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FIVE THINGS TO KNOW ABOUT ...

# Monoclonal gammopathy of undetermined significance

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### Monoclonal gammopathy of undetermined significance is a diagnosis of exclusion

The condition, also known as benign monoclonal gammopathy, is characterized by the presence of a monoclonal immunoglobulin or light chain on immunofixation of the patient's serum or urine.[1,2] Such a diagnosis can only be considered if underlying causes, most notably multiple myeloma, are excluded (Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.122090/-/DC1).[1] Because monoclonal immunoglobulins may be transient, this condition should only be diagnosed if they persist.

### All cases should be investigated

Because this condition can evolve into multiple myeloma or, less frequently, other B-cell malignancies,[5] investigation is required to exclude a malignant cause (Appendix 1).[1] The condition is also associated with some nonmalignant diseases, including neuropathy, autoimmune disease and chronic infections with viruses such as HIV and hepatitis C.[6] Most of these reported associations are coincidental and not causal.[6]

### Monoclonal gammopathy of undetermined significance is a common problem

About 4.2% of people aged 50 years or older have this condition, and its prevalence increases with age — almost 10% of men older than 80 years are affected.[2] It is more common in men than in women, and it occurs 2–3 times more frequently among black people than among white people.[3] The available evidence suggests that this racial disparity is a function of genetic predisposition,[3] although other risk factors, such as obesity[3] and underlying HIV infection,[4] may also contribute to the differences seen. There is no evidence to support population screening for the condition. Appendix 1 outlines indications for testing.[5]

### Tools are available to assess the risk of evolution into malignant disease

Almost all cases of multiple myeloma are preceded by monoclonal gammopathy of undetermined significance.[5] Nevertheless, many patients have a very low risk of the condition undergoing malignant transformation, and they should be reassured. Proper risk stratification is important.[5] A commonly used risk stratification tool is the Mayo Clinic model, in which 3 parameters are associated with increased risk of progression to multiple myeloma: a paraprotein concentration greater than 15 g/L, the presence of nonimmunoglobulin G paraprotein and an abnormal free light-chain ratio in the serum.[5] The 20-year absolute risk of multiple myeloma developing is only 5% in patients with no risk factors (low risk), but 56% in patients with all 3 risk factors (high risk).[5]

### No known treatment exists and follow-up should be individualized

This condition requires no treatment, and no therapy is known to prevent its progression to multiple myeloma. Patients with monoclonal gammopathy of undertermined significance must be monitored for malignant transformation or toxicity related to the presence of paraprotein (e.g., renal impairment, neuropathy). Guidelines suggest follow-up and repeat serum electrophoresis 3–6 months after the initial diagnosis, with risk-adapted follow-up thereafter if the paraprotein concentration remains stable. Patients at intermediate or high risk should be seen every 3–6 months, whereas those at low risk require review every 2–3 years.[1]

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