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Maybe It's Multiple Myeloma? The Role of Family Physicians in Improving Patient Outcomes

Maybe it’s Multiple Myeloma?

Awareness of the signs and symptoms with a prompt referral to haematology can improve patient outcomes

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Maybe it's Multiple Myeloma? The Role of Family Physicians in Improving Patient Outcomes

Dr Chiang Shu Hui Grace

SFP2026; 52(4)

Globally, multiple myeloma (MM) is the second-most common haematologic malignancy in adults, with a median age of diagnosis of 69 years old.1 Locally, it affects 100–120 individuals per year.[2,3]

MM is an incurable lymphoproliferative disorder of malignant clonal plasma cells originating in the bone marrow. While there is currently still no cure for MM, with the advances in drug therapies and availability of novel drug classes in routine care, the survival of patients with MM has improved significantly over the past 25 years.[4] Patients are now living more than a decade after diagnosis.[5] Mohty et al suggest that there might be a realistic prospect of cure and early diagnosis is the best window for cure.[6] Asymptomatic disease states, in particular smouldering MM (SMM), might offer a preclinical window. There is also new evidence to suggest that intervening early in high-risk SMM might significantly delay the progression to overt MM.[6]

As family physicians are often the first point of contact for most patients, they play a crucial role in the early detection of MM should there be any clinical or laboratory suspicion. Early referral and diagnosis are critical in preventing complications of MM and mortality.

As patients with MM continue to live longer with the disease, family physicians can also play a collaborative role with the haematologist-oncologists in ensuring that their quality of life is preserved. Family physicians who have a close relationship with their patients can address and optimise cardiovascular and neuropsychiatric issues that may arise; and manage the psychosocial impact of the disease.

This issue of the Singapore Family Physician provides an overview on how family physicians can improve patient-outcomes in individuals with MM.

In Unit 1, Dr Cinnie Soekojo provides a comprehensive guide for family physicians on when they should suspect multiple myeloma.

In Unit 2, Dr Sanjay de Mel shares an approach to the diagnosis of multiple myeloma.

In Unit 3, Professor Chng Wee Joo details why early diagnosis is important and what can be done for individuals with multiple myeloma.

In this issue, A/Prof Goh Lee Gan has selected ten current readings on topics related to multiple myeloma.

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Distance Learning Course on "Maybe It's Multiple Myeloma?"

- Unit 1: Who to Suspect of Having Myeloma?
- Unit 2: Approach to the Diagnosis of Multiple Myeloma
- Unit 3: Why Does It Matter, and What Can We Do for Myeloma Patients

Unit No. 1

WHO TO SUSPECT OF HAVING MYELOMA?

Dr Cinnie Soekojo

ABSTRACT

Multiple myeloma (MM) is the second most common haematological malignancy worldwide, yet its non-specific presentation frequently leads to diagnostic delays in primary care. This article highlights the key clinical and laboratory features that should prompt suspicion for MM. Primary care physicians are often the first point of contact for these patients and play a crucial role in early investigation and timely referral. Early identification is essential in preventing irreversible end-organ damage and to enable prompt initiation of treatment, which could substantially improve patient outcomes.

Keywords: multiple myeloma, CRAB features, diagnosis, primary care, early referral

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INTRODUCTION

Multiple myeloma is a malignancy of plasma cells characterised by the production of a monoclonal protein and associated end-organ damage, including osteolytic bone lesions, renal impairment, hypercalcaemia, anaemia, and immunosuppression. It is the second most common haematological malignancy in the world, with approximately 100 to 120 people being diagnosed with MM in Singapore per year.1 Multiple myeloma occurs slightly more often in men than in women and is most commonly diagnosed in individuals aged 65–74 years.[2]

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Rather than reflecting anatomical extent of disease, staging in MM is based on biochemical and genetic markers that indicate tumour burden and disease biology. The primary purpose of staging is to guide prognosis and risk stratification. This helps haematologists determine disease aggressiveness and tailor treatment strategies. Importantly, advanced-stage disease does not preclude a meaningful response to modern treatment and should therefore not preclude referral or treatment consideration.

Treatment outcomes in multiple myeloma have improved dramatically over the past two decades, with many patients now living for years beyond diagnosis. Modern therapy typically combines several novel agents, followed by autologous stem cell transplant in eligible patients and ongoing maintenance therapy, most of which can be delivered in the outpatient setting. Clinical trial data have demonstrated impressive results, with 4-year progression-free survival exceeding 84 percent in transplant-eligible patients,[3] and median progression-free survival was not yet reached at over 56 months of follow-up in transplant-ineligible patients.[4] Nevertheless, a proportion of patients still fare poorly, and research efforts continue to focus on improving outcomes for this group.

WHEN TO BE SUSPICIOUS OF MULTIPLE MYELOMA

Multiple myeloma can present with a broad spectrum of non-specific features that frequently mimic common conditions, often resulting in significant diagnostic delays in primary care. In some cases, it may be entirely asymptomatic, with myeloma first suspected on the basis of incidental laboratory abnormalities.

Importance of Early Detection and Role of Primary Care Physician in Identifying Suspicious Cases

Early detection of multiple myeloma is critical for preventing irreversible end-organ damage and severe complications such as spinal cord compression, pathologic fractures, or advanced renal impairment. In addition, prompt initiation of therapy is associated with improved outcomes.[5] Increasing awareness of the varied presentations in MM among primary care physicians therefore remains an essential priority.

SIGNS AND SYMPTOMS

Multiple myeloma classically presents with a constellation of features remembered by the acronym CRAB: hyperCalcaemia, Renal impairment, Anaemia, and Bone lesion. Recognising these features early in primary care is crucial, as each reflects significant underlying disease burden and should prompt urgent further investigation.

HyperCalcaemia

Hypercalcaemia in primary care is most often due to hyperparathyroidism, but myeloma must be considered—especially when accompanied by anaemia, unexplained renal impairment, and bone lesions. In myeloma, hypercalcemia arises from osteoclastic bone resorption driven by malignant plasma cells. Serum calcium level should be interpreted after correction for albumin.

Renal Impairment

Renal impairment in myeloma is due to cast nephropathy, where excess monoclonal free light chains combine with Tamm-Horsfall protein to form obstructive tubular casts, causing inflammation and injury. It is one of the most serious complications of myeloma and it is reversible if recognised and treated early. Primary care physicians should refer urgently without waiting for a formal myeloma diagnosis, ensure adequate hydration, and avoid nephrotoxins such as NSAIDs and contrast agents. Rapid reduction of free light chains through prompt myeloma-directed therapy is the key to renal recovery.[6]

Anaemia

Anaemia in myeloma is typically normochromic and normocytic, resulting from plasma cell infiltration suppressing normal bone marrow haematopoiesis. Mild macrocytosis may also be seen.[7] PBF may show rouleaux formation, where the positively-charged proteins coat the negatively-charged surface of the red blood cell, causing them to stack together.[8]

Bone Lesion

Many MM patients suffer from bone pain.[9] Myeloma cells drive osteoclast activity without compensatory bone repair,[10] producing lytic lesions visible on imaging. Plain X-rays may miss early lytic lesions but can sometimes detect established disease, and thus should be evaluated carefully. A normal X-ray does not exclude myeloma, and further imaging should be sought if suspicion remains. Pathological fractures can occur even at presentation. Vertebral collapse causing spinal cord compression is an oncological emergency requiring immediate assessment and management.

Immunosuppression/Infection

Recurrent or severe infections are a significant clinical feature of multiple myeloma, arising from the profound immunosuppression.[11,12]

Constitutional Symptoms

Patients may also present with constitutional symptoms, including malaise, fatigue, or unintentional weight loss.

WHAT CAN PRIMARY CARE PHYSICIANS DO?

The majority of patients with myeloma initially present to primary care, often visiting several times before a haematology referral is made. To prevent diagnostic delays that lead to irreversible organ damage, primary care physicians should initiate directed investigations and early referral when there are suspicious signs and symptoms.

Initial Diagnostic Tests in Primary Care

- Full Blood Count (FBC): Anaemia is typically normocytic and normochromic, and mild macrocytosis can be seen. Sometimes, especially in more advanced disease, patients can have leukopenia or thrombocytopenia. Low reticulocyte count may reflect impaired bone marrow erythropoiesis due to infiltration by malignant plasma cells.
- Peripheral blood film (PBF): PBF might show rouleaux formation.
- Renal function test and serum biochemistry: Specifically evaluate renal function (serum creatinine or eGFR), albumin, and corrected calcium.
- Imaging: X-ray or CT scans might show lytic lesions. Early lesions might manifest as focal bone lesion on MRI.

Be alert to elevated total protein and globulin levels.[13] Serum total protein includes both albumin and globulin. In multiple myeloma, the presence of monoclonal protein drives an elevation in globulin levels, consequently raising the total serum protein concentration and affecting the albumin/globulin ratio. However, suspicion should still remain even when total protein and globulin are not elevated, as can be seen in some myeloma cases, especially light chain myeloma.

A matched case-control study in UK primary care found that during the year before diagnosis, 85 percent of myeloma patients had an abnormal ESR compared with 46 percent of controls.[14] However, this remains non-specific and should not be used as a screening tool for myeloma.

If available, myeloma screening panel, which consists of serum electrophoresis (SPEP), serum immunofixation (IFE), and serum-free light chain, can be sent. Including serum-free light chain testing in addition to SPEP and IFE is essential, as it substantially improves detection rates, particularly given that approximately 20 percent of myeloma patients produce light chains only, thereby eliminating the need for cumbersome 24-hour urine collection for Bence Jones protein (which represents a homogeneous population of light chains) detection.[2,15]

Supportive Care and Management

Primary care physicians can provide symptomatic relief while facilitating referral. Bone pain can be managed with analgesia, although nonsteroidal anti-inflammatory drugs (NSAIDs) are generally avoided in MM patients due to their potential to exacerbate renal impairment.[16] Additionally, hydration could be encouraged and infections managed promptly due to patients' underlying immunosuppression.

REFERRAL TO HAEMATOLOGIST

Patients with suspected myeloma should be referred to a haematologist. For most cases, referral can be done as an early outpatient referral. However, in patients with new or worsening neurological deficit suspicious of spinal cord compression, acute kidney injury with rapidly declining renal function, or symptomatic hypercalcaemia, same-day referral to the emergency department for urgent haematology review is warranted.

CONCLUSION

Primary care physicians play a pivotal role in the early detection of multiple myeloma. By recognising the key clinical and laboratory features and initiating timely investigations and referral, primary care physicians can make a meaningful difference to patient outcomes. With modern therapies offering unprecedented survival benefits, every earlier diagnosis is an opportunity to change a patient's trajectory for the better.

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LEARNING POINTS

- **Multiple myeloma often presents with non-specific features, including unexplained anaemia, back pain, hypercalcaemia, and renal impairment, that can mimic common conditions.**
- **Familiarity with the CRAB criteria and other features is essential for timely recognition in primary care.**
- **Early referral is critical, with same-day emergency referral required for red flag presentations such as spinal cord compression, acute kidney injury, or symptomatic hypercalcaemia.**

Unit No. 2

APPROACH TO THE DIAGNOSIS OF MULTIPLE MYELOMA

Dr Sanjay de Mel

ABSTRACT

Multiple myeloma (MM) is the second most common haematologic malignancy and is characterised by a clonal proliferation of plasma cells along with specific clinical manifestations. The diagnosis of MM requires the demonstration of a clonal plasma cell infiltrate along with at least one clinical manifestation from among anaemia, renal impairment, bone lesions, and hypercalcaemia. Monoclonal proteins are detected in the majority of patients with MM and require laboratory evaluation for accurate characterisation. Awareness of the clinical presentation of MM and prompt evaluation with a view to obtaining a definitive diagnosis are key steps towards timely initiation of treatment.

Key Words: Multiple myeloma; Diagnosis; Monoclonal protein; Myeloma-Defining Events

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INTRODUCTION

Multiple myeloma (MM) is the second most common blood cancer worldwide and affects 100–120 people per year in Singapore.[1,2] Recognising the clinical manifestations and performing the initial investigations leading to the suspicion of MM are key steps in the diagnostic process. MM is part of a spectrum of plasma cell dyscrasias whereby Monoclonal Gammopathy of Undetermined Significance (MGUS) and Smouldering Multiple Myeloma (SMM) are recognised precursor stages of MM.[3] MGUS and SMM are characterised by monoclonal paraproteinaemia and bone marrow plasma cell infiltration at specific levels in the absence of clinical manifestations (known as MM-defining events).[4] The management of patients with MGUS and SMM currently involves close observation rather than treatment.[4–6] This review elucidates the current approach to confirming a diagnosis of MM based on the international myeloma working group (IMWG) diagnostic criteria.

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INTERNATIONAL MYELOMA WORKING GROUP DIAGNOSTIC CRITERIA FOR MULTIPLE MYELOMA

The diagnosis of MM requires the presence of clonal plasma cells infiltrating the bone marrow (>/=10 percent), or a histopathologically proven bony or extramedullary plasmacytoma alongside one or more MM-defining events denoted by the acronym "SLiM-CRAB".[3,7] The IMWG definitions of MM-defining events are summarised below.

- **S:** Sixty percent or more clonal plasma cells infiltrating the bone marrow
- Li: Serum-free light chain ratio (Involved/Uninvolved) ≥100
- **M:** Magnetic Resonance Imaging (MRI) based bone lesions (>1 focal bone lesions ≥5 mm in size)
- **C:** Hypercalcaemia (>2.75 mmol/L or >0.25 mmol/l greater than the upper limit of normal)
- **R:** Renal impairment (creatinine clearance <40 ml/min or serum creatinine >177 mmol/L)
- **A:** Anaemia (Haemoglobin <10 g/dL or >2 g/dl below the lower limit of normal)
- **B:** Bone lesions: One or more osteolytic lesions detected by skeletal imaging

Although monoclonal proteins are found in the majority of patients with MM, their presence is not a requirement for the diagnosis of MM, as a minority of patients have non-secretory disease.[8] Importantly, the discovery of a monoclonal protein does not equate to a diagnosis of MM, as paraproteins are also found in patients with MGUS, SMM, and other plasma cell disorders such as light chain amyloidosis.9 Plasma cell leukaemia is an aggressive variant of MM in which the diagnostic criteria for MM are met along with 5 percent or more circulating plasma cells.[10]

DIAGNOSTIC APPROACH TO PLASMA CELL DISORDERS

Screening for Monoclonal Proteins

Monoclonal proteins are detected in approximately 97 percent of patients with MM[3] and a systematic approach to their characterisation is crucial for accurate diagnosis. Serum immunofixation (sIFE) is required to confirm monoclonality and the serum-free light chain assay (SFLC) is important in the diagnosis of patients with light chain MM who may have MM-defining events and a negative sIFE.[11] The SLFC also plays a role in the prognostication of patients with MGUS and SMM.[12] It is noteworthy that SFLC readings are sensitive to renal impairment and the IMWG has published SFLC reference ranges adjusted for creatinine clearance.[13]

The Singapore Myeloma Study Group (SMSG) currently recommends that serum protein electrophoresis (SPEP), sIFE, and SFLC are used in the format of a screening panel for monoclonal proteins.[2] When SPEP, sIFE, and SFLC are available, urinalysis for a monoclonal protein is of doubtful added value and is not routinely recommended. While 24-hour urinary protein quantification is used in the assessment of patients with light chain amyloidosis, spot urine IFE, m band quantification, or urine-free light chain assays are not routinely recommended.[14]

Confirmation of Bone Marrow Plasma Cell Infiltration and Myeloma-Defining Events

Bone marrow aspiration and trephine biopsy (BMAT) are essential for the diagnosis of MM, with confirmation of plasma cell clonality being demonstrated by immunohistochemistry.[3] Flow cytometric immunophenotyping is another means of demonstrating light chain restriction of plasma cells but is not mandatory for the diagnosis of MM.[15] BMAT is particularly important in the 3 percent of patients with non-secretory MM.

The initial evaluation of myeloma-defining events requires a full blood count (FBC), serum creatinine, and corrected calcium, investigations that can be performed in the primary care setting when MM is suspected. Quantification of the serum monoclonal protein by densitometry is required at diagnosis as a baseline for assessment of response to treatment. Quantification of individual immunoglobulins by turbidimetry is recommended in patients with IgA, IgM, or IgD paraproteins, which are not reliably measured by densitometry of the M protein.[16]

Confirming the presence of bone lesions is a key step in the diagnostic evaluation for MM. While the whole-body skeletal survey was historically the standard imaging modality, whole-body low dose computed tomography (WBLDCT), whole-body magnetic resonance imaging (MRI), and positron emission tomography (PET) scans have since been proven as more sensitive options.[17,18] The SMSG and Asian myeloma network (AMN) consensus currently recommend WBLDCT as the minimal requirement for bone imaging.[19,20] An MRI of the spine is required in the evaluation of spinal cord compression while whole-body MRI is recommended at the initial diagnosis of SMM as the finding of more than one focal lesion >5 mm will upstage these patients to MM.[7] The AMN imaging consensus[20] and SMSG guidelines[2] provide more information on each of these modalities and detailed guidance on their use.

Staging and Prognostication

Prognostication of MM was traditionally based on the international staging system (ISS) where albumin and β2 microglobulin (B2M) were used to calculate a prognostic score.[21] Genomic information obtained through fluorescent in situ hybridisation (FISH) and conventional karyotyping from the diagnostic bone marrow sample also play a key role in risk stratification.[22] Key chromosomal abnormalities driving adverse prognosis including t(4;14) 17p del, t(14;16), t(14;20), 1p loss, and 1q gain[22] can be detected by FISH performed on bone marrow samples enriched for plasma cells.[23] The latest international myeloma society/IMWG risk stratification defines high risk MM based on combinations of genomic abnormalities and/or high B2M (>5.5 mg/dl) with normal renal function.[24] The recommended investigations for diagnosis and risk stratification of MM are summarised in **Table 1**.

Table 1. Recommended Investigations for Confirmation of Diagnosis and Risk Stratification in Multiple Myeloma

Blood Investigations	Bone Marrow Investigations	Imaging
Serum M protein quantification (In addition to SPEP/SFLC and IFE)	Bone marrow aspirate and trephine biopsy	Whole-body low-dose CT scan (WBLDCT) as the minimum first-line screening modality
FBC, Serum electrolytes, and renal function assessment including urea/ creatinine, corrected Calcium	FISH myeloma panel including the following probes: FGFR3/MMSET t(4;14), MAF-B t(14;20), and MAF-C t(14;16) translocations, copy number changes for 17p, 1q, and 1p	Non-Contrasted diffusion weighted whole-body MRI or Non-Contrasted FDG PET-CT to be considered if WBLDCT is not conclusive/ unavailable
Serum β2 microglobulin, albumin, and LDH		MRI whole-body is the modality of choice when evaluating patients with SMM for high-risk biomarkers, which may result in upstaging to active MM

CONCLUSION

The diagnosis of MM requires awareness of the key clinical manifestations and knowledge of which initial investigations are required. Close collaboration between primary care and specialist haematology services is important for the timely referral and evaluation of patients with suspected plasma cell disorders. Key advancements in the diagnostic process include the advent of mass spectrometry for the detection and monitoring of paraproteins,[25] as well as ongoing improvements in imaging techniques.[26] The diagnostic landscape is likely to evolve further in the coming years with the integration of these tools into routine clinical practice.

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LEARNING POINTS

- **The diagnosis of multiple myeloma requires the demonstration of a clonal plasma cell infiltrate along with myeloma-defining clinical events.**
- **Serum immunofixation, electrophoresis, and the serum-free light chain assay are the key investigations required to identify monoclonal proteins.**
- **The presence of a monoclonal protein is not equivalent to a diagnosis of myeloma as it can be found in the precursor states and other plasma cell disorders.**

Unit No. 3

WHY DOES IT MATTER, AND WHAT CAN WE DO FOR MYELOMA PATIENTS

Prof Chng Wee Joo

ABSTRACT

Multiple myeloma has been the poster child for drug development in oncology, with more than 10 new drugs approved in the last two decades. These drugs and their combinations have resulted in deeper responses and longer survival, with generally good tolerability and quality of life for patients. However, the situation is becoming even more promising with the emergence of immunotherapy. These exciting therapeutic agents are producing unprecedented response and survival duration, even in relapse and high-risk disease. More importantly, the treatments are in general well tolerated and patients have good quality of life. It is therefore critical to diagnose myeloma early so that patients can benefit maximally from the improvement in therapy.

Keywords: Myeloma, Therapy, Prognosis, Immunotherapy

SFP2026; 52(4): 12-14

INTRODUCTION

What Is Myeloma?

Multiple myeloma is a malignancy arising from post-germinal centre B cells. Phenotypically, most of these cells are plasma cells, which are normally antibody-producing cells that reside in the bone marrow. It is commonly diagnosed in the 6th decade of life or later. We see a rising incidence in Singapore, which is reflective of trends across the world. This is likely due to a combination of factors such as an ageing population and increasing diagnostic awareness.

PROF CHNG WEE JOO
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Patients tend to present with one or more of the following clinical features[1]:

- **Hypercalcaemia**, which may result in non-specific pain and changes in mental state
- **Renal impairment**, which may result in non-specific symptoms
- **Anaemia**, which may result in fatigue, breathlessness, dizziness
- **Bone involvement** (plasma cell infiltration or lytic lesions), which may cause pain, pathological fracture, or serious spinal cord compression resulting in bilateral lower limb weakness and loss of sensation

In addition, there should be a measurable clonal fraction in the form of monoclonal proteins measurable in the blood (intact monoclonal immunoglobulin or monoclonal light chain) and clonal plasma cells in the bone marrow. However, the monoclonal immunoglobulins or plasma cells might also be present as a person ages (especially when at lower levels) in conditions such as monoclonal gammopathy of undetermined significance (MGUS) or smouldering myeloma (SMM), which does not require treatment. As some of the above myeloma-defining clinical features are non-specific, it is often important to exclude other potential causes before diagnosing myeloma and instituting treatment.

PROGNOSIS

Outcomes of patients to treatment is quite heterogenous, mainly driven by underlying heterogeneity in biology. One of the key drivers of biological heterogeneity is the genetic aberrations present in the myeloma cells. Some of the recurrent genetic abnormalities such as t(4;14); t(14;16); t(14;20), 1q21 gain, 1p32 loss, and 17p13 loss have been incorporated into the IMS/IMWG high-risk criteria.[2] Outcomes of standard risk patients are good, while that of high-risk patients remain a challenge with short disease-free periods and a propensity towards drug resistance. Tumour burden reflected by beta-2-microglobulin is another important prognostic factor.

While the current genetic risk classification is good, it does not take into account some important phenotypic elements that may also be important for prognosis such as age and frailty, response to treatment, extramedullary disease, and presence of significant renal impairment.

GOALS OF TREATMENT

Once the diagnosis of myeloma requiring treatment is made, the goals of the treatment will depend on the age and performance status of the patients, pre-morbid conditions, and transplant eligibility.

In a younger, transplant-eligible patient, the focus is more on getting the patient into remission with a potent treatment that can induce a response quickly and to consolidate with treatment that will get the patient into the deepest remission conceivable and to maintain this for as long as possible. The ideal response is to reach minimal residual disease (MRD)[3] negativity at a sensitivity of 10-5. There are standardised methodologies using either flow cytometry or genomic sequencing for the detection of MRD. This may be at a cost of higher toxicity in exchange for treatment that will also produce a longer period of remission and survival. With today's regimen, a proportion of these patients may well be cured with a single line of treatment, yet more will probably die of other conditions rather than myeloma (similar to well-controlled chronic disease such as diabetes).

In older patients who are too frail, or too old for transplant to be considered, the goal will be disease control with a good quality of life. The treatment intensity might be lower, with the aim of providing effective treatment that is less toxic. With this approach, the maximal response might take longer, and the depth of response may not be as much as in the approach for younger patients. As a result, the remission time and survival might also be shorter, but this is acceptable as the time from age of diagnosis to normal expected lifespan is also shorter.

TREATMENT PATHWAYS

Supportive Care

One of the first things is to manage the complications. If there is hypercalcaemia, hydration is started and sometimes a bisphosphonate is needed.

If there is renal impairment, again hydration is important, and likewise avoidance of imaging contrast and nephrotoxic drugs. Sometimes, dialysis support might be necessary.[4]

For anaemia, if this is severe and patient is symptomatic, blood transfusion might be necessary.

For pain related to myeloma bone lesions, analgesia may be needed. If there are fractures in the vertebra or long bone, surgical consult and sometimes a surgical intervention may be needed to stabilise the bone. If lytic lesions and myeloma bone disease is present, bisphosphonates (mainly zoledronate acid) have been shown to reduce bone events.[5]

Myeloma lesions are very radiosensitive. If there are isolated myeloma lesions (plasmacytomas) that may be causing cord compression or other symptoms, they may be irradiated. If there is cord compression due to vertebral plasmacytomas, this is a medical emergency that requires urgent referral to orthopaedic surgery and radiation oncology. High-dose steroids can be started while waiting for these consults.

Clone Eradication

Once the acute symptoms are managed, consideration should be given to the main myeloma treatment that is effective in eradicating the myeloma clones. For transplant-eligible patients (fit and relatively young), treatment usually includes a 4-drug combination of a monoclonal antibody targeting CD38 (Daratumumab or Isatuximab), a proteasome inhibitor (Bortezomib), an immunomodulatory drug (Lenalidomide or Thalidomide), and Dexamethasone.[6,7] This combination is given for 4–6 cycles during the induction phase. This is usually followed by an autologous stem cell transplant following high-dose melphalan for consolidation. Subsequently, at least two years of maintenance therapy with lenalidomide will take place.[8]

In patients who do not have high-risk disease and have achieved an MRD-negative response, one can consider stopping maintenance after two years. If patients have high-risk disease or are still MRD positive, it is prudent to continue maintenance.

For transplant-ineligible patients, they are typically treated with a triplet such as Daratumumab plus lenalidomide plus dexamethasone in a continuous manner.[9] To reduce toxicity, dexamethasone is usually stopped after 3–6 months. The treatment usually continues until progression.

In very frail patients, a 2-drug combination of lenalidomide and dexamethasone can be used. Similar to transplant-eligible patients, if the patient has standard risk disease and manages to achieve MRD negativity, treatment could potentially be stopped after two years.

Follow-up

Whether on treatment or off treatment, myeloma patients should be regularly followed up in clinic to assess for treatment toxicity and response. In patients in remission, they should be followed up for surveillance of relapse so that salvage therapy can be initiated early prior to clinical symptoms.

Lenalidomide is a commonly used drug and often used for prolonged duration in maintenance. It can be associated with increased risk of developing a secondary malignancy.[10] It is therefore important to do cancer surveillance during follow-up.

Management of Relapse Disease[11]

It is common for myeloma patients to experience relapse. The first period free of progression is highly variable but is 4–5 years on average; however, this may extend to more than 10 years for new patients treated with today's regimen.

When patients progress or relapse, they are usually identified prior to symptomatic relapse. Treatment for relapse disease is usually started before the development of symptoms. Myeloma patients are fortunate that many effective treatments are available. The choice of treatment will depend on a number of factors such as the patient's condition, comorbid medical conditions, their prior treatment and response, how they presented, and if they have high-risk disease.

The development of new immunotherapy such as bispecific T-cell engagers and Chimeric Antigen Receptor (CAR)-T cells, several of which have been approved for the treatment of myeloma, is an important advancement as they are producing very high response rates and deep responses with long progression-free survival even in relapse disease as well as in high-risk patients.

CONCLUSION

With the treatment options available today, the outcomes of myeloma patients and their quality of life during therapy are very good. Access to treatment might pose a challenge as some of the newer treatments can be quite expansive and are not yet on the MOH cancer drug list. Nevertheless, it is important to have myeloma as one of the differential diagnoses to consider in patients, as their symptoms can be non-specific and common in populations of their age, so that they are diagnosed early and can benefit from therapy.

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LEARNING POINTS

- **Tremendous progress has been made in the treatment for multiple myeloma, resulting in a marked improvement in survival of patients.**
- **Treatment is based on supportive care for affected organs and effective non-chemotherapy-based eradication of tumour cells followed by consolidation to deepen response and maintenance to prevent early relapse.**
- **Emergence of immunotherapy is heralding an even more exciting era in myeloma treatment, with Bispecific T-cell Engagers and CAR-T targeting BCMA, producing excellent responses and progression-free survival even in advanced disease.**
- **Treatment is also mainly outpatient-based with favourable toxicity profile, resulting in good quality of life.**

ASSESSMENT OF 15 MCQS

FPSC NO : 134
MCQS ON MAYBE IT'S MULTIPLE MYELOMA
SUBMISSION DEADLINE: 7 JULY 2026, 12 NOON

INSTRUCTIONS
- **To submit answers to the following multiple choice questions, you are required to log on to the College Online Portal (https://lms.wizlearn.com/cfps/)**
- **Please contact sfp@cfps.org.sg if you have not received an email on the new LMS account.**
- **Attempt ALL the following multiple-choice questions.**
- **There is only ONE correct answer for each question.**
- **The answers should be submitted to the College of Family Physicians Singapore via the College Online Portal before the submission deadline stated above.**
- **There will be NO further extension of the submission deadline**

1. A 68-year-old man presents with persistent lower back pain, fatigue, and a serum creatinine of 180 µmol/L. His full blood count reveals normocytic, normochromic anaemia with Hb 9.2 g/dL. Which acronym best captures the core organ-damage features of multiple myeloma that should guide your clinical assessment?

A. CRASH
B. CRAM
C. CARB
D. GRAB
E. CRAB

2. A 68-year-old man presents to his GP with a 6-week history of worsening fatigue, diffuse back pain, and decreased urine output over the past 3 days. He has no history of diabetes or prior kidney disease. Blood results show: haemoglobin 8.8 g/dL, creatinine 480 µmol/L (baseline 90 µmol/L one year ago), corrected calcium 2.6 mmol/L. He takes ibuprofen regularly for back pain. Which of the following is the most appropriate immediate next step in management?

A. Reassure the patient, stop ibuprofen, and arrange a routine nephrology outpatient referral in 4–6 weeks to investigate the renal impairment
B. Order a 24-hour urine collection for Bence Jones protein and review results in two weeks before deciding on further action
C. Prescribe oral prednisolone empirically and review in one week to assess if renal function improves
D. Stop ibuprofen, same-day emergency department referral for acute kidney injury in the context of suspected multiple myeloma, ensure the patient is adequately hydrated, and avoid nephrotoxins while awaiting urgent haematology review and myeloma-directed therapy
E. Start a renal-dose ACE inhibitor to slow progression of renal impairment and schedule a non-urgent haematology referral within the next month

3. A primary care physician suspects multiple myeloma in a 70-year-old patient with back pain, hypercalcaemia, and a markedly elevated ESR. Which combination of investigations constitutes the most appropriate initial workup in primary care?

A. Full blood count, liver function tests, and urine dipstick
B. Full blood count, renal function, corrected calcium, ESR, serum total protein, and myeloma screening panel if available
C. Bone marrow biopsy, CT chest-abdomen-pelvis, and 24-hour urine collection
D. Serum ferritin, thyroid function, and chest X-ray
E. Peripheral blood film, reticulocyte count, and direct Coombs test

4. A patient with suspected multiple myeloma develops new-onset bilateral leg weakness and urinary retention. What is the most appropriate next step in management?

A. Prescribe NSAIDs for pain relief and review in two weeks
B. Arrange an outpatient MRI spine within one month
C. Initiate empirical corticosteroids and refer to haematology within one week
D. Same-day emergency referral for suspected spinal cord compression
E. Order urgent serum-free light chains and await results before referring

5. Which of the following statements about anaemia in multiple myeloma is correct?

A. It is typically microcytic and hypochromic, consistent with iron deficiency
B. It is always macrocytic due to vitamin B12 deficiency from malabsorption
C. It is usually normochromic and normocytic, sometimes slightly macrocytic, and the peripheral blood film may show rouleaux formation
D. It is caused exclusively by renal failure-related erythropoietin deficiency
E. It is rarely seen at initial presentation and usually develops only in advanced disease

6. Which of the following is NOT a myeloma-defining event according to the IMWG diagnostic criteria?

A. Anaemia
B. Lytic bone lesions

C. Monoclonal protein quantification above 50 g/dl
D. Renal impairment
E. Hypercalcaemia

7. Which of the following is mandatory when making a diagnosis of myeloma?

A. Bone marrow plasma cell infiltration of at least 10% or biopsy proven plasmacytoma
B. Circulating plasma cells at least 5%
C. Presence of a monoclonal protein in the serum
D. Presence of a monoclonal protein in the urine
E. Monoclonal protein quantification above 30 g/dl

8. Which of the following is recommended as part of the screening panel for monoclonal proteins?

A. Serum immunofixation
B. Erythrocyte sedimentation rate
C. Total protein
D. Albumin
E. Globulin

9. How does the IMWG define anaemia as a myeloma-defining event?

A. Haemoglobin <13 g/dL or >1 g/dl below the lower limit of normal
B. Haemoglobin <10 g/dL or >2 g/dl below the lower limit of normal
C. Haemoglobin <8 g/dL or >3 g/dl below the lower limit of normal
D. Haemoglobin <7 g/dL or >2 g/dl below the lower limit of normal
E. Haemoglobin <6 g/dL or >3 g/dl below the lower limit of normal

10. How does the IMWG define renal impairment as a myeloma-defining event?

A. Creatinine clearance <30 ml/min or serum creatinine >199 µmol/L
B. Creatinine clearance <20 ml/min or serum creatinine >200 µmol/L
C. Creatinine clearance <50 ml/min or serum creatinine >160 µmol/L
D. Creatinine clearance <40 ml/min or serum creatinine >177 µmol/L
E. Creatinine clearance <60 ml/min or serum creatinine >100 µmol/L

11. Myeloma patients survive a median of:

A. 1 year
B. 3 years
C. 5 years
D. 10 years
E. 20 years

12. Which of the following is true of myeloma treatment?

A. Combination cytotoxic chemotherapy is used
B. Treatment of newly diagnosed patients requires prolonged hospitalisation
C. Treatment usually continues in some form until disease progression
D. Stem cell transplant is never used
E. Quality of life is very poor

13. Which of these is a medical emergency that might arise from myeloma?

A. Toxic Shock Syndrome
B. Spinal cord compression
C. Hypertensive Crisis
D. Stevens Johnson Syndrome
E. Respiratory Distress Syndrome

14. Which of the following is NOT useful imaging to pick up myeloma bone disease?

A. Skeletal survey
B. Low dose CT whole body
C. Whole-body PET-CT
D. Bone scan
E. Whole-body MRI

15. Which of the following is an exciting new treatment that is changing the outcome of myeloma patients?

A. Daratumumab
B. Blinatumumab
C. Rituximab
D. CD19 CAR-T
E. Siltuximab
F. Enable

READINGS

A SELECTION OF TEN READINGS ON TOPICS RELATED TO
MAYBE IT'S MULTIPLE MYELOMA

A SELECTION OF TEN READINGS ON TOPICS RELATED TO MAYBE IT'S MULTIPLE MYELOMA

FPSC134 – SATURDAY, 2 MAY 2026 (via Zoom)
All are available as Free full text

Selection of readings made by A/Prof Goh Lee Gan

READING 1. RHEOLOGICAL PROPERTIES OF BLOOD IN MULTIPLE MYELOMA PATIENTS

Ptaszek B,[1] Podsiadło S,[2] Jandziś Z,[3] Teległów A,[4] Piotrowska A,[4] Czerwińska-Ledwig O,[4] Jurczyszyn A.[5] Rheological properties of blood in multiple myeloma patients. Sci Rep. 2024 Feb 21;14(1):4260. PMID: 38383860.

doi: 10.1038/s41598-024-54947-4. PMID: 38383860. Free Full Text.

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ABSTRACT

Multiple myeloma (MM) is considered to be one of the haematological malignancies formed by excessive and abnormal proliferation of plasmocytes. Among other parameters, several blood tests are used to diagnose multiple myeloma. The haemorheological profile in multiple myeloma is not widely studied.

Haemorheology includes the study of measuring the deformability and aggregation of erythrocytes, blood viscosity, and sedimentation rate. The degree of deformability of blood cells is necessary to maintain proper vital functions. Proper deformability of red blood cells ensures proper blood circulation, tissue oxidation, and carbon dioxide uptake. The aim of the study was to compare morphology and blood rheology parameters in patients with MM and healthy individuals. The study included 33 patients with MM and 33 healthy subjects of the same age. The haematological blood parameters were evaluated using ABX MICROS 60 haematology analyser. The LORCA Analyser was used to study erythrocyte aggregation and deformability. Patients with MM had lower red blood cell count (RBC) (9.11%) ($p<0.001$) and half time of total aggregation (T1/2) (94.29%) ($p<0.001$) values; and higher mean corpuscular volume (MCV) (5.50%) ($p<0.001$), aggregation index (AI) (68.60%) ($p<0.001$), total extent of aggregation (AMP) (87.92%) ($p<0.001$) values than the healthy control group. Aggregation in patients with MM is different compared to healthy individuals.

It was observed that the percentage of cell aggregation is almost 50 percent higher than in the control group. The study of morphology, aggregation, and deformability of erythrocytes in patients with suspected MM might be helpful in making clinical decisions.

READING 2. EPIDEMIOLOGY AND TREATMENT OPTIONS OF MULTIPLE MYELOMA IN ASIA

Chng WJ,[1,2] Nagarajan C,[3,4] Huang SY,[5] Malhotra P,[6] Hwang YY,[7] Blunk V,[8] Singh M,[9] Wang L.[9] A systematic review on the epidemiology and treatment options of multiple Myeloma in Asia. Heliyon. 2024 Oct 22;10(21):e39698. PMID: 39553611.

doi: 10.1016/j.heliyon.2024.e39698. PMID: 39553611. Free Full Text.

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ABSTRACT
Multiple myeloma (MM) accounts for almost 15 percent of all neoplastic malignancies around the globe. This systematic review intends to analyse data on the treatment and management of MM in selected regions in Asia to identify and prioritise areas that need attention.

A comprehensive review of original articles, published in English from 2005 to 2022 and derived from the PubMed/MEDLINE database, was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

There were 98 studies from select regions of Asia (China, India, Taiwan, Hong Kong, and Singapore) on newly diagnosed MM and relapsed/refractory MM. This review evaluated the trends in disease outcomes with the gradual shift in treatment regimens from doublet to triplet. Additionally, this review also explored autologous stem cell transplant outcome and anti-B-cell maturation antigen (BCMA) chimeric antigen receptor (CAR) T-cell therapy in MM patients. This is the first systematic review attempting to collect data on the utility and comparison of innovative agents and modifications in treatment regimens in the context of the Asian population. This review established that the body of evidence for the management of MM was generally of poor quality and there is a need for more versatile studies in the region. Novel and innovative drug regimens may help in combating the illness but consorted efforts by researchers, industry partners, policymakers, and the government are key factors in the long-term survival of MM patients.

In the current systematic review, the authors have tried to give a comprehensive account of the available treatments, trends in MM management, and prognosis for MM in Asia.

READING 3. MULTIPLE MYELOMA PRESENTING AS CHRONIC PAIN MIMICKING DEGENERATIVE CONDITIONS

Mo B,[1] Markar J,[1] Sacks S.[1,2] Unmasking Multiple Myeloma: The Importance of Suspecting Malignancy in Atypical Chronic Pain Mimicking Degenerative Conditions—A Case Report. Clin Case Rep. 2025 Jan 16;13(1):e70129. PMID: 39822886.

doi: 10.1002/ccr3.70129. PMID: 39822886. Full Free Text.

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ABSTRACT
Heightened clinical vigilance for multiple myeloma is essential in patients presenting with atypical chronic pain progression. Symptoms may overlap with degenerative musculoskeletal conditions, frequently leading to misdiagnosis. This underscores the necessity of a thorough evaluation when symptoms are refractory to conventional therapies, in order to facilitate timely diagnosis and effective management of malignancy.

READING 4. UNUSUAL PRESENTATION OF MULTIPLE MYELOMA AS LIVER TUMOUR (CASE REPORT)

Abdel-Samad N,[1–3] Nahri S,[1,4] Bharadwaj L,[5] Ross L.[5] Unusual Presentation of Multiple Myeloma as a Liver Tumour at Initial Diagnosis: A Case Report. Am J Case Rep. 2025 Aug 14;26:e946709. PMID: 40811143.

doi: 10.12659/AJCR.946709. PMID: 40811143. Free Full Text.

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ABSTRACT

BACKGROUND: Multiple myeloma (MM) is a haematologic cancer marked by malignant plasma cells in the bone marrow, often leading to bone pain, anaemia, and renal issues. Rarely, MM presents as extramedullary myeloma in organs such as the liver and is associated with a poor prognosis.

CASE REPORT: We report a 64-year-old woman with a history of aortic stenosis and transient ischaemic attack who presented with severe anaemia, epistaxis, and fatigue. Initial test results showed elevated liver enzymes, hypercalcemia, and kidney injury, with imaging revealing suspected liver metastases. Cancer markers, such as carcinoembryonic antigen, cancer antigen 15-3, and cancer antigen 125 were elevated. Liver biopsy showed plasma cells positive for CD138, CD38, and CD56, confirming MM. Additional tests found IgA kappa monoclonal proteins and 60 percent plasma cells in bone marrow, without bone lesions. The patient required an extended hospital stay, due to recurrent pleural effusions, hypercalcemia, and cholangitis requiring stent placement. After recovery from complications, including COVID-19, she was treated with seven cycles of daratumumab-dexamethasone-lenalidomide and was scheduled for an autologous stem cell transplant. After four months of treatment, the patient had positive clinical outcomes in myeloma parameters and liver lesions. The patient had improved haemoglobin, white blood cells, neutrophils, and platelets. The patient's IgA decreased, hepatic enzymes improved, monoclonal protein bands disappeared, and liver lesions resolved.

CONCLUSIONS: This case highlights an uncommon MM presentation with liver involvement, underscoring the importance of considering MM in the differential diagnosis of atypical liver lesions and of early identification to improve treatment outcomes.

READING 5. PERIPHERAL NEUROPATHY IS A COMMON COMPLICATION OF MULTIPLE MYELOMA

Huang J,[1] Xie Y.[1] Diagnostic Potential of the Risk Factors Associated with Peripheral Neuropathy in Multiple Myeloma: Evidence from Logistic Regression Analysis. Br J Hosp Med (Lond). 2025 Nov 25;86(11):1–14. PMID: 41284234.

doi: 10.12968/hmed.2025.0795. PMID: 41284234. Free Full Text.

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ABSTRACT

AIMS/BACKGROUND: Peripheral neuropathy (PN) is a common and debilitating complication in patients with multiple myeloma (MM), which results from both disease-related mechanisms and treatment-induced neurotoxicity.

Despite its clinical significance, comprehensive investigations assessing PN risk in MM, along with examining demographic, clinical, nutritional, and inflammatory factors, remain limited. Therefore, this study aimed to investigate independent risk predictors associated with PN in MM patients using univariate and multivariate logistic regression analysis, thereby enhancing clinical risk management and improving treatment outcomes.

METHODS: This retrospective observational study included 161 MM patients who were treated at Ganzhou People's Hospital between February 2020 and February 2024. Study participants were divided into the PN (n=45) and non-PN (n=116) groups. PN diagnosis was conducted based on new neurological signs and symptoms post-treatment, confirmed through abnormal sensory, motor, autonomic, or nerve conduction assessments. Baseline characteristics, including demographic information, clinical features, and laboratory parameters, were compared between the two groups using Mann-Whitney U and Chi-square tests. Univariate logistic regression analysis evaluated potential parameters associated with PN. Furthermore, a multivariate logistic model was used to assess independent risk predictors. Finally, model performance was evaluated via receiver operating characteristic (ROC) curve analysis.

RESULTS: This study analysed 161 patients, of whom 45 (27.95%) developed PN. Patients in the PN group were significantly older and had higher body mass index (BMI), increased immunoglobulin G (IgG) and interleukin-6 (IL-6) levels, and increased diabetes prevalence than the non-PN group. However, they exhibited lower haemoglobin (Hb) and serum 25-hydroxyvitamin D [25(OH)D] levels ($p<0.05$). Multivariate logistic regression analysis identified older age (odds ratio [OR] = 1.49, 95% confidence interval [CI]: 1.07–2.08), higher BMI (OR=2.05, 95% CI: 1.01–4.17), reduced 25(OH)D levels (OR=0.54, 95% CI: 0.29–0.97), elevated IgG (OR=1.64, 95% CI: 1.12–2.41), and increased IL-6 (OR=2.07, 95% CI: 1.10–3.88) as independent PN predictors. The model showed excellent discrimination capability (area under the curve [AUC] = 0.998, 95% CI: 0.996–1.000, $p<0.001$).

CONCLUSION: This study identified older age, higher BMI, vitamin D deficiency, elevated IgG, and increased IL-6 levels as independent risk predictors for PN. Assessing these parameters in the early stages facilitates the identification of high-risk patients, allowing for targeted preventive strategies and personalised nursing interventions in MM patients, which can reduce PN incidence and enhance overall clinical outcomes.

READING 6. MULTIPLE MYELOMA PRESENTING AS PERICARIAL EFFUSION—A CASE REPORT

Kebede LM,[1] Woldeamanuel AM,[2] Mehammed FM,[2] Girma HG,[2] Tafa ME,[2] Abraham YB.2 Unmasking multiple myeloma first presentation as pericardial effusion with tamponade physiology: a case report. J Med Case Rep. 2026 Jan 18;20(1):89.

doi: 10.1186/s13256-025-05795-x.

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ABSTRACT
BACKGROUND: Multiple myeloma is a malignant plasma cell disorder primarily involving the bone marrow and skeleton, leading to anaemia, renal dysfunction, and lytic bone lesions. Extramedullary disease, seen in about 9 percent of cases, reflects aggressive disease biology with poor prognosis. Common sites include the pleura, liver, and gastrointestinal tract, while pericardial involvement is exceedingly rare and often detected postmortem. Fewer than 25 cases of pericardial effusion or cardiac tamponade due to multiple myeloma have been reported, usually in advanced disease. The mechanism likely involves hematogenous spread or direct extension from adjacent lesions, often associated with high-risk cytogenetic abnormalities. This case presents an unusual first manifestation of multiple myeloma as pericardial effusion with tamponade physiology, emphasising the need to consider haematologic malignancy in unexplained pericardial effusion, especially in resource-limited settings.

CASE PRESENTATION: A 60-year-old Ethiopian man presented with a 6-month history of progressive dry cough, dull chest pain, and worsening shortness of breath. He had been repeatedly treated for pneumonia and pulmonary tuberculosis without improvement. Chest-computed tomography revealed a large pericardial effusion with features of cardiac tamponade. Echocardiography confirmed pericardial fluid causing right atrial and ventricular collapse. Pericardiocentesis drained 800 mL of haemorrhagic fluid, and cytology showed atypical plasma cells. Further evaluation, including serum protein electrophoresis and bone marrow biopsy, confirmed multiple myeloma. The patient was managed with Pericardiocentesis and systemic chemotherapy, showing clinical and radiologic improvement, highlighting the rarity of pericardial involvement as an initial presentation of multiple myeloma.

CONCLUSION: Pericardial involvement in multiple myeloma is an extremely rare and serious manifestation, usually signifying advanced or aggressive disease. While malignant pericardial effusions are commonly due to solid tumours, multiple myeloma should also be considered when no other cause is identified. Early echocardiography-guided pericardiocentesis is lifesaving, and definitive procedures such as a pericardial window may prevent recurrence. This case highlights the importance of suspecting haematologic malignancy in patients with unexplained pericardial effusion or cardiac tamponade. Early recognition and prompt initiation of systemic therapy can improve survival, particularly in resource-limited settings where diagnostic challenges are common.

READING 7. ESTABLISHING A MULTIPLE MYELOMA CLINICAL REGISTRY IN ASIA PACIFIC REGION

Aoki N,[1] Chen PY,[1] Moore E,[1] Oliver L,[1] Waters NA,[1] Wellard C,[1] McQuilten ZK,[1,11] Chen W,[2] Chng WJ,[3] Gan GG,[4] Goh YT,[5] Hou J,[6] Huang J,[7] Kim K,[8] Lee JJ,[9] Lu J,[10] Min CK,[12] Wood EM,[13–15] Yeh SP,[16] Spencer A[17–19]; APAC MRDR Investigators. The establishment of a multiple myeloma clinical registry in the Asia-Pacific region: The Asia-Pacific Myeloma and Related Diseases Registry (APAC MRDR). BMC Med Res Methodol. 2024 May 2;24(1):102.

doi: 10.1186/s12874-024-02227-0.

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ABSTRACT

BACKGROUND: Multiple myeloma (MM) is the second most common haematological cancer worldwide. Along with related diseases including monoclonal gammopathy of undetermined significance (MGUS), plasma cell leukaemia (PCL), and plasmacytoma, MM incidence is rising, yet it remains incurable and represents a significant disease burden. Clinical registries can provide important information on management and outcomes, and are vital platforms for clinical trials and other research. The Asia-Pacific Myeloma and Related Diseases Registry (APAC MRDR) was developed to monitor and explore variation in epidemiology, treatment regimens, and their impact on clinical outcomes across this region. Here we describe the registry's design and development, initial data, progress, and future plans.

METHODS: The APAC MRDR was established in 2018 as a multicentre collaboration across the Asia-Pacific, collecting prospective data on patients newly diagnosed with MM, MGUS, PCL, and plasmacytoma in Korea, Singapore, Malaysia, and Taiwan, with China recently joining. Development of the registry required a multidisciplinary team of clinicians, researchers, legal and information technology support, and financial resources, as well as local clinical context from key opinion leaders in the APAC region. Written informed consent is obtained and data are routinely collected throughout treatment by hospital staff. Data are stored securely, meeting all local privacy and ethics requirements. Data were collected from October 2018 to March 2024.

RESULTS: Over 1,700 patients from 24 hospitals have been enrolled onto the APAC MRDR to date, with the majority (86%) being newly diagnosed with MM. Bortezomib with an immunomodulatory drug was most frequently used in first-line MM therapy, and lenalidomide-based therapy was most common in second-line. Establishment and implementation challenges include regulatory and a range of operational issues.

CONCLUSION: The APAC MRDR is providing "real-world" data to participating sites, clinicians, and policymakers to explore factors influencing outcomes and survival, and to support high quality studies. It is already a valuable resource that will continue to grow and support research and clinical collaboration in MM and related diseases across the APAC region.

READING 8. PREVALENCE OF MILD COGNITIVE IMPAIRMENT AND ITS ASSOCIATION WITH MALNUTRITION IN OLDER CHINESE ADULTS IN THE COMMUNITY

Liu Y,[1] Parks AL.[2] Diagnosis and Management of Monoclonal Gammopathy of Undetermined Significance: A Review. JAMA Intern Med. 2025 Apr 1;185(4):450–456.

doi: 10.1001/jamainternmed.2024.8124.

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ABSTRACT

IMPORTANCE: Nearly 5 percent of adults have the precursor malignant condition monoclonal gammopathy of unknown significance (MGUS). Management centres on differentiating MGUS from more serious conditions to determine additional diagnostic testing, monitoring, and potential therapy.

OBSERVATIONS: MGUS is defined by the absence of end-organ damage or symptoms, a small amount of monoclonal immunoglobulin (M protein), and low volume of plasma cells. MGUS must be distinguished from overt malignant diseases like multiple myeloma (MM), immunoglobulin light-chain (AL) amyloidosis, and monoclonal gammopathy of clinical significance (MGCS), all of which cause organ damage or symptoms. Although testing for M proteins is often prompted by clinical findings (e.g., osteoporosis or autoimmune disease), recent evidence from screened populations suggests that previous MGUS disease associations were likely overestimated and that testing for M proteins should be reserved for when malignant disease or MGCS is suspected. Risk of progression to malignant disease ranges from 0.5 to 1 percent, meaning most patients have indolent disease. Guideline-concordant management of MGUS is determined by predicted risk of progression to malignant disease, which depends on subtype of immunoglobulin, M protein concentration, and free light chain ratio. Patients with low-risk MGUS can safely defer bone marrow biopsy and advanced imaging, and should undergo periodic laboratory monitoring. Intermediate- and high-risk MGUS should trigger bone marrow biopsy and bone imaging to detect overt MM and shorter monitoring intervals. Advanced molecular testing may improve on current risk stratification to target monitoring and treatment to those with highest risk of malignant progression and avoid overtreatment of those with low-risk disease. Management will also be informed via results of several clinical trials to clarify the risks and benefits of screening, optimal monitoring strategy, predictors of progression, and potential preventive or curative therapies.

CONCLUSIONS AND RELEVANCE: Evidence-based management of MGUS currently rests on separating clinically indolent from high-risk precursor disease. Research using novel detection methods, incorporating molecular testing into risk stratification, and evaluating screening, monitoring, and therapeutic or lifestyle interventions has the potential to improve outcomes.

READING 9. DETECTING SYMPTOMATIC PROGRESSION IN PATIENTS WITH MULTIPLE MYELOMA

Pietsch C,[1,2] Herget GW,[1,2] Schmal H,[1,2] Frodl A,[1,2] Wäsch R,[2,3] Engelhardt M,[2,3] Ihorst G,[4] Wystrach L,[5] Jung J,[6] Terpos E.[7] Analysis of skeletal pain, general symptoms and patient-reported outcome measures and their value in detecting symptomatic progression—An interdisciplinary prospective study in patients with multiple myeloma. J Bone Oncol. 2025 May 8;52:100685.

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ABSTRACT
BACKGROUND/AIM(S): Globally, studies have shown that the dental disease burden among persons with intellectual and/or developmental disabilities (IDD) is high and can be attributed to lower utilisation levels of dental services. The aim of the study was to assess the influence of income and financial subsidies on the utilisation of dental care services among persons with IDD in Singapore.

In this prospective study, we analysed skeletal pain, general symptoms, and patient-reported outcome measures (PROMs) in patients with MM and their value in detecting symptomatic progression. We evaluated 502 patients, 47 with initial diagnosis (ID) of MM and 455 follow-up patients. At ID, 74 percent reported bone pain, mostly in the spine. General symptoms, particularly fatigue, were present in 89 percent of the patients. 88/455 (19%) of the follow-up patients experienced PD. Of these, 65 percent reported skeletal pain and 81 percent exhibited general symptoms, with fatigue being the most common. PD was suspected and confirmed as the cause of clinical symptoms in 59/88 (67%) and not suspected in 29/88 (33%). Occurrence and character of bone pain and general symptoms differed significantly between patients with and without PD, as did QoL and health-related status. Logistic regression analysis demonstrated that bone pain at night, pain in various locations, pain of known character with occurrence in different location, pain in the chest, pelvis, and thigh as well as fatigue and weight loss were associated with an increased risk of PD.

In conclusion, bone pain and general symptoms are helpful in identifying both MM and PD. PROMs can aid in the diagnosis of PD through symptom-based patient assessment. Serologic and, especially in the case of skeletal complaints, additional radiologic diagnostics are required to confirm suspected and detect unexpected PD.

READING 10. HEALTH SUPPORT OF PEOPLE WITH INTELLECTUAL DISABILITY AND THE CRUCIAL ROLE OF SUPPORT WORKERS

de Mel S,[1] Soekojo CY,[1] Ooi MG,[1] Chng WJ,[1,#] Tso AC,[2] Lee LK,[2] Cao L,[2] Lim CC,[3] Teo C,[4] Chen YX,[5] Tan M,[5] Manjeri A,[5] Goh YT,[5] Nagarajan C,[5,#] Lee ZY,[6] Tan D.[7] Singapore Myeloma Study Group consensus guidelines for the management of patients with newly diagnosed multiple myeloma. Ann Acad Med Singap. 2025 Sep 25;54(9):561–584.

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ABSTRACT
Plain Language Summary: Multiple myeloma (MM) is the second most common haematologic malignancy and remains incurable.

Significant advances have been made in both supportive care and definitive therapy for MM, leading to marked improvements in survival and quality of life. The availability of potent novel agent-based induction regimens, as well as methods to assess deeper levels of response, has transformed the landscape of MM therapy. Balancing therapeutic efficacy against toxicities and cost-effectiveness remains a key challenge to be addressed.

Here, the Singapore myeloma study group provides consensus recommendations on the management of newly diagnosed MM, incorporating key developments in diagnostics, response assessment, supportive care, and definitive therapy.

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Tables should be submitted on a separate page. Label them in Roman-numeric sequence [I, II, III, etc] and ensure they are clear and with explanatory legends as required. Give each column a short or abbreviated heading. Place Table explanations in the footnotes, not in the heading. Explain in footnotes all non-standard abbreviations that are used in each Table.

Illustrations
Illustrations must be submitted in a separate page, and should be provided whenever appropriate. Illustrations should be numbered consecutively in Arabic numerals (e.g., Figure 1, 2, 3) according to the order in which they have been first cited in the text. When required, it is the author's responsibility to obtain permission to reproduce illustrations. Authors need to ensure that photographs, illustrations, and figures do not contain any information that will reveal the identities of the patients and authors. From 1 January 2012, all photographs and illustrations taken from any human subject must be accompanied by the respective endorsed consent form. Clear captions to the figures should be provided.

Concluding Paragraph
Summarise your main findings and its clinical implication, preferably in a single paragraph and no more than 3-4 sentences. Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, distinguish between clinical and statistical significance, and avoid making statements on economic benefits and costs unless the manuscript includes the appropriate economic data and analyses. Avoid claiming priority or alluding to work that has not been completed. State new hypotheses when warranted, but label them clearly.

Learning Points (for invited Family Physician Skills Course article)
Include a minimum of three (3) Learning Points as a take-home message for readers.

Author Contributorship for Original Article Submission
Author details must be included in the relevant fields when submitting an article. Only those who have made substantial contributions to the study and/or preparation of the article should be acknowledged as authors and named in full. The SFP follows the International Committee of Medical Journal Editors (ICMJE) criteria pertaining to authorship (refer to http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html). The precise role(s) of each author should be included in the "contributorship" declaration.

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Declaration of Conflicts of Interest
The SFP requires the author(s) to provide full and detailed declarations of any conflicts of interest. Where there are none, please use the following declaration: *"The author(s) declare(s) that he/she/they has/have no conflict of interest in relation to this article."*

RECOMMENDED FORMAT FOR CASE RECORDS OF FAMILY MEDICINE SECTION

The Case Records of Family Medicine is a newly created series to encourage submissions from Family Medicine teaching programmes and for Family Medicine departments to submit cases of learning value to the *Singapore Family Physician*. Cases discussed during peer review learning and Family Medicine grand ward round teachings are just some examples of submissions that are suitable for this

series. Authors planning to submit their case studies to the Case Records of Family Medicine section should structure their article according to these headings:

Title
The title should define the key focus of the case study.

Case Presentation
The author(s) will provide a pertinent summary of the medical and/or psychosocial issue pertaining to the health or disease management of the case. It should cover the situation and relevant background of the case. Author(s) should conceal the identity of the subject and/or related or accompanying personnel; abbreviation should be used instead, if necessary.

Diagnoses/Problems identified
The assessment of the diagnoses/problems identified will constitute a problem list and will serve as a focus for the management of the case. If the case was a diagnostic dilemma, the author(s) should showcase the diagnostic challenges and their work in narrowing to the correct diagnosis and/or differential diagnoses.

Management of the case
This section covers the approach to the management of the case by the author(s).

Literature review on latest evidence/guidelines (related to diagnosis and/or management)

The author(s) should provide a literature review of current evidence/guidelines, if any, of the basis of the case's diagnosis/management, or to highlight the gaps of knowledge if such evidence is lacking.

The author(s) will provide a concise summary of the lessons learnt from this case study.

Clinical Practice pointers (up to three (3))
The author(s) will suggest ways to apply the new knowledge in clinical practice or to highlight the limitations of its applications, if any.

RECOMMENDED FORMAT FOR PRISM (Patients' Revelations as Insightful Studies of their Management) SECTION

Authors planning to submit their case studies to the PRISM section should structure their article according to these headings:

Title
The title should be framed into a question to define the key focus of the case study.

Patient's revelation: What happened?
The author(s) will provide a concise description of the setting in which the subject raised his/her medical or psychosocial issue pertaining to their health or disease management. It should cover the background, encounter, and interaction of patient with the healthcare professional (doctor, nurse, or allied healthcare professional).

Author(s) should conceal the identity of the subject and/or related or accompanying personnel: abbreviation should be used instead, if necessary.

Gaining insight: What are the issues?
The issue(s) raised by the patient should be framed into question(s). The question(s) will constitute a problem list and will serve as a focus for the management of this subject.

Study the management: How do we apply in our clinical practice?
This section covers the approach to the management of the subject by the author(s). The author(s) should provide a literature review of current evidence, if any, of the basis of the subject's management, or to highlight the gaps of knowledge if such evidence is lacking. The author(s) will suggest ways to apply the new knowledge in clinical practice or to highlight the limitations of its applications, if any.

Conclusion
The author(s) will provide a concise summary of the lessons learnt from this case study.

The article submitted to the PRISM section should be written by no more than three authors. Each article should not exceed 2,000 words. Photographs or charts may be included but should conform to the specific instructions for any other articles submitted to *The Singapore Family Physician*.

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Manuscripts may be returned to their respective authors for revision. This will be accompanied by an Editor's email for which comments and recommendations may be made. The authors are advised to read and to take note of these comments carefully and to revise their articles accordingly. The authors need to reply to the editor's email to outline their response before the resubmission of the revised manuscript. They should exclude the identity of the authors and their institutions, as the email may be redirected to the reviewers during the resubmission process. The resubmitted manuscripts should include the revised complete version, as well as the anonymised version as before.

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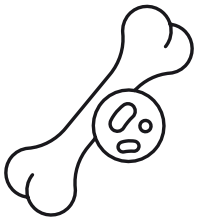
Maybe it's Multiple Myeloma?

1

Multiple Myeloma is a blood cancer that arises from plasma cells in the bone marrow

While ~75% of Multiple Myeloma diagnoses are in people **aged 65 and over,** it can **affect younger people too.** One in 3 patients is younger than 65, and rates in the under 40s are increasing.[1]



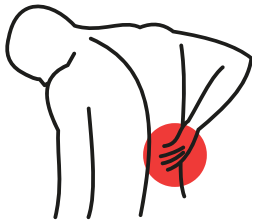
2

Symptoms are often **non-specific**

Challenging to diagnose and often **confused with signs of ageing.** Median time to diagnosis is 108.6 days

Common symptoms include;

- Fatigue
- Breathlessness
- Recurring infections
- Unexplained bone pain
- Unintentional weight loss



3

General Practitioners (GPs) play a **key role in recognizing symptoms** at the earlier stages

Survival rate increases by >1.5X when diagnosis is through the primary care referral pathway, rather than emergency route

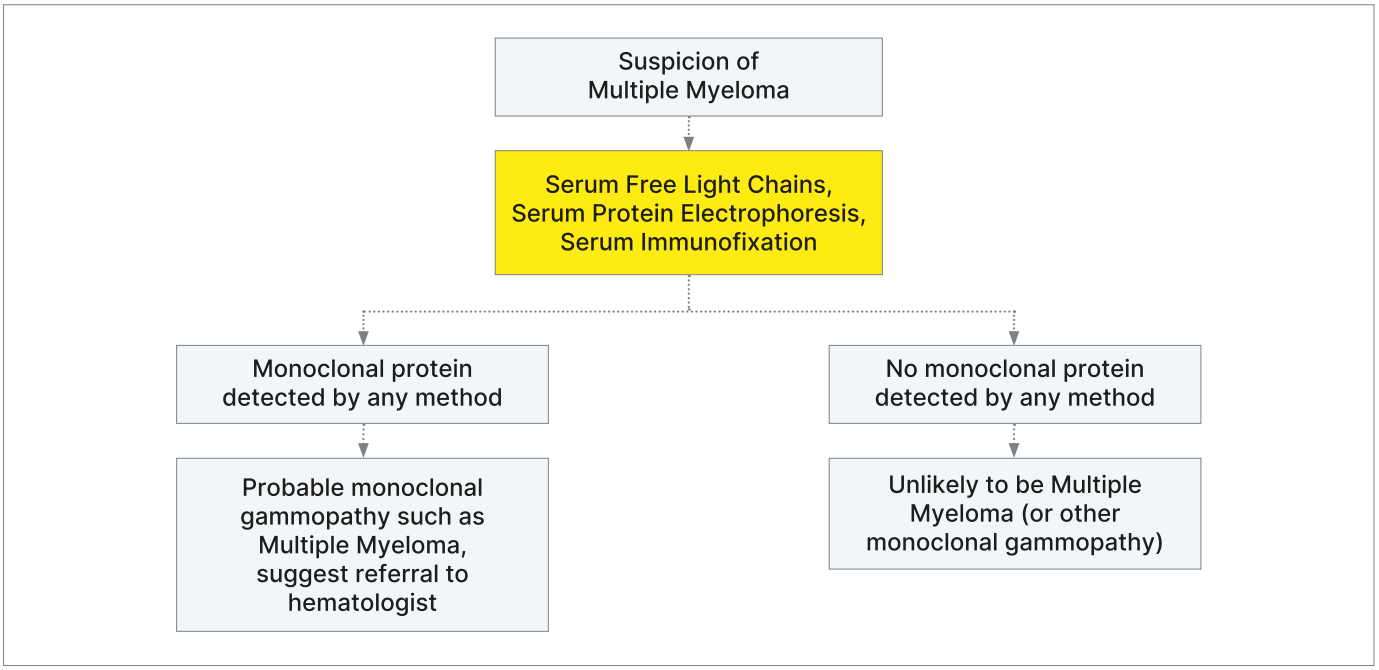
4

Earlier diagnosis helps preserve kidney function. Most patients do not have renal impairment at initial presentation, but as time to diagnosis increases, so does renal impairment.

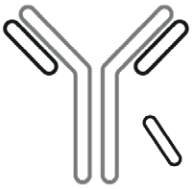
- In patients whose time to diagnosis is <200 days, 20% have renal impairment.
- In patients whose time to diagnosis is >200 days, **56% have renal impairment.**

Recommended Guidelines for Multiple Myeloma diagnosis

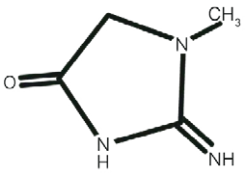
International and national guidelines recommend including serum free light chains (sFLC) testing alongside serum protein electrophoresis (SPE) and serum immunofixation (sIFE) when Multiple Myeloma is suspected to maximize the detection of monoclonal proteins. It is important to include sFLC testing when Multiple Myeloma is suspected, as ~15-20% of patients have Light Chain Only Multiple Myeloma. The monoclonal protein produced by these patients may not be detected by SPE, but will be detected by a test, such as Freelite® assays by the Binding Site, which are designed to detect free light chains.



Complete blood count to check for anemia and raised Erythrocyte Sedimentation Rate



Serum free light chain tests, serum protein electrophoresis and immunofixation to check for a monoclonal protein



Chemistry to check for raised calcium, raised creatinine and low albumin

Refer to hematology

Early referral and diagnosis of Multiple Myeloma are critical.
Delays can lead to severe comorbidities and reduced 5-year survival rates.
Timely intervention can markedly improve patient outcomes.

View the Multiple Myeloma guidelines for Singapore

Learn more about Multiple Myeloma

1 Zhang J, Zhang T, Huang G, Liu C, Wu H, Zhou L: Global burden of multiple myeloma in adolescents and young adults, 1990-2021. Blood Global Hematology 2026, 2(1).

2 Kariyawasan CC, *et al.* Multiple myeloma: causes and consequences of delay in diagnosis. QJM 2007; 100:635-640

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Delayed diagnosis can lead to serious clinical complications

These complications are often referred to as 'CRAB' symptoms and include Hyper**C**alcemia, **R**enal insufficiency, **A**nemia and **B**one lesions (bone pain, fractures and compressions)

Primary care providers play a critical role in improving patient outcomes by ensuring a prompt referral to haematology

The diagram below shows the most common pathways for a myeloma diagnosis

- **Up to 47%** of Multiple Myeloma patients are diagnosed through emergency and urgent care routes
- **51%** one-year relative survival in patients diagnosed via emergency presentation
- **81%** one-year relative survival in patients diagnosed via GP referral route
- **2.7-fold higher frequency** of renal disease in patients diagnosed more than 6 months after first symptom onset compared with those diagnosed within 6 months[2]