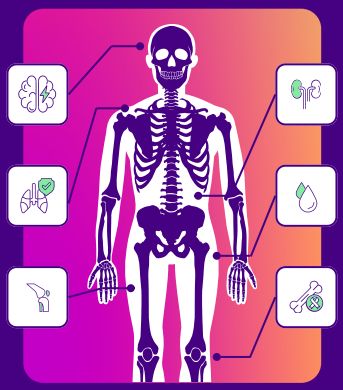
Myeloma considerations for general practice: a practical review

For more details regarding the considerations provided below, please refer to the cited references.

Diagnostic testing relevant to myeloma:

Test	Detects	Relevance
Serum protein electrophoresis (SPEP) and serum immunofixation (IFE)	Detects monoclonal (M) proteins and identifies monoclonal protein type (commonly IgG, IgA, IgM, kappa FLC, lambda FLC)	Identify and quantify monoclonal protein Confirm and type SPEP results
Serum free light chain (sFLC) testing	Free light chain tests provide three values: a concentration of free kappa light chains and free lambda light chains, as well as a kappa/lambda ratio	Most myeloma patients will have elevated kappa or lambda free light chains (but not both). An abnormal kappa/lambda ratio is a sensitive marker of plasma cell clonality[1]
Random urine protein studies and PEP	Detects monoclonal protein in urine	May indicate active paraprotein-related kidney disease



Diagnostic pathway for myeloma:[2]

Clinical suspicion of myeloma based on symptoms and/or relevant laboratory abnormalities

Additional testing to identify monoclonal proteins
SPEP, IFE, sFLC

Imaging
Low-dose CT skeletal survey (if negative, consider PET-CT or MRI* for bony pain)

Referral to haematology for additional testing and definitive diagnosis

*PET/MRI not covered by medicare when ordered by a GP

IMWG diagnostic criteria for myeloma:[3]

Clonal bone marrow plasma cells ≥ 10% or bony or extramedullary plasmacytoma.

Plus, one or more of the following myeloma defining "CRAB-SLiM" events:[3]

HyperCalcaemia	Raised serum calcium
Renal insufficiency	Reduced creatinine clearance or raised serum creatinine
Anaemia	Low haemoglobin
Bone lesions	1 or more Osteolytic lesion on X-ray, CT or PET-CT
Sixty percent	≥ 60% Clonal bone marrow plasma cells
Light chains	Involved/uninvolved sFLC results ≥ 100 with an involved sFLC ≥ 100mg/L
MRI focal lesions	>1 focal lesions ≥ 5mm in size on MRI studies

Diagnostic testing can help diagnose myeloma

The role general practice specialists play in improving outcomes for patients with myeloma

myeloma less likely ⟷ **myeloma more likely**

- normal SPEP* and
- normal sFLC tests* and
- lack of myeloma defining events (CRAB/SLiM)[2,3]

- abnormal sFLC ratio and/or SPEP with no accompanying myeloma defining events, see considerations below

- any elevated SPEP and/or sFLC ratio accompanied by one or more CRAB-SLiM criteria[2,3]
- malignant disease risk increases with increasingly elevated M protein concentration[2,3,5]
- as the ratio of involved /uninvolved FLC increases, so does the probability of malignant disease[4-6]

An individual's risk of myeloma is not constant and may change over time.[7]

Management considerations for the general practice specialist

Laboratory results should always be evaluated in the context of clinical symptoms. The considerations on this page are not a substitute for haemotologist consultation.

With normal SPEP, IFE, and sFLCs, there is a decreased likelihood of monoclonal gammopathy, consider other potential causes for symptoms[2*]

- For additional analysis, consider results from low-dose CT[2]
- Borderline abnormal κ/λ ratios can occur in patients with renal impairment. Results must be considered alongside appropriate renal function tests[8]
- Ad hoc sFLC ratio cut-offs may help increase specificity for identifying monoclonal gammopathies that warrant more immediate clinical action/referral[4,5,8]
- plasma cell burden on bone marrow ≥10% but <60% may meet the criteria for smouldering myeloma which requires haematology management

When clinical symptoms and/or test results indicate a high likelihood of myeloma, promptly referl to haematology[2]

*** A small percentage of myeloma patients will not secrete measurable M proteins[3]**

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