CANCERtalk
› CONNECTING WITH MANITOBA'S HEALTH PROFESSIONALS
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MYELODYSPLASTIC SYNDROMES

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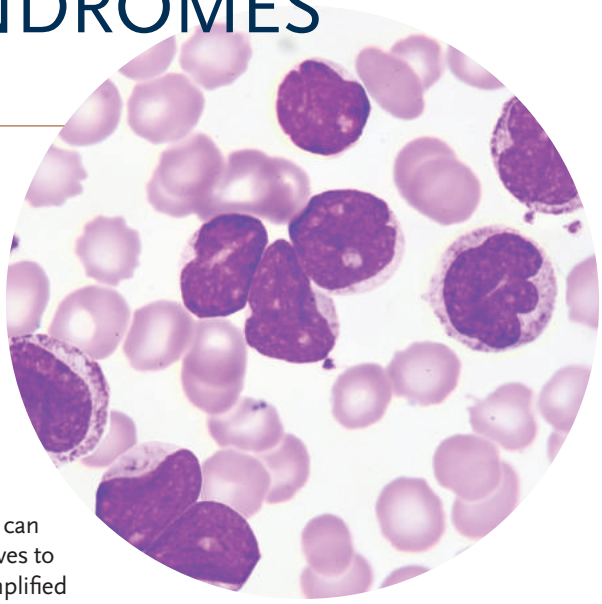
Myelodysplastic syndromes (MDS) are a heterogeneous group of clonal bone marrow disorders usually presenting with progressive anemia. The incidence is 3-4/100,000 population per year, increasing ten-fold in patients older than 70 years. It is characterized by ineffective hematopoiesis, leading to one or more cytopenias, marrow dysplasia, and a tendency for leukemic progression. Many patients die due to the complications of cytopenias, while transformation to acute myeloid leukemia occurs in 30%.

Diagnosis

When unexplained persistent blood cytopenias occur, usually in the elderly, MDS should be suspected. Diagnosis is challenging, as the lab features are non-specific. Cytopenias and dysplasia (in blood or bone marrow) may occur in infective, toxic, inflammatory and nutritional deficiency states. Cytogenetic abnormalities occur in only 50% cases. Hence, the diagnosis of MDS requires expertise and should be done in a hematology center.

The major diagnostic criteria recommended by the World Health Organization (WHO) in 2016 are given in Table 1. Once the diagnosis is established, the prognosis should be assessed. Based on the number and severity of cytopenias, blast percentage and cytogenetic characteristics, the Revised International Prognostic Scoring System (IPSS-R) was proposed in 2012. This framework can estimate the survival, and also serves to guide therapeutic decisions. A simplified diagram highlighting the principles of prognostication and therapeutic options is presented in Figure 1.

The only curative therapy is hematopoietic cell transplantation (HCT), with inherent toxicity. All other modalities are effective for a limited time; the disease eventually becomes refractory and progresses in spite of therapy. Hence supportive therapy plays a pivotal role and the family physician plays an important part in management. Participation in clinical trials is recommended, to determine the role of new molecules.



Supportive Care

For patients with low IPSS-R risk and asymptomatic cytopenias, watchful waiting is justified, with blood counts every 3 months. Almost 90% patients with MDS have anemia at some point. Eventually most need regular red cell transfusions. For thrombocytopenia, platelet transfusions are the only treatment, but must be used judiciously, as platelet refractoriness is a complication. There is no specific treatment for neutropenia.

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Infections should be treated aggressively, as recommended in guidelines for neutropenic patients.

Specific therapy for low-risk MDS

High dose erythropoietin (or darbepoietin) may be used in selected patients having mild anemia with serum erythropoietin levels <500 mU/ml, and may be effective in half to one third of cases. Lenalidomide is a useful drug effective in patients with deletion (5q). About 70% of such patients become transfusion independent on lenalidomide, usually within 4-6 weeks. In a small subset of young patients with hypocellular bone marrow, immunosuppressive drugs are effective.

Therapy for high-risk MDS

Potentially toxic therapy is justified in higher risk patients with poor survival indicators. Allogeneic HCT is indicated if patients are fit and have a donor. Unfortunately, most patients are ineligible due to old age and co-morbidities.

Younger (usually less than 70 years) patients should be referred to a transplant center.

Azacitidine is a hypomethylating agent, which prolongs survival and brings about hematological improvement in 50% cases, with complete remission in 10-20%. Age is not a limiting factor and the benefit may last for a few years.

Recommended Reading

1. Malcovati L, Hellstrom-Lindberg E, Bowen D, et al. Diagnosis and treatment of primary myelodysplastic syndromes in adults: recommendations from the European LeukemiaNet. Blood. 2013;122(17):2943-2964.
2. Arber DA, Orazi A, Hasserjian A, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 2016; 127:2391-2405.
3. NCCN Practice Guidelines in Oncology. Myelodysplastic Syndromes. 2016 (*www.nccn.org*)
4. MDS Clear Path: A Canadian physician Consensus. *http://www.mdsclearpath.org*

Table 1.

Diagnosis MDS (WHO criteria)
Peripheral blood
Cytopenias (one or more): Hb <100 g/L; Plat <100x10^9/L; ANC <1.8x10^9/L
+ Bone Marrow
Dysplasia: 10% or more in erythroid, myeloid or megakaryoctes **OR**
Myeloblasts: ≥ 5% (or ≥ 1% in blood) **OR**
Cytogenetics: MDS defining, by conventional karyotyping
Exclude Reactive Causes or Dysplasia

Before, During, After and Beyond
Psychosocial Oncology at CancerCare Manitoba

Elizabeth Payne
SUPPORTIVE CARE COORDINATOR, COMMUNITY CANCER PROGRAM NETWORK

While distress associated with a diagnosis of cancer is normal, over 30% of cancer patients experience clinically significant anxiety or depression, and the incidence is even greater for their partners (*www.cancer.gov*). Emotional, financial, relationship, and spiritual struggles are common. Depression and distress tend to peak at times of transition (such as suspicion of cancer, time of diagnosis, beginning and end of treatment, time of recurrence, end of life, and bereavement). Psychosocial Oncology services at CancerCare Manitoba are available to patients and family members at any point on the cancer trajectory, including bereavement.

The Department of Psychosocial Oncology at CancerCare offers specialized counseling, support groups and programs for patients and families affected by cancer. Programs include a variety of disease site specific support groups, and one specifically for young adults. A number of structured eight to ten week programs are offered as well, including Brain Fog for patients struggling with cognitive side effects, Mindfulness Meditation, Expressive Arts, and several programs focusing on physical activity and recovery post treatment. More detailed program information is available in the Navigator, a monthly newsletter produced by Patient and Family Support Services. The Navigator can be accessed at *http://www.cancercare.mb.ca/pfss* on the CancerCare Manitoba website or you can request that hard copies be mailed to your office every month.

Referrals and inquiries are welcome from community health care providers. Persons affected by cancer may also self-refer.

Department of Psychosocial Oncology
Phone 204-787-2109
Fax 204-786-0623
Email ccmbpfssinquiry@cancercare.mb.ca

CANCER PATIENT JOURNEY: FIVE-YEAR UPDATE

Judy Edmond
CCMB, COMMUNICATIONS & PUBLIC AFFAIR

June 2016 marked five years since the launch of the Cancer Patient Journey Initiative, also known as In Sixty. The project's steering committee met in June to reflect on the successes of the project and to discuss next steps.

At the meeting, steering committee co-chair and CCMB President and CEO Dr. Sri Navaratnam, remarked that the key learning of the project was that the quality of the patient's experience was equally important as timely access to cancer services.

After five years, project participants identified seven key achievements:

1. The patient voice significantly influenced improvements. The emphasis on the quality of the patient journey was due to the guidance of cancer patients and their families.
2. For the first time, Manitoba healthcare professionals came together as a team with the goal of streamlining and fast-tracking cancer services. More than 5,000 Manitobans have been referred for navigation services. One phone call connects the patient with a team of cancer experts who ensures tests are conducted to get a timely diagnosis and provides the patient and family with emotional support during this stressful time.
3. Cancer pathways have been developed and posted on cancercare.mb.ca for breast, lung, colorectal and prostate cancer and lymphoma. Each pathway sets out the ideal timeline to get patients from suspicion to treatment within 60 days. They are a handy tool for physicians that outline the steps to a diagnosis of cancer.
4. System-wide process changes have been introduced to shorten the patient wait times: "Out the Door in 24" to get referrals out of primary care offices faster; Direct Referral from a suspicious mammogram directly to the next needed test up to and including surgery consiltation, if needed; Central Referral for colonoscopies; and other process improvements at clinics, diagnostic sites and hospitals throughout Manitoba.
5. Urgent Cancer Care established at CCMB has seen more than 5,500 patients. This means fewer cancer patients waiting in emergency rooms.
6. Made-in-Manitoba cancer resources developed by patients, for patients with current information about services and supports including a tool to track their own cancer journey are available on cancercare.mb.ca

Early results are showing that wait times are coming down. For example, 41 per cent of patients with breast cancer now get a diagnosis within 60 days, compared to 18 per cent five years ago.

The next stage is the establishment of a provincial oncology council composed of health care professionals and patients, who will continue to work together to achieve further improvements to the cancer patient journey.

Please go to *cancercare.mb.ca* for more information

HYPERGLYCEMIA, STEROIDS & CHEMO

Mark Kristjanson
MEDICAL LEAD, PRIMARY CARE, COMMUNITY ONCOLOGY PROGRAM

Have you ever been tempted to give your diabetic patient 300 mg of prednisone, just to see what would happen to their blood sugars? Probably not – but high dose steroids are an integral part of many chemotherapy regimens, and even non-diabetic patients on chemotherapy sometimes run into serious problems from marked hyperglycemia complicating their steroid therapy. Responsibility for managing dysglycemia during chemotherapy does not fall squarely on the shoulders of any single discipline, whether family medicine, medical oncology, oncology nursing, pharmacy or endocrinology. Nor is it the sole responsibility of the patient. We all own it.

In one study of hyperglycemia related to the steroids administered as part of Hyper –CVAD (a chemotherapy induction regimen for acute lymphoblastic leukemia) it was observed that patients with hyperglycemia were more prone to sepsis and infections generally, and had a shorter median survival.[1] Various studies of induction chemotherapy for ALL have documented rates of steroid-associated hyperglycemia ranging from 37 – 67%.[1 2 3]

A proactive approach to detecting and treating steroid-induced hyperglycemia requires the active participation of the patient in their own care. Self-management of glycemic control involves education of the patient in the technique of blood glucose monitoring and on the effects of steroid hormones, dietary carbohydrates, and exercise on blood glucose levels.

For those patients already on oral hypoglycemics, these agents can usually be continued throughout the chemotherapy regimen. Be ready to reduce or discontinue oral agents (especially metformin) if renal impairment develops as a complication of (for example) a platinum-based chemotherapy regimen. If a patient is on a daily steroid dose, such as with some metastatic prostate cancer regimens, and the blood sugar levels remain slightly above target, the initiation of metformin can help;

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for patients already on metformin, or who have significant renal dysfunction, the clinician might choose instead to add a low dose of NPH, the pharmacokinetics of which match well the arc of hyperglycemia across the day which one sees with steroids administered in the morning.

For those regimens involving high dose steroids and extreme fluctuations in blood sugar, Cancer Care Manitoba is currently in the process of developing a process for managing hyperglycemia and ensuring that appropriate communication takes place between oncologists, primary clinicians and (when necessary) endocrinologists.

Some family physicians and nurse practitioners are quite comfortable with teaching glucose self-monitoring. Alternatively, clinicians practicing in Winnipeg can visit the WRHA's Diabetes Services Directory (*http://www.wrha.mb.ca/healthinfo/a-z/diabetes/directory.php*) for a list of clinics that will do insulin starts and teach patients how to check their sugars. Urgent consultation with an endocrinologist can be obtained by paging the on-call endocrinologist at any of the following Winnipeg hospitals: Health Sciences Centre; St. Boniface General Hospital; Grace Hospital; or Victoria General Hospital.

1 Weiser MA, Cabanillas MD, Konopleva M, et al.: Relation between the duration of remission and hyperglycemia during induction chemotherapy for acute lymphocytic leukemia with a hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone/methotrexatecytarabine regimen. Cancer 2004;100:1179–1185

2 Sonabend RY, McKay SV, Okcu MF et al.: Hyperglycemia during induction therapy is associated with increased infectious complications in childhood acute lymphocytic leukemia. Pediatr Blood Cancer 2008;51:387–392

3 Matias Cdo N, Lima V, Teixeira HM, et al.: Hyperglycemia increases the complicated infection and mortality rates during induction therapy in adult acute leukemia patients. Rev Bras Hematol Hemoter 2013;35:39–43.

4 Brady V, Thosani S, Zhou S, Bassett R, Busaidy NL, Lavis V: Safe and Effective Dosing of Basal–Bolus Insulin in Patients Receiving High-Dose Steroids for Hyper-Cyclophosphamide, Doxorubicin, Vincristine, and Dexamethasone Chemotherapy. Diabetes Technology & Therapeutics 2014 Vol 16, Number 12: 874-879

ASK THE Cancer Expert

Your questions from Blood Disorders Day 2016 Answered

Q: When are serum iron levels of benefit?

A: (from Dr. Don Houston, CCMB Hematology)

1. First, note that serum iron should always be ordered with TIBC.
2. If ferritin is low, the patient is iron deficient; serum iron does not add anything so don't order it.
3. If ferritin is normal but MCV is low, serum iron will help to distinguish between thalassemia trait (normal serum iron) and either iron deficiency anemia or anemia of inflammation (low serum iron). [Remember that the quickest and cheapest way to rule out thalassemia trait is to find a previous CBC with a normal MCV]
4. Measurement of iron and TIBC may help a little in trying to sort out the patient in whom you suspect there may be both anemia of chronic disease AND iron deficiency (i.e. patient with a ferritin in normal range but evidence of inflammation). Serum iron will be low either way, but TIBC should be high if pure iron deficiency, low if pure chronic disease, and in the middle (like the ferritin) if both processes are present
5. Serum iron and TIBC should be ordered if ferritin is high, to distinguish ferritin response to inflammation (Transferrin saturation low) from iron overload (Tsat high). Once a diagnosis of hemochromatosis is made, ferritin is the parameter to follow treatment response to phlebotomy.

Q: Why would B12 fail to rise even with monthly injections?

A: (Dr. Ryan Zarychanski, CCMB Hematology) Some people have a genetic deficiency of haptocorrin (formerly called transcobalamin I or R-protein). Haptocorrin binds free vitamin B12 in the stomach to protect it from hydrochloric acid produced by the gastric mucosa. Haptocorrin also is present in plasma, where it binds the majority (75%) of vitamin B12 in the blood stream. However, B12 bound to haptocorrin is biologically inactive. Since a serum B12 assay reflects the total B12 in circulation, a deficiency in haptocorrin results in a low serum B12 value even though there are likely normal circulating levels of biologically active B12 bound to transcobalamin II, a glycoprotein carrier molecule that transports biologically active B12 to tissues. If a biochemical deficiency of B12 exists, serum levels of methylmalonic acid (MMA) are elevated. Normal MMA and homocysteine levels and absence of neurologic or hematologic findings are consistent with haptocorrin deficiency. Cautious observation and monitoring of MMA and homocysteine levels, instead of vitamin B12 levels, may be considered for a patient with suspected haptocorrin deficiency. Treatment with oral or subcutaneous B12 is felt to be unnecessary in this instance, but also unlikely to be harmful. Supplementation may further prevent complications of acquired B12 deficiency that may go unnoticed in patients with suspected haptocorrin deficiency.

COLON CANCER SCREENING

David Haligowski
B.SC., MD, RIVERGROVE MEDICAL CLINIC, WINNIPEG

I have been practicing family medicine in Winnipeg for 26 years. I work in a group practice of five doctors, each with his/her own patient load. As well, I attend upon approximately 180 residents of 2 personal care homes.

In implementing screening for colon cancer, as in screening for other disorders, I follow national or provincial guidelines. Here in Manitoba, the provincial guideline recommends screening for colon cancer in average risk patients with fecal occult blood testing every 2 years from age 50 to 74 years of age. Our clinic began using EMR and I use this to record reminders to perform FOB testing every 2 years.

Initially, I used FOBT kits distributed by our local private laboratory. But, as I learned of the improved accuracy of ColonCheck's FOBT kits, I switched over for patients aged 50 to 74 years. Also, I was impressed with the improved instructions included in ColonCheck's kit, the supplied toilet bowl liner to collect the sample (which was not offered by the private lab), the ease of returning the package via mail, and the follow up by ColonCheck in the form of letters to patients with negative results, phone calls to patients about positive results, and reminder letters to be sent to patients 2 years after their last known FOBT or 5 years after their last known colonoscopy.

Now, with the new FOBT request form, I offer to send in a request to ColonCheck when patients are seen at the clinic, or I send in the forms when I review results or prescription requests and I haven't seen the patient in some time. This eliminates the need for patients to call and request the kit, and it prevents procrastination on their part. It seems most, but not all, patients want to please their primary care provider and understand the importance of performing this test.

For patients who have a positive ColonCheck FOBT result I have opted to have ColonCheck schedule the colonoscopies for me, as I found the wait times were shorter and it was one less thing my office staff had to do. ColonCheck has taken the worry out of arranging these investigations and expedited the time it takes to complete them.

I think we as health care providers need to make FOBT "The new routine", thinking about it each time we see a patient for an unrelated problem. EMR can make this an easier and more effective way to protect our patients against the risks of colorectal cancer. I don't know how to make doing the test less icky when we ask patients to obtain samples for testing, but I know we can make it tolerable, easy, and effective for the betterment of our patients' health.

Expansion of Services: Rapid Diagnostic Clinic Winnipeg Cancer Hub

Zenith Poole and Dr. Helmut Unruh
ZENITH POOLE IS PROVINCIAL NAVIGATION LEAD, CANCERCARE MANITOBA; DR. UNRUH IS HEAD, SURGICAL ONCOLOGY, CCMB

A Rapid Diagnostic Clinic (RDC) at CCMB has long been recognized as something that has been lacking and was therefore established as a direct result of the 2016-2021 Manitoba Cancer Plan. The RDC was operationalized in November 2015 as an extension of services provided by the Winnipeg Cancer Hub (WCH). The initial phase was undertaken as a pilot project and referrals were limited to patients referred to the WCH by WRHA facilities or medical practitioners. It soon became apparent that patients with advanced disease were in particular need of urgent attention and that this was a significant gap in the services provided at CCMB.

To address gaps and differing availability of resources in regions outside Winnipeg the RDC/WCH in June 2016 expanded its scope of services to include accepting referrals from rural Regional Cancer Program Hubs. The RDC will see patients from rural regions in the early diagnostic phase of their journey. Referral criteria include:

- Patients exhibiting advanced stages of cancer and/or poor performance.
- Patients in need of symptom management.
- Patients who would benefit from early discussion of next steps irrespective of stage of cancer.
- Patients with metastatic disease from an unknown primary cancer.

To refer patients meeting the criteria, primary care providers should direct a referral (by phone or fax) to their Regional Cancer Program Hub. The referral letter should state explicitly that an assessment in the RDC is sought. It is recognized that many of the patients will be too ill to travel and consultation via TeleHealth is available.

For more information on Regional Cancer Program Hubs including referral forms and patient resources please go to *www.cancercare.mb.ca/navigation*

HOW TO REACH US

CCMB REFERRAL CENTRE
204-787-2176
FAX: 204-786-0621
M-F, 0830-1630, closed Stat Holidays
Emergency Referrals:
HSC PAGING: 204-787-2071
ST BONIFACE PAGING: 204-237-2053

CANCER QUESTION? HELPLINE FOR HEALTH CARE PROVIDERS
204-226-2262 (call or text / sms)
EMAIL: cancer.question@cancercare.mb.ca
WEB FORM: cancercare.mb.ca/cancerquestion
M-F, 0830-1630, closed Stat Holidays

CCMB SCREENING PROGRAMS BREASTCHECK – CERVIXCHECK – COLONCHECK
1-855-952-4325 | GetCheckedManitoba.ca

CANCERCARE MANITOBA
TOLL FREE: 1-866-561-1026
(ALL DEPARTMENTS + CLINICS)
www.cancercare.mb.ca
Inquiry & Reception
MACCHARLES UNIT (HSC) 204-787-2197
ST. BONIFACE UNIT 204-237-2559
Pharmacy: 204-787-1902

COMMUNITY CANCER PROGRAMS NETWORK (CCPN) OFFICE, CCMB
204-784-0225

MANITOBA PROSTATE CENTRE, CCMB
204-787-4461
FAX: 204-786-0637

PAIN & SYMPTOM MANAGEMENT
204-235-2033 ask for pain & symptom physician on call
M-F, 0830-1630

UPCON
204-784-0218

ANNOUNCEMENTS

Dr. Leonard Minuk

Dr. Leonard Minuk has joined the Department of Medical Oncology and Haematology, CancerCare Manitoba, and the Section of Haematology Oncology, Department of Internal Medicine, University of Manitoba, as of July 19th, 2016.

Dr. Minuk will be providing outpatient services in the Lymphoproliferative and General Hematology disease site groups and will be participating in the Adult Hematology Consultation Service at the Health Sciences Centre.

Dr. Craig Harlos

Dr. Craig Harlos graduated in 2010 from medical school at the University of Manitoba where he also pursued residency training in internal medicine followed by subspecialty training in Medical Oncology. He recently completed a clinical fellowship in Neuro-Oncology through the University of Toronto at the Princess Margaret Cancer Centre under Dr. Warren Mason.

Dr. David Haligowski

The Urgent Cancer Care clinic at the McCharles Unit is pleased to announce that Dr. David Haligowski (University of Manitoba medical school class of '85), a prominent Winnipeg family physician and long-time UPCON lead for the Rivergrove Medical Centre, will be joining the team in UCC on a part time basis.

Dr. Benjamin A. Goldenberg

Dr. Goldenberg was born and raised in Manitoba with family roots dating back more than a century to rural Western Manitoba and Winnipeg's North End.

He completed medical school (Class of 2009) and Internal Medicine Residency at the University of Manitoba, and subsequently trained in Medical Oncology at the BC Cancer Agency and the University of British Columbia in Vancouver.
He thereafter completed an advanced fellowship in Gastrointestinal Oncology at Princess Margaret Cancer Centre in Toronto, while at the same time doing an MSc in Health Services Research at the University of Toronto.

He will have a clinical practice in GI and Breast malignancies and is keenly interested in the Quality of Cancer Care delivery and the safe provision of oral systemic therapy.

Benjamin, his wife and two young boys are very happy to return home to a welcoming community of family and friends.

Dr. Belynda Salter-Oliver

Dr. Belynda Salter-Oliver is a family physician in Winnipeg. She completed medical school in 2002 and her Family Medicine residency in 2004 at the University of Manitoba. She currently has a family medicine practice at Prairie Trail Medical Clinic and recently started as an FPO at Cancer Care.

New Guidelines Posted

Four new guidelines have now been posted on CancerCare Manitoba's website CancerCare.mb.ca. These guidelines can be used to determine the best course of action when decisions about treatment options or care must be made. The ultimate goal is to ease the patient's journey through the cancer experience and keep patients and their families at the centre of care.

- Recommendations for Filgrastim Use in Adults by Disease Site
- Consensus Recommendations for the Routine Use of Positron Emission Tomography (PET) Scan Imaging for Lymphoma in Manitoba
- Consensus Recommendations for Management of Malignant Melanoma
- Consensus Recommendations for the Management of Chronic Lymphocytic Leukemia: Primary Care Guideline

CancerCare Manitoba's website contains all approved Clinical Practice Guidelines, Clinical Guides and Systemic Therapy Summaries.

Clinical Practice Guidelines and practice tools are updated periodically. We recommend that practitioners consult CancerCare.mb.ca to ensure they are using the most recent versions.