.

Minimal residual disease (MRD): The myeloma cells which remain when the patient is in remission, and which cannot be detected using standard methods.

Monoclonal gammopathy of undetermined significance (MGUS): A non-cancerous condition in which low levels of paraprotein are present in the blood. Patients do not have symptoms but have an increased risk of developing myeloma.

Myeloma bone disease: A complication in which bone is damaged by myeloma cells. Results can include lytic lesions, pathological fractures or spinal collapse.

Non-secretory myeloma: A type of myeloma in which there is no detectable paraprotein or light chains in either the blood or urine.

Oligosecretory myeloma: A type of myeloma where patients only secrete very low levels of paraprotein and/or free light chains.

Paraprotein: An abnormal antibody (immunoglobulin) produced in myeloma. Measurements of paraprotein in the blood can be used to diagnose and monitor the disease. Also known as M protein.

Plasma cells: A type of white blood cell that produces antibodies (immunoglobulins) to fight infection.

Plasmacytoma: A localised build-up of myeloma cells found either inside the bone (intramedullary plasmacytoma), or outside the bone (extramedullary plasmacytoma).

Plateau: A period of time when the myeloma, and the paraprotein level, is relatively stable. Often referred to as stable disease.

Prognosis: The probable outcome or course of a disease.

Prognostic marker: A characteristic that gives an indication of the likely progression of a disease.

Quality of life: A term that refers to a person's level of comfort, enjoyment, and ability to pursue daily activities. It is a measure of an overall sense of wellbeing.

Relapse: The point where disease returns or becomes more active after a period of remission or plateau.

Remission: The period following treatment when myeloma cells and paraprotein are no longer detectable, and there are no clinical symptoms of myeloma.

Seralite®: One of the brand names for the serum free light chain assay, a test used to detect and measure the type and amount of free light chains in the blood.

Smouldering myeloma: The term used to describe an early stage of myeloma in which there is paraprotein in the blood but no symptoms and no damage to organs. Smouldering myeloma patients generally do not require treatment.

Spinal cord compression: The term used to describe pressure on the spine. It can be caused by a collapsed vertebra or by the growth of a plasmacytoma within the spinal canal.

Staging: A measurement of how much a patient's myeloma has developed and how much it is affecting the body.

Stem cell transplant: The infusion of healthy stem cells into the body. This allows the bone marrow to recover and renew its blood-forming capacity following the administration of high-dose chemotherapy.

Tumour burden: The number of cancer cells, the size of a tumour, or the amount of cancer in the body.

Appendix 1: Blood tests and normal ranges

Blood tests	Test name	Normal range*	Notes
Full blood count	White cell count	4.0–11.0 x10^9/L	A low count makes you less able to fight infections
	Haemoglobin (men)	135–180 g/L	A low haemoglobin level causes anaemia and fatigue
	Haemoglobin (women)	115–160 g/L	
	Platelets	150–400 x10^9/L	A low count makes you bruise or bleed easily
	Absolute Neutrophil Count	1.5–7.5 x10^9/L	A low count makes you less able to fight infection
Urea, electrolytes and creatinine	Urea	2.5–6.7 mmol/L	Measure of kidney function
	Creatinine	70–150 µmol/L	Measure of kidney function
	Calcium (total)	2.12–2.6 mmol/L	Raised by myeloma bone disease
Proteins	Paraprotein	0 g/L	Abnormal protein found in certain conditions, including myeloma
	Total protein	60–80 g/L	Often raised in myeloma because of amount of paraprotein
	Albumin	35–50 g/L	Often lowered in myeloma because of presence of paraprotein
	Kappa (κ) light chain	3.3–19.4 mg/L	Part of an immunoglobulin (antibody). Levels are often raised in myeloma, with an abnormal ratio (normal ratio is 0.26κ to 1.65λ)
	Lambda (λ) light chain	5.71–26.3 mg/L	

* The normal range is an average, but each hospital laboratory has its own 'normal range' of values

Explanation of units

g/L number of grams there are in a litre of blood
x10^9/L number of billion cells there are in a litre of blood
mole a standard measurement for the amount of any chemica
mmol/L number of thousandths of a mole in a litre of blood
µmol/L number of millionths of a mole there are in a litre of blood

Please note that doctors do not use a litre of blood to make these measurements; they just take a small sample (a few millilitres) and then multiply up the results.

Useful organisations

Carers UK **www.carersuk.org**
0808 808 7777
Provides advice, information and support for carers.

Citizens Advice **www.citizensadvice.org.uk**
England: 03444 111 444
Wales: 03444 77 20 20
Scotland: call your local office
Northern Ireland: call your local office
Offers advice about debt and consumer issues, benefits, housing, legal matters and employment.

Macmillan Cancer Support **www.macmillan.org.uk**
0808 808 0000
Provides practical, medical and financial information and support to all cancer patients and their carers.

Maggie's **www.maggiescentres.org**
0300 123 1801
Provides free practical, emotional and social support to people with cancer and their family and friends.

Mind **www.mind.org.uk**
0300 123 3393
Provides advice and support to empower anyone experiencing mental health problems.

NHS 111 Service **www.nhs.uk/111**
111
Call 111 when you need medical advice fast but it's not a 999 emergency. NHS 111 is available 24 hours a day, 365 days a year.

We're here for everything a diagnosis of myeloma brings

Call our **Myeloma Infoline** on **0800 980 3332** for practical advice, emotional support and a listening ear.

Get answers to your questions by emailing **AskTheNurse@myeloma.org.uk**

Learn about myeloma from experts and meet other patients at our **Patient and Family Myeloma Infodays**.

Order or download our **information publications**, which cover all aspects of myeloma - call **0800 980 3332** or visit **myeloma.org.uk**

Join your nearest **Myeloma Support Group** to meet up and talk to other people face to face.

Visit **myeloma.org.uk**, a one-stop-shop for information on myeloma; from news on the latest research and drug discovery to articles on support, treatment and care.

Watch **Myeloma TV**, videos about myeloma presented by experts, patients and family members.

Use the **Discussion Forum** for the opportunity to share experiences and advice about living with myeloma.

We need your help

Thanks to our generous supporters we are able to provide information and support to patients and their families, as well as fund vital research that will help patients live longer and with a better quality of life.

Myeloma UK receives no government funding. We rely on fundraising activities and donations.

You can support Myeloma UK by:

- **Making a single donation or setting up a Direct Debit**
  Online at **myeloma.org.uk/donate**
  Over the phone **0131 557 3332**
  Or by posting a cheque payable to **Myeloma UK** to:
  Myeloma UK, 22 Logie Mill, Beaverbank Business Park, Edinburgh, EH7 4HG
- **Fundraising** – fundraising is a positive way of making a difference and every pound raised helps. As myeloma is a rare, relatively unknown cancer, fundraising is also a great way to raise awareness
- **Leaving a gift in your will** – legacies are an important source of income for Myeloma UK and help us to continue providing practical support and advice to myeloma patients and their families. They also help us to undertake research into the causes of myeloma and investigate new treatments

However you decide to raise funds, our Fundraising Team is here to support you. Contact us on **0131 557 3332** or email **fundraising@myeloma.org.uk**

Nobody ever forgets the moment they are diagnosed with myeloma. Myeloma UK advances the discovery of effective treatments, with the aim of finding a cure. That is what patients want, it's what they deserve and it's what we do.

Judy Dewinter – President, Myeloma UK

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We appreciate your feedback. Please fill in a short online survey about our patient information at **myeloma.org.uk/pifeedback** or email any comments to **myelomauk@myeloma.org.uk**

For a list of references used to develop our resources, visit **myeloma.org.uk/references**

Treatments and tests Infoguide:
Tests and investigations in myeloma

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