Patients with myeloma often present with an anemia of chronic disease; others present with fatigue, or bone pain (such as persistent back pain, with or without obvious lytic lesions and/or mottling of bones on plain radiography) or with weight loss or declining renal function. If laboratory investigations discover unexplained hypercalcemia, a normocytic or macrocytic anemia, unexplained renal dysfunction, or lytic bone lesions or vertebral compression fractures, myeloma should be entertained on the differential diagnosis.

The normal role of the plasma cell is to produce immunoglobulins, AKA antibodies. Myeloma is a malignant proliferation of a clone of plasma cells. Such a malignant clone typically secretes an antibody fragment (either an immunoglobulin heavy chain or a light chain) known as an M-protein. The M-protein can be detected by electrophoresis on serum (SPEP) or urine (UPEP); monoclonal light chain fragments can also be detected on serum free light chain testing. Prior to eventual transformation into myeloma, the underlying clonal plasma cell proliferation typically exists for many years or even decades as a benign disorder, viz., Monoclonal Gamopathy of Undetermined Significance, or MGUS. Estimated to be present in >3% of the North American population over age 50, most cases of MGUS never progress to a malignant form, and are detected incidentally during the work up of unexplained renal dysfunction, anemia, hypercalcemia, premature osteoporosis, unexplained neuropathies, or hyper- or hypogammaglobulinemia. Thus, Monoclonal Gamopathy of Undetermined Significance (MGUS) is a lymphoplasmacytic disorder caused by the proliferation of a clone of cells which produce an M-protein consisting of all or part of an immune globulin, whether IgG (most common), IgA, IgD, IgM, or pure light chains (which can be kappa or lambda). Over time, such benign plasma cell monoclonal proliferations can progress to meet diagnostic criteria for multiple myeloma, or, less commonly, Waldenström macroglobulinemia, AL (“primary”) amyloidosis, light chain deposition disease, heavy chain deposition disease, or POEMS. MGUS is diagnosed if a patient has a monoclonal gammopathy with a serum M-protein concentration <30 g/L, <10% monoclonal plasma cells on bone marrow biopsy, and no end-organ damage (hypercalcemia, renal dysfunction, anemia or bone lesions) attributable to the monoclonal plasma cells or to the protein they produce.
Smouldering myeloma is diagnosed if the M-protein rises above 30 g/L, or bone marrow biopsy demonstrates >10% but <60% monoclonal plasma cells, and there is no end-organ damage.

Multiple myeloma is diagnosed when two conditions obtain:

1. Clonal bone marrow plasmacytes constitute 10% (or more) of the cells on bone marrow biopsy (or there is a biopsy proven plasmacytoma of bone or soft tissue);
2. The neoplastic proliferation of the clone of plasma cells responsible for a monoclonal gammopathy, irrespective of the measured M-protein concentration, progresses to the point of causing end organ damage. That end-organ damage, to be diagnostic of myeloma, must meet one or more of the so-called CRAB criteria.

C = hypercalcemia, defined by a serum calcium > 2.75 mmol/L
R = renal dysfunction defined by an eGFR < 40 (or serum creatinine > 177 umol/L)
A = anemia defined by a Hb < 100 g/L (or > 20 g/L below normal)
B = bone lesions, meaning one or more lytic lesions measuring 5 mm (or more) in diameter on skeletal survey or other imaging test such as MRI.

Lab investigations to pursue in order to rule out or to diagnose myeloma should include a serum protein electrophoresis (SPEP), plasma free light chain (PFLC) ratio, BUN, Cr, corrected calcium, and a CBC. A skeletal survey should be obtained. In some instances (for example if there are neurologic findings suggestive of a radiculopathy or an evolving cord compression, vertebral compression fractures, unexplained osteoporosis, or persistent bony pain in spite of normal plain radiographic findings) an MRI should be ordered. For a concise summary on when to order an SPEP and how to work up suspected myeloma visit http://www.cancercare.mb.ca/resource/File/Cancer_Patient_Journey/When_to_Order_SPEP-CCMB_2015.pdf

You have a 64 year old patient with a history of multiple myeloma. He comes to your office today complaining of an ache to his right thigh and knee which has been worsening over the past 7 days. He reports that the pain is exacerbated by weight bearing, and wakes him at night. You request X-rays be done emergently, and your on-site X-ray clinic obtains a plain radiograph of the right hip, femur and knee. The X-rays reveal generalized slight mottling of the femur, as well as a more obvious 3 cm lytic lesion in the peritrochanteric region of the femur. Approximately 50% of the cortex appears to be eroded by this lesion.

What is your next step in the management of this complication of your patient’s myeloma?

In an article published in 1989 in Clinical Orthopaedics and Related Research entitled “Metastatic Disease in Long Bones: A Proposed Scoring System for Diagnosing Impending Pathologic Fractures”, Hilton Mirels recommended an evidence-based tool for estimating fracture risk in patients with bony metastases (see table below). In his retrospective chart review he found statistical correlations between the size of a lesion (specifically, the amount of cortical bone destruction present), the nature of the lesion (blastic, mixed, or lytic), and the degree of pain. He also incorporated a rating of risk by site of lesion, even though no statistically significant correlation has been obtained for this particular domain. When the various domains are scored and those numbers are summed, the total can range from 3 to 12. Patients whose total score was less than 7 were deemed not at risk for pathologic fracture and can be treated with radiotherapy, bisphosphonates, and/ or chemotherapy. A score of 8 carries a 15% fracture risk, and clinical judgement was recommended with respect to the need for prophylactic fixation of the bone. For all patients with a score of 9 or greater, the recommendation was to urgently refer to an orthopaedic surgeon for prophylactic fixation. Interestingly, irrespective of the total score all patients in whom pain was aggravated by function went on to fracture in Mirels’ study (p = 0.0001). In this case, your patient has a trochanteric lesion (score of 3), which involves about 1/2 of the cortex (score of 2), is lytic in nature (score of 3), and is worse with weight bearing (score of 3). This results in a total score of 11. Based on Mirels’ study, the recommendation would be to counsel your patient to avoid bearing weight on the affected limb pending an urgent consultation with an orthopaedic surgeon for consideration of prophylactic fixation.

<table>
<thead>
<tr>
<th>SCORE</th>
<th>SITE OF LESION</th>
<th>SIZE OF LESION</th>
<th>NATURE OF LESION</th>
<th>PAIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Upper limb</td>
<td>&lt; 1/3 of cortex</td>
<td>Blastic</td>
<td>Mild</td>
</tr>
<tr>
<td>2</td>
<td>Lower limb</td>
<td>1/3 – 2/3</td>
<td>Mixed</td>
<td>Moderate</td>
</tr>
<tr>
<td>3</td>
<td>Trochanteric region</td>
<td>&gt; 2/3 of cortex</td>
<td>Lytic</td>
<td>Functional</td>
</tr>
</tbody>
</table>
Fatigue is the most common symptom reported by cancer patients in Manitoba. Moderate fatigue (scores of 4-6) is reported on 25% of ESAS-r tools completed by patients. Severe tiredness (scores of 7-10) is reported on nearly 15%. This trend is consistent across time and has been observed across age groups, gender, and disease sites. While most individuals in the normative population will experience fatigue, the prevalence and severity is significantly higher in cancer patient populations; up to 90% of cancer patients will experience fatigue over the course of treatment, with one third experiencing persistent fatigue for years after treatment.

Fatigue affects many aspects of quality of life and is often reported by patients as the most distressing symptom experienced.¹,²

Want to support your patients to self-manage aspects of fatigue and promote consistent use of credible, evidence based resources between healthcare providers across the province? Visit the CCMB website to access high quality, evidence based patient resources, including a soon to be released Living Your Best Life: Cancer Related Fatigue Video Series.

**The CancerCare Manitoba Breast and Gyne Cancer Centre of Hope**

The CancerCare Manitoba Breast and Gyne Cancer Centre of Hope is a resource centre that provides education, information and support for women with breast or gynecological cancer.

If you would like to refer a patient for education support or have any questions, contact:

**Michelle Ellwood**, R.N., Gyne Cancer Patient & Family Educator

**Lori Santoro**, B.N., Breast Cancer Patient & Family Educator

Phone: 204-788-8080 or toll free at 1-888-660-4866
MYELOMA AND IMMUNIZATION

Dr. Eric Bow

Infections are a major cause of excess morbidity and mortality among patients with plasma cell dyscrasias, including multiple myeloma, Waldenstrom’s macroglobulinaemia (WM), and monoclonal gammapathies of uncertain significance (MGUS). There are some vaccines which can and should be given to patients with myeloma, but timing is everything. Read on...

Inactivated vaccines may be given safely to patients with myeloma. These vaccines should be administered at least 2 weeks before starting immunosuppressive therapy. The 13-valent pneumococcal conjugate vaccine should be followed in 8 weeks by the 23-valent polysaccharide vaccine. A single dose of the Haemophilus influenza conjugate vaccine may be appropriate if the patient has not received this previously. Lastly, the Meningococcal quadrivalent conjugate vaccine (Men-C-ACWY) and the Type B Meningococcal conjugate vaccine (4CMenB) may also be considered. The meningococcal vaccines should be followed in ≥ 8 weeks by a second dose.

Shingles afflicts 10-15% of myeloma patients, and is especially common with bortezomib and dexamethasone-based induction therapy. Prophylaxis with valacyclovir (500 milligrams orally twice daily) is recommended. Zoster vaccine may be considered for early stage (ISS I, or Salmon-Durie I) myeloma where the Haematologist/Oncologist has elected to observe without specific anti-myeloma therapy. It is essential that this decision be made in consultation with the patient’s haematology-oncology consultant.

Patients who have not received the Pneumococcal vaccine in advance (and who may be also at risk for Pneumocystis jirovecii pneumonia) might benefit from prophylaxis with trimethoprim-sulfamethoxazole (160/800 to 320/1600 milligrams orally daily); however, clinical trials to support such a strategy are lacking.

About 1 in 4 patients with hematological malignancies vaccinated for Hepatitis B develop protective levels of antibodies. Among patients receiving active chemotherapy and who have serological evidence of past HBV infection characterized by circulating Hepatitis B surface antigen (HBsAg) the risk for significant clinical and biochemical hepatitis is between 30-60%. Those with occult infection (HBsAg-negative but HB-core antibody-positive) are also at risk for re-activation, particularly if there is significant HBV DNAemia. Such patients may benefit from lamivudine-based prophylaxis.

Annual vaccination with inactivated influenza vaccine is strongly recommended, even for those patients undergoing active chemotherapy. Some centers have recommended oseltamivir (75 mg daily for 10 days) following patient exposure to a documented symptomatic case of influenza infection. Vaccination of members of the patient’s household is also strongly recommended.
BREAST HEALTH & YOUR PATIENTS: WHEN TO USE TARGETED BOOKING VS PROVINCIAL BREAST IMAGING CONSULTATION REQUEST FORM

The BreastCheck program is for your patient if she is over 50, is asymptomatic with no previous diagnosis of breast cancer, and does not have breast implants. Encourage her to phone 1-855-95-CHECK to book an appointment for a screening mammogram.

Targeted booking for under-screened patients

The BreastCheck Targeted Booking Form is intended for under-screened, average risk women age 52-69 that have never had a screening mammogram, or haven’t returned in 30+ months. You can help your reluctant patient by discussing the importance of routine screening for breast cancer, addressing her questions and concerns, and sending in a completed Targeted Booking Form. BreastCheck will confirm her eligibility and call her to book an appointment at the screening site most convenient for her.

Provincial Breast Imaging Consultation Request Forms

If a patient is not eligible for BreastCheck, she will need to be referred to a diagnostic centre using the Provincial Breast Imaging Consultation Request Form. This includes women who:

- Are symptomatic
- Have had a previous breast cancer diagnosis
- Who currently have breast implants
- Who are under 50 with a family history

Exceptions

The BreastCheck mobile program provides province-wide access to screening mammography. However, accommodation can be made for women living in areas with limited access who require diagnostic mammography on the mobile clinic. Please contact BreastCheck directly to discuss your referral options.

What’s new in cancer screening?

Laura Coulter

CancerCare Manitoba Screening Programs has recently welcomed the following individuals into newly appointed positions:

Kelly Bunzeluk, Director
k bunzeluk@cancercare.mb.ca
204-788-8636

Laura Coulter, ColonCheck Program Manager
lcoulter@cancercare.mb.ca
204-788-8084
Dr. Shrinivas Rathod  

We are pleased to announce that Dr. Shrinivas Rathod has joined the Department of Radiation Oncology, CancerCare Manitoba, as a Radiation Oncologist starting September 6, 2016.

Dr. Rathod received his medical degree and completed his internship at the Grant Government Medical College, Mumbai, India, in 2007. He completed his residency and obtained board certification from the Tata Memorial Center, Mumbai, India in 2011. He completed a 2-year senior residency at TMH implementing SBRT lung program in 2013. He pursued a Clinical Fellowship in the Radiation Oncology Program at the Princess Margaret Hospital, University of Toronto from July 2014 to August 2016. During his fellowship, he served as the Chief Fellow for the Radiation Oncology Program at the Princess Margaret Hospital, University of Toronto from July 2015 to June 2016.

Dr. Rathod will be joining the Gamma Knife team and the CNS disease site group. His office will be located at the MacCharles site. We look forward to his clinical and research contributions to CancerCare Manitoba and the University of Manitoba.

New Community Oncology Program Staff:

Anisa Baker  Professional Development Coordinator
Jill Sutherland  UPCON Professional Development Coordinator
Cody Watling  Research Assistant