

# The Microenvironment

August 2012



C H S C H

THE CANADIAN  
HEMATOLOGY  
SOCIETY

SOCIÉTÉ  
CANADIENNE  
D'HÉMATOLOGIE

**NEWSLETTER**

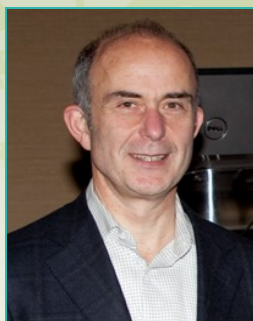
## Message from the President

### CHS activities focus on serving trainees and new hematologists

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#### *Dear Colleagues,*



**Dr. Stephen Couban**  
**President, CHS**

I want to let you know about the activities of the Canadian Hematology Society Executive and our central office over the last several months.

The CHS Executive held a one-day retreat in Ottawa in June, 2012. We reviewed the results of a recent survey of CHS members asking about how to improve communication among members of the society. We will be holding a follow-up meeting with Tanis Steward from Sosido

Networks to see if this novel social network can be a benefit for our membership.

We seek to continue to improve our collaboration with the Royal College of Physicians and Surgeons of Canada. With that in mind, Dr Darrell White who is Chair of the Hematology Speciality Committee and Dr. Marciano Rees who is Chair of the Hematopathology Speciality Committee joined us for part of the retreat. In addition, the Immediate Past President of the CHS will become a standing member of the Hematology Speciality Committee.

One of the items of discussion at the retreat was how we can improve the visibility and relevance of our society for trainees and new hematologists. In the regard, Aaron Schimmer, our

*(continued on page 2)*

## 2012 CHS Executive Committee

President  
Past-President  
Vice-President  
Secretary Treasurer  
Executive Vice-President

Dr. Stephen Couban  
Dr. Tom Nevill  
Dr. Aaron Schimmer  
Dr. Molly Warner  
Dr. Gail Rock

Editor

**The Microenvironment**  
**Dr. Tom Nevill**

*continued from page 1*

President Elect, spoke about the CHS at the recent Jerry Scott Day in Toronto. We also set up a booth and have been encouraged by the number of enquiries about membership which we received in Toronto.

As you all know, the CHS is highly supportive of research undertaken by Canadian trainees in hematology and acknowledges this at our annual CHS reception at ASH with a number of awards.

Also, we have the new R.K. Smiley Awards which also support academic endeavours by Canadian hematologists and there is information about the first three winners of these awards on pages 4 and 5 of this issue of the Microenvironment.

I would like to thank Drs. Dick Wells, David Anderson and Tom Nevill for all their work in reviewing the applications and selecting the three winners.

Finally, the CHS has made an application to the International Society of Hematology to hold the ISH 2018 meeting in Vancouver! This will be an excellent opportunity to showcase Canadian hematology accomplishments and to host the international hematology community. We will keep you posted on this project.

I look forward to seeing many of you at the CHS reception at ASH in Atlanta which will be on Sunday December 9, 2012. More information about the venue and agenda to come shortly. In the meantime, let me know how we are doing and what we can do to improve our society!

***Kind regards,  
Stephen Couban***

## Message du Président

### ***Chers collègues,***

Je voulais porter à votre connaissance les activités de l'exécutif de la société canadienne d'hématologie et notre bureau central durant plusieurs mois.

L'exécutif de la CHS a tenu une journée en retrait à Ottawa en Juin 2012. Nous avons revu les résultats d'une récente étude des membres de la CHS se demandant comment peut-t-on améliorer la communication parmi les membres de la CHS.

Nous tiendrons une réunion de suivi avec Tanis Steward de Sosido Communications pour voir si ce nouveau réseau social peut être bénéfique pour notre adhésion.

Nous visons à poursuivre l'amélioration de notre collaboration avec le Royal College of Physicians and Surgeons of Canada. Avec ça dans la tête, Dr Darrell White qui le président du comité de la spécialité hématopathologie, nous a rejoints durant une partie de la journée en retrait. En plus, l'ancien président de la CHS deviendra un membre éminent du comité de la spécialité hématologie.

L'une des questions de débat de cette journée en retrait était comment pouvons-nous améliorer la visibilité et la pertinence de notre société à destination des stagiaires et nouveaux hématologistes. Dans cet égard, Aaron Schimmer, notre président élu parla de la CHS durant la récente journée Jerry Scott à Toronto.

Nous avons également installé une cabine et avons été encouragés par le nombre de requêtes concernant l'adhésion reçues à Toronto. Comme

vous le savez tous, la CHS soutient hautement la recherche entreprise par les stagiaires canadiens en hématologie et la reconnaît lors de notre réception annuelle CHS à ASH avec un nombre de récompenses.

Egalement, nous avons les nouvelles récompenses R.K. Smiley qui soutiennent aussi les efforts académiques entrepris par les hématologistes canadiens et il y a information sur les premiers lauréats de ces récompenses ailleurs dans le microenvironnement.

Je souhaiterais remercier les Dr Dick Wells, Dick Wells, David Anderson et Tom Nevill pour leur travail dans l'examen des applications et la sélection des lauréats.

Finalement, la CHS a remis une demande à la société internationale d'hématologie pour tenir la réunion ISH 2018 à Vancouver! Ceci sera une excellente opportunité pour mettre en valeur les réalisations de l'hématologie canadienne et abriter le comité international de l'hématologie. Nous vous tiendrons informé sur ce projet.

Je souhaite vous voir nombreux lors de la réception à l'ASH à Atlanta qui aura lieu Dimanche 9 décembre, 2012. Plus d'informations sur le lieu et le sommaire seront bientôt disponibles.

Entre-temps, faites-moi savoir comment faites-vous et comment pouvons-nous pour améliorer notre société.

***Meilleures salutations,  
Stephen Couban***

## The Presidential Suite: a look at past CHS Presidents

**Dr. Peter Galbraith was the President of the Canadian Hematology Society from 1984-1986.**



**Dr. Peter Galbraith**

He graduated from Queen's University Medical School in 1956 and completed his Internal Medicine and Hematology training in Kingston and Toronto before travelling to Boston. There, he did a clinical and research fellowship with Dr. William Dameshek, the founder of the *Blood* journal and a pioneer in the field of myeloproliferative disease.

Upon his return to Kingston, Dr. Galbraith quickly assumed the role of Chief of Hematology in 1965 and Director of Undergraduate and Postgraduate Hematology Programs, positions that he held for the next 32 years. Working with Dr. R. Kennedy Smiley and other Hematology colleagues in Canada, Dr. Galbraith was instrumental in the formation of the Canadian Hematology Society in 1971.

He became the Chairman of the Division of Hematology/Oncology at Queen's University in 1970 and created the ambulatory chemotherapy clinic at Kingston General Hospital that same year. Dr. Galbraith's publications included numerous articles on the kinetics of granulopoiesis in health and disease, appearing in key journals including *Blood*, *British Journal of Haematology* and the *CMAJ*.

He co-authored two papers with Dr. Hal Broxmeyer, a pioneer himself in the field of umbilical cord blood stem cells. Following Dr. Galbraith's term as CHS President, he spent four years (1987-1991) as a Councillor for the American Society of Hematology. He was appointed Emeritus Professor, Queen's University in 1997 and remains committed to teaching. He created the 6-part HemeTeam Interactive Hematology website in 1996 which he continues to maintain.

Dr. Galbraith recently received a Clinical Skills Excellence in Teaching Award in October 2011.

## DO YOU KNOW THE DIAGNOSIS?

- A 55 year-old man, a life-time non-smoker, was referred for hematology consultation in 2006 with a 15-year history of asymptomatic, mild pancytopenia.

- His blood counts were: Hb 120 g/L, WBC 2.9 x 10<sup>9</sup>/L, neutrophils 1.8 x 10<sup>9</sup>/L and platelets 117 x 10<sup>9</sup>/L. Chemistry was normal.

- Physical examination revealed that he was tall (190 cm) and thin (70 kg) but aside from a scar on his lower lip from a recently resected squamous cell carcinoma, was entirely normal.

- Bone marrow examination revealed 70% cellularity with moderate erythroid dysplasia and 30% ring sideroblasts.

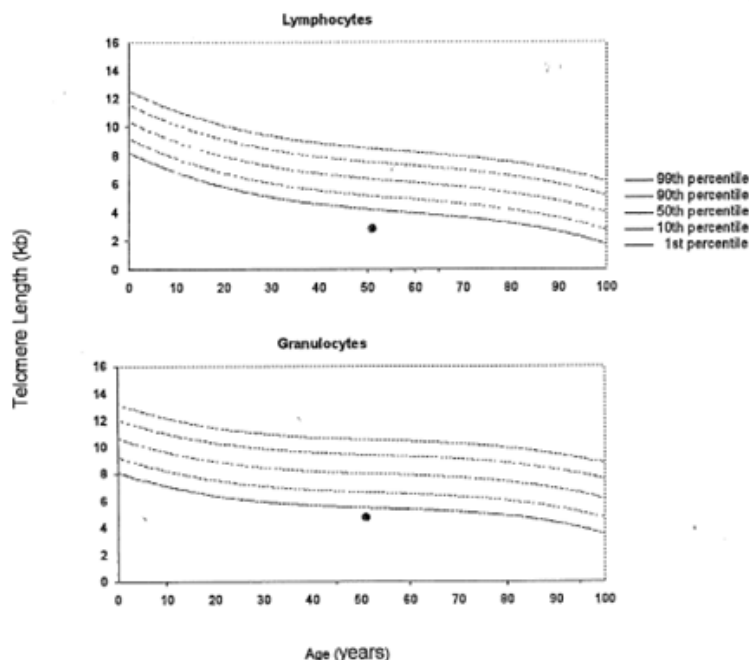
- Marrow blast count was 2% and karyotype was normal male in all 25 metaphases.

- A peripheral blood sample was sent further testing, with results shown in the accompanying picture.

Lymphocytes			Granulocytes		
MTL	MTLN	INT	MTL	MTLN	INT
(kb)	(kb)		(kb)	(kb)	
2.9	6.4	VL	4.8	8.0	VL

MTL = Patient Median Telomere Length  
MTLN = Normal MTL at age (50th percentile)  
INT = Telomere length interpretation

VH = Very High (≥ 99th percentile)  
H = High (≥ 90th and < 99th percentile)  
N = Normal (≥ 10th and < 90th percentile)  
L = Low (≥ 1st and < 10th percentile)  
VL = Very Low (< 1st percentile)



**What is the diagnosis?**

(SEE BOTTOM OF PAGE 15)



**Canadian Hematology Society**  
**Société Canadienne d'Hématologie**

## The Canadian Hematology Society congratulates the three winners of the first RK Smiley Research Grant awards.

Established in 2011, to mark the Fortieth Anniversary of the Canadian Hematology Society's service and support to hematology practitioners in Canada, this new award is named in honour of the **CHS Founding President, Dr. R. Kennedy Smiley.**

In response to the announcement of this new research grant program and the initial invitation for proposals, the CHS received many impressive submissions from across Canada. We are very pleased to announce that the following three proposals have been selected as the first winners of the award:

- ***Myeloid-derived suppressor cells as potential novel mediators of Factor VIII tolerance in Hemophilia A***  
Principal Investigator, Dr. Michael Rauh, PhD, MD  
Queen's University
- ***Prognostic markers in relapsed Hodgkin lymphoma***  
Principle investigator, Dr. Christian Steidl MD PhD  
BC Cancer Research Centre
- ***"Sensing" Hematopoiesis***  
Principal Investigator, Dr. Hubert Tsui MD PhD  
University of Toronto



**Dr. R. Kennedy Smiley**  
**1922 - 2010**  
**CHS Founding President**

*More information about each of  
these three winning proposals  
is given on the following page.*



## 2012 RK Smiley Research Grant Award Winners

### *Myeloid-derived suppressor cells as potential novel mediators of Factor VIII tolerance in Hemophilia A*

**Dr. MICHAEL RAUGH, Hematopathologist-Scientist, Queen's University, Kingston, ON**

About 25-30% of FVIII-treated Hemophilia A patients develop FVIII antibodies which jeopardize the effectiveness of treatment for this disorder. The investigator's laboratory have previously shown that plasma-derived FVIII is more tolerogenic than recombinant FVIII with regards to risk of inhibitor formation.

Dr. Rauh and colleagues hypothesize that myeloid-derived suppressor cells (MDSC), a heterogeneous immunosuppressive myeloid cell population that mediate allogeneic tolerance, may be differentially expanded with

plasma-derived versus recombinant FVIII treatment.

Their proposal involves investigating the role of endogenous MDSC in a mouse Hemophilia A model by measuring FVIII inhibitor levels and proportion of CD11b+Gr-1+(MDSC) cells in HA mice exposed to the two different FVIII products. The researcher also plans to generate MDSC from cultured murine bone marrow and explore the therapeutic potential of MDSC in preventing FVIII antibody production by adoptively transferring these cells into HA mice prior to FVIII treatment.

### *Prognostic markers in relapsed Hodgkin lymphoma*

**Dr. CHRISTIAN STEIDL, Research Scientist, Centre for Lymphoid Cancer, Vancouver, BC**

Hodgkin lymphoma (HL) is the most common lymphoma affecting young people in the Western World and, while there have been considerable therapeutic advances made, 25% of patients progress after initial therapy.

The majority of those with progressive HL proceed to high-dose therapy with stem cell support which cures ~50% of HL patients that receive this treatment. However, there is a lack of biological markers that can predict the success of salvage therapy and the malignant Reed-Sternberg cells in HL comprise only 1% of the tumour tissue. The investigator has recently shown that the composition of the microenvironment in HL can predict response to upfront

therapy and that gene expression measured in formalin fixed paraffin embedded (FFPE) biopsy specimens can predict overall survival. The hypothesis of the researcher's proposal is that paired FFPE biopsies from diagnosis and at first relapse will reveal that relapse specimens can provide superior information on outcome of salvage therapy.

The paired specimens will be examined by histology and immunohistochemistry for malignant cell and microenvironment composition. The results will provide the preliminary data for a submission to CIHR that will involve digital gene expression profiling of the paired samples.

### *"Sensing" Hematopoiesis*

**Dr. HUBERT TSUI, University of Toronto, Toronto, Ontario**

Recent publications have implicated neuroimmune mechanisms in the pathogenesis of Type I diabetes mellitus in which islet innervating sensory neurons contribute to a proinflammatory environment that can lead to autoimmune  $\beta$ -cell destruction.

The investigators plan to apply neuroimmunology to the field of hematology using their knowledge of the sympathetic nervous system controlling stem cell mobilization through innervation of mesenchymal stem cells

and the contribution of marrow Schwann cells to the stem cell niche by regulating TGF- $\beta$ . This research project will involve peripheral blood phenotyping in primary sensory nerve activation ion channel-deficient, substance P neurotransmitter-deficient and neonatal capsaicin-treated mice.

Immunohistochemistry will be used to localize sensory nerves in relation to sympathetic nervous system, mesenchymal stem cells, Schwann cells and the hematopoietic niche.

## SUMMER STUDENT RESEARCH: EPIDEMIOLOGICAL REVIEW

# Patient Referrals to Vancouver General Hospital Marrow Failure Syndromes Clinic

**Edward Nevill**

**and**

**Dr. Sujaatha Narayanan**  
**Leukemia/BMT Program of BC**  
**Vancouver, British Columbia**

Marrow failure syndromes are a group of disorders where hematopoietic cells are not produced by the bone marrow at a normal rate. These diseases include aplastic anemia, myelodysplastic syndrome, paroxysmal nocturnal hemoglobinuria, large granular lymphocytosis and primary myelofibrosis.<sup>1</sup>

Myelodysplastic syndrome (MDS) is believed to be the most common clonal hematologic disorder in North America with the majority of cases thought to develop in a susceptible individual by cumulative exposure to toxins and/or radiation.<sup>2-4</sup> However, identifying exposures that predispose to MDS is particularly challenging as the latency period between encountering toxins and the development of bone marrow failure may be decades.<sup>5</sup>

With this in mind, the lack of an identified data base for MDS cases is a key deficiency in understanding the epidemiology of this disorder. The creation of an MDS data base containing patient demographics and possible toxin exposures along with the interpretation of the collected data was the purpose of this summer project.

We collected and assembled data from 250 patients in British Columbia who were referred to a specifically created Marrow Failure Syndromes Clinic between January 2008 and June 2012. Of these patients, 185 were diagnosed

with MDS, 22 were diagnosed with acute myelogenous leukemia, 15 were diagnosed with primary myelofibrosis and 19 were diagnosed with aplastic anemia.

The primary focus of our study was the 185 patients referred with MDS as we sought to determine risk factors (such as age, gender, place of residence, occupation, and toxin exposure) that may cause a predisposition to developing marrow failure.

In the MDS patients, the median age was 64 years and the male:female ratio was 1.7:1. The median peripheral blood counts at diagnosis were a hemoglobin of 98 g/L, a WBC count of  $3.3 \times 10^9/L$  and a platelet count of  $93 \times 10^9/L$ . Median bone marrow blast count was 5%. Thirty-seven patients had fibrosis although only 16 had WHO grade 2-3/3 fibrosis.

Bone marrow karyotype was normal in 87 subjects (47%), with the most common cytogenetic abnormalities being complex changes (21 subjects, 11%), trisomy 8 (15 subjects, 9%) and deletion 5q (11 subjects, 6%). With this cytogenetic profile, not surprisingly, the majority of patients (70%) had either low-risk or intermediate-1-risk international prognostic scoring system (IPSS) scores and 112 patients (60%) remain alive at this time.

The project also included a comprehensive review of the patient's medical histories. Six cases of MDS occurred in the context of congenital

disorders known to predispose to its development -- 3 patients have been diagnosed with Dyskeratosis congenita; 2 patients have been diagnosed with MonoMAC syndrome and one patient has been diagnosed with Diamond-Blackfan syndrome.

Co-morbidities were recorded for all MDS patients referred and the most frequent were hypertension (36% of patients), diabetes mellitus (16% of patients), hypothyroidism (10% of patients) and ischemic heart disease (9% of patients). A history of another malignancy was also common with the most frequent being basal cell or squamous cell carcinoma of the skin (52% of cases), followed by breast cancer (11% of cases) and prostate cancer (9% of cases).

The study concluded with an in-depth look into regional trends and occupational exposures. The cities of Vancouver and Victoria contributed 25% and 17%, respectively, of the



**Edward Nevill**



**Dr. Sujaatha Narayanan**

**Leukemia/BMT Program of B C, Vancouver, BC**

## Toxin Exposure in MDS Patients

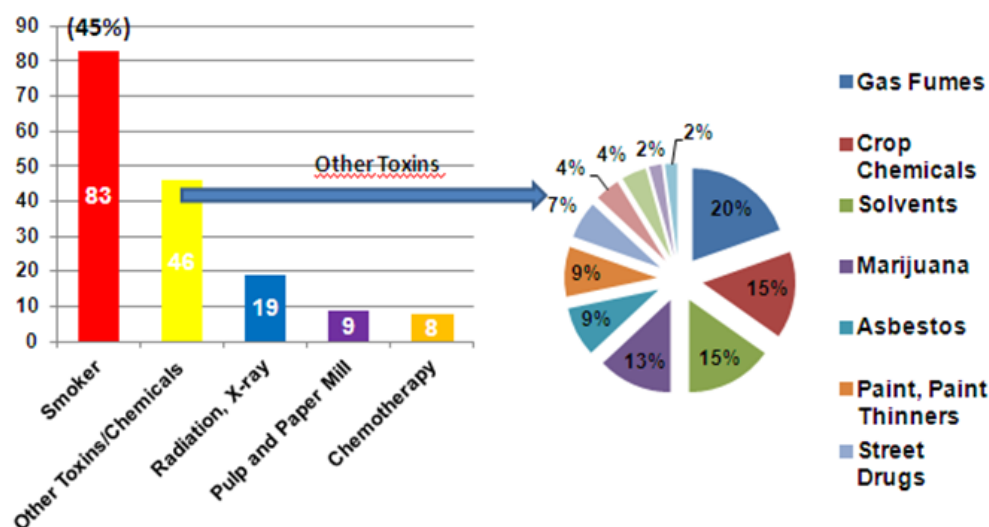


Figure 2

partially attributed to medical access and population demographics, recreational and occupational toxin exposures may also be contributing to this disproportionate contribution of MDS patients.

The study findings should act as a basis for a larger, more systematic review of the incidence of MDS in specific regions of BC and in identifiable at-risk professions.

**REFERENCES:**  
Are listed on the following page.

MDS patients referred for assessment. While both were over-represented in relation to the actual percentage of the BC population, Victoria (8% of the provincial population) was a disproportionately large contributor.

Although this finding may have been explained by access to medical specialty care or population demographics, there may have been some relevance to the fact that employment within the transportation industry, shipyards and on barges was identified in 20 patients, the most common of the "at-risk" professions.<sup>3,4</sup>

The second most common occupation was building construction/painting followed by healthcare professionals and heavy machinery operators or employment at a gas/oil refinery (Figure 1). Finally, we examined chemical and toxin exposure among MDS patients, with the most easily modifiable exposure, cigarette smoke, also being the most common (43% of patients). This figure contrasts with the 14% smoking rate reported in the general population in

2010 figures for British Columbia. Other common toxin exposures included gas fumes, crop chemicals and solvents (Figure 2).

During our research on marrow failure syndromes, we found important trends in regional distribution and occupational exposure. The Vancouver area and Victoria were over-represented, and although this can be

## INVITATION TO SUBMIT STUDENT RESEARCH ARTICLES

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

Queries should be directed to:

- The Editor of *The Microenvironment*
- Email: [chs@uniserve.com](mailto:chs@uniserve.com)

## OCCUPATION OF MDS PATIENTS

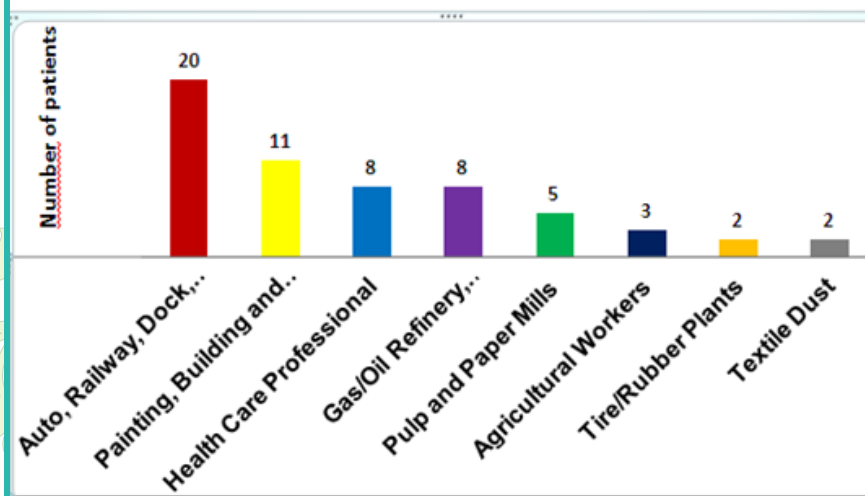


Figure 1



**Summer Student Research:***continued from page 7***Epidemiological Review:**  
Patient Referrals to  
Vancouver General Hospital  
Marrow Failure Syndromes  
Clinic**References**<sup>1</sup>Young NS. Acquired aplastic anemia. *Ann Intern Med* 2002;136:534-536.<sup>2</sup>Look TA. Molecular pathogenesis of MDS. *Proc Am Soc Hem* 2005;156=160.<sup>3</sup>Rigolin GM. Exposure to myelotoxic agents and MDS: case-control study and correlation with clinicobiological findings. *Br J Haematol* 1998;103:189-197.<sup>4</sup>West RR. Cytogenetic abnormalities in MDS and occupational or environmental exposure. *Blood* 2000;95:2093-2097.<sup>5</sup>Kamada N. Preleukemic states in atomic bomb survivors in Japan. *Nouv Rev Fr Hematol Blood Cells* 1976;17:57-65.**INVITATION TO SUBMIT  
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**WE WANT TO HEAR  
FROM YOU**

# La greffe de sang de cordon chez l'adulte

La greffe de sang de cordon est une modalité thérapeutique ayant connu un essor important au courant de la dernière décennie chez l'adulte souffrant d'une maladie hématologique grave.

Selon les données rapportées au CIBMTR, à Eurocord ainsi qu'au registre japonais, plus de 25 000 greffes de sang de cordon ont été réalisées à travers le monde entre 1994 et 2011. De ce nombre, environ 9000 ont eu lieu au Japon, 7000 en Amérique du Nord et 5500 en Europe.

La proportion de la clientèle adulte par rapport à la clientèle pédiatrique a également significativement augmenté. Notamment, depuis 2005, plus d'allogreffes de sang de cordon ont été réalisées chez l'adulte que chez l'enfant. Fondée en 1993, la banque de New-York a été la première banque publique de sang de cordon. Elle rapporte aujourd'hui un inventaire de plus de 50 000 unités ce qui la place au deuxième rang dans le monde après la banque du NMDP qui possède plus de 120 000 unités.

Il existe un réseau international de banques publiques de sang de cordon et on estime à environ 600 000 le nombre total d'unités de sang de cordon entreposées dans près de 150 banques publiques.

Les 5 pays fournissant le plus d'unités de sang de cordon à travers le monde sont, par ordre décroissant, les États-Unis, le Japon, l'Espagne, la France et l'Italie. Au Canada, il existe 2 banques publiques, soit Alberta Cord Blood Bank fondée en 1996 et Héma-Québec fondée en 2004.

Chez l'adulte nécessitant une allogreffe, cette nouvelle source de cellules est en général privilégiée dans les deux situations suivantes : 1) aucun donneur compatible (apparenté



**Geneviève Gallagher md**  
Service d'hématologie  
Hôpital l'Enfant-Jésus

ou non) n'a été identifié 2) aucun donneur apparenté compatible n'est disponible et il y a une urgence à procéder à l'allogreffe.

Dans ce dernier cas, le processus de recherche de donneur non-apparenté est écarté, puisqu'il existe un délai minimum de deux à trois mois avant l'identification d'un donneur potentiel. Les indications principales de procéder à une allogreffe sont par ailleurs les mêmes peu importe la source de cellules souches.

Selon les données de l'Eurocord, les cancers hématologiques (principalement les leucémies aiguës et les syndromes myélodysplasiques) représentent 96% des maladies sous-jacentes des patients recevant une greffe de sang de cordon.

Seulement 4% des adultes souffrent d'un désordre bénin, principalement une insuffisance médullaire. Ces données contrastent avec celles de la



clientèle pédiatrique où 25% des allogreffes de sang de cordon sont réalisées chez des patients souffrant de conditions non cancéreuses.

Les recommandations générales actuelles sont de sélectionner des unités de sang de cordon avec une compatibilité HLA 4/6, 5/6 ou 6/6 avec le patient ainsi qu'une dose cellulaire totale  $\geq 3 \times 10^7$  cellules nucléées par kg de poids du receveur. Chez l'adulte cette dose est le plus souvent atteinte avec deux unités plutôt qu'une seule. Lorsque deux unités sont sélectionnées pour un même patient, il demeure controversé à savoir si les deux unités doivent présenter entre elles une compatibilité HLA d'au moins 4/6.

Il existe plusieurs avantages à employer cette source de cellules souches. Les unités de sang de cordon sont rapidement accessibles, leur utilisation est flexible du fait qu'elles sont cryopréservées, l'incompatibilité HLA est permise, les cellules sont hautement prolifératives, il y a absence d'inconfort pour le donneur et la quasi-totalité des unités sont exemptes du cytomégalovirus.

Les inconvénients rapportés sont principalement la dose cellulaire limitée et la prise de greffe tardive, la qualité variable des greffons selon les banques et les années de collecte, l'impossibilité d'obtenir des cellules additionnelles ainsi que le coût prohibitif, principalement lors de la double greffe de sang de cordon.

La dose cellulaire limitée représente la limitation principale et on estime que chez seulement le quart des adultes il est possible d'identifier une unité de sang de cordon suffisamment riche et de compatibilité adéquate pour procéder à une greffe de façon sécuritaire.

Plusieurs stratégies ont été

développées pour contrer cette limitation et la double greffe de sang de cordon est la modalité la plus employée(1). En plus de permettre à plus d'adultes d'être éligibles à ce type de greffe, une possible augmentation de l'effet du greffon contre la leucémie a été rapportée(2).

D'autres méthodes plus expérimentales sont à l'étude dont l'expansion ex vivo des précurseurs et progéniteurs inclus dans le cordon, l'injection intra-médullaire du greffon et la co-infusion d'un greffon de cellules souches provenant d'un donneur haplo-identique ayant subi une déplétion en lymphocytes T.

Les données cliniques relatives à la greffe de sang de cordon sont en constante évolution et ne sont pas toujours faciles à interpréter(3). Les études provenant des grands registres tels que le CIBMTR et Eurocord ont l'avantage d'inclure un nombre important de patients, mais il y a une hétérogénéité importante des données en termes de diagnostic, stade de la maladie, âge des patients, dose cellulaire infusée et régime de conditionnement.

Les études publiées par un seul centre ont pour leur part le désavantage d'inclure un nombre limité de patients. Les résultats cliniques sont mieux définis chez les patients souffrant de leucémies aiguës puisqu'il s'agit de l'indication principale de traitement.

Eapen et al. ont rapporté en 2010 les données de 1525 patients provenant du CIBMTR et de Eurocord en comparant la greffe de sang de cordon avec une compatibilité HLA 4-6/6 à la greffe non apparentée de moelle osseuse ou de cellules souches sanguines avec une compatibilité HLA 7-8/8(4). Bien que la mortalité liée au traitement était plus élevée dans le groupe de sang de cordon (33% vs 23%, RR 1.62,  $p < 0.01$ ) la survie sans

maladie à 2 ans était identique peu importe le type de greffon (33% sang de cordon vs 39% HLA 8/8 vs 34% HLA 7/8,  $p = 0.09$ ). Cette étude a renforcé l'idée d'utiliser le sang de cordon chez les patients sans donneur non-apparenté compatible.

Plusieurs plus petites études ont également comparé le sang de cordon par rapport aux autres sources de cellules souches et ont publié des résultats comparables(5-9).

En conclusion, la greffe de sang de cordon est une option thérapeutique relativement nouvelle en constante évolution.

La limitation principale chez l'adulte est la faible dose cellulaire contenue dans chacune des unités, mais beaucoup de centres ont contré ce problème en procédant à une double greffe de sang de cordon.

Lorsque comparés aux autres sources de cellules souches, les résultats cliniques supportent l'emploi d'une ou deux unité(s) de sang de cordon HLA 4-6/6 lorsque aucun donneur non apparenté HLA 8/8 n'est disponible ou que la transplantation est jugée urgente.

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# Cord blood transplantation in adults

## Bref Rapport:

Submitted by

**Dr. Geneviève Gallagher**

Service d'hématologie  
Hôpital l'Enfant-Jésus

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Continue de page 9

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Cord blood transplantation is a therapeutic modality that has shown considerable growth over the past decade for adults suffering from severe hematologic diseases.

According to the data reported to CIBMTR from the Eurocord registry as well as the Japan registries more than 25,000 cord blood transplants were performed worldwide between 1994 and 2011. Of these, about 9,000 were done in Japan, 7,000 in North America and 5,500 in Europe.

The proportion of adults relative to the pediatric population has also increased significantly. Notably, since 2005, more cord blood allografts were performed in adults than children.

In 1993, The New York Blood Center established the first public cord blood bank. It now has an inventory of over 50,000 units which is second in the world after the National Marrow Donor Program (NMDP) bank which has over 120,000 units.

There is an international network of public cord banks with an estimated 600,000 units of cord blood which are stored in nearly 150 public banks. Internationally the five countries providing the most cord blood units are, in descending order,

the United States, Japan, Spain, France and Italy.

In Canada, there are two public banks, the Alberta Cord Blood Bank which was established in 1996 and the *Héma-Québec* bank, founded in 2004.

In adults requiring an allograft, this new source of cells is generally preferred in the following two situations: 1) no compatible donor (related or not) has been identified 2) no related donor is available and there is an urgency to proceed with the allograft. In the latter case, the process of finding a non-related donor is not feasible, since it takes a minimum of two to three months to identify a potential donor.

The main indications for performing an allograft are the same regardless of the source of stem cells. According to data from the Eurocord, hematological malignancies (primarily acute leukemias and myelodysplastic syndromes) represent 96% of the underlying diseases in patients receiving a cord blood transplant.

Only 4% of adults suffer from a benign disorder, mainly bone marrow failure.

These data contrast with those of pediatric patients where 25% of allogeneic cord blood transplants are performed in patients with non-cancerous conditions.

Current the general recommendations are to select units of cord blood with an HLA 4/6, 5/6 or 6/6 with the patient and a total cell dose  $\geq 3 \times 10^7$  nucleated cells per kg of the recipient.

In adults this dose is most often achieved with two units rather than one. When two units are selected for the same patient, it remains controversial as to whether the two units must have an HLA compatibility between them of at least 4/6.

There are several advantages to using this source of stem cells. The units of cord blood can be quickly accessed, their use is flexible as they are cryopreserved, HLA incompatibility is permitted, the cells are highly proliferative, there is no discomfort for the donor and the majority of the units are exempt from cytomegalovirus.

The disadvantages reported are mainly the limited cell dose and late engraftment, the varying quality depending on the bank and the years of collection, the inability to obtain additional cells and the prohibitive cost, mainly for double cord blood transplants.

The limited cell dose is the main limitation and it is estimated that in only a quarter of adults is it possible to identify a unit of compatible cord blood rich enough to safely proceed to transplantation.

Several strategies have been developed to overcome this limitation and double cord blood

transplant is the most widely used method (1). In addition to allowing more adults to be eligible for this type of transplant, a possible increase in the graft versus leukemia effect has been reported (2).

Other more experimental methods are being studied including ex vivo expansion of the progenitors and precursors, intramedullary injection of the graft and the co-infusion of a stem cell transplant from a haploidentical donor after T cell depletion.

Clinical data related to cord blood transplantation are constantly evolving but are not always easy to interpret (3). Studies from large registries such as the CIBMTR and Eurocord have the advantage of including substantial numbers of patients, but there is significant heterogeneity of data in terms of diagnosis, disease stage, patient age, cell dose infused and conditioning regimen.

Studies published from a single center have the disadvantage of including a limited number of patients. The clinical results are better defined in patients with acute leukemia as this is the main indication for treatment. In 2010, Eapen et al. reported data from 1,525 patients from the CIBMTR Eurocord and compared cord blood transplant with an HLA 4-6/6 to transplantation of unrelated bone marrow or blood stem cells with an HLA 7-8/8 (4).

Although treatment-related mortality was higher in the cord

blood group (33% vs. 23%, RR 1.62,  $p < 0.01$ ) disease-free survival at 2 years was identical regardless of the type of graft (33% cord blood vs. 39% HLA 8/8 vs. 34% HLA 7/8,  $p = 0.09$ ).

This study has reinforced the idea of using cord blood in patients without an apparently compatible donor. Several smaller studies have also compared cord blood to other sources of stem cells and have published similar results (5-9).

In conclusion, transplantation of cord blood is a relatively new therapeutic option which is in constant evolution.

The main limitation in adults is the low cell dose contained in each unit, but many centers have countered this problem by performing a double cord blood transplant.

When compared to other sources of stems cells, the clinical results support the use of one or two unit(s) of HLA 4-6/6 cord blood when no unrelated HLA 8/8 donor is available or transplantation is considered urgent.





## 2012 National Hematology Resident Retreat

**In July of each year, hematology trainees from across Canada gather in Toronto, Ontario for the National Hematology Resident Retreat.**

This event spans a weekend of educational activities including a mock oral examination, specialized workshop (topics changing yearly), Jerry Scott Half-Day of expert lectures, and morphology exam/review.

The retreat is coordinated with the Annual Hematology Web-based Written Exam which is offered in July, to provide a full spectrum of examination preparation for senior trainees and expert teaching for all levels of trainee.

In addition, this weekend provides opportunity to meet and socialize with fellow trainees and hematology faculty from across the country, forging new contacts for future collaboration and friendships.

Retreat Coordinators are **Drs. Christine Chen** and **Gena Pilotis**, of the University of Toronto.



**Dr. Roopesh Kansara**, LEFT, Hematology Fellow at the University of Manitoba and **Dr. Janet Lui**, Hematology Fellow, University of Ottawa, look over materials at the CHS information booth at the recent Jerry Scott Educational Half-Day, Saturday, July 21, 2012 at the Princess Margaret Hospital in Toronto, held in conjunction with the 6th Annual Hematology Residents Retreat, July 20 – 22 in Toronto.

## Upcoming Events

- The Canadian Hematology Society Annual Reception, Awards Presentation & Dinner, will be held (during ASH) Sunday December 9, 2012, in Atlanta GA.  
For more information: [chs@uniserve.com](mailto:chs@uniserve.com)
- The American Society of Hematology (ASH) 54th Annual Meeting and Exposition, will be held December 8 – 11, 2012, in Atlanta GA.  
For information: [www.hematology.org](http://www.hematology.org)
- The Canadian Bone Marrow Transplant Group (CBMTG) April 10—13, 2013, Fort Garry Hotel, Winnipeg, Manitoba.  
For information: [www.cbmtg.org](http://www.cbmtg.org)
- Canadian Apheresis Group & Canadian Association of Apheresis Nurses Annual General Meeting, April 11—13, 2013, Fort Garry Hotel, Winnipeg, Manitoba.  
For information: [cag@cagcanada.ca](mailto:cag@cagcanada.ca)
- International Society of Laboratory Hematology (ISLH) May 10—12, 2013, at the Sheraton Centre in Toronto, Ontario.  
For information: [www.islh.org/ISLH\\_2013](http://www.islh.org/ISLH_2013)

# About the Canadian Hematology Society

The Canadian Hematology Society (CHS) is a professional organization, representing all physicians and scientists with an interest in the discipline in Canada. Currently, the CHS has approximately 350 members.

## Established in 1971

The first annual meeting of the Society was held in the Richelieu Room of the Chateau Laurier in Ottawa on the 20th of January 1971. Fifty-six members attended that meeting, where the draft bylaws, presented by the executive were approved.

**R.K. Smiley** was appointed as the first President. **Al Cousineau** was named Vice President, and **W. Corbett** as Secretary Treasurer.

In 2008, for the first year since its inception, the society did not hold an annual meeting in Canada and since that year, the annual business meeting has been held in conjunction with the American Society of Hematology (ASH) December meetings.

Historically, Canadian Hematologists have gathered for a social evening on the Sunday evening of the American Society of Hematology's annual meeting. This tradition remains unchanged from the founding days and included an awards night in which selected abstracts from the ASH meeting are reviewed.

## Research Awards

Today, awards are generally presented for the two best resident abstracts, the two best abstracts from PhDs and one award for a junior faculty member.

In 2008 the CHS began a new tradition of combining the reception, awards evening and a gala dinner for all Canadian hematologists. This is a major function for the CHS — it is very well attended and brings together the largest group of Canadian hematologists under one roof. It is a great chance to network!

In 2011, to mark its fortieth anniversary, the society established the RK Smiley Research

Award Program, in honour of the founding president.

## Communications

The CHS has published this newsletter for the past many years. It is distributed via the web site <http://www.canadianhematologysociety.org/> A printed copy is also mailed to each member.

The newsletter, *The Microenvironment*, under the editorship of **Dr. Tom Nevill**, carries a Message from the President in each issue, which gives a good overview of activities, ongoing initiatives and plans on behalf of the executive committee. It also carries several regular features as well as information about membership, career opportunities, awards programs, and upcoming events.

## Membership in the CHS

Membership is open to physicians engaged in the practice of clinical or laboratory hematology in Canada or Canadian physicians engaged in such practice, or persons with university degrees making continuing contributions to research in physiology or pathology in hematology in Canada.

In appropriate cases, the requirement for a university degree or other qualifications may be waived if, in the opinion of the Executive Committee, the candidate is making significant continuing contributions to science.

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.

Active Members only may vote, hold office and pay dues. Honorary, Emeritus and Associate (fellows-in-training) members shall have the privileges of the Corporation except for voting, holding office and paying the \$75. annual dues.

Membership forms are available on the CHS website or from CHS Administration office at 613-748-9613, or by email:

[canadianhematology@uniserve.com](mailto:canadianhematology@uniserve.com).

# Career Opportunities

## Full-Time Hematologist

St. Michael's Hospital, a fully-affiliated University of Toronto teaching hospital located in downtown Toronto, is seeking a full-time Hematologist to join our academic Division of Hematology and Oncology, as a clinician-teacher or clinician-educator.

He or she will join a dynamic group of 5 Hematologists and 4 Medical Oncologists with wide-ranging interests, and specialized expertise in congenital and acquired bleeding disorders, lymphoproliferative diseases, and cancers of the breast and gastrointestinal tract. The successful candidate will have the opportunity to establish a practice in general clinical Hematology, with a focus on benign diseases will participate fully in the Division's undergraduate and post-graduate medical education program, with academic activities based on education and/or clinical research.

All candidates must have RCPSC subspecialty certification in Hematology or equivalent, and must be eligible for appointment in the Faculty of Medicine at the University of Toronto at the rank of Lecturer or Assistant Professor.



Leading with Innovation  
Serving with Compassion

**ST. MICHAEL'S HOSPITAL**  
*A teaching hospital affiliated with the University of Toronto*

All interested candidates are invited to reply  
**on or before October 1, 2012**

with a current CV, by mail or email to:

**Dr. Jerry Teitel, Division Head, Hematology and Oncology,**  
St. Michael's Hospital, 2-080 Queen Wing, 30 Bond Street  
Toronto, ON, M5B 1W8  
**teitelj@smh.ca**

## Hematologist or Hematologist/Oncologist

We are currently seeking a Hematologist or Hematologist/Oncologist to join the practice of two general hematologists in Victoria, British Columbia, for the Fall 2013.



**BC Cancer Agency**

CARE + RESEARCH

*An agency of the Provincial Health Services Authority*

Academic appointment is given through the University of British Columbia and the University of Victoria. This would be a possible joint appointment with the BC Cancer Agency. Candidates need to have a broad knowledge of benign and malignant oncology, work independently, be self-motivated and have a strong interest in patient care. Research and medical education opportunities are also available.

The estimated catchment area is approximately 900,000 people, with the majority of patients from the Greater Victoria area (population 400,000). We provide predominantly outpatient clinical care and consultative in-hospital care. On-call responsibilities are shared with medical oncology. Chemotherapy for malignant hematology is administered through the BC Cancer Agency, Vancouver Island Centre in Victoria. Our office has electronic medical records and shared office space is available. We are supported by a team of three hematopathologists, providing a full range of laboratory services. There is also a DVT clinic overseeing anticoagulation.



For further details please contact :

**Dr. Jason Hart: [jhart@bccancer.bc.ca](mailto:jhart@bccancer.bc.ca)**

or

**Dr. Adrian Yee: [ayee@bccancer.bc.ca](mailto:ayee@bccancer.bc.ca)**



# Fellowships

## **Thrombosis Fellowship 2012-2013 Jewish General Hospital, McGill University, Montreal, Quebec**

The JGH Thrombosis Program is currently accepting applications for a one year fellowship (July 1, 2013 - June 30, 2014) to acquire and consolidate expertise in Thrombosis. Specific areas of clinical activity include the Thrombosis Clinic, Anticoagulation Clinic and In-patient Thrombosis Consultation Service.



Jewish General Hospital

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.

For information, please contact:

**Dr. Susan Kahn**

**514-340-7587**

**[susan.kahn@mcgill.ca](mailto:susan.kahn@mcgill.ca)**

## **Thrombosis Clinical & Research Fellowships - Up to 3 positions**

Applications are encouraged from MDs who have completed or who will complete General Internal Medicine, Respiriology and/or Hematology training. Foreign medical graduates with equivalent qualifications are eligible.

Applicants may apply to one of three training streams:

- 1.) Clinical Fellowship**, one-year—To consolidate expertise in thrombosis.
- 2.) Clinical and Research Fellowship**, 2-3 years (to become a clinician investigator in thrombosis (Fellows enroll in the Master's of Clinical Epidemiology Program at the University of Ottawa).
- 3.) Clinical and Education Fellowship**, 2-3 years (to become a clinician educator in Thrombosis. (Fellows enroll in a Master's in Education).

To apply, please contact:

**[nlangois@ohri.ca](mailto:nlangois@ohri.ca)**

*Details are also available on the CHS website.*



*...from Page 3:*

## THE DIAGNOSIS?

### **The Answer:**

The picture shows telomere length results for peripheral blood neutrophils and lymphocytes that are far below the 1st percentile.

Follow-up DNA sequencing showed a Del441E mutation in the TERT gene, a known pathogenic mutation for Dyskeratosis Congenita.

The history of a squamous cell carcinoma of the lip in a non-smoker in combination with a bone marrow failure syndrome prompted the telomere testing in this patient.

## **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.

**For more information: [leukemiabmtprogram.org](http://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](mailto:dforrest@bccancer.bc.ca)**



## Membership Matters

**The Canadian Hematology Society** has represented all physicians and scientists with an interest in the discipline in Canada since its founding 40 years ago in 1971. Our society now has over 300 members.

**Active Membership is open** to physicians engaged in the practice of clinical or laboratory hematology in Canada and to any persons doing scholarly research in hematology in Canada.

In appropriate cases, the requirement for a university degree or other qualifications may be waived if in the opinion of the Executive Committee the candidate is making significant continuing contributions to science.

**We welcome residents and fellows** in approved university training programs in hematology or hematological pathology as **Associate Members**. Associate members will not be required to pay dues until the completion of training.

**Emeritus Membership** is open to individuals at the age of 65 or those who were active members and request a transfer of status with adequate reason. Emeritus members will not be required to pay a membership fee.

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 ...**

to please remit your 2012 Annual Dues. **Your \$75. annual dues payment** may be made online at the CHS website: [www.canadianhematologysociety.org](http://www.canadianhematologysociety.org)

Or mailed to: **Canadian Hematology Society, 199-435 St. Laurent Blvd., Ottawa, Ontario K1K 2Z8**

Please provide the following information with your payment:

### **2012 Membership Renewal: Canadian Hematology Society**

#### **Membership Status**

**Active** ☐

**Associate** ☐

**Emeritus** ☐

#### **Has your status changed?**

**Yes** ☐

**No** ☐

**Name:** \_\_\_\_\_

**Title:** \_\_\_\_\_

**Email:** \_\_\_\_\_

**Work Address:** \_\_\_\_\_

**Work Phone:** \_\_\_\_\_

**Work Fax:** \_\_\_\_\_