The Microenvironment

THE CANADIAN HEMATOLOGY SOCIETY

SOCIÉTÉ CANADIENNE D'HÉMATOLOGIE

NEWSLETTER

August 2017

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2017 CHS Executive Committee

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MICROENVIRONMENT

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MESSAGE FROM THE PRESIDENT

Dr. Lynn Savoie
President, CHS

Dear Colleagues,

Change and renewal:

these are two words top of mind for me right now. Some of you already know this but I am currently on leave from my position in Calgary and heading to London for a sabbatical year. In order to do this I have had to revisit all of my training with some degree of nostalgia. This fits right in with this time of year when new residents have joined our training programs and new full-fledged staff hematologists have started their first positions. I welcome them all to join us at the CHS and keep us posted of their news locations and contact information.

Welcome Co-Chief Residents!

Within the CHS executive I am pleased to welcome our new Co-Chief residents: Drs. **Cindy Hickey** from Dalhousie and **Siraj Mithoowani** from McMaster. I am excited to see what innovations this young blood will bring to the table as all of our previous chief residents certainly have. I want to take this opportunity to thank **Zach Liederman** for all his hard work as outgoing chief resident.

CHS Gala Event at ASH 2017

There are lots of activities coming up. Registration has just come and gone for ASH and as per usual we will be hosting our gala dinner on the Sunday night. Stay tuned for your invitation. We invite you to attend and meet all of us in the executive and your colleagues from around the country. Of course, this is also when we recognize the best of research our country has to offer. The deadline for the submissions for the Canadian Paper of the Year is upon us at the end of September and we encourage you to submit your publications. Also, by the time you read this ASH abstracts will have been submitted. We expect another banner year of applications for the CHS trainee awards at ASH.

CHS to host ISH 2018, Vancouver

Finally, it is exciting to remind you that the CHS will be hosting the **International Society of Hematology bi-annual meeting in Vancouver in September 2018**. If this is not a meeting you usually attend, please keep it in mind when planning your CME for 2018. As **co-chairs Drs. Rock and Nevill** have been working very hard at ensuring a wonderful conference for us.

I will remain your president until ASH of this year despite being out of the country so please feel free to be in touch if you have any questions, concerns or thoughts. I can be contacted at lynn.savoie@ahs.ca, through the CHS email at chs@uniserve.ca or through our web portal.

Dr. Lynn Savoie,
President, CHS

Le message du Présidente

Dr. Lynn Savoie, Présidente, CHS

Chers collègues

Changement et renouvellement : ce sont les deux mots qui viennent à l'esprit en ce moment. Certains d'entre vous le savent déjà, mais je suis actuellement en congé de mon poste à Calgary et je me dirige vers Londres pour une année sabbatique. Pour ce faire, j'ai dû revoir toute ma formation avec un certain degré de nostalgie. Cela correspond parfaitement à cette période de l'année où les nouveaux résidents se joignent à nos programmes de formation et les nouveaux hématologues commencent leurs premiers postes. Je vous invite à vous joindre à nous au CHS et de nous tenir au courant de vos nouvelles, votre lieu de travail et vos coordonnées.

Bienvenue co-chef résidents!

Au sein de l'exécutif de la CHS, je suis heureuse d'accueillir nos nouveaux co-résidents: les Drs Lynn Hickey de Dalhousie et Siraj Mithoowani de McMaster. Je suis ravi de voir quelles innovations ce jeune sang apportera à la table comme tous nos anciens résidents en chef ont fait. Je tiens à remercier Zach Liederman pour son travail acharné en tant que résident en chef sortant.

Soirée Gala du CHS à ASH 2017

Il y a beaucoup d'activités à venir. L'inscription pour ASH est maintenant ouverte et, comme d'habitude, nous organisons notre souper gala pour le dimanche soir. Surveillez pour votre invitation. Nous vous invitons à participer à cet événement et de rencontrer l'exécutif et vos collègues de notre pays. Bien sûr, c'est aussi lorsque nous reconnaissons les meilleures recherches que notre pays a à offrir. La date limite pour les soumissions pour le document canadien de l'année, approche rapidement et nous vous encourageons à soumettre vos publications avant la fin de septembre. En outre, au moment où vous lisez ces lignes, les résumés ASH auront été soumis. Nous nous attendons à une autre année à haut nombre de candidature pour les prix de stagiaires CHS à ASH.

CHS accueille ISH 2018, Vancouver

Finalement, il est excitant de vous rappeler que CSH accueillera la réunion bi-annuelle de la Société internationale d'hématologie à Vancouver en septembre 2018. Si ce n'est pas un rendez-vous que vous fréquentez habituellement, gardez-le à l'esprit lors de la planification de vos credits pour 2018. En tant que co-présidents, les Drs Rock et Nevill ont travaillé fort pour assurer une merveilleuse conférence pour nous tous.

Je vais continuer à être votre présidente jusqu'à ASH de cette année, malgré le fait que je serai hors du pays, alors n'hésitez pas à prendre contact si vous avez des questions, des préoccupations ou des pensées. Je peux être contacté à lynn.savoie@ahs.ca, par courrier électronique du CHS à chs@uniserve.ca ou par l'intermédiaire de notre portail Web.

Dr. Lynn Savoie,
Présidente, CHS

ACKNOWLEDGEMENT

Dr. Mohammad Bahmanyar: outstanding contribution to CHS Portal

Dr. Mohammad Bahmanyar

The Canadian Hematology Society Executive Committee and general membership, gratefully acknowledge the excellent work of Dr. Mohammad Bahmanyar as the CHS Hematopathology Editor for the CHS interactive web portal.

"*Dr. Bahmanyar's commitment and expertise in developing hematopathology cases for the CHS webportal went above and beyond our expectations and contributed strongly to the ongoing education of residents and hematologists across Canada*," said Dr Lynn Savoie, CHS President.

The teaching modules that Dr. Bahmanyar helped to create will continue to be presented on the CHS web portal and will serve as an important component of the CHS education library.

Welcome to the CHS Portal !

- ⇒ Academic Case Review
- ⇒ Image Challenge
- ⇒ Continuing Medical Education
- ⇒ Product Reimbursement Library
- ⇒ Members

https://chsportal.ca/

UPDATE: ISH-CHS Congress, September 13 - 16, 2018 / Vancouver

The ISH 2018 congress will begin on Thursday, September 13, 2018, opening with a plenary session. The closing session will be on Sunday, September 16.

PROMOTIONAL ACTIVITIES AND PLANS

The CHS will have a booth at ASH in December, 2017, to promote attendance at the Vancouver 2018 meeting. We will also be sending promotional materials to other international meetings.

We have developed some flyers and banners and are developing a more detailed information pamphlet about ISH 2018 to augment the current material.

Vancouver Convention Centre ISH/CHS 2018 Congress venue

THE SCIENTIFIC PROGRAM

The Scientific Program will be packed with a broad selection of current and controversial topics of interest in benign and malignant hematology.

We hope to see all of the CHS members there!

Dr. Tom Nevill, *Scientific Committee Chair*
Dr. Gail Rock*, Organizing Committee Chair*

Visit the Congress Website: http://www.ish2018.com/

- **Program at a Glance**
- **Program Highlights**
- **Important Dates**
- **Abstract Submissions**
- **Registration & Housing**
- **Early Bird Deadline**

For information: ish2018@ICSevents.com

Do you know the diagnosis?

By Danielle Hammond, MD, Department of Medicine, University of Toronto, Toronto

"What's DAT?!"

A patient on daratumumab will exhibit:

a) Invariably a positive direct antiglobulin test (DAT) and antibody screen with pan-reactivity.

b) A variably positive DAT; invariably positive antibody screen with pan-reactivity.

c) Only the DAT but not the antibody screen is affected.

Answer: See Page 12

Your 2017 CHS Executive Committee

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Dr. Lynn SAVOIE
Calgary

Past—President
Dr. Aaron SCHIMMER
Toronto

Vice—President
Dr. Nicole LAFERRIERE
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Dr. Siraj MITHOOWANI
Toronto

Co—Chief Resident
Dr. Cindy HICKEY
Halifax

WHO'S WHO / WHAT'S HAPPENING: CHS Members on the Move

Based on members' feedback and comments about their interest in *The Microenvironment* content — the CHS Executive decided at the May 15, 2017 Executive Retreat, held in Toronto — to launch this column as a regular feature, beginning with this summer of 2017 issue.

To help keep CHS members up to date and informed about news regarding peers across this vast country, this column will feature news of promotions, heads of international committees, important grants or publications, mid-career moves, retirements, etc.

Our outgoing president, **Dr. Lynn Savoie**, has recently traveled to London where she will be spending a year sabbatical. She will be doing leukemia and clinical trials work at St Bart's and University College London.

After many years of dedicated service to the field of hematology in Calgary **Dr. Karen Valentine** has retired.

Dr. Zach Liederman our recent chief resident is excited to start the Alexandra Yeo Fellowship in Thrombosis and Hemostasis this fall. He will continue to be involved in medical education and is enrolled in the Health Practitioner Teacher Education Masters at the University of Toronto.

Preliminary partnership discussions have recently begun between the International Society for Laboratory Hematology (ISLH) and the Canadian Hematology Society to jointly plan, organize and operate the **2019 Congress of ISLH in Vancouver, BC, Canada, May 9–11, 2019**.

The following new Hematological Pathology specialists were certified by the Royal College of Physicians and Surgeons of Canada on June 30, 2017:

- **Mohammad Bahmanyar**, Toronto, Ontario
- **Habib Moshref Razavi**, Vancouver, British Columbia
- **Jason Quinn**, Halifax, Nova Scotia
- **Ashish Rajput**, Warman, Saskatchewan
- **Mahmood Roshan**, Tariq, Nepean, Ontario
- **Audi Setiadi**, Vancouver, British Columbia

Introducing our new Co-Chief Canadian Hematology Residents

The CHS recently announced the appointments of **Dr. Cindy Hickey** and **Dr. Siraj Mithoowani** as **Co-*Chief Canadian Hematology Residents***. The term for this position is from July 1, 2017 to June 30, 2018. As the Chief Canadian Hematology Residents, Cindy and Siraj will be part of the CHS executive and will provide the voice and perspective of hematology trainees across the country.

Cindy is originally from Newfoundland and obtained her medical degree at Memorial University of Newfoundland. She moved to Halifax, Nova Scotia where she completed her Internal Medicine residency and is currently now a PGY-5 and the chief hematology resident at Dalhousie University. Cindy has clinical interest in malignant hematology, specifically bone marrow transplantation.

Dr. Cindy Hickey

"I am really excited to be working alongside Siraj as your co-chief resident for the Canadian Hematology Society. We are hopeful that the CHS portal will only continue to expand and be an excellent resource for interesting cases and learning opportunities for trainees. Please do not hesitate to contact myself or Siraj if there are any ideas or suggestions on ways we can help with your hematology training!"

Siraj is a PGY-5 Hematology resident at McMaster University in Hamilton, Ontario and the current Chief Resident of that program. He completed medical school and Internal Medicine residency at McMaster. Siraj has clinical and research interests in benign hematology and in medical education.

Dr. Siraj Mithoowani

"I'm excited to act as your resident representative to the Canadian Hematology Society. Cindy and I look forward to keeping you informed about CHS events, awards and educational content and we welcome your input on how the organization can improve your residency experience and transition to practice!"

CHS members are invited to send news items regarding promotions, heads of international committees, huge grants or publications, mid-career moves, retirements, or other notes of significance for this column.

For further information or to submit items, please contact *The Microenvironment* at **chs@uniserve.com**

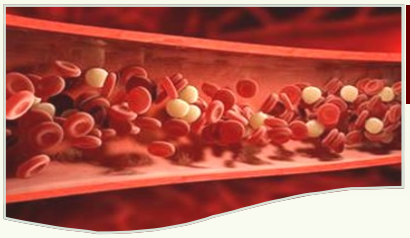
Danielle Hammond joins the Microenvironment editorial team

Danielle Hammond MD

I am honoured to be joining Dr. Nevill on The Microenvironment editorial team. I am currently a PGY4 hematology at Queen's University, and I completed my internal medicine training at the University of Toronto. What I appreciate most about hematology is that it is rational medicine epitomized. If you can identify at the molecular level what is going wrong, you can begin to find ways to fix it!

Early academic interests include bone marrow failure syndromes and approaches to treating the frail and/or elderly patient with a hematologic malignancy. I previously was the editor-in-chief for an undergraduate faculty newspaper, so I am pleased to find a new outlet for my passion for communication. My aim is to offer accessible educational content as well as important membership updates. I encourage your feedback and submissions.

Danielle Hammond, MD
PGY4 Hematology
77dh@queensu.ca



Thrombosis & Hemostasis Corner

Submitted by Danielle Hammond, MD
Department of Medicine
University of Toronto

Questions:

1. Giant platelets are seen in:

A. Glanzmann Thrombasthenia
B. Bernard-Soulier Syndrome
C. Type 2A von Willebrand Disease
D. Thrombotic thrombocytopenic purpura

2. The treatment for pseudo or platelet type von Willebrand Disease (PT-vWD) is:

A. Tranexamic acid
B. vWF:FVIII concentrates
C. DDAVP
D. Platelet transfusions

3. A 67-year-old male is brought to the emergency department after a fall from a l a d d e r while intoxicated. He is found to have a left subdural hematoma. No further history is available. Hgb 142, Plt 233, INR 3.4, PTT 31. An eager resident ordered additional factor levels: Factor II 0.25, Factor V 1.22, Factor VII 0.07, Factor IX 0.26. The most likely diagnosis is:

A. Vitamin K deficiency.
B. Early DIC.
C. Coagulopathy of liver disease.
D. Hemophilia B.

4. Which of the following is TRUE regarding anti-phospholipid syndrome (APS)?

A. When using VKAs, a target INR of 3-4 to superior to the standard 2-3 after first presentation of a venous thrombotic event.
B. There is no dose dependence when it comes to thrombotic risk and number of positive lab criteria.
C. Most patients with catastrophic antiphospholipid syndrome (CAPS) have a prior diagnosis of APS or underlying collagen vascular disease.
D. The leading hypothesis as to how antiphospholipid antibodies result in a hypercoagulable state is that they lead to an acquired activated protein C resistance by interference with the protein C pathway.

Answers: See page 12

Save the Date!

for the

Canadian Hematology Society Members Annual Reception, Awards Presentations and Dinner at ASH

Sunday, December 10, 2017 at 7:00 pm

Omni Hotel, 100 CNN Centre, Atlanta

Hope you can join us!

Lynn Savoie
President, CHS

CHS@uniserve.com
http://canadianhematologysociety.org/

CHS Paper of the Year: 2016 WINNER

Pretreatment with anti-thymocyte globulin versus no anti-thymocyte globulin in patients with haematological malignancies undergoing haematopoietic cell transplantation from unrelated donors: a randomised, controlled, open-label, phase 3, multicentre trial

Lancet Oncology, 17:164-173, 2016

Irwin Walker

McMaster University and Juravinski Hospital and Cancer Centre, Hamilton, ON

By Dr Tom Nevill
Editor-in-Chief, The *Microenvironment*

Dr. Irwin Walker, McMaster University and Juravinski Hospital and Cancer Centre, Hamilton, Ontario, addresses the CHS meeting at ASH 2016, San Diego, accepting the CHS 2016 Paper of the Year Award.

Allogeneic stem cell transplantation (AlloSCT) is a curative therapy used in a wide variety of hematological malignancies but the development of graft-versus-host disease (GVHD) contributes to the significant morbidity and mortality associated with the procedure. Chronic GVHD occurs in ~50% of patients undergoing AlloSCT and appears to be increasing in incidence with the use of peripheral blood stem cells and the rising median age of those undergoing transplantation.

Strategies to limit acute and/or chronic GVHD have largely resulted in an increased risk of post-transplantation relapse and infectious complications leading to the absence of a clear survival advantage. Anti-thymocyte globulin (ATG) administration as part of conditioning has been shown to reduce chronic GVHD in some studies but the use of ATG has not been uniformly adopted because of concerns about its overall benefits.

In this multicentre study by Walker et al, on behalf of the Canadian Bone Marrow Transplant Group (CBMTG), 196 unrelated donor AlloSCT patients receiving standard Cyclosporine or Tacrolimus plus either Methotrexate or Mycophenolate mofetil were randomized 1:1 to receive rabbit ATG 4.5 mg/kg over 3 days (99 patients) or not (97 patients).

The cohort included patients age 16-70 years (median 49 in both study arms) accrued over a 3-year period (2010-2013) with ~2/3 in both groups having acute leukemia or MDS; 80-90% of participants received blood stem cells from an 8/8-matched unrelated donor.

Notably, the study included patients receiving reduced-intensity conditioning (~1/3 of both arms) in addition to patients receiving standard myeloablative preparative regimens.

The primary study endpoint was freedom from immunosuppression at 12 months post-SCT and was observed in 37% of the ATG group versus 16% of the No ATG group (p=0.001). In a variety of subgroup analyses, the endpoint was also seen significantly more frequently in the ATG arm with the exception of the small number of patients receiving bone marrow grafts when ATG did not appear to provide any benefit. The non-relapse mortality at 3, 6 and 12 months did not differ between the ATG and non-ATG group.

Interestingly, relapse rates at 12 months were higher in the non-ATG group (16% versus 11% in the ATG group) although this did not reach statistical significance. Furthermore, overall survival at 12 months was not significantly different in the two arms although it was higher in the ATG group (75% versus 65%, p=0.24).

In this study, the cumulative incidence of acute GVHD at 100 days was higher in the No ATG group (65% versus 50% in the ATG group, p=0.012). The cumulative incidence of chronic GVHD at 12 months was 33% in the No ATG group versus 22% in the ATG group (p=0.065) and the risk of moderate or severe chronic GVHD was higher in the No ATG group 29% versus 13% in the ATG group (p=0.008).This reflected in thedifference in chronic GVHD incidence and severity was results of quality of life questionnaires; both the Lee Chronic

... continued from previous page

GVHD Scale and the Atkinson Happiness Score were significantly better in the ATG arm.

The ATG arm in this study did have some important adverse reactions. Two patients experienced significant reactions during the infusion of rabbit ATG but this was adequately medically-managed. EBV reactivation was identified in 1/3 of patients although 20% of the patients were accrued at centres that did not routinely screen for EBV reactivation. Only 2 patients in the No ATG group showed evidence of EBV reactivation. None of the patients with reactivation in either arm died of EBV-related causes.

This important study suggests that ATG should be added to the conditioning regimen in most, if not all, patients undergoing unrelated donor SCT. Infusional reactions are uncommon but screening for EBV reactivation must be done and appropriate treatment instituted when this common complication occurs. It is probably too early to comment on whether the risk of relapse, especially late relapse, is increased by the addition of ATG in this fashion. -ed.

CANADIAN RESEARCH

Dr. Irwin Walker, RIGHT, receives the 2016 CHS Paper of the Year Award for the best hematology paper in Canada, published between August 31, 2016 and August 31 2017. Presenting the award, at the CHS gala evening at ASH in San Diego, December 4, 2016, is CHS Executive Secretary, Dr. Vikas Gupta.

2017 CHS Paper of the Year

DEADLINE: Sept 30, 2017

- The Canadian Hematology Society is now accepting nominations for ***"the best hematology paper in Canada"***.
  - Individuals may nominate themselves or may nominate others.

Please include:

- A PDF of the paper
- A one-paragraph description of the work and its significance to hematology

Eligibility requirements:

- Papers must have been published **between August 31, 2016 to August 31 2017**.
- Nominated individuals must be CHS members in good standing.
- The recipient or designate must be available to accept the award.
- Awards will be presented at ASH, December 10, 2017 in Atlanta.
- Papers addressing clinical or lab-based hematology research will be considered.
- Applicants of all levels are encouraged to apply.

Nominations are now open

Material must be submitted to the Canadian Hematology Society office by email to chs@uniserve.com **by the deadline, September 30, 2017**.

CANADIAN RESEARCH AT EHA 2017

By Dr Tom Nevill
Editor-in-Chief, The *Microenvironment*

The European Hematology Association Annual Meeting was held June 22-25, 2017 in Madrid, Spain. It was a meeting that featured record-breaking weather with daily highs of 35-38°C but the city and its famous cuisine did not disappoint. The scientific program was excellent with many good oral presentations and two well-attended poster sessions. What follows are some of the interesting presentations from Canadians at EHA 2017.

Assessing the Risk-Benefit of Anticoagulants in Elderly Patients with Cancer-Associated Venous Thromboembolism.

⇒ ***Alejandra Lazo-Langer**, Epidemiology & Biostatistics, Institute of Clinical Evalutive Sciences, University of Western Ontario, London, ON.*

Cancer patients have a higher risk of venous thromboembolism (VTE) which can increase their risk of mortality. Unfortunately, due to tumour anatomy and chemotherapy-induced thrombocytopenia, cancer patients also have a higher risk for major bleeding (MB). However, the consequences of VTE and MB may be different – previous studies have suggested similar case fatality rates for these two events although these studies included quite heterogeneous patient populations.

In this study, Lazo-Langer and colleagues sought to estimate the risk and benefit of anticoagulant therapy in cancer patients who develop VTE. The investigators did so by interrogating a patient data base to determine case fatality rates and the MB:VTE fatality rate ratio. The population selected were those patients >65 years old who developed a VTE within 6 months of developing a cancer. Data was then collected on this cohort examining for recurrent VTE and MB that occurred within 6 months of the initial event and subsequent death within 7 days of the recurrent VTE or MB.

Between 2004 and 2014, almost 7000 patients over age 65 with cancer developed a VTE. Of these patients, 60% were treated with LMW Heparin, 22% were treated with Warfarin and 15% received both agents. Recurrent VTE was observed in 1184 patients (17%) and 6 of these patients died (0.5%). MB occurred in 235 patients (3%) of whom 26 died (11%). The MB:VTE mortality rate ratio was 21.8 (95% CI 9-53) with no difference in this rate regardless of the anticoagulant used. The authors concluded that while recurrent VTEs in this patient population are over 5 times as common as MB, the consequences of the latter are more serious with a mortality rate that was at least 9 times that of recurrent VTE.

Double Umbilical Cord Blood Transplantation in Adults: Correlation of Allele-Level Matching With Outcome and Which Cord Will Become Dominant.

⇒ ***Mara Westendorp**, Leukemia/BMT Program of British Columbia, Vancouver, BC*

While umbilical cord blood (UCB) is a viable source of stem cells for allogeneic transplantation, fewer hematopoietic precursor cells and higher degrees of histoincompatibility between the cord unit and the recipient has led to higher rates of graft failure and an increased risk of graft-versus-host disease (GVHD) – especially in adult patients.

Graft failure rates have been reduced by the infusion of two cord blood units in adults (double UCB transplantation or DUCBT) although it has clearly been shown that only one of the two units provides long-term hematopoiesis (i.e. becomes dominant). That unit that will become dominant is not always predictable but previous studies have suggested the more closely HLA-matched unit and/or the unit with the highest total nucleated cell count (TNC) will often win out and persist.

In this retrospective review, Westendorp et al summarized the outcomes for 31 adults in the Province of British Columbia, ages 19-59 years (median 49 years), who underwent DUCBT from 2009-2017. A Fludarabine/Total body irradiation (1350 cGy) conditioning regimen was utilized along with Tacrolimus/ Mycophenolate mofetil GVHD prophylaxis.

All patients recovered an ANC >0.5 x 10^9/L (median 20 days; range 14-72) and 26/31 (84%) reached a platelet count >20 x 10^9/L (median 36 days; range 24-188). Acute GVHD developed in 28 patients (88%) and chronic GVHD in 19 of 25 patients (76%) that survived to day +100. Eighteen patients (56%) remain alive and in continuous complete remission, with a median follow-up of 3 years. Ten patients died of complications (31%) and four patients have relapsed (13%).

Outcomes following DUCBT were better when recipients received a best matched cord that was 0-2 antigen-mismatched

continued, page 9 ⟶

(Ag-M/M; 9/12 alive and well) compared to 3 Ag-M/M (3/9 alive and well, p=0.20). Unexpectedly, 7/11 patients who received best matched cords that were ≥4 Ag-M/M also remain alive.

In 21 patients, data was available on which of the two cords became dominant and in 19 cases, the dominant cord was an equal or better HLA match. The TNC of the units was less predictive with the lower TNC unit being dominant in 3/5 cases when it was a better HLA match than the other cord and in 5/14 cases when the degree of HLA mismatch was the same for both cords.

In this study, DUCBT was shown to be an effective therapy for adults with life-threatening hematologic disorders with an acceptable long-term outcome in excess of 50%. Graft failure is rare despite the low TNC of the products and the significant degree of histoincompatibility between donor and recipient although GVHD is almost universally seen. The cord that becomes dominant is more frequently determined by being a better HLA match with TNC playing a The

Cost Effectiveness of Rituximab in Addition to Standard of Care Chemotherapy for Adult Patients With ALL.

⇒ ***Matthew Seftel**, Hematology and Medical Oncology, Cancer Care Manitoba, Winnipeg, MB*

The GRAALL-R study (Maury *et al*) supported the improvement in clinical outcomes for patients with Ph-negative CD20+ precursor B-ALL with the addition of Rituximab to standard of care chemotherapy (SOCC). The investigators wanted to examine the cost effectiveness of this strategy in the publicly-funded Canadian health care system.

The SOCC that was used in the analysis included either HyperCVAD or the Dana Farber Consortium Protocol. The decision analytic model over a 15-year time-horizon included event-free survival (EFS), relapsed/resistant disease, cure (≥5 years of EFS) and death. Costs that were included in the analysis included first, second and third-line treatment administration, disease management, palliative care and SAE-related treatments using public data, literature review and input from Cancer Care Manitoba.

The authors found that life years increased by 1.33 years with the addition of Rituximab to SOCC versus SOCC alone and quality-adjusted life-years increased by 1.15 years with the addition of the monoclonal antibody. The incremental cost of Riuximab added to SOCC was $46,624 CDN which was primarily drug acquisition costs. A superior EFS drove lower second line treatment and palliative care use creating modest cost savings. The mean Incremental Cost-Effectiveness Ratio (ICER) was calculated to be $40,405/QALY; at a standard threshold of $100,000/QALY, the probability of cost-effectiveness was 96%. Based upon these calculated figures, adding Rituximab to SOCC is an appropriate and cost-effective intervention in adults with Ph-negative CD20+ precursor B-ALL.

Perception of Symptom Burden and Treatment Goals Between Physicians and Patients with MPNs: An Analysis From the International MPN Landmark Survey.

⇒ ***Lynda Foltz**, St. Pauls' Hospital, Vancouver, BC*

This study was based upon an online survey and evaluated the impact of MPNs – Myelofibrosis, Essential Thrombocytosis and Polycythemia Vera – on patients from six countries. This project was designed to investigate differences between independently-recruited patients and physicians with regards to their perceptions of symptom burden, treatment goals and disease management.

A total of 699 patients (302 ET, 223 MF, 174 PV) participated in the survey and ~3/4 were within 2 years of first developing symptoms. Two hundred and nineteen physicians from Canada, the UK, Germany, Italy, Japan and Australia answered the survey of which 81% were hematologists or oncologists. Of the physicians, 71% used a prognostic score although only 54% of patients were aware of their prognostic score. Physicians evaluated patients by asking how they were feeling 80% of the time but only 26% used a validated symptom assessment form.

Both patients and physicians agreed that MPNs had a high symptom burden with MF patients having the highest degree of burden on daily living. However, physicians felt that the emotional burden and impact on quality of life was more of an issue than the patients reported. This could have related to the fact that some patients did not associate classic MPN symptoms with their disease – 20% of patients did not realize that night sweats were a manifestation of MPNs.

While patients and physicians were both focused on treatments that could alleviate symptoms of the disease, patients also wanted to pursue treatments that might delay progression and physicians expressed more interest in prevention of thrombotic and vascular events in ET and PV. Of interest, only ~25% of physicians "completely agreed" with their patients on treatment goals although 87% of patients were satisfied with the communication with and treatment given by their physicians.

This study certainly suggests a need for standardized symptom evaluation in MPNs and a lack of patient awareness of their disease manifestations. It emphasizes a need for better communication and education between caregivers and their patients in order to overcome a disconnect between those afflicted with MPNs and their hematooncologist.

CANADIAN RESEARCH @ EHA EUROPEAN HEMATOLOGY ASSOCIATION

HISTORY CORNER

The Birth of Pediatric Hematology/Oncology in Canada

By Dr Tom Nevill
Editor-in-Chief
The *Microenvironment*

In 1944, **Dr. Bruce Chown** and his colleague, **Marion Lewis**, began their work in hemolytic disease of the newborn (HDN or "Rh disease") (see History Corner in *The Microenvironment* Summer 2014). Their story of searching for patients to study is fascinating in its own right – they travelled about Winnipeg and rural Manitoba by car, street trolley and even bicycle looking for subjects.

In 1945, Dr. Chown received a National Research Grant of $1000 that allowed for the hiring of a research technician to investigate maternal immunization. This led to the founding of the Rh laboratory in Winnipeg and it is interesting to find how important Rh disease research was in forming the foundation for the development of pediatric hematology programs.

Dr. Louis Diamond

In 1946, **Dr. Ronald Denton** returned to Montreal after training with **Dr. Louis Diamond**, the legendary hematologist at Boston Children's Hospital.

Dr. Denton quickly established the first hematology unit at **Montreal Children's Hospital** where he went on to perform pioneering work in diagnostic blood grouping and the use of exchange transfusions in Rh disease and acted as the Director of Red Cross Blood Transfusion Services for Quebec.

Montreal Children's Hospital

Montreal soon had a second unit when **Dr. Albert Royer** returned from his training in Boston and set up another pediatric hematology unit in 1950 at Hôpital Sainte-Justine.

In Canada's second largest city at the time, Toronto, a pediatric hematology program was grinding to life. In 1947, **Dr. Bernard Laski**, who trained with **Dr. Carl Smith** in New York, NY, returned to Toronto as the first trained pediatric hematologist in the city. Although he was ultimately responsible for helping to establish hematology as a distinct pediatric subspecialty, Dr. Laski

Hospital for Sick Children, Toronto

worked for years as a member of the Department of Pathology at **The Hospital for Sick Children**. In addition, he ran a busy general pediatric practice and also did important work in Rh disease.

By the early 1950s, Rh disease management was a heavy workload – 300 exchange transfusions were carried out annually at Sick Children's – although the technique was crude! Exchange transfusions were done by "letting blood drip into the saphenous vein and out a slit in the radial artery into a bowl".

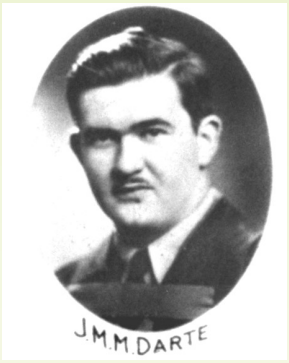
CANADA'S FIRST PEDIATRIC ONCOLOGY UNIT

In 1958, a pediatric oncology unit – the first of its kind in

Princess Margaret Hospital

continued, page 11 ⟶

HISTORY CORNER (continued)



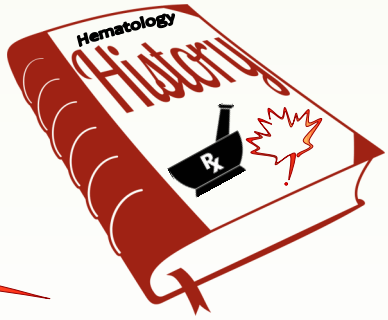
Canada – was opened at **Princess Margaret Hospital** in Toronto, directed by **Dr. John Darte**, a pediatric hematologist and radiation oncologist. Dr. Darte was also given the responsibility of being the Director of Hematology at The Hospital for Sick Children.

Two key developments led to the expansion of pediatric hematology/oncology units across the country in the 1960s. Firstly, radiation and chemotherapy treatments in Hodgkin lymphoma and acute lymphoblastic leukemia began to show major breakthroughs (See History Corner in *The Microenvironment* March 2015). However, the implementation of National Health Insurance in 1967 was equally important in that it guaranteed all citizens access to hospital-based medical care.

Through the 1960s, comprehensive programs for hemophilia care and, particularly in Montreal and Toronto, hemoglobinopathies, were developed. The development of blood component therapies allowed for the eventual launch of the first home infusion program for children with hemophilia, run out of the Montreal Children's Hospital by **Dr. Hanna Strawynski**.

Reference

A. Zipursky, Pediatric Hematology and Oncology, 1991



37th World Congress of the International Society of Hematology (ISH)
...hosted by the
Canadian Hematology Society (CHS)
Sept 13-16, 2018
Vancouver Convention Centre
Contact: http://www.ish2018.com/

Canadian Society for Transfusion Medicine (CSTM)
Transfusion Medicine Education Day
September 8, 2017
Toronto, Ontario
Contact: maria.wadden@nshealth.ca

Canadian Blood and Marrow Transplant Group (CBMTG)
Theme: *Pre & Post-Transplant Issues in Blood and Marrow Transplant*
September 8—9, 2017
St. John's, Newfoundland and Labrador
Contact: http://www.cbmtg.org/page/2017ThemedMeetings

15th Annual CBS International Symposium
September 9, 2017
Chestnut Conference Centre, Toronto, ON
Contact: blood.ca/professionaleducation

Canadian Apheresis Group (CAG) *...in conjunction with the* **Canadian Association of Apheresis Nurses (CAAN) Annual Meeting**
September 22—24, 2017
Montreal, Quebec
Contact: http://cagcanada.ca/annual-general-meeting/

Canadian Hematology Society (CHS)
Annual Reception, Dinner & Awards Evening
December 10, 2017
Atlanta, Georgia, USA
Contact: chs@uniserve.com

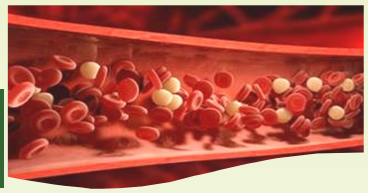
American Society for Apheresis (ASFA)
2018 Annual Meeting
April 25—28, 2018
Chicago, IL, USA
Contact: http://www.apheresis.org/page/ASFA2018

35th International Congress of the International Society of Blood Transfusion (ISBT)*...in conjunction with the* **Annual Conference of the Canadian Society for Transfusion Medicine (CSTM)**
June 2 – 7, 2018
Toronto, Ontario
Contact: http://www.transfusion.ca/Events/

Canadian Blood and Marrow Transplant Group (CBMTG)
2018 Annual Meeting & Conference
June 7—9, 2018
Ottawa, Ontario
Contact: http://www.cbmtg.org/

European Hematology Association (EHA) 23rd Congress
June 14—17, 2018
Stockholm, Sweden
Contact: https://www.ehaweb.org/ or eha@mci-group.com

ANSWERS ...FROM PAGE 5



Thrombosis & Hemostasis Corner

1. B - Both Glanzmann Thrombasthenia and Bernard-Soulier syndrome are hereditary platelet disorders in which platelet receptors are deficient or defective. In Glanzmann, IIb-IIIa is deficient, meaning that platelets are unable to properly aggregate. In Bernard-Soulier, Ib is abnormal, meaning that platelets are unable to bind von Willebrand factor in the subendothelium, leading to defective adhesion. Patients with Bernard-Soulier (but not Glanzmann) also have giant platelets. Giant platelets are not seen in most cases of vWD nor in TTP.

2. D - Platelet-type von Willebrand disease (PT-vWD), or pseudo-vWD, and type 2B vWD share a common bleeding phenotype with different etiologies. Both PT-vWD and type 2B vWD represent an enhanced binding between von Willebrand factor (vWF) to its platelet ligand, glycoprotein Ib alpha. However, type 2B vWD results from a functionally abnormal vWF molecule, whereas PT-vWD is caused by hyper-responsive platelets. Differential diagnosis is important because the two diseases are treated differently: normal exogenous vWF is required in 2B vWD versus platelet transfusions for PT-vWD.

3. A - Tests are consistent with vitamin K deficiency, likely from warfarin use. Vitamin K dependent coagulation factors include: II, VII, IX, X, and proteins S and C often remembered by reference to the famous Soviet Union-Canada hockey game = "1972 SC."

4. D - (A) There are two trials which show standard (2-3) INR targets to be equivalent to elevated (3-4) primarily in those with first presentation of VTE, one of which is: Crowther MA, Ginsberg JS, Julian J, et al. A comparison of two intensities of warfarin for the prevention of recurrent thrombosis in patients with the antiphospholipid antibody syndrome. N Engl J Med. 2003;349(12):1133-1138. (B) "Dose dependence" was highlighted in the 2006 revised Sydney Criteria: those with a single lab criterion positivity have a much lower thrombotic risk than those with multiple lab criteria in any combination, with "triple positivity" being at the highest risk. (C) Surprisingly, 50% of patients with CAPS do not have a prior diagnosis of APS or underlying rheumatologic condition.

Do you know the diagnosis?

"What's DAT?!" - ANSWER ...FROM PAGE 3

Daratumumab (DARZALEX®) is an IgG monoclonal antibody against CD38, an antigen that is highly expressed on myeloma cells.

This is the rationale for approval by Health Canada in April of 2017 for daratumumab, in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.

However, CD38 is also expressed ubiquitously on adult red cells. This leads to variable DAT positivity without clinically significant hemolysis and invariably a positive antibody screen (i.e. indirect antiglobulin test) with a pseudo pan-reactive autoantibody picture. Importantly, unlike a true red cell autoantibody, it cannot be removed by adsorptions.

Therefore, all patients should have an antibody screen on record before being started on daratumumab. One strategy to resolve the daratumumab interference with blood compatibility testing is to treat the panel red cells used in the antibody screen with dithiothreitol (DTT) to remove CD38.

However, this risks also removing certain clinically relevant RBC antigens, such as Kell (K1).

JOB POSTINGS

HEMATOLOGIST – OAKVILLE, ONTARIO

The Department of Medicine at Oakville Trafalgar Memorial Hospital is recruiting a full-time Hematologist, for predominantly benign hematology with cross-coverage of malignant hematology inpatients. The successful applicant will provide inpatient hematology consultation in rotation with two existing hematologists and will be supported by a nurse practitioner. The selected candidate will have access to outpatient clinic time in the hospital for consultations, procedures, phlebotomy, transfusions and infusions. There is also an expectation that the candidate will provide care in a community-based office practice.

Expressions of interest will be accepted until **September 30th** and must include a covering letter, up-to-date curriculum vitae, a description of previous specialty and any subspecialty training, and previous working experience. For details please **contact: Dr. John McPhaden, Medical Director, Cancer Services c/o Andrea D'Sa, Director of Medical Affairs, at ADSA@haltonhealthcare.com**

HEMATOLOGISTS – TORONTO, ONTARIO

The Division of Medical Oncology and Hematology at the University Health Network (UHN) is seeking energetic and innovative physicians with expertise in Hematology. As one of the top health networks in the world, the UHN encompasses the Princess Margaret Cancer Centre and the Toronto General Hospital along with each of their respective research institutes. The Division is comprised of roughly 85 physicians and 20 clinical assistants working in the Solid Tumour Oncology Program, Malignant Hematology Program, Blood Disorders Program, Medical Genetics Program and our GIM-Oncology Program.

Available positions are:

- **Scott-Whitmore Chair in Hematology**
- **General Hematologists**
- **Hematology & Thromboembolism Physicians**
- **Malignant Hematologists**
- **Clinical Assistants**
- **Nocturnists**

For information contact:
Dr. Amit Oza - Chief, Division of Medical Oncology and Hematology
C/o Michelle Williams – Administrative Coordinator
Princess Margaret Cancer Centre,
University Health Network
Suite 7-925, 700 University Avenue,
Toronto, Ontario, Canada, M5G 1Z5
Office: 416.946.4501 x2432
Mobile: 647.642.4031
Fax: 416.946.2082 E-mail: **michelle.williams@uhn.ca**

HEMATOLOGIST – BARRIE, ONTARIO

Department of Internal Medicine

The Royal Victoria Regional Health (RVH) Centre, is a state-of-the-art facility located in Barrie, one of Canada's fastest growing cities.

- Completely Hospital Based GIM Model
- Internal Medicine Ambulatory Clinics
- Closed ICU and CCU
- Community/Hospital Haematology Practice, without GIM responsibilities
- Excellent Subspecialty back up
- Well established GP Hospitalist services
- Outpatient Clinic Access
- Subspecialty Practice On-call only with reasonable parameters
- Regional Practice Potential
- Strong Family Medicine Teaching Unit and Opportunity for University of Toronto Faculty Appointment

Contact: Brittany Peterson, Physician Recruitment Coordinator: petersonb@rvh.on.ca

CLINICAN/CLINICAN SCIENTIST – CALGARY, ALBERTA

The Department of Oncology, Cancer Control Alberta, Alberta Health Services, Community Oncology and Cumming School of Medicine, University of Calgary invite applications for a full-time clinician/clinician scientist within the discipline of Hematology and Hematological Malignancies at the Assistant Professor level.

The successful applicant will become a member of a multidisciplinary cancer program located at the Central Alberta Cancer Centre (CACC) site in Red Deer, Alberta, and will join a team of Medical and Radiation Oncologists, Nurse Practitioners and medical support staff working in the Central Zone.

Please submit a CV, a statement of career goals and the names of three referees to: **Dr. Peter Duggan, MD, FRCPC**, 1331 29 Street NW Calgary, Alberta T2N 4N2 E-mail: **peter.duggan@ahs.ca**

JOB POSTINGS

MEDICAL ONCOLOGY, APP – BELLEVILLE, ONTARIO

The Dr Douglas A MacIntosh Cancer Clinic in partnership with The Cancer Centre of South-eastern Ontario (CCSEO) are searching for a Medical Oncologist. This 1.0 FTE position is fully funded by MOH as a ONT MOA APP position with competitive salary. The successful applicant will possess Royal College Certification in Internal Medicine, or equivalent and will have completed sub-speciality training in Medical Oncology with eligibility for APP under the ONT MOA agreement.

To apply, please send a letter of intent and a CV to: Dr Roger Lévesque, Head Medial Oncology, Quinte Health Care, 265 Dundas Street East, Belleville, Ontario, K8N 5A9.; Tel: 613-969-7400 ext. 2371; Fax 613-969-0486; email: **rlevesque@qhc.on.ca**

BENIGN HEMATOLOGIST—RICHMOND HILL, ONTARIO

Mackenzie Health is a major regional healthcare organization that is rapidly expanding to meet the needs of the growing community of Southwest York region. The current Mackenzie Richmond Hill Hospital is a 515 bed community hospital in Richmond Hill. Training and interest in thromboembolic disease and management would be an asset.

Interested applicants should send a CV and letter of intent to:

Dr. Matilda Ng MD, RCPC, Head, Division of Medical Oncology/ Hematology, Mackenzie Richmond Hill Hospital
10 Trench Street, Richmond Hill, ON L4C 4Z3
Phone: (905)883-2153
Email: **matilda.ng@mackenziehealth.ca**

HEMATOLOGIST – TORONTO, ONTARIO

Humber River Hospital is seeking applications for a hematologist with an interest in benign hematology. The successful candidate will have the opportunity to participate in our thrombosis clinic as well as our cancer clinic. Some malignant hematology will be required.

Humber River Hospital is a large community hospital in an urban part of the GTA. There are opportunities to participate in clinical trials and teaching, should the candidate be interested. Interested candidates can contact our Chief of Medicine, Dr. D. Fishbein, Humber River Hospital, 1st floor, 1235 Wilson Ave., Toronto, ON

Email: **sfishbein@hrh.ca**

FELLOWSHIPS

JAMES DREWRY STEWART FELLOWSHIP IN MULTIPLE MYELOMA AND MALIGNANT HEMATOLOGY—TORONTO, ONTARIO

The James Drewry Stewart Fellowship in Multiple Myeloma and Malignant Hematology will provide financial assistance in the form of fellowship grants to oncology trainees at St. Michael's Hospital who have completed their core training in oncology and are seeking additional clinical training in myeloma and other blood cancers.

Application Procedure
Applicant must submit the following:
1. Completed James Drewry Stewart Fellowship in Multiple Myeloma and Malignant Hematology form
2. CV
3. Statement of intent
4. Applications will be reviewed by the Stewart Fellowship Committee
CONTACT NAME: Maryana Ghazula
ROLE: Administrator
TELEPHONE: 416-864-5632
EMAIL: **gazhulam@smh.ca**
MAILING ADDRESS: St. Michael's Hospital, 30 Bond Street, Room 2 – 084,
Toronto ON M5B 1W8

Invitation to submit ...

STUDENT RESEARCH ARTICLES

The Microenvironment **will be happy to consider for publication, articles submitted by members who have sponsored student summer projects.**

Queries should be directed to:

- **Dr. Tom Nevill, The Editor, *The Microenvironment***
- **Email: chs@uniserve.com**

FELLOWSHIPS

Malignant Hematology Fellowship - Hamilton, Ontario

The Department of Oncology, McMaster University has several clinical research fellowship positions available in Malignant Hematology.

The Department of Oncology is located at the Juravinski Cancer Centre, Hamilton, Ontario and offers one of the largest cancer treatment services in Ontario. Over 5,000 new patients are referred to the centre each year by physicians in the region.

Duration:
1—2 year Fellowships

Start Date:
July 1, 2018

Funding:
Available at the PGY6 level

Invitations for interviews will be given to selected applicants. Incomplete applications will not be accepted. Application deadline September 1, 2017.

Leukemia/Bone Marrow Transplantation Fellowship, Vancouver, BC

The Leukemia/Bone Marrow Transplantation Program of British Columbia offers 1 or 2 Year fellowships to provide advanced training in the management of adults with hematological malignancies including all aspects of allogeneic and autologous hematopoietic stem cell transplantation (HSCT).

Candidates should be registered in, or completed a recognized hematology or oncology training program.

For more information: leukemiabmtprogram.org

Interested candidates should submit a CV and names of three references to:

Dr. Sujaath Narayanan, Fellowship Director Leukemia/ BMT Program, BC Cancer Agency
& Vancouver General Hospital
Phone: (604) 875-4089
FAX: (604) 875-4763
Email: SNarayanan@bccancer.bc.ca

Two-year Fellowship Program, Princess Margaret Cancer Centre, Toronto

Allogeneic Blood and Marrow Transplantation – Clinical Research Fellowship

The 2-year Fellowship Program at Princess Margaret Cancer Centre/University of Toronto is designed to provide the opportunity for trainees in hematology and medical oncology to define and refine career goals, enhance their ability to pursue a successful career as consultants, clinical researchers and clinician scientists.

Both funded and unfunded opportunities are available.
For further information, please contact:

Auro Viswabandya
Fellowship Director, Allotransplant
Telephone: +1-416-946-4501 x 3256
E-mail: Auro.Viswabandya@uhn.ca

Mailing Address:
Princess Margaret Cancer Center
Division of Medical Oncology and Hematology
610 University Avenue, Rm 5-110
Toronto, ON, Canada M5G 2M9

Your Canadian Hematology Society
Société Canadienne d' Hématologie Newsletter

Membership Matters

The Canadian Hematology Society has represented all physicians and scientists with an interest in the discipline in Canada since it was founded in 1971, and currently has over 500 members.

Active Membership

- Physicians in the practice of clinical or laboratory hematology in Canada
- Scientists with PhD degrees making continuing contributions to research related to hematology in Canada
- Allied Health Professionals making sustained contributions to clinical or laboratory hematology practice or hematology research in Canada.

Only active members shall:

- **vote**
- **hold office**
- **receive CHS grants, and**
- **pay dues.**

Associate Members

- Residents and fellows engaged in hematology training
- Masters and PhD graduate students
- Post-doctoral fellows engaged in hematology research

Associate members will not be required to pay dues until completion of their training.

Emeritus Members

- All individuals who have retired from full time hematology practice or research, or those who were active members and request a transfer of status with adequate reason.

Honorary Membership

- Non-members may be invited to become Honorary Members of the corporation by virtue of their outstanding contributions to any discipline which is of importance to hematology.

CHS members are reminded ... that dues for the year 2017, are now due.

Your $75. annual dues payment may be made online at the CHS website: **www.canadianhematologysociety.org**

Or by mail to: **Canadian Hematology Society, 199-435 St. Laurent Blvd., Ottawa, Ontario K1K 2Z8**
Please provide the following information with your payment:

2017 Membership Renewal / Address Change: Canadian Hematology Society

Membership Status

Active ☐
Associate ☐
Emeritus ☐

Has your status changed?

Yes ☐
No ☐

Name: _____

Title: _____

Email: _____

Work Address: _____

_____

Work Phone: _____

Work Fax: _____