

Smouldering myeloma

Related conditions Infosheet

This Infosheet provides information on what smouldering myeloma is, how it is diagnosed and managed, and the links between smouldering myeloma and active myeloma.

Smouldering myeloma is part of a spectrum of conditions, and is related to both active myeloma and monoclonal gammopathy of undetermined significance (MGUS).

All three involve changes to the plasma cells. These cells, normally found in the bone marrow, form part of the immune system. Normal plasma cells produce antibodies (also called immunoglobulins) to help fight infection.

What is myeloma?

Myeloma, also known as multiple myeloma or active myeloma, is a type of blood cancer arising from plasma cells in the bone marrow.

In myeloma, plasma cells become abnormal. They multiply uncontrollably and produce a large amount of a single type of antibody, known as paraprotein, which has no useful function.

Paraprotein molecules are made up of two light chains and two heavy chains. In some cases, light chains can be produced without

heavy chains and they are known as free light chains.

Most of the symptoms related to myeloma are caused by the build-up of abnormal cells in the bone marrow and the presence of paraprotein in the body.

What is MGUS?

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

For more information see the **MGUS Infosheet** and **Myeloma – an Introduction** from Myeloma UK

What is smouldering myeloma?

Smouldering myeloma (less commonly known as asymptomatic myeloma) is an early form of myeloma which usually progresses to active myeloma, but may take some time to do so.

In smouldering myeloma, abnormal plasma cells can be detected in the bone marrow, and abnormal protein can be detected in the blood and/or

urine. However, patients do not have the typical symptoms related to active myeloma, such as those associated with kidney, immune system, or bone problems.

Generally, patients with smouldering myeloma do not require treatment. However, they are monitored regularly for signs that they may be progressing to active myeloma.

How is smouldering myeloma diagnosed?

Smouldering myeloma does not normally cause symptoms, so it is often diagnosed by chance, following a routine health check or blood tests for another condition. Blood tests may show an increased level of overall protein and this will usually prompt further investigation.

To confirm the diagnosis, tests and investigations are carried out including blood and urine tests, imaging scans and a bone marrow biopsy.

For smouldering myeloma to be diagnosed the blood and urine tests will show:

- A blood paraprotein measurement of 30g/L or above (and/or urinary monoclonal protein of 500mg or more per 24 hours)

- Normal blood calcium*
- Normal kidney function*
- No anaemia*

(* unless abnormal due to some unrelated cause)

A bone marrow biopsy and imaging scan will show:

- Between 10 and 60% myeloma cells in the bone marrow
- No bone lesions

For patients to be confirmed as having smouldering myeloma, they may have either the abnormal blood/urinary protein results or the myeloma cell percentage in the bone marrow, or possibly both.

Table 1 summarises how MGUS, smouldering myeloma and active myeloma are diagnosed.

Will smouldering myeloma develop into active myeloma?

Most patients with smouldering myeloma will at some point progress to active myeloma (or in rare cases to other related conditions). However, the time to this point varies from patient to patient, and it is not possible to say exactly when it will happen in any individual patient.

Data have shown that the chance of progressing to active myeloma

is higher in the early years after smouldering myeloma is diagnosed.

In two studies with a total of 700 patients with smouldering myeloma, 10-18% (10-18 in 100) had progressed to active myeloma in the first year, 10% (10 in 100) per year in the next three years, and by 10 years after diagnosis this had reduced to about 1% (1 in 100) per year. The data from the studies are summarised in Table 2.

Active myeloma without symptoms of organ damage

Some patients who have no symptoms of organ damage are still considered to have active myeloma on the basis of specific test results. The test results are one or more of:

- 60% or more myeloma cells in the bone marrow
- Serum free light chain ratio 100 or more
- Evidence of more than one area of bone damage on MRI scan

These patients would previously have been considered to have very high-risk smouldering myeloma, but are now considered to have active myeloma and would start treatment straight away.

MGUS	Smouldering myeloma	Active myeloma
Less than 10% myeloma cells in the bone marrow	10 - 60% myeloma cells in the bone marrow And/or	At least 10% myeloma cells in the bone marrow Plus any one or more of the following test results or signs of organ damage:
Paraprotein level in the blood of less than 30g/L	Paraprotein level in the blood of 30g/L or more, and/or urinary monoclonal protein 500mg or more per 24 hrs	Evidence from test results in the absence of organ damage: <ul style="list-style-type: none"> ● Serum free light chain ratio 100 or more ● 60% or more myeloma cells in the bone marrow ● More than one bone lesion that is at least 5mm or larger in size as picked up by an MRI scan
No symptoms of organ damage (normal kidney function, no anaemia, no bone lesions)	No symptoms of organ damage (normal kidney function, no anaemia, no bone lesions)	Evidence of organ damage: <ul style="list-style-type: none"> ● Serum calcium >2.75mmol/L ● Kidney damage – indicated by creatinine clearance <40mL/min or serum creatinine >2mg/dL ● Anaemia – indicated by haemoglobin <100g/L ● Bone lesions – one or more shown on X-rays, CT or PET/CT scan
Does not require treatment but will be monitored	Is not normally treated but will be monitored	Requires treatment

Table 1. Simplified criteria for diagnosis of MGUS, smouldering myeloma and active myeloma.

Number of years after diagnosis	Proportion of patients that may progress to active myeloma
1	10 - 18%
2 - 4	10%
5	4 - 10%
6 - 10	3 - 4%
10 - 20	1%

Table 2. Percentage of smouldering myeloma patients that may progress to active myeloma in the years following diagnosis.

How is disease progression assessed?

Whether someone has progressed from smouldering to active myeloma is established through a number of factors including:

- Changes to kidney function
- Increases in blood calcium levels
- Development of anaemia
- New damage to bones seen on X-rays or other types of scans

These changes are often accompanied by an increase in the paraprotein level over time (e.g. over three or more readings).

It is therefore important that patients are regularly monitored by their doctor. It is recommended that smouldering myeloma patients should have blood tests approximately every three months for the first five years. Blood tests

may be done less often after this time, depending on how stable the condition is.

This should also be balanced with the needs and preferences of patients. If patients, for whatever reason, wish to be monitored more regularly then this should be considered.

The development of signs and symptoms such as pain, fatigue or weight loss can coincide with changes to test results so it is important for patients to be vigilant about any new symptoms and report them promptly to the doctor.

What is the treatment for smouldering myeloma?

Currently, the majority of smouldering myeloma patients are not treated until active myeloma develops. This is

because, at present, there is not clear evidence that treatment would provide a significant benefit, in terms of delaying progression to active myeloma or prolonging overall lifespan. In the absence of clear benefits, patients who may not progress to active myeloma for some time, may be exposed to potential side effects of treatment.

Smouldering myeloma is a very variable condition, and some patients are considered as “low-risk”, while others are at higher risk of progressing to active myeloma sooner. It is still not certain what combination of factors influence whether an individual patient is at higher or lower risk of disease progression, but the factors are thought to include:

- The percentage of myeloma cells in the bone marrow
- The level of paraprotein in the blood
- The serum free light chain ratio
- Some specific changes to the genetics of the myeloma

One clinical trial has shown encouraging results in patients with high-risk smouldering myeloma. Drug treatment was compared with active monitoring

only, and the treatment group had a longer time to progression compared with the observation group. Potential treatments for high-risk smouldering myeloma are being studied in various clinical trials at present (see Future Directions section).

For the majority of smouldering myeloma patients, monitoring remains the standard of care.

Coping with the diagnosis

This is often a difficult and uncertain time for patients and their families. Smouldering myeloma is even rarer than myeloma and dealing with a diagnosis can feel isolating. It can also be challenging for a patient to be told they have smouldering myeloma, but that treatment is not yet recommended.

Many patients find talking with their nurse at the hospital clinic helpful and supportive. You can also call the Myeloma Infoline on [0800 980 3332](tel:08009803332), or join the [Myeloma UK Online Discussion Forum](#) and speak directly to other patients who have been diagnosed with smouldering myeloma.

Future directions

Research is ongoing into different ways of identifying

which smouldering myeloma patients are at higher risk of progression to active myeloma. A number of clinical trials are also underway, to see if particular drugs or combinations are of benefit in high-risk patients. Steroids, immunomodulatory drugs, proteasome inhibitors and monoclonal antibodies are among those being investigated.

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.

To give feedback about this publication, email myelomauk@myeloma.org.uk or fill in a short survey at myeloma.org.uk/pifeedback

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

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Myeloma UK has a range of publications available covering all areas of myeloma, its treatment and management. Download or order them from myeloma.org.uk/publications

To talk to one of our Myeloma Information Specialists about any aspect of myeloma, call our Myeloma 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



We're here for everything a diagnosis of myeloma brings

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

Call the Myeloma Infoline on

 **0800 980 3332**

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 **AskTheNurse@myeloma.org.uk**

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