The Microenvironment

April 2016

THE CANADIAN HEMATOLOGY SOCIETY

SOCIÉTÉ CANADIENNE D'HÉMATOLOGIE

C H S C H

NEWSLETTER

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2016 CHS Executive Committee

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MESSAGE FROM THE PRESIDENT

Dr. Lynne Savoie
President, CHS

Dear Colleagues,

It is with great pleasure that I write this, my first column as president of the Canadian Hematology Society as it enters its 46th year of existence. Yes, the **CHS in now 45 years old!** How things have changed since 56 hematologists came together in Ottawa in January of 1971 in the first annual gathering of Canadian Hematologists. Having said that, I believe the CHS still serves its original purpose of bringing together hematologists across the country, if not in person then at least electronically. We have grown to a membership of over 400 in those 45 years.

Once a year we gather face to face at our **Gala dinner during ASH**. This is always a fun event where yes, we conduct business and give out awards, but also connect with our colleagues spread across the country. Seeing many colleagues we may not see otherwise - those we trained under, worked with or have helped train but now live and work elsewhere, and in a specialized field different than ours such that our paths do not tend to cross. This is personally my favorite part of the evening.

Under past president **Dr. Aaron Schimmer** the development of our interactive web portal has also served to bring the community together. I hope you are all participating in our educational Leaderboard challenge. I must say I am sad that I can no longer compete as I have access to the answers ahead of time.

If you are reading this you are clearly aware of ***The Microenvironment***, our newsletter, however I would like to take this opportunity to remind you of some of our other activities. We have recently completed the process of reviewing the applications for the **2016 RK Smiley Research Grants**, $10,000 grants aimed at pilot studies (by the way - Dr Smiley was our first president).

Read more about these CHS winners: pages 6, 7, 8 & 9.

We give out **awards to our junior investigators** who have abstracts at ASH, as well as an award for the **best Canadian paper of the year**.

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The **web portal** has a focus on education but also has a members list that allows you to connect with others, those whom you may have lost touch with or do not yet know personally. There is also a **Product Reimbursement Library listing** drug reimbursement details across the country.

One of our most ambitious endeavors headed by Drs **Gail Rock** and **Tom Nevill** is the organization of the **2018 International Hematology Society** biannual meeting to be held in Vancouver, BC.

Finally, we liaise with the Royal College and other associations where our voice needs to be heard and we can help effect change. Most recently, for example, we participated in the **Choosing Wisely Canada** campaign.

As a society we are always eager to hear from our members, anything from suggestions, comments, constructive criticism or a desire to volunteer. Please feel free to email me at lynn.savoie@ahs.ca and don't forget to pay your dues!

Dr. Lynne Savoie,
President, CHS

Le message du Président

C'est avec grand plaisir que j'écris mon premier article en tant que présidente de la Société canadienne d'hématologie qui célèbre son 46e anniversaire. Eh oui, la SCH a maintenant 45 ans! Comme les choses ont changé depuis le premier rassemblement des 56 hématologues à Ottawa en janvier 1971.

Cela dit, je crois que la SHC sert toujours son objectif initial qui est de rassembler tous les hématologues à travers le pays, sinon en personne, du moins par voie électronique. Le nombre de nos membres s'est agrandi de plus de 400 en 45 ans. Une fois par an, nous nous réunissons en face à face lors d'un dîner de gala de la Société américaine d'hématologie (SAH). Ceci est toujours un événement amusant au cours duquel nous exerçons nos activités et offrons des récompenses, et où nous pouvons également communiquer avec nos collègues répartis partout dans le pays. Nous pouvons ainsi voir de nombreux collègues que nous ne pourrions pas voir autrement - ceux qui nous ont formés, ceux avec lesquels nous avons travaillé ou qui ont contribué à la formation, mais qui, maintenant vivent et travaillent ailleurs, et dans un domaine spécialisé différent du nôtre de telle sorte que nos chemins n'ont pas la possibilité de se croiser. Personnellement, c'est ma partie préférée de la soirée.

Sous l'ancien président, le Dr Aaron Schimmer, l'élaboration de notre portail web interactif a également servi à rassembler la communauté. J'espère que vous projetez tous de participer à notre défi pour le tableau de classement éducatif. Je dois dire que je suis triste de ne plus y participer ayant accès aux réponses à l'avance.

Si vous lisez ceci, vous êtes parfaitement au courant de notre bulletin d'information « The Microenvironnement », mais je voudrais profiter de cette occasion pour vous rappeler quelques-unes de nos autres activités. Nous sommes actuellement en train d'examiner les demandes de subventions de recherche RK Smiley, 10 000 $ de subventions destinées à des études pilotes (je vous signale en passant que le Dr Smiley était notre premier président). Nous offrons des récompenses à nos jeunes chercheurs qui ont soumis des résumés à la Société américaine d'hématologie, ainsi qu'un prix pour le meilleur article canadien de l'année.

Le portail web met l'accent sur l'éducation, mais offre également une liste de membres qui vous permet de vous connecter avec d'autres, par exemple avec ceux dont vous avez perdu le contact ou n'avez encore jamais rencontré personnellement. Il y a également une bibliothèque de remboursement de produits énumérant les détails de remboursement de médicaments à travers le pays. Un de nos efforts les plus ambitieux dirigé par les Drs Gail Rock et Tom Nevill est l'organisation de la réunion internationale bimensuelle de la société d'hématologie de 2018 qui se tiendra à Vancouver, en Colombie-Britannique.

Enfin, nous sommes en liaison avec le Collège Royal et avec d'autres associations où notre voix doit être entendue et nous pouvons vous aider à effectuer des changements. Plus récemment, par exemple, nous avons participé à la campagne « Choisissez judicieusement Canada ».

En tant que société, nous sommes toujours impatients d'entendre ce que nos membres proposent, que ce soit leurs suggestions, leurs commentaires, leurs critiques constructives ou leur désir de faire du bénévolat. N'hésitez pas à communiquer avec moi à lynn.savoie@ahs.ca et n'oubliez pas de payer vos cotisations!

Dr. Lynne Savoie,
President, CHS

UPDATE: ISH-CHS 2018 VANCOUVER

PASSING THE FLAG

Co-chairs for the 45th World Congress of the International Society of Hematology—to be hosted by the CHS in 2018 in Vancouver—Dr. Tom Nevill, Scientific Committee Chair and Dr. Gail Rock, Chair of the Organizing Committee, are officially presented with the ISH Flag, on April 18, 2016 during the opening ceremonies of the very successful 44th ISH World Congress in Glasgow, Scotland, hosted by the British Society of Haematology.

This *"passing of the flag"* marks the international launch of the Canadian Hematology Society as host of the ISH 2018 World Congress.

In addition to the participation of Drs. Rock and Nevill at ISH 2016, an information booth promoting the Vancouver 2018 meeting, was also organized by the CHS and staffed by the professional conference organizer for the Vancouver meeting at this year's Exhibits at the ISH Glasgow Congress.

Pictured above, **FROM LEFT**, presenting the ISH flag, on behalf of the ISH Executive Board are **Prof. Emin Kansu**, Chair-of-Council and **Prof. Adrian Newland**, President of ISH 2016; and accepting the ISH flag on behalf of the CHS, **Dr. Tom Nevill** and **Dr. Gail Rock.**

The program for ISH 2018 in Vancouver will highlight both Canadian and International activities and will include:

- **Educational and *"Meet-the-Professor"* Sessions**
- **Simultaneous Scientific Symposia covering all hematology disciplines**
- **Plenary and poster abstract presentations**
- **A full Social Program with President's Welcome Reception and Congress Dinner**

Please send suggestions for scientific program articles to the Chair of the Scientific Program, Dr. Tom Nevill.

Email: TNevill@bccancer.bc.ca

Your 2016 CHS Executive Committee!

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HISTORY CORNER: Dr. Vera Peters (1911-1993)

Pioneer in radiation treatment for Hodgkin diesase

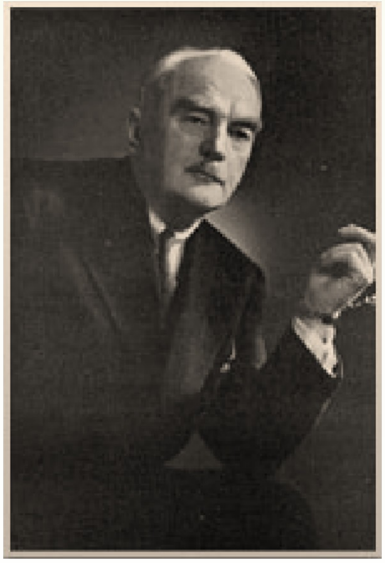
Mildred "Vera" Peters

Mildred "Vera" Peters was born April 28, 1911 on a farm in Rexdale, Ontario, educated in a one-room schoolhouse in Thistletown and completed high school at the age of 16.

She enrolled in the **University of Toronto** but was too young to study Medicine, forcing her to spend one year studying mathematics and physics before pursuing her dream of becoming a physician. During her time off her studies in the summer, she met and ultimately married Ken Lobb and they would go on to raise two daughters.

Vera Peters graduated from the Faculty of Medicine in 1935 and spent two years as a surgical resident at **St. John's Hospital in Toronto** where she cared for many patients with malignant disease.

In 1935, she joined **Dr. Gordon Richards**, the Director of the Department of Radiology at Toronto General Hospital and a pioneer in the field of radiation treatment, who had treated her mother for breast cancer.



Dr. Gordon Richards

Dr. Richards installed a state-of-the-art 400-kV radiation machine at the Ontario Radiotherapy Institute at TGH in 1937, the same year that Dr. Peters was appointed as a full-time junior assistant radiotherapist, and they treated many patients together over the next 10 years.

In 1947, Dr. Richards, in a fortuitous hallway discussion, suggested to Dr. Peters that she review their experience with radiation treatment in Hodgkin disease (HD). At the time, HD was considered a fatal condition in which surgical removal of involved lymph nodes was often considered the best management.

Dr. Richards and Dr. Peters were accumulating a cohort of patients that they had treated with radiation that "appeared to be cured". This led to **Vera Peters' 1950 landmark paper in the American Journal of Roentgenology, Radium Therapy and Nuclear Medicine** in which she reported on the **results of 113 HD patients treated with radiation** over the previous 20 years. In this paper, Dr. Peters developed the first staging system for HD which she put forward as the most important determinant of survival.

She clearly noted that for stage I HD patients (involvement of a single lymph node region or a single non-lymph node lesion) had a distinct flattening of the survival curve at 8-9 years suggesting cure was possible.

Finally, she emphasized the importance of radiation to adjacent, apparently uninvolved nodal regions in order to improve survival rates in stage I patients. Surprisingly, considering current knowledge of the biology and treatment of HD, Vera Peters' publication was either ignored or met by great skepticism around the world, even after her eloquent update involving 291 cases in the same journal in 1958.

Work done in the 1960s by Easson and Russell at the Holt Radium Institute in England led to more openness to the possibility of cure of HD with radiation treatment.

Slowly, practitioners began to accept this concept but it was not until the 1974 edition of Harrison's Principle of Internal Medicine that the curability of HD was even mentioned, following the dramatic results reported with combination chemotherapy treatments developed by De Vita at the NCI in Bethesda, MD.

Dr. Peters moved to the newly built Princess Margaret Hospital, the largest radiotherapy facility in North America, in 1958. There, she expanded her interest into breast cancer and helped demonstrate that treatment of localized breast cancer with breast-conserving surgery (lumpectomy) and radiation was as effective as the traditional radical mastectomy.

Vera Peters was praised for her individualized approach to her oncology patients. She advocated for as little intervention as possible to allow for a cure and had a modern approach of providing information about the disease they had, the various

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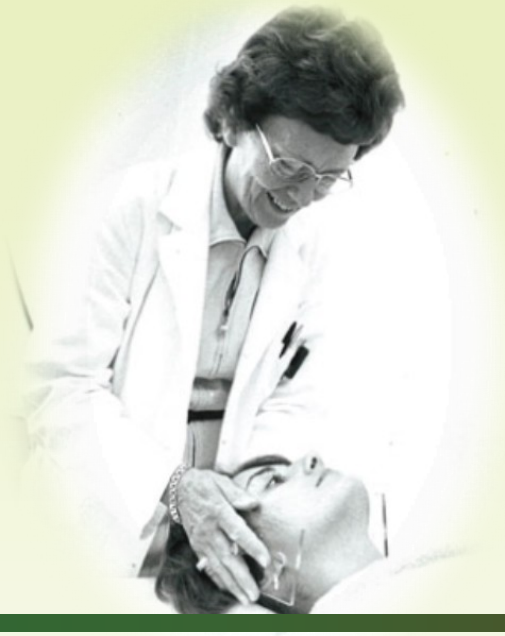


HISTORY CORNER: Dr. Vera Peters

treatment alternatives and the right to seek a second opinion.

Dr. Peters was appointed a Member of the Order of Canada in 1975 and this was raised to Officer in 1977.

She was awarded the Gold Medal by the American Society for Therapeutic Radiology and Oncology in 1979 and was appointed Professor Emeritus at University of Toronto in 1982.

After retiring from PMH in 1976, she acted as a part-time consultant at Oakville Trafalgar Memorial Hospital until 1988.

She died October 1, 1993 at Princess Margaret Hospital from complications of breast cancer.

Dr. Mildred Vera Peters was named to the Canadian Medical Hall of Fame in 2010.

References

Cowan D.H. Curr Oncol 15:206, 2008

Do you know the diagnosis?

CASE 1

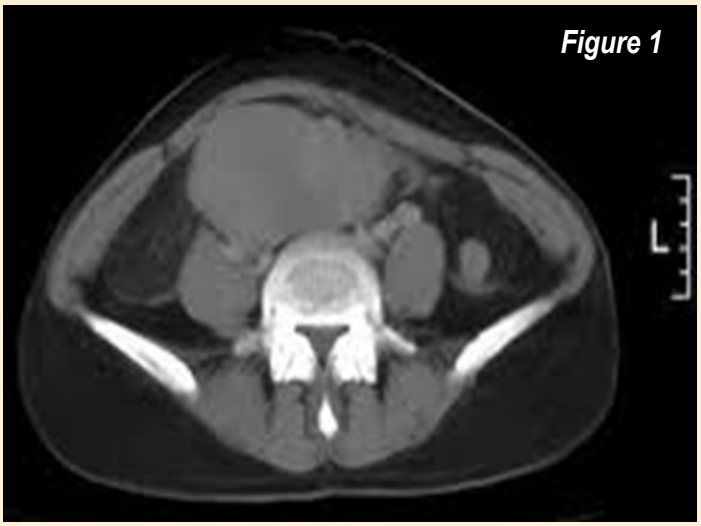
A 32-year-old nulliparous woman presented with a 6-month history of dyspareunia, intermittent right-sided pelvic cramping and menorrhagia.

- Past medical history was non-contributory.
- Blood work revealed a hemoglobin of 123 g/L, WBC 4.8 x 109/L (with a normal differential) and Platelets of 417 x 109/L.
- Renal and hepatic function and LDH were normal.
- A CT scan of the abdomen was performed (Figure 1).

Do you know the diagnosis?

See Page 14

Figure 1



CASE 2

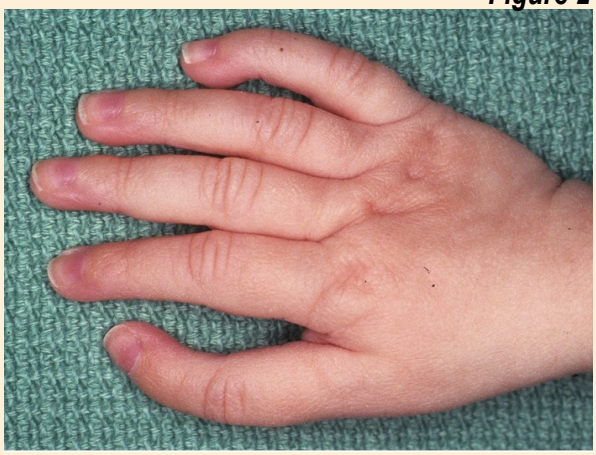
A 12-year-old girl was brought to a GP by her paternal grandmother, who she had recently met for the first time.

- The girl, who lived with her single mother in a different province, had a history of being "anemic" and had been on iron supplements intermittently for a number of years.
- The paternal grandmother indicated the girl's father and her paternal uncle had both suffered from anemia and was particularly concerned about the appearance of the girl's hand (Figure 2).

Do you know the diagnosis?

See Page 14

Figure 2



2015 CHS Abstract Award Winners

John H. Crookston Award

Risk Factors Predictive of Occult Cancer Detection in Patients with Unprovoked Venous Thromboembolism

Dr. Ryma Ihaddadene

Department of Medicine, University of Ottawa & Ottawa Hospital Research Institute Ottawa, Ontario

Venous thromboembolism (VTE) may be the earliest sign of cancer and the risk factors predictive of an underlying occult malignancy in first unprovoked VTE are unknown. This study sought to determine these risk factors through a post-hoc, pre-defined analysis of the randomized "SOME" trial (Carrier *N Engl J Med,* 2015). This trial compared limited screening for an occult cancer (history, physical examination, basic laboratory testing, chest x-ray and breast/ cervical/prostate screening) to this same limited screening plus comprehensive computed tomography in patients with a first unprovoked VTE. Cox proportional hazards models were used to analyze the effect of certain risk factors on the outcome of documented cancer within 12 months of the VTE event.

The SOME study included 854 randomized patients with a mean age of 54 years and a male:female ratio of 2:1. By 12-month follow-up, 33 patients (3.9%) had received a new diagnosis of cancer. In univariate analysis, age ≥60 years was a predictor of an underlying cancer compared to age <60 years [hazard ratio (HR) 2.90, p=0.003] as was a prior history of provoked VTE (HR 3.57, p=0.009). In multivariable analysis, age ≥60 years (HR 3.0, p=0.002), and prior provoked VTE (HR 3.8, p=0.006) remained significant risk factors and the presence of a DVT without pulmonary embolism showed a trend towards also being a predictor of cancer at 12 months (HR 2.1, p=0.06).

***The SOME study** has the potential to greatly influence the investigation of patients with first unprovoked VTE. Aggressive screening of all such individuals for an occult cancer appears to be of limited value. Targeted testing of high-risk patients (age ≥60 years or those with a prior history of provoked VTE) is more likely to become a winning strategy.*

Dr. Ryma Ihaddadene, *(Photo on RIGHT)* of the Department of Medicine, University of Ottawa and the Ottawa Hospital Research Institute, accepts the most prestigious CHS annual award to a Resident, the **John H. Crookston Award** for the best paper given by a Resident, at the CHS Gala evening at ASH, December 6, 2015 in Orlando, Florida.

YOUR CHS NEWSLETTER

Member submissions welcome!

2015 CHS Abstract Award Winners

Residents and Fellows Award

Sharing Post-AML Consolidation Supportive Therapy with Local Centers Reduces Patient Travel Burden without Compromising Safety and Efficacy

Samantha A. Hershenfeld, BMSc

Princess Margaret Cancer Centre, Ontario Cancer Institute and UNH Toronto, Ontario

Acute myelogenous leukemia (AML) is treated with induction chemotherapy to achieve remission, frequently followed by intensive post-remission consolidation chemotherapy (CCT). CCT can be effectively administered to many patients in an ambulatory setting, which has traditionally been given in centralized quaternary cancer centres. This model requires patients to travel long distances to the quaternary centre at considerable time and cost. The investigator studied the outcomes with a newer shared-care model involving centralized delivery of CCT but follow-up testing, blood product support and management of febrile neutropenia was performed at the patient's local hospital.

Over a four-year period (2009-2013), 73 patients with AML in CR1 (including 12 with acute promyelocytic leukemia) with a median age of 57 years (range 21-78) received their care after 137 CCT cycles at 14 local Ontario hospitals. These regional cancer centers treated a median of two patients during the study period and were staffed by a hematologist/oncologist experienced in management of cytopenias and febrile neutropenia. The mean travel distance for patients was 99.5 km to Princess Margaret Hospital (PMH) versus 26.3 km to the regional treatment center ($p<0.001$), with estimated travel times (calculated from Google Maps) of 71.6 minutes versus 23.3 minutes ($p<0.001$). By receiving post-CCT care at their local center rather than PMH, patients saved a mean of 146.5 km and 96.7 minutes of round-trip travel per visit. Safety and efficacy of the shared-care model was evaluated by comparing the 73 patients with the 344 AML patients who remained at PMH for their entire CCT care during the same time period. Patient characteristics did not differ between the two cohorts. Overall survival at 30, 60 and 90 days from the start of CCT was no different in the locally treated patients (98.6%, 97.2% and 95.9%) compared to the PMH-treated patients (90.8%, 97.1% and 95.3%).

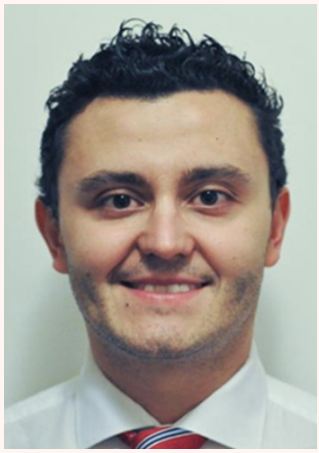
***This study does show** that a shared-care model does not influence survival at 90 days following CCT and therefore, in the broadest sense, does not appear to be inferior to the traditional quaternary care model. A more detailed analysis of morbidity and longer-term follow-up will be needed to allow this model to gain wider acceptance.*

Samantha A. Hershenfeld, BMSc, *(Photo on RIGHT) of the* Princess Margaret Cancer Centre, Ontario Cancer Institute and UNH Toronto, Ontario, is presented an award in the **Residents and Fellows** category, at the CHS Gala evening at ASH, December 6, 2015 in Orlando, Florida. Presenting the award is outgoing CHS Secretary, **Dr. Molly Warner**.

2015 CHS Abstract Award Winners

Residents and Fellows Award

Influence of Prophylactic Antibiotics Aiming at Gut Decontamination on Gastrointestinal Graft-Versus-Host Disease and Overall Survival Following Allogeneic Haematopoietic Stem Cell Transplantation



Dr. Bertrand Routy

Gustav Roussy Comprehensive Cancer Centre Villejuif, France

Commensal bacteria in the GI tract are thought to be etiologically important in acute graft-versus-host disease (GVHD) and infections, two lethal complications following allogeneic stem cell transplantation (SCT). High-dose conditioning chemotherapy can disrupt the epithelial barrier and bacteria then translocate into the blood influencing T-cell response and cytokine production. In an effort to decrease gram-negative bacterial translocation, gut decontamination has been used and this study was designed to determine whether such treatment can reduce the risk of acute GVHD and influence overall survival.

Dr. Routy reviewed the charts of 543 patients who underwent a single allogeneic SCT for a hematologic malignancy at two hospitals in Québec between January 2005 and December 2012 – Hôpital Maisonneuve-Rosemont (HMR) and Centre hospitalier universitaire de Québec (CHU). HMR routinely initiated Ciprofloxacin or Moxifloxacin at the start of conditioning during this timeframe, except in patients allergic to Fluoroquinolones or Penicillin or during nosocomial infection outbreaks. CHU did not routinely administer prophylactic antibiotics. A total of 500 patients were included in the analysis and 240 (48%) had received antibiotics during conditioning (ATB group). The incidence of grade II-IV acute GVHD was 42% in the ATB group and 28% in the non-ATB group ($p < 0.05$) with stage 2-4 GI acute GVHD being higher in the ATB than in the non-ATB group (20.7% versus 10.8%, respectively; $p < 0.01$). The stage of skin and liver acute GVHD did not differ between the two groups.

Pneumatosis coli, a complication of GI GVHD, was only seen in patients receiving Ciprofloxacin prophylaxis (12 patients) and was associated with an 80% mortality rate. Neutrophil count at day +14 was significantly lower in the ATB group ($p < 0.05$). Furthermore, overall survival was significantly higher in the non-ATB group at both one and five years post-SCT.

This interesting study does appear to finally lay to rest the role of gut decontamination prior to allogeneic SCT. The hypothesis that such treatment may reduce T-cell and cytokine response and thereby reduce acute GVHD clearly must be rejected. In fact, gut decontamination may actually increase the risk of acute GVHD, especially GI GVHD, following allogeneic SCT.

Dr. Bertrand Routy accepts an award in the **Residents and Fellows** category, at the CHS Gala evening at ASH, December 6, 2015 in Orlando, Florida. Presenting the award is then CHS Secretary, **Dr. Molly Warner**.

2015 CHS Abstract Award Winners

PhD and Postdoctoral Award

Mutational and Transcriptomic Landscape of AML with Core-Binding Factor Rearrangements

Dr. Vincent-Phillippe Lavallée

Hôpital Maisonneuve-Rosemont
Montréal, Quebec

Core-binding factor (CBF) AML includes leukemias with t(8;21) or inv(16)/t(16;16) and these disorders are often characterized by distinct gene expression profiles involving mutations in KIT, FLT3 and RAS pathway genes. This study was intended to compare the mutational profile and transcriptomic landscape in a large cohort of CBF and non-CBF AML samples. The investigators analyzed 415 AML specimens of which 48 were CBF AMLs – 20 samples with t(8;21) and 28 samples with inv(16)/t(16;16).

Dr. Lavallée found that specimens from CBF AMLs most frequently showed mutations in activated signaling genes – KIT (46%), NRAS (31%), FLT3 (25%) and KRAS (4%). In 38% of the mutated samples, 2-5 mutations were found with the sum of their variant allele frequency never exceeding 50%, consistent with each mutation occurring in a different subclone. Additionally, there were a number of unique observations reported from this analysis. Mutations in ZBTB7A encoding a transcription factor of the POK/ZBTB family was seen in three t(8;21) samples but only one of the other 395 samples (p=0.0004). Likewise, ASXL2 mutations were seen in four t(8;21) samples but only two of all other AML samples (p <0.0001). Furthermore, in five t (8;21) samples, mutually exclusive mutations in cohesin complex genes (SMC1A, SMC and STAG2) were noted. Lastly, a novel non-activated signaling gene, PRRC2B, was found to be mutated in three inv(16) samples.

The investigators went on to identify 145 and 127 gene signatures specific to the t(8;21) and inv(16)/t(16;16) groups, respectively; ~80% of these genes have not previously been described in gene enrichment analyses of CBF AML and may be novel CBF diagnostic markers. The CBF subgroup gene signaling cluster together homogeneously with one exception – a sample with t(16;21), which fuses RUNX1 and CBFA2T3, unambiguously grouped with t(8;21) specimens. This fusion shares structural characteristics to the RUNX1/RUNX1T1 fusion seen with t(8;21) whereas eight other RUNX1 fusions found in the non-CBF cohort demonstrated unique and different transcriptomic profiles.

This paper provides compelling information regarding the mutational and gene expression profiles of CBF AMLs. Dr. Lavallée's work will add to our understanding of this unique subgroup of AML and certainly has the potential to improve diagnostics and therapeutics.

Dr. Vincent-Phillippe Lavallée (Left) accepts the **PhD and Postdoctoral Award**, at the CHS Gala at ASH, Dec. 6, 2015 in Orlando, Florida—from then CHS Secretary, **Dr. Molly Warner**.

Chief Resident's Report

CHS online resources connect Canadian Hematology trainees

Eric Tseng PGY5
University of Toronto

April is an important month for most Canadian hematology trainees. The PGY4s are in the midst of preparing for their internal medicine licensing exams, while PGY5s (and above) are preparing for their next step, be it a foray into independent practice or further training.

We also reflect at this time on the role that the Canadian Hematology Society has played over the past year for trainees. I continue to believe that the CHS has potential for connecting trainees across the country at social gatherings, and in the online sphere via our WebPortal and social media. Even as we differentiate into our own career paths, I encourage you all to stay connected with each other, as the Canadian hematology community is a relatively small and collegial one.

"I continue to believe that the CHS has potential for connecting trainees across the country at social gatherings, and in the online sphere via our WebPortal and social media."

I also encourage you to continue to participate in our online educational resources, which have expanded this year to include monthly academic cases, the images challenge, drug reimbursement database, and CME webinars. Any contributions from CHS members in terms of content would also be welcomed and appreciated.

On a personal note, as I end my term as the inaugural CHS Chief Resident, I would like to thank the CHS membership for their continued participation and support, and to our executive and administrative team.

I also welcome the next Chief, who will undoubtedly improve and expand our educational portfolio.

Eric Tseng PGY5
University of Toronto

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**

Dr. Marc Carrier *receives the* ***2015 CHS Paper of the Year Award,*** *from outgoing CHS Secretary,* ***Dr. Molly Warner****, on Dec. 6, 2015 at the CHS Gala Evening at ASH in Orlando. Dr. Carrier's winning paper, "****Screening for Occult Cancer in Unprovoked Venous Thromboembolism****," was published in the* ***New England Journal of Medicine*** *in 2015.*

2015 CHS Paper of the Year Award

Screening for Occult Cancer in Unprovoked Venous Thromboembolism

N Engl J Med 373:697-704, 2015

Dr. Marc Carrier
Department of Medicine, Ottawa Hospital Research Institute, University of Ottawa
Ottawa, ON

Venous Thromboembolism (VTE) may be the earliest sign of underlying cancer in a patient. The SOME study sought to assess the efficacy of screening for occult cancers in patients with otherwise unprovoked VTE. A previous study by Dr. Carrier had suggested ~10% of patients with unprovoked VTE will ultimately be diagnosed with a malignancy in the year following the event (*Ann Intern Med* 149:323, 2008), with the incidence of a malignancy gradually declining to that of the general population thereafter. As a result, physicians and policy makers have questioned how aggressive one should be in screening for occult malignancies in the setting of an unprovoked VTE. Is there evidence to support that the early detection of an occult malignancy in this patient population will meaningfully influence cancer-related mortality? If so, a more intensive screening strategy would be justified following an unprovoked VTE. To answer this important question, Dr. Carrier and his co-investigators designed and performed this recently published randomized study.

Between October 2008 and April 2014, almost 3200 patients were assessed for eligibility in the SOME trial and 854 patients with a first unprovoked, symptomatic VTE were included in an intention-to-treat analysis.

- Group 1 included 431 patients assigned to limited occult cancer screening – history, physical examination, CBC, creatinine, electrolytes, liver function, chest X-ray and, when appropriate by accepted age criteria, mammography, PAP smear and PSA levels were performed; 427 patients (99.1%) actually received this intervention.
- Group 2 included 423 patients assigned to limited occult cancer screening plus a standardized comprehensive CT scan of the abdomen and pelvis (limited screen + cCT); 388 patients (90.9%) actually received this intervention. Abnormal findings were further investigated as directed by the local treating physician.

Primary outcome of the study was the incidence of confirmed cancers that were missed by the screening strategy but detected by the end of the 1-year follow-up.

In the limited screening cohort, 14.4% of patients were referred for additional investigations following initial screening to rule out an occult malignancy. This compared to 14.9% of patients referred for additional investigations in the limited screen + cCT. Following these investigations, 10 limited screening patients and 14 limited screen + cCT patients were found to have an occult malignancy (p=NS). By one year follow-up, 4 additional malignancies were discovered in the former group and five additional malignancies were found in the latter group (p=NS). In total, by one year follow-up, occult malignancies were found in 3.2% of limited screening patients and 4.5% of limited screen + cCT patients (p=0.28).

The types of malignancies seen with the two screening methods differed. The most common cancers found in the limited screening group were gynecologic (4 patients) and pancreatic (3 patients) malignancies. In the limited screen + cCT cohort, the most common occult cancers were colorectal, lymphoma and urologic (3 patients each). The mean time to cancer diagnosis was similar in both groups – 4.2 months in limited screening patients and 4.0 months in limited screen + cCT patients (p=0.88).

The rates of recurrent VTE (3.3% and 3.4%, respectively; p=1.0) and all-cause mortality (1.4% and 1.2%, respectively; p=1.0) were identical in the two cohorts. Rate of detection of cancers at an early stage was insignificantly lower in the limited screening group compared to the limited screen + cCT group (0.23% versus 0.71%, p=0.37) and cancer-related mortality was insignificantly higher (1.4% versus 0.9%, p=0.75).

The investigators conclude that more aggressive screening of patients with first unprovoked VTE that included comprehensive CT scan did not have a significant impact on incidence of detection of occult malignancy, the time to cancer diagnosis or on cancer-related mortality. Furthermore, the incidence of developing a malignancy over the first year following a negative screen was only ~1%. The paper suggests that the significant radiation exposure associated with comprehensive CT scan exposes patients to risk without a clinically significant benefit.

Dr. Carrier and colleagues do note that the incidence of occult cancer in first unprovoked VTE was lower than previously indicated in their 2008 publication. However, more recent studies have suggested that a more realistic incidence is in the range of 3-5% at 2.5 years follow-up (Prandoni, *J Thromb Haemost* 8:1126, 2010 and Van Doormaal *J Thromb Haemost* 9:79, 2011).

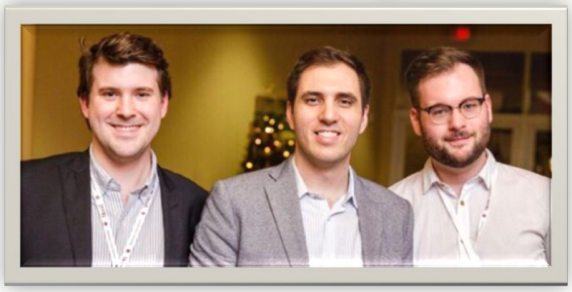
Despite the fact that unprovoked VTE may be the first sign of an underlying malignancy, this pivotal randomized, controlled trial provides the best evidence that the incidence of an occult cancer is low and a limited screening strategy is sufficient in this setting.

CHS at ASH 2015

Abstract Awards!

Networking

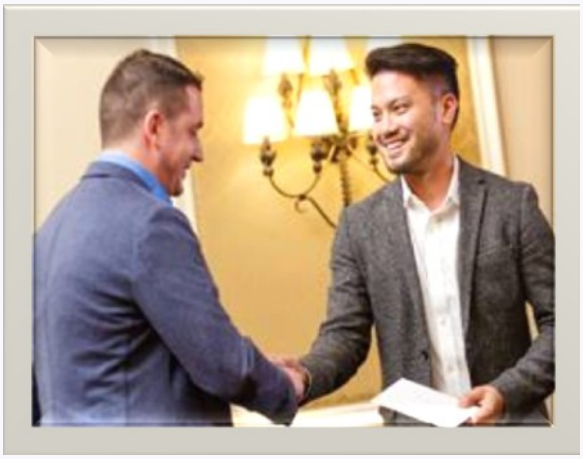
Socializing



Paper of the Year

Good Food & Fun

CHS Points First Prize!



Umberto Falcone, (LEFT) Lymphoma Fellow at Princess Margaret Hospital in Toronto, receives the first prize for achieving the **highest number of CHS Points for July-December 2015**. Making the presentation, at the CHS Gala Evening at ASH 2015 in Orlando, Florida, is **CHS Chief Hematology Resident, Dr. Eric Tseng**, University of Toronto.

Meet Old Friends & Make New Friends

Upcoming Events

Canadian Blood and Marrow Transplant Group (CBMTG)
Apr 24 - 27, 2016
Vancouver, BC, Canada
Contact: http://cbmtg.org/2016-annual-conference

American Society for Apheresis (ASFA)
May 4 - 7, 2016
Annual Meeting: Palm Springs, California, USA
Contact: http://www.apheresis.org/?page=ASFA2016

Conference of the Canadian Society for Transfusion Medicine (CSTM)
Start May 11 - 15, 2016
Vancouver, BC, Canada
Contact: http://www.transfusion.ca/en/cstm2016

21st European Hematology Association (EHA)
Jun 9 - 12, 2016
Copenhagen, Denmark
Contact: http://www.ehaweb.org/congress-and-events/21st-congress/key-information-3

XXXII World Congress Federation of Hemophilia (WFH)
Jul 24 - 28, 2016
Orlando, Florida, USA
Contact: http://www.wfh.org/congress/en/home

3rd World Congress of Cutaneous Lymphomas
Oct 26 - 28, 2016
New York, New York, USA
Contact: http://www.columbiacme.org/

Canadian Hematology Society (CHS)
Annual Reception, Dinner & Awards Evening
Sunday, December 4, 2016
San Diego, CA
Contact: chs@uniserve.com

ISH & Canadian Hematology Society (CHS) Joint Congress:
37th World Congress of the International Society of Hematology (ISH)
Sept 13-17, 2018
Vancouver Convention Centre
Contact: http://www.ish2018.com/

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The DIAGNOSIS? Answer: (from Page 5)

CASE 1: ANSWER

The CT scan revealed a 10 x 9 cm. mass that was felt to be consistent with a uterine fibroid. The patient underwent a laparotomy and was found to have a nodular mass involving the right ovary and bladder with pelvic and para-aortic lymphadenopathy. A BSOH and lymph node dissection was performed and the pathology revealed extensive infiltration with malignant cells that expressed CD34, CD117 and myeloperoxidase. The final diagnosis was granulocytic sarcoma. A subsequent bone marrow examination was normal with a normal female karyotype.

Granulocytic sarcoma (extramedullary myeloblastoma or chloroma) can present before, at the same time as or after AML involving the bone marrow. ~30% of granulocytic sarcomas (GS) precede the diagnosis of AML by months (or sometimes years). GS can be found in the lymph nodes, CNS, oral/nasal mucosa, breast, chest wall/pleura, GI or GU tract. When isolated GS is the initial presentation, 90-100% of patients treated with local therapy will ultimately develop AML.

Only 40-45% of isolated GS patients treated with systemic chemotherapy will go on to develop AML. Therefore the recommended treatment for this presentation is conventional AML therapy. Allogeneic stem cell transplantation has been proposed to lead to optimal long-term outcomes in isolated GS.

CASE 2: ANSWER

This girl was noted to have triphalangeal thumbs, short stature and a systolic ejection murmur due to a bicuspid aortic valve. She had an isolated profound anemia of 64 g/L but normal WBC and platelet counts. Her reticulocyte count was 5 x 10^9/L. Bone marrow examination revealed red cell aplasia and a normal karyotype. Genetic testing showed a mutation in the ribosomal protein RPS19 consistent with a diagnosis of Diamond-Blackfan anemia (DBA).

DBA is an autosomal dominant ribosomopathy with incomplete penetrance that usually presents in the first two years of life but mildly affected individuals may not be diagnosed until adolescence or as young adults. Presentation is typically with symptomatic anemia but those affected may have a variety of congenital abnormalities including craniofacial, thumb and upper limb abnormalities, cleft palate and cardiac or urogenital defects.

Corticosteroids are helpful in at least 80% of patients although their efficacy may wane leading to chronic transfusion support or, occasionally, allogeneic bone marrow transplantation. Spontaneous remissions may also occur. DBA patients are at modest increased risk for AML and other malignancies.

Opportunities

LEUKEMIA/BONE MARROW TRANSPLANTATION FELLOWSHIP VANCOUVER

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.

BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

For more information: leukemiabmtprogram.org

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

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

McGill University Thrombosis Fellowship 2017-18

McGill University Thrombosis Fellowship 2017-18 at Jewish General Hospital in Montreal, Quebec.

Hôpital général juif
Jewish General Hospital

The JGH Thrombosis Program is currently accepting applications for a one year fellowship (July 1, 2017 - June 30, 2018) to acquire and consolidate expertise in Thrombosis.

Specific areas of clinical activity include the Thrombosis Clinic, Anticoagulation Clinic and In-patient Thrombosis Consultation Service. Our Thrombosis Program also encompasses a broad range of research activities that relate to diagnosis, risk factors and treatment of venous and arterial thromboembolic disease.

To obtain more information please contact Dr. Vicky Tagalakis or Maureen Morganstein 514-340-7587 maureen.morganstein@ladydavis.ca.

More details about these opportunities can be found on the CHS website - http://canadianhematologysociety.org/

PRINCE EDWARD ISLAND CANCER TREATMENT CENTER

MEDICAL ONCOLOGIST OR HEMATOLOGIST

Health PEI is seeking a Medical Oncologist or Hematologist to join the small multidisciplinary oncology team at the center. Either specialty will be considered for this position, and some cross coverage will be required.

The successful candidate must have certification by the Royal College of Physicians and Surgeons of Canada (RSCPC), or equivalent training considered acceptable to the RSCPC. US Board exams are acceptable.

CONTACT:
Dr. Philip Champion
philip.champion@mac.com
902-894-2027

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Division of Hematology, Department of Medicine, The Ottawa Hospital and the Faculty of Medicine, University of Ottawa

HEMATOLOGISTS

We seek hematologists to join in our expansion and to lead in clinical care, education and/or research in Malignant Hematology and Benign Hematology.

Hematologist at an Assistant Professor level or higher; Bilingualism (French & English) an asset; Masters in Epidemiology or Education an asset; Eligible for licensure in Ontario. All qualified candidates are encouraged to apply: Canadian citizens & permanent residents will be given priority.

The Ottawa Hospital
L'Hôpital d'Ottawa

uOttawa

For application details:
Dr. Marc Rodger
mrodger@ohri.ca

thinkOttawaMedicine.ca
DEPARTMENT OF MEDICINE

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 400 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 with university degrees 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 2016, 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:

2016 Membership Renewal / Address Change: Canadian Hematology Society

Membership Status

Active ☐
Associate ☐
Emeritus ☐

Has your status changed?

Yes ☐
No ☐

Name: _____
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Work Phone: _____
Work Fax: _____