

MGUS

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

What is MGUS?

Monoclonal **g**ammopathy of **u**ndetermined **s**ignificance, or 'MGUS', is a benign (non-cancerous) condition. MGUS does not cause any symptoms and is usually diagnosed incidentally when tests are performed to investigate other problems. It does not require any treatment.

MGUS is characterised by the presence of an abnormal antibody in the blood and/or urine. Antibodies (also called immunoglobulins) help fight infection in the body and are produced by plasma cells, which are formed in the bone marrow. In MGUS, abnormal plasma cells in the bone marrow release an increased amount of a single type of antibody, known as paraprotein, which has no useful function.

MGUS can be categorised on the basis of the type of abnormal antibody affected. The categories of MGUS are: Non-IgM MGUS (for example IgG or IgA MGUS), IgM-MGUS and light chain MGUS.

While most MGUS patients have a stable condition which has no effect on their general health, a small proportion of patients will go on to develop a cancer called myeloma. MGUS can also progress to other conditions such as Waldenström's macroglobulinemia, AL amyloidosis or lymphoma.

Who can develop MGUS?

MGUS is a common condition which increases with age. About one in 30 people aged 50 years or older will have the condition and this rises to one in 20 people aged over 70 years, and to nearly one in 10 people aged over 85 years. It is about 1.5 times more common in men than in women.

The condition also appears to be nearly twice as common in people of African origin as Caucasian origin.

About four out of five 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?

There are no symptoms associated with MGUS and it does not require treatment. Generally, any symptoms that MGUS patients have are associated with other medical problems.

However, MGUS patients need to look out for any new symptoms that might indicate the development of a more serious diagnosis, such as myeloma. Common signs and symptoms of myeloma include bone pain, kidney damage, fatigue and being prone to recurring infection. It is important to report any new symptoms as early as possible to your doctor or nurse so that you can be appropriately managed.

How is MGUS diagnosed?

As MGUS is not associated with any symptoms, the paraprotein is usually discovered when tests are being performed to rule out other health issues, for example kidney

problems, osteoporosis or an inflammatory disorder; or it can be detected during routine pre-operative tests. Once paraprotein is discovered, it is important to make sure that it is not due to a more serious diagnosis such as myeloma, and so further tests are likely to be carried out.

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

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

If a bone marrow biopsy or X-rays are carried out they will show:

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

Some MGUS patients may have an abnormal result for one or more of these tests due to an unrelated condition. For example, it may be possible to have MGUS with anaemia caused by iron deficiency.

After a diagnosis of MGUS has been made the patient will have a regular blood test, usually for

the rest of their lifetime. Regular monitoring is important because of the small chance that MGUS will develop into a more serious diagnosis, such as myeloma. The aim of monitoring is to catch any changes at the earliest possible stage.

What is the link between MGUS and myeloma?

Myeloma, also known as multiple myeloma, is a type of bone marrow cancer arising from plasma cells. MGUS is a condition which resembles myeloma due to the presence of abnormal plasma cells in the bone marrow and paraprotein in the blood and/or urine, but at much lower levels than in myeloma. Also, unlike myeloma, MGUS does not cause symptoms.

Before a diagnosis of MGUS is made, other investigations will be carried out (see above) to ensure that there is no evidence of myeloma or other blood condition.

Will MGUS develop into myeloma?

It is generally now accepted that all myeloma patients have had MGUS first, whether it was identified or not. However, only a small percentage of MGUS

patients will go on to develop myeloma - each year around one in 100 MGUS patients will be diagnosed with myeloma and will need treatment.

MGUS usually remains stable for many years without progressing to myeloma. Data suggests that if MGUS remains stable for two years then, on average, it will remain stable for 10 years before there is progression to myeloma.

Is there any way to tell if MGUS will develop into myeloma?

It is not yet clear why only a small minority of patients progress to myeloma and, unfortunately, when MGUS is diagnosed no definitive test exists that shows who will progress to myeloma and who will remain stable long-term.

However, research does point towards certain factors that are associated with an increased risk of progression:

- An abnormal serum free light chain ratio* (see below)
- Non-IgG MGUS
- Higher paraprotein level (≥ 15 g/L)

The more of these factors that are present, the higher the risk of developing myeloma, although

the risk still remains low. This affects how closely MGUS patients are monitored.

*The Serum Free Light Chain Assay is a very sensitive test that can be used to monitor MGUS patients and may help to detect early signs of progression to myeloma. Patients can usually have this test done at the same time as other blood tests are being carried out. It measures part of the paraprotein called light chains, and the ratio between them in the blood.

For more information see the [Serum Free Light Chain Assay Infoguide from Myeloma UK](#).

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

How is MGUS managed?

Current guidance recommends that MGUS is actively monitored but not treated. MGUS patients are usually checked every 3 - 4 months for the first year following diagnosis. The checks can then be reduced to every 6 - 12 months as long as no symptoms develop.

Paraprotein levels can rise and fall in MGUS - this is normal.

However, any steady increase in paraprotein level, or development of symptoms, requires further tests to investigate whether MGUS has progressed to myeloma or another condition. It is important that MGUS patients are vigilant about any new symptoms and report them to their doctor as soon as possible.

Future directions

MGUS is a benign condition. A diagnosis of MGUS does not lead to the development of a serious diagnosis such as myeloma in the majority of cases.

Ongoing research aims to better understand what influences the progression of MGUS to myeloma. For example, research has shown that overproduction of an enzyme called PADI2 is associated with MGUS progression to myeloma. Over expression of PADI2 also causes an increase in an

important cytokine (a protein released by cells which can affect the behaviour of other cells) called interleukin-6 which is known to help myeloma cells grow and survive. This research provides a simple way of identifying MGUS patients at higher risk of progressing to myeloma and enables them to be monitored more closely.

Research into the genetics of myeloma will also continue to provide clues as to who is most likely to progress from MGUS to myeloma.

About this Infosheet

The information in this Infosheet is not meant to replace the advice of your medical team. They are the people to ask if you have questions about your individual situation. All Myeloma UK publications are extensively reviewed by patients and healthcare professionals prior to publication.

Other information available from Myeloma UK

Myeloma UK has a range of Essential Guides, Infoguides and Infosheets available covering many areas of myeloma, its treatment and management.

To order your free copies or to talk to one of our Myeloma Information Specialists about any aspect of myeloma, call the **Myeloma Infoline: 0800 980 3332** or **1800 937 773** from Ireland.

The Myeloma 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 www.myeloma.org.uk

Notes

Published by: Myeloma UK
Publication date: August 2009
Last updated: February 2017
Review date: February 2019

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Myeloma Awareness Week 21 - 28 June