Quebec Chapter

Just the Guys Father-Son Weekend–Testosterone at work

On the weekend of October 29, eight young hemophiliacs and their fathers went on an outing to L'Avenir, in the Drummondville area. Martin Kulczyk, our host for the weekend, and Dany Blanchette, gave us a warm welcome.

On Saturday, Catherine Sabourin, a nurse at Montreal Children's Hospital, ran the workshop on injections, which was crowned by a few successes. For the weekend's activities, every older hemophiliac and his father were paired with a younger hemophiliac and his father. People gradually started to feel more comfortable with one another. After lunch, everyone headed for the stables for a riding lesson. The afternoon was hot, and a lively game of soccer broke out. For many of us, this was the highlight of the weekend.

There was also a treasure hunt, a game of pool by the jukebox, and horseshoes. We hung out and talked, and everyone had a great time.

The evening Olympics were a source of laughter and fun, and prizes were awarded to the winners on Sunday morning. More important than the competition and games, each of us made new friends.

Obviously we boys find it harder to talk about what is important to us. But there, at L'Avenir, something very important and memorable happened. We all left feeling stronger and better prepared.

And that's what really counts.

We all left feeling stronger and better prepared.
–A father who participated in the weekend

Hemophilia Ontario

Hemophilia Ontario Youth – Summer Event – The Hiking Trip

On August 12-14, six youth and two supervisors took a trip to the Bruce Peninsula National Park of Canada to hike for three days. This was a first time trip for two youth who have shown enthusiasm for the coming events. The hiking trip was a trial for a summer event and the youth executive will discuss the pros and cons at their next upcoming event in February 2007. Thank you to Baxter and Bayer for their donations and to Julia Sek and Dane Pedersen for leading the youth through the Bruce Peninsula.

OEOR (Ottawa and Eastern Ontario Region)

On August 12, 2006, OEOR held the 12th Annual Shawn Duford Golf Tournament for Hemophilia at the Meadows Golf & Country Club. It was a sunny day, great for golf. Throughout the day there were games and contests, some requiring skill, others for fun. The day concluded with a roast beef buffet dinner, silent and live auctions and a special memorial tribute to Shawn. A great time was had by all and we realized a profit of approximately $23,000.00. We hope to continue this community-building event started by Shawn, as his legacy.

Fiesta Salsera

Fiesta Salsera, the first of what is hoped will become an annual fundraiser, took place this past November 4th.

Benoît Lefebvre, a talented stand-up comedian, acted as Master of Ceremonies throughout the evening as ten groups of dancers, all volunteers, offered remarkably lively and sunny performances, including not only salsa dancing accompanied by latin rhythms, but hip-hop and tap-dancing.

More than 270 participants turned out, contributing to the cause. *Fiesta Salsera* was made possible by the financial support of eleven sponsors.

This new fundraising activity raised $15,000 ($10,350 in net profit). Excellent for a first initiative.

The recipe? A devoted administrative assistant, Geneviève, who as a lover of salsa was determined to blend her passion with fundraising for hemophilia; combined with finding the right sponsors, appropriate advertising of the event, dedicated and optimistic salespeople, and volunteers always ready to help. In short, the work of a team motivated to make this event a success.

Thank you to all our sponsors, volunteers, participants, employees and partners who came together to make this first edition of the *Fiesta Salsera* a resounding success. We hope to see you all again next year.

Camp Wanakita

Camp Wanakita

Another successful year for Camp Wanakita! This year we were able to send 47 campers over a two-week period with three campers participating in the Senior Counselor program. This year we were able to support the 50 campers through generous donations from the Dewdney Foundation, Toronto Star Fresh Air Fund, Wyeth, Baxter and Bayer.

Thank you to the nursing staff who assisted in making the 2006 camp year a very safe and fun summer. Thank you to Betty Ann Paradis, Ann Marie Stain, Diane Bissonnette, Kay Decker, Georgina Floros and Sherry Purcell. A special thank you to Julia Sek and Dane Pedersen for volunteering their time to assist in the Bayer Den.

For 2007, families will need to register with Hemophilia Ontario to ensure their spot at Camp Wanakita. Please contact Sarah Crymble if you have any questions or concerns about the registration process for 2007.

Just the Guys Getaway Camp Ki-Way-Y

SWOR (South Western Ontario Region)

Just the Guys

The fifth annual Just the Guys Getaway was held September 15-17, 2006 at Camp Ki-Way-Y near Kitchener. All of the guys had a chance to try for a bull's eye during archery, swing like Tarzan on the low ropes course, and balance across the beam that was strung high up in the trees. The beautiful weather made it possible to go swimming, canoeing and kayaking. We decorated mini guitars, played messy pudding games, and relaxed around the campfire. The action-packed weekend also included a few education sessions on accessing the emergency room, celebrating your son, and an overview of the services provided by the Society.

A special thanks to Lori Laudenbach, Kay Decker and Keira Evans who were on site all weekend to provide training and medical support to the guys. This joint event between CWOR and SWOR was made possible through the generous support of Bayer, Baxter, and Wyeth.

Pinecrest celebrates

Every day at Pinecrest Adventures Camp is a celebration filled with fun games, silly songs and yummy food. This year there were even more surprises as Pinecrest celebrated its 15th anniversary. It was also the 50th anniversary of Hemophilia Ontario - South Western Ontario Region. Pinecrest Adventures Camp was held August 23 to 27 at Camp Menesetung, near Goderich. Our theme this year was "Every day is a Holiday" and each morning when the campers woke up, they discovered what holiday we would be celebrating that day. Meal times were always a surprise with crazy utensils, Halloween costumes, winter toques, and a favourite of everyone, backwards lunch – you get dessert first! There were lots of holiday crafts and lots of time for games, songs, swimming and campfires.

> Our theme this year was "Every day is a Holiday."

TCOR (Toronto and Central Ontario Region)

2006 TCOR Community Retreat Weekend at Camp Wanakita

The TCOR Community Retreat Weekend at Camp Wanakita was held September 15-17, 2006. The weekend was an opportunity for families within the TCOR community and some special guests from NEOR, to enjoy the benefits, pleasures and overall serenity of being north of the city in a scenic environment. For those who are not familiar with Camp Wanakita, it is located south of Haliburton, Ontario and borders the beautiful Koshlong Lake.

Many participants expressed that they rarely had the opportunity to travel outside the busy city, let alone travel to a camping retreat. The weekend was marked with activities designed to appeal to both the young and young at heart. There were informational sessions that covered such diverse topics as inhibitors, joint replacement and accessing emergency care, as well as more physically challenging sessions such as strength training. Alongside these educational programs there were also camp-oriented activities such as a high ropes course, kayaking and water sports, just to name a few. This provided the opportunity for adults to attend information sessions or check out camp activities while knowing that the younger children were entertained and well taken care of.

Saskatchewan

Guys Getaway

My Dad and I got the chance to go to the Guys Getaway at the Blackstrap Youth Camp, south of Saskatoon. We did a lot of things such as archery, canoeing, camping, having a campfire, swimming and fishing.

On Saturday the first thing we did was talk about home infusions. We practiced mixing the factor and then practiced hitting a vein. This was so we could learn how to give ourselves an infusion. After this A.J. told us what it was like when he was a kid. He shared some of the things that I think most of us could relate to.

The dads and the boys then split up and the kids did scenarios about what to do if… and the dads shared stories of their experiences.

The weekend was a blast. If there is a Guys Getaway next year, I will definitely want to participate and would encourage all other boys and dads to do the same.

> If there is a Guys Getaway next year, I will definitely want to participate and would encourage all other boys and dads to do the same.
>
> **- A child who participated in the weekend**

Manitoba

Just the Guys Getaway, Camp Assiniboia, Manitoba

On September 8 to 10, 2006, six Chapter boys and their fathers/guardians attended the *Step-By-Step* retreat held at Camp Assiniboia. The program for the weekend included information sessions on sporting activities, wrapping joints, making slings, information on how and when to present to the E.R., and much more. All the boys on home treatment were asked to pre-treat on Saturday morning and our care team nurse, Rose Jacobson, facilitated the treatments.

> We all laughed so much and really had a fantastic time.
>
> **–A child who participated in the weekend**

The guys were split into two teams for the weekend: the "Blue Dragons" and the "G.I. Joes". They participated in challenges based on the shows *Survivor* and the *Amazing Race*. It was a fantastic way to encourage team building. Some challenges were pure fun and others required the guys to demonstrate what they had learned. We all laughed so much and really had a fantastic time.

Thank you to Christine Keilback and Rose Jacobson for developing and executing the program for the weekend. Thank you to Cory Prestayko and Hannah Shin for volunteering. Thank you to all the guys who participated. Thank you to CHS and the *Step-by-Step* program for making this possible.

CHS FOCUS ON RESEARCH

The mission of the Canadian Hemophilia Society is to strive to improve the health and quality of life for all people with inherited bleeding disorders and to find a cure. Therefore, research is at the heart of our activities. Over the past 15 years, thanks to the Hemophilia Research Million Dollar Club endowment, generous individual donors, committed corporate sponsors and CHS chapters and regions across the country, the Society has invested more than four million dollars in both clinical and basic peer-reviewed research in Canada. The cure may not yet have been achieved but it is closer every year.

In 2006 the CHS operated three research programs: the CHS Research Program, the Care until Cure Research Program in collaboration with Wyeth, and the Novo Nordisk Canada Inc. – CHS – Association of Hemophilia Clinic Directors of Canada Fellowship in Congenital and Acquired Bleeding Disorders. Descriptions of the programs and the research projects funded in 2006 follow on pages 22 to 25.

The goal of this special feature on research, published each year at this time, is to inform the community of the tremendous work being accomplished and to acknowledge the commitment of the researchers who have worked to improve the quality of life of people with bleeding disorders over the last year.

We would also like to highlight the behind-the-scenes work of the scientists who have volunteered their time in 2006 on the Peer Review Committees to evaluate the grant applications. Without them, the CHS would not be able to operate its research programs. They are:

Dr. Patricia McCusker, *Chair of the Committees*
CancerCare Manitoba
Dr. Lawrence Jardine,
Children's Hospital of Western Ontario
Dr. Michael Nesheim, *Queen's University*
Dr. Fred Ofosu, *McMaster University*
Dr. Bruce Ritchie, *University of Alberta*
Dr. Mary-Frances Scully,
Memorial University of Newfoundland

Looking ahead to 2007, the CHS hopes to attract even more interest in its research programs. To this end, we are holding a Research Summit on February 2, 2007 in Toronto to seek input from researchers, physicians, allied health care providers and other key stakeholders with an interest in bleeding disorders research to advise the CHS on future strategies.

–David Page, *Director of Programs and Public Affairs*

Hemophilia Research Million Dollar Club Report

Joel Hershfield, *Chair*

The Hemophilia Research Grants Review Committee, under the chairmanship of Dr. Patricia McCusker, earlier this year announced the 2006 Hemophilia Research Program grant recipients. Summaries of their projects can be seen on pages 22 to 25. These grants total $140,000 and were made possible by funding provided by the Canadian Hemophilia Society and the Hemophilia Research Million Dollar Club. The Million Dollar Club and the CHS have contributed over $2,600,000 to support hemophilia research in Canada since 1990.

The past couple of years have brought positive changes to the Million Dollar Club. The new Resolution and Policy was unanimously approved by the Canadian Hemophilia Society's Board of Directors and the majority of voting class certificates holders. The resolution clearly establishes the relationship between CHS and the Club.

The Club was also approached by a chapter which wanted to make a generous contribution. As there were no certificates available at the time of their request, the administrators held a meeting and recommended that the voting members approve a motion that there would be no restrictions as to the number of voting class certificates available for purchase. In February 2006, this recommendation was approved by more than a 2/3 majority of the voting class members.

Voting certificates can now be purchased at any time for $5,000 or $1,000 a year for five years and the money placed in the endowment fund. We are prohibited from touching the endowment so that it may generate funding into perpetuity. However, the interest from the fund can be put immediately towards funding current research. Our thrust is two-fold: first to increase the endowment part of the fund which will enhance the ability to generate dollars in the future and, second, to promote donations of non-voting class and honorary certificates that, combined with the interest earned from the growing endowment, will make more money available for research on a current basis.

The Hemophilia Research Million Dollar Club is the most effective way in which you can support bleeding disorders research in Canada. This is "our" fund; it is a tangible and visible evidence of our commitment to research. Every single dollar, whether you purchase a membership or make a donation, goes to research (there are no administration or fundraising costs) and is tax-deductible.

Each year in Hemophilia Today we acknowledge the Canadian Hemophilia Society and all its chapters and regions, and the individuals, families and groups who are members of the Million Dollar Club or have supported us through donations. We also recognize them in the Administrators' Annual Report to the members, and at the Annual General Meeting of the Canadian Hemophilia Society. Once again we thank all of you who are dedicated to supporting bleeding disorders research.

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Enid & Douglas Page
Poyser, O'Shaughnessy & CHS
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Lois Lindner Diane Rudd George
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(In Memory of Gregory Bott)
Jamie Hill
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(In Memory of Andras J. Hordos)
Volunteers from the 1st Annual Road Hockey
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Villeneuve)
Friends and Family of Marjorie Calderwood
(In Memory of Marjorie Calderwood)
Tanya and Flavio Antenucci
(In Honour of Andris Antenucci)

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New Brunswick Chapter
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Nova Scotia Chapter
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Quebec Chapter
Hemophilia Saskatchewan
Hemophilia Ontario
Hemophilia Ontario (On Behalf of the Maynard
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In Memory of Ann Lois Brown
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Elena Kanigan
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In Memory of Raymond
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For Persons with Hemophilia who have Died from AIDS
"So We Never Forget"
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In Memory of Glen Sprenger
In Memory of John Strawa
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Frank and Candy Terpstra
In Memory of Frank Terpstra
In Memory of Troy Christian Trépanier
Dr. Chris Tsoukas
Dr. Irwin Walker
Barbara Webster
Glen Webster

DONORS

The following represent general donations, and those made in honor of Mary MacLeod, and Marjorie Calderwood, and in memory of Ray Abate, Norman Babinec, Martin Bott, George Forbes-Bentley, John Fulton, Jacqueline Hébert, Reverend Stephen Hill, Dr. Barry Isaac, Hazel MacDonald and Art Olson.

Valerie Alexander and Greg Rumpel
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Jean & Ed Maskiewich
Ruth Mesich
Everett Person
Louise Watson
Carole & Dan Young

Canadian Hemophilia Society
Help Stop the Bleeding

CHS Research Program

Supporting research towards improving the quality of life for persons with hemophilia and finding a cure have been goals of the Canadian Hemophilia Society (CHS) since it was founded in 1953. Since 1990, through funds provided by the **Hemophilia Research Million Dollar Club and the CHS**, the Society provides basic scientific research grants and studentships aimed at developing treatments for hemophilia and finding a cure. The following reports describe the projects funded in 2006.

CHS Research Program

The role of X-inactivation in the expression of hemophilia A in women

1st year funding
Wenda L. Greer, PhD
Dalhousie University, Halifax, Nova Scotia

Hemophilia A is an X-linked recessive bleeding disorder resulting from mutations in the factor VIII (FVIII) gene. It is usually expressed in males who inherit only one X chromosome from their mothers. Females inherit one X from each parent. Those who inherit only one mutated FVIII gene usually do not express the disease. Rare examples of hemophilia A manifesting in heterozygous females occur due to an unusual pattern of X chromosome inactivation. This is a mechanism that causes one X in every female cell to be inactivated early in development. It is a mechanism which compensates for the fact that females have a double dose of X chromatin compared to males. In most females, approximately half of the cells inactivate their maternal X and half their paternal X. In rare cases, X chromosome inactivation is skewed. If it is skewed toward the expression of a mutated X chromosome, a heterozygous female can be affected with an X-linked recessive disease.

A family has presented with several males and several females affected with hemophilia A. Analysis of one female showed that most of her cells were expressing the mutated paternal X chromosome. We therefore hypothesized that affected females in this family are expressing hemophilia A due to non-random X inactivation patterns. It is unlikely that random chance could account for the putative dramatic skewing of X chromosome inactivation leading to 3 affected females. This led us to consider that these females have inherited a pre-disposition to skewed X chromosome inactivation patterns.

XCI is controlled in cis by an untranslated RNA coded by the XIST gene. XIST is regulated by the Tsix RNA that is antisense to XIST. It is believed from studies in mice that there is an X chromosome controlling element (XCE) that down regulates Tsix expression and alters the probability of an X chromosome being inactivated.

Our objective is to understand why females in this family are expressing hemophilia A. Our hypothesis is that their X chromosomes containing the normal FVIII gene have been selectively inactivated, leaving only the mutated FVIII available for expression. More specifically, we propose to test the hypothesis that there is a region on the X chromosome that contains an XCE that influences selection and accounts for disease in this family.

Our specific aims are:

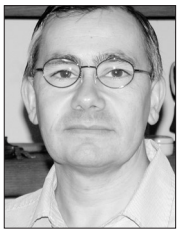
1. To use polymorphic microsatellite markers at 5 cm intervals to compare the X chromosomes of affected and unaffected female siblings with skewed and random X-inactivation patterns, respectively. Hypothetically, regions where they differ should define the critical region of the putative XCE.
2. To further compare these X chromosomes using micro-array CGH to look for regions of duplication, deletion and differential methylation (collaboration with Dr. Wan Lam, Toronto).
3. To develop a cell culture model system to study the process of X-chromosome inactivation in females. With this testable system, we will determine if X-inactivation is under genetic control. It will also provide a tool to localize the XCE gene.

This study will provide answers for this family and insight into the basic biology of X-chromosome inactivation.

CHS Research Program

Implantable microcapsules as gene therapy for hemophilia A

1st year funding
Dr. Gonzalo Hortelano
McMaster University, Hamilton, Ontario



We will evaluate the feasibility of cell transplantation therapy to reverse severe hemophilia A in mice. Although current factor VIII (FVIII) products are safe, patients must endure life-long, regular FVIII infusions. Thus, a safe and more economic treatment is desirable.

Gene therapy is an alternative. Gene therapy strategies use virus as vehicles to introduce the FVIII gene, but they are associated with undesirable immune responses. Alternatively, transplanted cells producing FVIII are only temporarily functional. We propose the transplantation of non-autologous cells (not from the patient), genetically engineered to continuously produce FVIII. To avoid rejection of the transplanted cells, they are enclosed in tiny microcapsules (less than 1 mm in diameter) before being transplanted. The microcapsules allow the free flow of FVIII, but are impermeable to immune cells, therefore protecting the enclosed cells.

We found that mice transplanted with microcapsules containing muscle cells engineered to secrete factor IX (FIX) contained high amounts of factor IX in the blood for at least 120 days and did not mount an immune response to human FIX. More importantly, this treatment was able to reverse the disease in severe hemophilia B mice. If this were achieved in humans, it would eliminate severe and moderate hemophilia. Therefore, we will apply the same strategy to hemophilia A.

Initially, we will engineer muscle cells to produce FVIII, and determine the amount of FVIII they produced. Second, we will enclose FVIII-producing cells in microcapsules that will then be transplanted into mice to determine how much FVIII is found in blood, and for how long. Any immune responses to FVIII will be studied. Finally, the correction of the disease

in hemophilia A mice will be investigated.

This transplantation therapy could reduce and ultimately eliminate the need for regular FVIII injections. Importantly, the microcapsules can be removed, increasing the safety of the treatment.

CHS Research Program

Genetic differences between obligate carriers of Type 3 VWD and individuals with Type 1 VWD

2nd year funding
Dr. Paula James
Queen's University, Kingston, Ontario

Von Willebrand disease (VWD) is the most common known inherited bleeding disorder in humans, affecting as many as 1% of the population. People with VWD have difficulty with bleeding from mucous membranes such as the nose, mouth or lining of the uterus, or can have problems with bleeding after injuries, dental work or surgical procedures. There are 3 subtypes: Type 1 VWD is the most common and least severe and is caused by a mild to moderate deficiency of a blood clotting factor called von Willebrand factor (VWF). Type 3 VWD is the least common and most severe and is caused by a severe deficiency of VWF. Type 2 VWD is caused by VWF that doesn't function properly.

Type 1 VWD is inherited from one parent while Type 3 VWD is inherited from both parents. In this study, we are interested in examining the genetic changes in VWD. A person affected with Type 1 VWD would have inherited it from one parent, while a person affected with Type 3 VWD must have inherited it from both parents. A parent of an individual with Type 3 VWD is usually not affected by any bleeding problem and is referred to as a "carrier". By using special techniques that allow us to examine an individual's genetic make-up, we hope to improve our understanding of the types of genetic changes that might lead to Type 1 VWD and those that would lead to being a carrier for Type 3 VWD.

Care Until Cure

The **Care Until Cure Research Program** was established in the year 2000 in collaboration with **Wyeth Canada**. Wyeth Canada is engaged in the discovery, development, and commercialization of human pharmaceuticals through recombinant DNA and other technologies.

This program allows Canadian investigators to conduct research on various medical and psychosocial aspects of bleeding disorders. Grants are given for clinical research, including outcome evaluation, in fields relevant to improving the quality of life of persons with hemophilia, persons with von Willebrand disease or other inherited bleeding disorders, persons with related conditions such as HIV or hepatitis C as well as carriers of an inherited bleeding disorder. The following reports describe projects funded in 2006.

Care Until Cure

Creating meaningful messages for individuals with mild hemophilia through consultation: integrating grounded theory and action research

1st year funding
JoAnn Nilson, PT
Saskatoon, Saskatchewan

This multi-phased project brings individuals with mild hemophilia and physiotherapists together to create more meaningful educational materials *specifically* for people with mild hemophilia. The Canadian Physiotherapists in Hemophilia Care (CPHC) have serious concerns about gaps in patients' understanding of mild hemophilia. Young adults with mild hemophilia are often seen in the emergency room days after a traumatic incident with an uncontrolled bleed which then takes weeks or months to totally resolve. These clinical experiences suggest that the educational materials and strategies currently in use that target individuals with severe hemophilia are not effective in providing information that facilitates those with mild hemophilia to seek care in a timely manner.

The purpose of this study is to consult young adults with mild hemophilia, parents of children or adolescents with mild hemophilia and Physical Therapists (PTs) from across Canada in order to identify appropriate communication strategies to be used in educational material about health and healthcare *specifically for people with mild hemophilia*. In Phase 1 we will focus on the lived experiences of young adults with mild hemophilia from four locations in Canada. Through semi-structured interviews, we will learn about participants' internal 'processes' and choices that they make in accessing medical care after injury, learn about messages, information and knowledge that participants feel would motivate them to seek care in a timely manner. During Phase 2, the knowledge gained in Phase 1 will be used to guide a group of PTs from across Canada. They will identify educational strategies that are grounded both in the experiences and attitudes of individuals with mild hemophilia and in the realities of the health care system. In Phase 3, these strategies will be further refined during focus groups of young adults and PTs and parents of children with mild hemophilia and PTs in both French and English. This phase will also include written or telephone consultation with young adults with mild hemophilia who live in rural settings. Participants from each phase will be invited to continue their involvement in the project through written or verbal feedback after each phase.

This research will help to develop a model that demonstrates a viable way of integrating the perspectives and knowledge of patients and health care professionals in order to create the most meaningful, client-centred, realistic educational strategies specifically for people with mild hemophilia.

Care Until Cure

Haemostatic changes during pregnancy in healthy women and women with inherited bleeding disorders presenting with menorrhagia

2nd year funding
Dr. Christine Demers
Centre hospitalier universitaire affilié de Québec
Quebec City, Quebec

Inherited bleeding disorders are associated with a wide spectrum of clinical symptoms depending on the type and the severity of the disease. During pregnancy, the risk of bleeding is generally low in affected women, because the levels of many of the coagulation factors naturally rise over the course of a pregnancy. However, the risk of bleeding can be significant at delivery and after the pregnancy (during the postpartum period), because these levels once again fall to the baseline. In fact, it has been demonstrated that the risk of postpartum hemorrhage is increased to 10 to 25% in women with bleeding disorders compared to less than 1% in the general population. Management is difficult, in part, because there is a lack of information concerning variation of the coagulation factors during pregnancy both in normal women and in women with bleeding disorders.

In this study we are planning to recruit 2 groups of women: 20 normal and 25 with an inherited bleeding disorder. The first objective of this study is to evaluate how the levels of coagulation factors vary over the course of pregnancy in both groups, and also to determine the rate with which these coagulation factors return to the baseline after delivery. Coagulation factors will be measured 3 times during pregnancy, at delivery and 4 times in the 4 weeks postpartum. We will try to co-ordinate this blood testing, whenever possible, with the regular testing of pregnancy

Postpartum bleeding is very difficult to assess and at the present time there is no way of objectively measuring it. However, there is a graphical chart that has been extensively evaluated in women with heavy periods. The second objective of the study is to evaluate

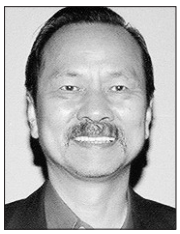
if a modified version of the chart is a useful tool to measure postpartum bleeding. All women will complete the pictorial chart during the four weeks postpartum.

With this study, we hope that a better understanding of coagulation during and after pregnancy will result in a better management of pregnancy for women affected with inherited bleeding disorders.

Care Until Cure

Investigation of clotting factor activity heterogeneity in severe hemophilia A

2nd year funding
Dr. Man-Chiu Poon
University of Calgary
Calgary, Alberta



People with severe hemophilia (clotting factor activity below 1%) tend to bleed frequently and spontaneously into joints, leading to disabling arthritis. The current standard of treatment is regular, preventative factor concentrate infusion. This primary prophylaxis started at an early age improves quality of life but the treatment is intensive, representing a burden to those with hemophilia and their families. It is also expensive. Often, a device is implanted to facilitate infusion and this may be complicated by infection and thrombosis.

Among severely affected individuals, approximately 10-15% have milder than expected bleeding symptoms. It is important to identify these people so that their treatment can be customized, avoiding unnecessary infusion. We believe that some severe patients have factor VIII in their blood, but below the 1% detectable by routine laboratory methods. Furthermore, in the ongoing Canadian Prophylaxis Trial (Dr. Victor Blanchette), some severely affected need only once or twice weekly FVIII infusion – the FVIII levels would be below 1% for a period before the next infusion and yet appear protective.

The focus of this research is to develop a sensitive assay to accurately measure circulating factor VIII levels between 0 and 1%, based on measurement of the activity of the enzyme, thrombin, that develops in proportion to the level of FVIII activity present. Three aspects of hemophilia treatment will then be investigated with participation from clinics across Canada. First, we will measure FVIII activity on 200 severe hemophilia A persons at a time when they have not been treated for 5 days or more (or at diagnosis) to determine if their "baseline" FVIII levels have a bearing on when they had their first spontaneous joint bleeding. We will take into account whether the affected individuals have inherited other mutations thought to promote clotting despite very low FVIII activity. Secondly, for patients in the Canadian Dose Escalation Prophylaxis study (Dr. Blanchette), we will measure the plasma FVIII level prior to their next FVIII injection. This may help discover the minimal FVIII level that will protect against bleeding and hence determine the frequency of FVIII infusions. Lastly, we will investigate (with Dr. Carcao) if the baseline FVIII level of severe hemophilia A persons can be related to how much FVIII is recovered after an injection, and how quickly the recovered FVIII disappears.

The focus of this research is to develop a sensitive assay to accurately measure circulating factor VIII levels between 0 and 1%, based on measurement of the activity of the enzyme, thrombin, that develops in proportion to the level of FVIII activity present.

In conclusion, this study will assess the minimum level of FVIII below 1% that is still protective to help customize treatment for individuals with severe hemophilia.

The Novo Nordisk Canada Inc. – Canadian Hemophilia Society – Association of Hemophilia Clinic Directors of Canada Fellowship in Congenital and Acquired Bleeding Disorders
is a fellowship program established in the fall of 2001. Novo Nordisk has a leading position within areas such as coagulation disorders, and manufactures and markets pharmaceutical products and services that make a significant difference to patients, the medical profession and society.

The goal of this fellowship program is to provide fellows in hematology or other relevant fields the opportunity to acquire clinical or research skills necessary to improve the care and quality of lives of patients with hemophilia and other congenital or acquired bleeding disorders. The following report describes the project funded in 2006.

Novo Nordisk Fellowship

Evaluation of thromboelastography (TEG) as a tool in monitoring the effect of recombinant factor VIIa in hemophilia A animal models

Dr. Maha Ahmed Othman
Queen's University, Kingston, Ontario

Despite similar factor levels, hemophiliacs often display variable tendencies for bleeding and heterogenous responses to factor VIII (FVIII) therapy. To date, no routinely used coagulation assay has proven ideal in predicting the bleeding pattern in hemophilia or reflecting the individual patient's response to therapy. Conventional assays typically use clot formation as the end point and underestimate the impact of other components of the hemostatic process.

Thromboelastography (TEG) is a global assay that assesses the quality of the blood clot and monitors different aspects of the hemostatic process. It provides information about the kinetics of the blood clot and thus a more comprehensive picture of coagulation than standard tests. Recombinant coagulation factor VIIa (rFVIIa) (Novoseven™) is a safe and effective treatment for hemophilia A and B patients with inhibitors. However, laboratory monitoring of the therapeutic efficacy of this product is still a problem. Bleeding risk does not correlate well with the standard clotting tests and the treatment response also cannot be adequately monitored.

In this study, we have two major goals: 1) to investigate the TEG pattern in hemophilia A animal models with and without inhibitors and evaluate the sensitivity of this test to variations in clinical phenotype and 2) to evaluate changes in the TEG pattern following administration of rFVIIa in therapeutic doses to these animals and to correlate this to clinical phenotype correction.

These studies have the potential to significantly improve our understanding of the clinical heterogeneity among hemophiliacs. This may help predict individual bleeding risks and improve the laboratory monitoring of rFVIIa therapy.

Important international study looks for causes of inhibitors

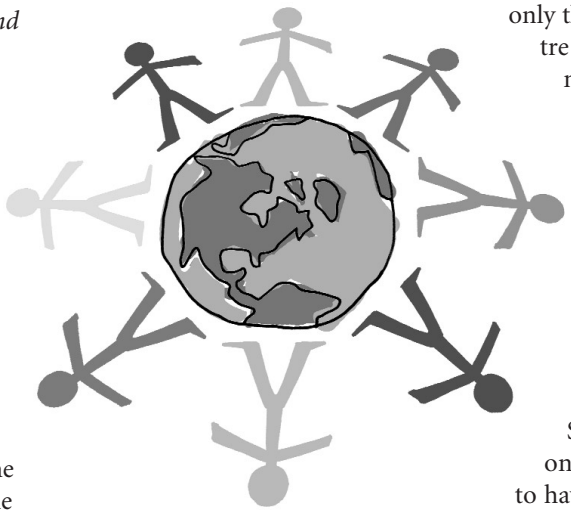
More participants needed

David Page, *CHS Director of Programs and Public Affairs*

As of October 31, 2006, investigators from 63 centres in Europe, North America and Australia have agreed to participate in the Hemophilia Inhibitor Genetics Study (HIGS).

The objective of the HIGS is to determine genetic factors, other than mutations within the factor VIII gene, that are associated with the development of inhibitors in severe hemophilia A. The chief investigator is the renowned Erik Berntorp, MD, PhD, of the Malmo University Hospital, Malmo, Sweden.

With the advent of safe clotting factor concentrates, it is well accepted that inhibitors currently represent the most important complication of hemophilia. Up to 30% of people with severe hemophilia A develop inhibitors at one time or another in their lives. Up to 10% of these patients are affected by a persistent inhibitor which makes treatment more difficult and less effective.



Unfortunately, their causes remain unclear.

Inhibitors are rare, their causes likely varied. It is only through large, international, multi-centre studies with many participants that the mystery will be unravelled.

As of this writing three Canadian centres, Hôpital Ste-Justine in Montreal, Hospital for Sick Children in Toronto and the Dr. John Akabutu Comprehensive Centre for Bleeding Disorders in Edmonton, are among the 63 centres that have agreed to participate. Hôpital Ste-Justine, under the leadership of Georges-Étienne Rivard, Sylvie Lacroix and Claude Meilleur, is one of the six centres around the world to have enrolled 60% of the 130 families currently participating.

Recruitment of families and centres is continuing. The study is open to families with severe hemophilia A and a history of inhibitors. Families interested in participating should contact their hemophilia clinic director or CHS at 1 800 668-2686 for more information.

OUR STORIES

Amber and Karine: a harrowing experience

Patricia Stewart,
Member, CHS Program Committee

When 11-year-old Karine Loiselle went in for a routine tonsillectomy in North Bay, Ontario in 2005, her life, and that of her mother, Amber Chevrette, was changed forever. Karine's surgery lasted twice as long as usual, and her mother began to worry that something was wrong. Afterwards, the surgeon explained that there was difficulty with Karine's bleeding, and that they should get this checked out. They went home to Timmins the next day, but nine days later, before they had had a chance to arrange an appointment for testing, Karine woke up during the night coughing up blood. They rushed her to Timmins and District Hospital where she began vomiting blood. Once the bleeding was stopped, they returned home, but were told to return immediately if it happened again. Within hours they had to rush back to the hospital where Karine continued vomiting blood and eventually fainted.

"Karine's father and I thought we were going to lose our daughter," said her mother Amber. "I have never seen someone lose so much blood. The basin was full!"

Karine was weak, terrified and confused. It's a nine-hour drive from Timmins to the Children's Hospital of Eastern Ontario in Ottawa, so their pediatrician, Dr. Willem Verbeek, immediately had Karine transferred by air ambulance. There, her bleeding was controlled by surgery and she then underwent testing and was diagnosed with mild Type 1 von Willebrand disease (VWD).

In hindsight, with the information she learned from the CHS Web site, Amber says she now realizes that Karine had all the symptoms of a bleeding disorder… and so did she. They both bruise easily and suffer from heavy menstrual bleeding (menorrhagia). Since this incident, Amber is still undergoing testing for VWD. As a young girl, she suffered from menorrhagia, but didn't know it could be caused by a bleeding disorder. No one spoke about her menstrual periods. Amber also noted that she sometimes suffered from bleeding following sexual relations. She would regularly miss two to three days of work each month due to menorrhagia and eventually had a hysterectomy to solve the problem. Her daughter's diagnosis with VWD arrived two days before her own surgery.

Karine, now 13 years old, also suffers from menorrhagia, sometimes having two periods a month, and is undergoing treatment to control it. She has learned to live with her VWD, and wears a MedicAlert bracelet. Both Karine and her mother are now registered at the Hemophilia Treatment Centre in Ottawa. Amber's two other children, a 3-year-old son and an 11-year-old daughter, will be tested soon so as to avoid having to go through similar experiences should they have this disorder. Amber sent out emails to her whole family following Karine's diagnosis with VWD, and referred them all to the CHS Web site for information.

Medication will help her have a normal life, and education about VWD will enlighten her life experiences.

"Reviewing my history and seeing the symptom list now gives me answers as to why my life experiences were what they were. I am so glad that we now know what to do and that Karine will not have to suffer through her 'womanhood' like I did," writes Amber. "Medication will help her have a normal life, and education about VWD will enlighten her life experiences."

Amber wishes to thank the Cochrane District Social Services Administration Board (CDSSAB), the Emergency Medical Services in Timmins, Derrick Cremin and Jeff Fletcher, and their pediatrician, Dr. Willem Verbeek, for their quick action in helping her daughter.

FAMILIES IN TOUCH

Karen Creighton
Mississauga, Ontario

Back to basics

Some things never change, withstanding the test of time and confirming the need to keep these good practices in place. Our ability to support each other is the very foundation of our organization. The Canadian Hemophilia Society has recently launched two on-line support initiatives to help our members connect with each other and keep in touch.

The *Step by Step Forum*, is an interactive meeting place for parents across Canada. On a regular basis, an issue related to raising a child with a bleeding disorder is posted. Read what parents are talking about or add your own thoughts and questions, the choice is yours. *Parent to Parent* is an on-line program intended to help users identify other parents they would like to communicate with directly, by matching parents up with other parents who may have had similar experiences and can share some thoughts and understanding. You are truly missing out on something special if you haven't had the opportunity to connect with other parents like yourself.

To learn more about the CHS *Step by Step Program* and to participate in the *Forum* or *Parent to Parent* please visit www.hemophilia.ca/en/stepbystep.php. Registration is free and you only have to register once in order to participate.

In Medicine Hat, Alberta, families of children with bleeding disorders are not feeling isolated. On the contrary, these families get together regularly to help each other by providing emotional support, listening to each other, providing understanding and relating to each other in a way only people who share the same challenges can.

Lori and Mike Watt have four children, ranging in age from seven to thirteen. Dylan is the youngest of the Watt children, the only boy and the only child with a bleeding disorder. He was diagnosed at 31 gestational weeks, shortly after his premature birth. By eight months he was diagnosed with inhibitors to factor VIII as well as porcine factor VIII. Medicine Hat is a three-hour drive from the Hemophilia Treatment Centre in Calgary. Lori recalled feeling very alone. Dylan was the first new case of hemophilia in the region in 35 years. She and Mike gathered as much information as they could and began to learn about and experience the reality of raising a child with hemophilia. Fortunately, they had the interest and support of a wonderful local pediatrician, Dr. Hendrik Hak, who made himself available to deal with their questions and their needs from day one and onwards. He was instrumental in supporting them as a family and in supporting the nurses and staff in paediatrics as well. Their sense of isolation, however, was acute.

The staff at the Calgary Hemophilia Treatment Centre provided Lori with the name of a parent willing to speak with her. In Lori's words, "She was a breath of fresh air to my overwhelmed soul." Even though Susan had an older child, Lori realized she could ask her questions; she was encouraged by her and by meeting her son who was doing well. Lori also got in contact with an adult with hemophilia. Todd visited Dylan and his parents during many hospital stays. Once again she was struck by his ability to offer them so much encouragement and practical information. It was great for Dylan as well to connect with a fellow patient. Both experiences left them feeling hopeful. The role of the clinic in connecting them with patients had been handled professionally, safeguarding confidentiality and giving the patients the choice to meet and or be put in contact with each other.

"She was a breath of fresh air to my overwhelmed soul."

Not surprisingly, when Lori heard about a mom from her hometown in Saskatchewan who had a son with hemophilia, she made contact. She called Clara Penner. Clara and Curtis Penner have two children. Braxton is eight and his little sister Blayne is five. Clara remembers the night Lori called her. "I was so thankful to have someone to talk to who did not feel sorry for me and Brax, but understood all my fears as I did hers." Clara reflects, "We became fast friends and still keep in touch seven years later. This friendship for me has been amazing."

Lori and Dylan Watt.

Guess who was matched up with Chrissy and Sean Eld, when their son Greyson was diagnosed with hemophilia? The Elds agreed to be contacted by another patient family as part of the voluntary support made available to new families at the Hemophilia Treatment Centre. Lori made the initial call, only this

time Chrissy wasn't ready to talk with another mom. However, when her son Greyson needed his first treatment because of a muscle bleed, Chrissy found Lori's number and called right away. Lori arranged to meet them, as she had to pick up blood products for her son that day at the hospital. They met while they were waiting for Dr. Hak to arrive on the paediatric floor. Lori provided whatever assistance she could during Greyson's first treatment. Chrissy later realized there was more than another mom on the paediatric floor that day, there was a supportive medical team and a history with processes developed to deal with the needs of another family that had come before Greyson. In Chrissy's words, "Mike, Lori and Dylan made it so much easier for us. The path was set out for us to follow and Lori was able to help us see we were doing fine and we could look forward to the future."

> "We became fast friends and still keep in touch seven years later. This friendship for me has been amazing."

Balancing the demands of working, taking care of other children in the family and their needs, and being available for medical support is an ongoing challenge for all families. Our solutions are different depending on how we handle each of these areas in our lives. Chrissy and Clara manage most of the front line care issues for their sons, while either Mike or Lori manage Dylan's needs. Mike appreciates the times he and Clara have talked things over on the phone. The association these families have with each other has enabled all family members to benefit from meeting each other… not just the moms, and not just the boys. Gatherings feel like social events. It is creating these opportunities that is so important. The encouragement flows naturally from the shared experiences and common challenges.


Clara and Braxton Penner with Chrissy and Greyson Eld.

Between Greyson, Braxton and Dylan, there have been ports, serious bleeds, inhibitors and hospital stays. All these things can take an emotional toll on young children. Clara recounted the first time her son Braxton met Dylan Watt. The boys are about a year apart in age. When they met for the first time, they both had ports. It didn't take long for the boys to show each other their ports and talk about them. This experience had a positive emotional impact on the boys, especially in regards to feeling different from other children.

The benefits this group is deriving from their combined efforts are invaluable to each of them. Clara and Curtis decided to move to Medicine Hat to be close to the outstanding medical support they knew Dylan was receiving. They believe this has been the right move for Braxton and their family and wish they had done it even sooner. Clara is particularly aware of quality of care issues, having been diagnosed with mild hemophilia at the age of thirteen. Now that Braxton is medically well supported, she is finding the confidence to expect and access quality care for herself. Clara recently sought and received treatment for a hip bleed that she admits, she may have not pursued in earlier days.

For Chrissy and Sean Eld, access to families that had already experienced ports, inhibitors and immune tolerance therapy helped them cope with the challenges they were experiencing with their son. This support gave them strength, knowledge and helped Chrissy manage the front line care issues with growing confidence. In Chrissy's words, "I feel we have been so blessed through our struggle with this disorder." She describes Dr. Hak as "the perfect paediatrician". Their local support team also includes an RN, Kara, who knows the boys, the families and their bleeding histories. The local care team and families all rely on the back-up of the Hemophilia Treatment Centre at the Alberta Children's Hospital in Calgary and the hands-on support of the Nurse Coordinator, Morna Brown, and the clinic team. Greyson's entry into the school system has been a positive experience. Staff have been willing to learn about hemophilia and how to accommodate Greyson. He is attending the same school Braxton goes to, and this has been helpful for both families.

Lori and Mike have helped and been helped by these families. The impact on the children has also been invaluable. Lori talked about the many times she called Clara for a second opinion, especially when a problem came up during non-clinic hours. Clara and Curtis were the first couple they met with a child close to Dylan's age and with a similar medical profile. Lori, Chrissy and Clara emailed me some of their thoughts on the gift of mutual support they have created amongst themselves. The theme of appreciation for each other is apparent. Mike Watt included his thoughts and captures the essence of it all in these words.

There is an African proverb which states:"It takes an entire community to raise a child." We feel this is very much applicable to the world of hemophilia. Our community naturally includes doctors, nurses, physiotherapists and lab techs. But it also includes other parents and patients. The benefit of having people involved in our lives and the life of our son who have travelled this road before us cannot be underestimated. A new diagnosis of hemophilia can be terribly overwhelming. But having someone else come along side and tell you, "It's going to be okay," to help you through those times of fear and doubt, and to talk you through those periods of questioning and uncertainty not only offers you strength, encouragement and support, but it gives you hope.

There are now a total of eight families giving and receiving support in Medicine Hat. I sincerely hope people who read this article and wish they had this type of encouragement, will take the time to get involved in the CHS *Step by Step Forum* and the *Parent to Parent* on-line meeting place. The understanding of someone who shares the same situation is one of the greatest coping mechanisms we have.

Many thanks to the Watt, Penner and Eld families for sharing their experiences with us. Your achievements are inspirational.

Hep C Press Review

Jeff Rice, *CHS Hepatitis C Program Coordinator*

New drug combo helps hepatitis C

ORLANDO, Fla., Oct. 30 — Researchers from Saint Louis University School of Medicine are reporting preliminary results of a study that suggests a new drug combo may help between 15 percent and 20 percent of people who don't respond to current therapies for treatment of the hepatitis C virus.

Bruce R. Bacon, MD, principal investigator, indicates that patients who typically do not respond to the current treatments — pegylated interferon and ribavirin therapy — have the most severe liver disease. "We are desperately trying to find things to use to treat this group of patients," Dr. Bacon said.

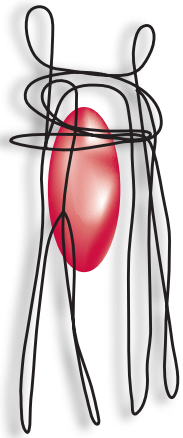
> "There really isn't anything for this population of non-responders, and now it looks like there's something and there's some evidence that shows it works."

He and colleagues tested the combination of ribavirin and Infergen — a highly potent form of interferon — on more than 500 patients, more than three-quarters of whom had severe liver disease. Between about 15 percent and 20 percent of the patients tested negative for the hepatitis C virus after six months after the end of treatment.

While the results are preliminary, Dr. Bacon says he's encouraged by what he's seen so far. "There really isn't anything for this population of non-responders, and now it looks like there's something and there's some evidence that shows it works."

Making babies the old-fashioned way

Earlier this year, the CHS produced the booklet, *Family Planning Options: A Guide for Serodiscordant Couples*, available for download at: www.hemophilia.ca/en/pdf/5.0/Sero_Int_EN.pdf.



A recent report suggests that natural conception may be a safe option for serodiscordant heterosexual couples. The conclusions of the Spanish study reported in the November 1 issue of the *Journal of Acquired Immune Deficiency Syndromes* suggest that unprotected vaginal intercourse to achieve pregnancy, provided that the HIV-positive partner is on HIV drug treatment and has an undetectable viral load, may be associated with a minimal risk of HIV transmission.

Previous studies have documented that HIV-positive people with "maximally suppressed" virus while on HIV drug treatment are significantly less likely to pass their virus along to their sexual partners. Spanish researchers took a look at the transmission risk associated with natural conception among mixed-status couples, in which the HIV-positive partner had an undetectable viral load as a result of antiretroviral therapy.

The authors reported that, in all cases, the HIV-negative partner remained uninfected. There was, however, one case of mother-to-child transmission. Aside from their conclusion that mixed-status couples "attaining natural pregnancy are exposed to a negligible risk of sexual transmission of HIV when the infected partner has an undetectable viral load while on HIV drug treatment," the researchers also provided the following useful conception recommendations:

"If the couple has opted for natural pregnancy, undetectable viremia is mandatory and pregnancy is discouraged in patients with any levels of HIV replication. Other transmissible infections (e.g., viral hepatitis), cofactors that can increase the risk of transmission (e.g., inflammation, infection or dysplasia of the genital tract), and fertility potential should all be evaluated carefully before attempting natural conception. It is important to advise these couples to restrict overt sexual contacts to fertile days exclusively, for which the use of ovulation tests may be recommended. Pregnancy attempts should be limited in number, and couples should receive medical reassessment if conception does not occur in three to six months."

Positive interim results of phase 2 trials of Albuferon™ with ribavirin in patients with chronic hepatitis C

BOSTON, October 31 — According to Dr. David Nelson from the University of Florida, interim results of two Phase 2 clinical trials to evaluate the efficacy and safety of Albuferon™ (albumin-interferon alpha 2b) in combination with ribavirin in patients with chronic hepatitis C, "continue to suggest that Albuferon may offer efficacy at least comparable to pegylated interferon for treatment-naïve patients, with similar safety, fewer injections and the potential to improve health-related quality of life".

"The results emerging from our Phase 2 program continue to build support for our belief that Albuferon could become an important therapeutic option for patients with chronic hepatitis C," said Mani Subramanian, MD, PhD, Senior Director of Clinical Research, Infectious Diseases, Human Genome Sciences (HGS).

Interim results from the first 24 weeks of treatment were presented from a randomized, open-label, multi-centre, active-controlled dose-ranging Phase 2b trial of Albuferon in combination with ribavirin in treatment-naive patients with genotype 1 chronic hepatitis C. The interim results suggest that Albuferon in combination with ribavirin was safe, well tolerated and showed robust antiviral activity in these patients.

Albuferon is a novel, long-acting form of interferon alpha, which was created by HGS using the Company's proprietary albumin fusion technology. This technology enables scientists to improve the pharmacological properties of therapeutic proteins by fusing the gene that expresses human albumin to the gene that expresses the active protein. Albuferon results from the genetic fusion of human albumin and interferon alpha 2b. Recombinant interferon alpha is approved for the treatment of hepatitis C, hepatitis B and a broad range of cancers.

THE BLOOD FACTOR

David Page,
CHS Director of Programs and Public Affairs

Quebec introduces no-fault compensation legislation for blood injury

The Quebec government has introduced legislation that would create Canada's first no-fault compensation plan for injuries acquired through transfusion.

Bill 45 modifies existing legislation regarding Héma-Québec and the Hemovigilance Committee. If passed by the National Assembly, it would create a system to provide financial assistance to anyone injured from a transfusion or transplant distributed by Héma-Québec without regard to negligence.

Such legislation has two principal benefits: rapid assistance to those injured without the burden of lengthy legal action, and protection for Héma-Québec from the need to contract expensive insurance coverage. There have been no claims against the manufacturer and distributor of blood, blood products and their substitutes, cells, tissues and organs since its creation in 1998.

The proposed legislation would allow three years from the onset of symptoms of injury in which to make a claim. Appeals would go before an Administrative Tribunal. Injured individuals would not be barred from making civil claims against other parties. Compensation would follow the model of the Quebec Automobile Insurance Plan which provides lump sums based on degree of injury, salary replacement, reimbursement of certain medical costs and re-training.

The Canadian Hemophilia Society has long called for no-fault insurance for blood injury. Compensation claims for injuries suffered in the 1980s, specifically hepatitis C infection acquired before 1986 and after 1990, are not yet completely settled.

Niastase approved for acquired hemophilia in U.S.

The U.S. FDA has approved Niastase®, recombinant factor VIIa manufactured by Novo Nordisk, for the treatment of acquired hemophilia, a rare and potentially fatal bleeding disorder.

"The approval of NovoSeven®* for use in patients with acquired hemophilia offers an effective choice for treating this life-threatening disorder," said Craig Kessler, Professor of Medicine and Pathology, Georgetown University Medical Center.

Acquired hemophilia can strike without warning. People affected have no inherited bleeding disorder; the causes of the condition are not well known.

Acquired hemophilia happens in up to 4 persons per million per year. It disrupts the body's natural blood clotting process, causing spontaneous, uncontrolled bleeding to occur, most often, in the skin and soft tissues. Acquired hemophilia can strike without warning. People affected have no inherited bleeding disorder; the causes of the condition are not well known.

Niastase is already approved in many countries, including Canada, for use with patients with hemophilia A and B and inhibitors which reduce the effectiveness of traditional clotting factors. Niastase was first introduced in 1999.

* The brand name of Niastase outside Canada is NovoSeven.

Novo Nordisk announces development of heat-stable Niastase

Novo Nordisk has announced that it expects to file for regulatory approval of a heat-stable version of NovoSeven (Niastase) in mid-2007. This would allow room-temperature storage.

The company also announced that a Phase III study for the use of the blood-clotting drug in prophylactic treatment of hemophilia patients with inhibitors is expected to be initiated during the first half of 2007.

Possible competitor for Niastase

GTC Biotherapeutics Inc. has created an agreement with LFB, a French company, to develop a treatment for hemophiliacs from the milk of genetically altered rabbits.

LFB Biotechnologies, a subsidiary of LFB S.A. of Paris, will invest $25 million in GTC and become its largest shareholder as the two companies collaborate on the development of a recombinant form of factor VIIa, a protein in blood plasma that is involved in clotting.

GTC will develop the rabbits and hold exclusive rights to products in North America. LFB will handle clinical development and regulatory matters and have exclusive commercial rights in Europe.

If the firms are successful, their product would compete with Niastase (NovoSeven), a recombinant form of factor VIIa sold by Novo Nordisk.

GTC is best known for developing female goats that carry human genes, which makes them capable of producing milk loaded with human proteins that can be processed and used in medical treatments. The company's goats make a recombinant version of antithrombin III, a clotting regulator, which was approved this year by regulators for sale in Europe under the name ATryn®.

GTC officials said that they will use rabbits instead of goats to make a recombinant factor VIIa because LFB has done some of its research in rabbits and because rabbits will produce enough milk and protein to meet the demand for factor VIIa for human studies and commercial sales.

"Remarkably, a rabbit produces somewhere between six and ten liters of milk a year," a company official said.

THE female FACTOR

Patricia Stewart

All About Carriers

Meeting the needs of hemophilia A & B carriers

The term *carrier* is a bit of a misnomer. Men who "carry" the defective hemophilia gene are called hemophiliacs, while women are "only carriers". The needs of women who are carriers of hemophilia are becoming more and more evident. They have long been unrecognized, including by the women themselves. As mothers or siblings, they have been so focused on the hemophiliacs' condition that they never thought that their own symptoms might be related to their carrier status.

The Carrier Project was created in order to offer women and girls information and tools to deal with their medical and psychological needs as carriers. In order to have a better idea of these needs, a Task Force with women from various age groups along with hemophilia medical personnel developed a questionnaire that was distributed to focus groups held across the country and through chapters and clinics. Topics ranged from family history to personal medical needs related to a bleeding disorder, to psychosocial needs as carriers and mothers of children with hemophilia. To date, over 60 questionnaires have been completed by women from 2 to 82 years of age having factor levels ranging from less than 1 percent to 82 percent.

Mild hemophilia is defined as a condition that occurs when clotting factor levels are between 5 percent and 30 percent. This means that many women with these levels actually have mild hemophilia, but this is seldom recognized. They are simply referred to as carriers, continuing the myth that women can't have hemophilia. However, many women stated that despite having levels higher than 30 percent, they had experienced bleeding problems that were discounted.

"As a mother, I was expected to diagnose bleeding episodes in my son. I can't imagine why I would not be competent to know when I am bleeding!"

"I lived with extremely heavy periods ruling my life and seeing doctor after doctor with none of them testing me until I was 40."

The majority of women surveyed were diagnosed as carriers after the birth of their child with hemophilia, even when hemophilia was in the family. Many indicated the benefits of early diagnosis as carriers. They said that support in the form of genetic counselling before pregnancy and after the birth of a child with hemophilia amounted to little more than a quick explanation of the facts and was seldom sufficient.

Early diagnosis as carriers of hemophilia would have permitted some women to make life decisions based on the information.

"If I had known my status, I might have decided against having children."

"I think I was in denial that even though it was in my family, I didn't think it would happen to me."

The decision to have a second child after having a first child with hemophilia, or even because of a carrier status, sometimes elicits harsh judgement from family, friends, and even from medical personnel. But by far one of the most difficult emotions that carriers expressed is the guilt associated with passing on hemophilia to their children. Some are living with the complications of a blood transfusion, while others are still fearful of another virus infecting treatment products.

"I feel responsible for putting my son through so much pain and agony."

According to studies, 52 percent of carriers suffer from heavy menstrual bleeding (menorrhagia). For many women who answered the questionnaire, their understanding of not only their gynecological problems but also other medical problems fell into place with their diagnosis as carriers. Few women, however, are registered at their local Hemophilia Treatment Centres. The need to work with hemophilia health care providers to ensure standardized practice in terms of access to care for carriers was recognized by all women surveyed.

All About Carriers, the new information booklet for women and girls, will be launched in May 2007 in Quebec City during *Rendez-Vous Québec*. Along with the booklet, a workshop will be organized for carriers. The CHS will be funding one woman per chapter to attend with the goal that they will bring the knowledge and workshop model back to their own chapters to share with other women.

CANADIAN PHYSIOTHERAPISTS IN HEMOPHILIA CARE

PHYSIOTHÉRAPEUTES CANADIENS EN HÉMOPHILIE

Where do you find 25 wheelchairs?

Catherine van Neste, PT, *Centre hospitalier universitaire affilié de Québec, Quebec City*

Where do you find 25 wheelchairs? How do you get a physiotherapy plinth from the hospital to the Conference Centre? These were just a few of the challenges with establishing the first Physiotherapy Treatment Room at the 27th World Federation of Hemophilia Congress. Yes, it was an exciting year for the Hemophilia Clinics of British Columbia with Vancouver as the host of WFH Congress 2006. It was an honour to have the responsibility for organizing the first Physiotherapy Treatment Room at a WFH Congress.

The physiotherapy treatment room was located in the Convention Centre adjacent to the medical treatment room. Physiotherapists were able to provide treatment for the management of acute bleeds to people with hemophilia (PWH) alongside the physicians and nurses. The Canadian Physiotherapists in Hemophilia Care (CPHC) and a consulting team of international physiotherapists who specialize in hemophilia care staffed the room.

During the conference the CPHC treated 38 PWH from 27 countries. It was a great learning experience for the CPHC to have the opportunity to treat the global community of PWH. The team of physiotherapists was kept busy with treating numerous joint bleeds of which 40% were ankle bleeds and 35% knee bleeds. The members of CPHC were able to use their therapeutic skills to assess and treat all of the acute joint bleeds.

Some of the treatments included providing walking aids and wheelchairs to the PWH to help rest painful joints yet enabling the PWH to attend the various meetings and, of course, to enjoy Vancouver's sights and scenery. We used numerous boxes of tubigrip as the word got around that the compressive sleeves were easy to pull on the affected limb and an excellent aid for swelling control. Other treatments included the use of ice, fabrication of splints and modification of footwear. We provided exercises to help with range-of-motion, strength and balance, always with the goal to improve functional mobility.

The positive experience of managing acute bleeds without the use of factor

A survey was conducted to give the CPHC the opportunity to reflect and comment on their experiences in the Physiotherapy Treatment Room. Many positive comments were received and the most rewarding aspect was the opportunity to treat and educate the many PWH who had never seen or been treated by a physiotherapist who is specialized in hemophilia care.

With the lessons learned at the treatment room in Vancouver, a physiotherapy treatment room will hopefully be included in a comprehensive treatment centre at the next WFH Conference in Istanbul, Turkey in 2008.

THE GLOBAL PERSPECTIVE

Twinning makes a difference

Candace Terpstra, *Toronto and Central Ontario Region (TCOR)*

Simply stated, *twinning* is all about improving the quality of life for people with hemophilia as well as improving care and treatment. The Jordanian Hemophilia and Thalassemia Society (JHTS) was officially twinned with TCOR early in 2003 as hemophilia organizational twins (HOT). A medical centre twinning between the St. Michael's Hemophilia Program and Al-Bashir Hospital in Amman was officially recognized by the World Federation of hemophilia (WFH) in November of 2005. Our most recent visit to the Kingdom of Jordan took place in July 2006.

The Society, now operating under the patronage of Queen Rania, has built a solid reputation among patients and key hemophilia health care providers. The Society continues to organize patient meetings for educational and support purposes, publish two newsletters per year, run a Mothers and Young Children Group as well as a Youth Group (formed in 2005), and a voluntary physiotherapy clinic initiated this year. In July of 2006, Board members, together with key volunteers, held their first strategic planning event with good results. Also in July, the Society held its first ever "Heroes for Hemophilia Youth Camp" – a raging success, enjoyed by all who were fortunate enough to attend. Youth spoke of the importance of their "shared experience", getting to know others with hemophilia, the willing participation of doctors in camp activities, and with Ann Harrington as Camp Nurse, how much they learned about themselves, their condition and the importance of teamwork. They left with renewed resolve, having brainstormed a significant list of goals for themselves – a small group of courageous young men facing an uncertain future.

In January of 2005, the Minister of Health signed an agreement with the WFH to institute the Global Alliance for Progress or GAP program. Through this WFH program, much needed resources have been applied to medical training in order to improve care, particularly in the Ministry of Health facilities. For each of the past three years, the Society has worked in collaboration with the World Federation of Hemophilia and the Jordanian Ministry of Health and hemophilia treaters to sponsor an annual symposium on hemophilia care and outreach presentations to the north and south of Amman. Dr. Bernadette Garvey from St. Michael's Hospital has been instrumental in educating medical personnel in Jordan as well as increasing cooperation among physicians from the various levels of care. Considerable effort has also been made to train nurses, physiotherapists and laboratory technicians using Canadian volunteers including Ann Harrington, hemophilia nurse, and Kathy Mulder, physiotherapist, along with other WFH volunteers, Dr. Paul Giangrande, Dr. Jerome Wiedel and Lara Oyesiku, RN. Upcoming plans for 2007 include a laboratory technician and two nurses traveling to St. Michael's for training.

For the very first time on this most recent trip we were able to meet with doctors in the southern part of the country, only to discover a shortage of product and a lack of identifiable hemophiliacs. Without product, patients are forced to travel north to Amman for treatment or forego treatment altogether.

Most significantly, the differences for the person with hemophilia are notable. Hemophilia treatment is now considered a priority in Jordan. A plan to test and confirm the diagnosis for all patients with hemophilia was instituted in 2006 and to date approximately eighty people have been tested. This screening forms the basis of a National Registry for the country of Jordan. For the first time, these patients have been tested, not only for bleeding disorders, but also for inhibitors and hepatitis, including hepatitis C. The collaboration between the JHTS, the Ministry of Health and key medical personnel has been essential to the success of this process.

…through the twinning, patients are learning about their condition, what they can do to manage their bleeding episodes, the importance of prompt treatment, the need to learn self-infusion…

Perhaps, the most remarkable difference for patients is the increased availability of factor VIII concentrates, a good thing in a country which continues to rely on cryoprecipitate to address any shortfall in concentrate. Also through the twinning, patients are learning about their condition, what they can do to manage their bleeding episodes, the importance of prompt treatment, the need to learn self-infusion… and more significantly, their role in the Society as advocates for optimal support, education, care and treatment for all patients with bleeding disorders.