

MGUS

Related conditions Infosheet

This Infosheet explains what Monoclonal Gammopathy of Undetermined Significance (MGUS) is and how it is diagnosed and managed.

What is MGUS?

Monoclonal Gammopathy of Undetermined Significance, or 'MGUS', is a condition where there is an abnormal protein in the blood. It is not a cancer.

The abnormal protein (called a paraprotein) in the blood is produced by abnormal plasma cells in the bone marrow.

MGUS does not generally cause any symptoms or need treatment. It is usually diagnosed by chance, when tests are being done for other reasons.

Plasma cells and the bone marrow

Bone marrow is the spongy centre of bones where blood cells are made. This includes a type of white blood cell called plasma cells. Normal plasma cells help fight infection by producing antibodies (also known as immunoglobulins).

Antibodies

Antibodies are Y shaped proteins and are made up of four parts – two identical heavy chains and two identical light chains. Figure 1 (below) shows an antibody, with the two heavy chains in purple and the two light chains in blue.

There are five types of possible heavy chain: G, A, D, E and M. Antibodies using these heavy chains are called IgG, IgA, IgD, IgE and IgM. There are two types of light chain: kappa (κ) and lambda (λ).

Normal antibodies are part of the immune system. They bind to bacteria and viruses and flag them for removal.

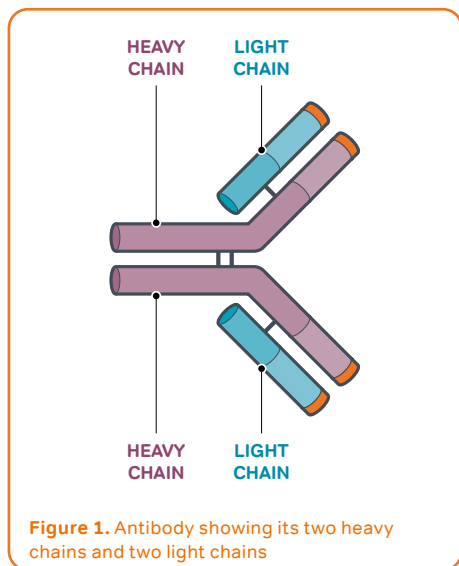


Figure 1. Antibody showing its two heavy chains and two light chains

Paraprotein

In MGUS, plasma cells in the bone marrow become abnormal and release an increased amount of a single type of antibody. This is known as a paraprotein and it has no useful function.

Paraprotein can also be called M protein, monoclonal protein or abnormal protein (this protein is not related to dietary protein in any way).

Types of MGUS

MGUS is named according to the type of heavy chain the paraprotein is made from:

- IgM MGUS
- Non-IgM MGUS – i.e. IgG, IgA, IgD or IgE MGUS
- Light chain MGUS – where there are no heavy chains at all, only light chains

Who can develop MGUS?

MGUS is more likely to develop in older people. The average age at diagnosis is 70 years. About one in 30 people aged 50 years or older will have the condition, rising to one in 20 people aged over 70 years and to nearly one in 10 people aged over 85 years.

Other factors, besides age, can increase the risk of developing MGUS:

- **Gender:** MGUS is more common among men than women
- **Ethnicity:** MGUS is more common among people from black ethnic groups than in white or Asian people, and more likely to develop at a younger age
- **Family history:** MGUS is more common among people who have a close relation with MGUS or myeloma

Most people with MGUS will never know that they have the condition because it usually does not cause any symptoms or lead to a more serious diagnosis.

What causes MGUS?

The exact cause or causes of MGUS are not yet known but is thought to involve complex changes at the genetic level.

What are the symptoms of MGUS?

People with MGUS generally have no symptoms. Usually, any symptoms that they have are caused by other medical issues.

Having MGUS can mean you are at a slight increased risk of several medical issues. These include bone fractures, osteoporosis, blood clots and infections.

However, most people with MGUS will not be affected by these issues, and in some who do have them, there may be no connection with MGUS. You may be given some tests and/or treatment for these issues.

Speak to your doctor (GP or haematologist) if you have any new symptoms, or any symptoms that you are concerned about.

Monoclonal Gammopathy of Clinical Significance (MGCS)

In some people, the abnormal plasma cells cause specific problems in the body. This happens when the low levels of paraprotein, or the light chain part of the paraprotein, cause tissue or organ damage.

This can include kidney damage, certain skin rashes, or peripheral neuropathy (damage to the nerves, causing symptoms such as numbness or tingling).

In these cases, the condition may sometimes be referred to as Monoclonal Gammopathy of Clinical Significance (MGCS). It may also be called Monoclonal Gammopathy of Renal Significance (MGRS) when it is the kidney that is affected. If you have MGCS you may need treatment for the complications involved. Your doctor will tell you if you have MGCS.



For more information see the **Monoclonal Gammopathy of Clinical Significance (MGCS)** Infosheet from Myeloma UK

How is MGUS diagnosed?

As MGUS is not normally associated with any symptoms, the paraprotein is usually discovered when tests are being done for unrelated reasons.

Once a paraprotein is discovered, it is important to make sure that it is not due to a more serious diagnosis, such as myeloma. Some of the tests that are recommended may be done for this reason.

In MGUS, blood and/or urine tests will show:

- A paraprotein level in the blood of 30 g/L or less
- Little or no protein in the urine
- A normal calcium level
- Normal kidney function
- No anaemia

A bone marrow biopsy and X-rays or scans are only carried out in some people during initial investigations. If they are done they will show:

- Less than 10% abnormal plasma cells in the bone marrow
- No bone damage

Some people with MGUS may have an abnormal result for one or more of these tests due to an unrelated condition.

How is MGUS managed?

Current guidance recommends that MGUS should be actively monitored (with blood tests and checks for symptoms) but not treated. This is because most people with MGUS remain well and never develop any problems related to it.

However, a very small number of people with MGUS go on to develop another, more serious condition. For this reason, it is important

to have blood tests at intervals to check for any change in your condition.

This is to make sure that if you need treatment, you can have it as soon as necessary. There is more about this in the section “Can MGUS develop into another condition?” on page 6.

When will your MGUS be monitored?

You may have blood tests every 3–6 months for the first year, followed by checks every 6–12 months after that. Your tests may be less often if you have a very low risk of progression to serious disease. There is more about risk of progression in the section “Is there any way to tell if MGUS will develop into myeloma or a related condition?” on page 7.

Your blood tests may be arranged by your GP, a specialist nurse or haematologist. You will also be monitored for any symptoms that could indicate a change in your condition.

Your GP may find the publication **Myeloma and MGUS: A guide for GPs** helpful. This can be ordered from Myeloma UK.

What blood and urine tests will be done?

Your regular blood and urine tests will include:

- Paraprotein in your blood and/or urine, and sometimes also free light chain
- Red and white blood cells and platelets
- Tests to check kidney function
- Blood tests for bone disease

Paraprotein levels can rise and fall in MGUS – this is normal. However, if there is a steady or large increase in paraprotein or free light chain, or if you develop symptoms, further tests will be done.

Keep track of your tests results with a free **MGUS Diary** from Myeloma UK. Order now from myeloma.org.uk

What symptoms should you watch out for?

It is important to report any new or worsening symptoms, as soon as possible. Don't wait for your next routine blood test appointment. Symptoms to watch for in particular are:



General deterioration in health or ability



Pain, particularly in your back or ribs



Fatigue



Having frequent infections, or infections that don't clear easily



Unexpected bone breaks



Swollen legs or abdomen



Breathlessness



Bruising or bleeding



Numbness or tingling in the feet, hands or legs



Unexpected weight loss

Can MGUS develop into another condition?

It is important to remember that most people with MGUS will have a stable condition with no effect on their general health throughout their lifetime.

In a very small proportion of people, MGUS eventually develops into a more serious condition, such as myeloma, AL amyloidosis or a type of lymphoma.

Myeloma, also known as multiple myeloma, is a type of blood cancer arising from plasma cells in the bone marrow. It causes symptoms and requires treatment. Each year around one in 100 people with MGUS will be diagnosed with myeloma or related conditions and will need treatment. Some of these people may develop an intermediate condition called smouldering myeloma. This is an early stage of myeloma which is not usually treated.



For more information see [Myeloma – An introduction](#) and the [Smouldering myeloma Infosheet](#) from Myeloma UK

AL amyloidosis is a condition where an abnormal protein made of light chains builds up in different tissues or organs. It can develop in rare cases from MGUS.

For more information see

AL amyloidosis: Your Essential Guide
from Myeloma UK



Lymphoma can develop in a small proportion of people with IgM MGUS, and this is explained in the section “IgM MGUS” on page 8.

Is there any way to tell if MGUS will develop into myeloma or a related condition?

It is not yet clear who will be in the small number who eventually progress to myeloma or a related condition. There is no definitive test to show who will progress and who will remain stable long-term.

Certain factors are associated with an increased risk of progression (although the risk is still very low).

These factors are:

- An abnormal serum free light chain ratio – this is the ratio between the two different types of light chain (kappa and lambda) that can be produced. An abnormal ratio shows that there is an increase in the production of one type of light chain

- Types of MGUS other than IgG type
- Higher paraprotein level (15 g/L or more)

If you do not have any of these three risk factors (meaning your MGUS is called low-risk), your risk of progressing to myeloma is extremely low – over 20 years, only around two in 100 people with low-risk MGUS progress to myeloma or related conditions. Your risk of progression is higher the more of the risk factors you have, but it is still very low overall. Your risk level may affect how closely you are monitored.

The cause of progression from MGUS to myeloma or related conditions is unknown but probably involves further changes at the genetic level. This is an area of active research.

IgM MGUS

IgM MGUS is where the paraprotein produced is of the IgM type. This type of MGUS can, although rarely, progress to a different condition rather than myeloma. This condition is a low-grade non-Hodgkin lymphoma (sometimes called Waldenström's macroglobulinaemia).

Non-Hodgkin lymphoma is a different blood cancer from myeloma and the symptoms can include fatigue, anaemia, swollen glands and sometimes, sweats at night.

For more information, contact **WMUK (wmuk.org.uk)** or **Lymphoma Action (lymphoma-action.org.uk)**



Living well with MGUS

For most people, the diagnosis of MGUS has no effect on daily life. However, we know from speaking to people that anxiety can be caused by knowing that you have a condition for which there is no treatment and a (very small) possibility of developing a more serious condition.

You may find you are anxious at certain times, for example in the period after your diagnosis, and also when your blood tests and

follow-up appointments are due. This is not unusual for people with MGUS.

However, you can be reassured that very few people do progress to a more serious condition, and that your healthcare team are monitoring you and will take any action needed.

Sources of support

It's important to reach out for any help that you need, and there are many sources of support for people with MGUS. You can get support from:



Your healthcare team – if you are concerned about your tests or about any new symptoms, you should speak to your healthcare team



You can call the Myeloma UK Infoline on **0800 980 3332** or email **AskTheNurse@myeloma.org.uk** for information, advice or just a listening ear



Family and friends – who you tell about your diagnosis (and when) is a personal decision. However, the friends or family that you do tell can be an important source of support



Chatting with someone else who has MGUS – speaking to someone who understands can help. The Myeloma UK Peer Buddy service is designed to facilitate one-to-one support by Peer Buddies who are happy to share their experience of MGUS. You can also speak to others living with MGUS on the Myeloma UK Discussion Forum

Myeloma UK is here for everything a diagnosis brings. Get in touch to find out more about how we can support you by calling the Infoline on **0800 980 3332** or visiting our website myeloma.org.uk

Staying positive and getting on with life

It is important not to let worry about your diagnosis of MGUS take over. Use the sources of support, and remember that in the great majority of cases MGUS does not cause any problems.

Key points

- MGUS is a condition where abnormal plasma cells in the bone marrow produce a protein called a paraprotein
- MGUS is not a cancer
- MGUS normally has no symptoms and is not treated
- In a very small number of cases, MGUS can develop into other conditions, such as myeloma
- People with MGUS will be monitored
- In most people, MGUS remains stable and has no effect on general health

About this Infosheet

The information in this Infosheet is not meant to replace the advice of your healthcare team. They are the people to ask if you have questions about your individual situation.

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

We value your feedback about our patient information. For a short online survey go to myeloma.org.uk/pifeedback or email comments to patientinfo@myeloma.org.uk

Other information available from Myeloma UK

Myeloma UK has a range of information booklets available covering all aspects of myeloma and related conditions.

Download or order them from myeloma.org.uk/publications

To talk to one of our Myeloma Information Specialists about any aspect of MGUS, call our Myeloma UK Infoline on **0800 980 3332** or **1800 937 773** from Ireland.

The Infoline is open from Monday to Friday, 9am to 5pm and is free to phone from anywhere in the UK and Ireland.

Information and support about myeloma is also available around the clock at myeloma.org.uk

Notes



Related conditions Infosheet:
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We're here for everything
a diagnosis brings

Get in touch to find out more about how we can support you

Call the Myeloma UK Infoline on

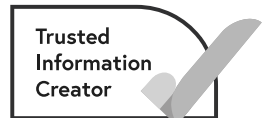
 **0800 980 3332**

Email Ask the Nurse at

 **AskTheNurse@myeloma.org.uk**

Visit our website at

 **myeloma.org.uk**



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