



**Network of Rare Blood Disorder  
Organizations**

**Réseau des associations vouées  
aux troubles sanguins rares**

## **2009 Progress in Comprehensive Care for Rare Blood Disorders Conference**

November 13-15, 2009 – Mississauga, Ontario, Canada

Presented by

**CSL Behring**

Biotherapies for Life™

***Conference proceedings***

*Version 2*

## Network of Rare Blood Disorder Organizations (NRBDO)

Aplastic Anemia and Myelodysplasia Association of Canada (AAMAC)  
Canadian Association for Porphyria (CAP)  
Canadian Hemophilia Society (CHS)  
Canadian Hereditary Angioedema Network (CHAEN)  
Canadian Immunodeficiencies Patient Organization (CIPO)  
Canadian Neuropathy Association (CNA)  
Canadian Organization for Rare Disorders (CORD)  
Canadian Sickle Cell Society (CSCS)  
Quebec Sickle Cell Anemia Association (QSA)  
Sickle Cell Association of Ontario (SCAO)  
Sickle Cell Disease Parents' Support Group of Ottawa (SCDPSC)  
Thalassemia Foundation of Canada (TFC)

[www.hemophilia.ca/en/about-the-chs/collaboration/network-of-rare-blood-disorder-organizations](http://www.hemophilia.ca/en/about-the-chs/collaboration/network-of-rare-blood-disorder-organizations)

E-mail: [nrbdo@hemophilia.ca](mailto:nrbdo@hemophilia.ca) Phone : 1-800-668-2686

The 2009 Progress in Comprehensive Care for Rare Blood Disorders  
Conference was made possible through the generous support of

**CSL Behring**  
Biotherapies for Life™

**ALEXION™** | innovators in  
pharma canada | complement  
inhibition™



**2009 Progress in Comprehensive Care for Rare Blood Disorders Conference**  
**Table of Contents**

Executive Summary .....	1
Friday, November 13 – Patient Registries .....	6
<b>Opening Remarks .....</b>	<b>6</b>
<b>Objectives of the Day .....</b>	<b>6</b>
<b>Session 1: Primer On Health Informatics .....</b>	<b>7</b>
<b>Session 2: What Is A Registry? .....</b>	<b>9</b>
<b>Session 3: Examples of Current Registries.....</b>	<b>12</b>
Observations on the International Blood and Marrow Transplant Registry .....	12
OneMatch Stem Cell & Marrow Network.....	14
European Society for Immunodeficiencies (ESID) Online Patient and Research Database .....	15
Alexion Global Paroxysmal Nocturnal Hemoglobinuria (PNH) Registry .....	17
Canadian Hemophilia Registry (CHR) .....	19
Canadian Hemophilia Assessment Resource Management information System (CHARMS).....	20
The Platelet type von Willebrand Disease (PT-VWD) Registry .....	21
Canada Vigilance Adverse Reaction Monitoring Program and Database .....	22
<b>Session 4: Privacy, Security, Ownership and Governance Issues .....</b>	<b>24</b>
<b>Session 5: Panel on How to Encourage the Establishment of Patient Registries .....</b>	<b>25</b>
<b>Day One Wrap-Up .....</b>	<b>29</b>
Saturday, November 14, 2009 – Progress in Comprehensive Care .....	30
<b>Objectives of the Day .....</b>	<b>30</b>
<b>Session 6: Review of Recommendations from 2006 NRBDO Conference .....</b>	<b>30</b>
<b>Session 7: Progress And Lessons Learned In Canada.....</b>	<b>33</b>
Edmonton Rare Blood Disorders Program .....	33
Quebec Primary Immunodeficiencies Network.....	34
Patient Perspective: Progress in Comprehensive Care for Hereditary Angioedema .....	36
Proposal for A Coordinated Adult Primary Immune Deficiency Clinic in British Columbia.....	37
Patient Perspective: From Intravenous to Subcutaneous Immunoglobulin Therapy.....	39
Home Treatment for Children with Primary Immunodeficiency Diseases .....	40
Canadian Guidelines for the Diagnosis and Treatment of Primary Immune Deficiency .....	41
Canadian Myelodysplastic Syndromes (MDS) Practice Guidelines .....	43
Comprehensive Childhood Bone Marrow Failure And Myelodysplasia Program.....	45
Standards of Care for Hemophilia .....	46
Transitioning from Pediatric to Adult Care in Sickle Cell Disease and Hemophilia .....	48
Canadian Thalassemia Treatment Guidelines.....	50
<b>Session 8: Models for Comprehensive Care .....</b>	<b>52</b>
Commissioning for Rare Conditions in England .....	52
Audit of Hemophilia Treatment Centres in the U.K. and Ireland.....	54
<b>Day Two Wrap Up.....</b>	<b>58</b>

Sunday, November 15, 2009 – Workshops ..... 59  
**Workshop 1: National Collaboration and the Role of Patient Organizations ..... 59**  
**Workshop 2: Barriers, Challenges, and Shortcomings ..... 61**  
**Workshop 3: Priority Areas Needing Action ..... 64**  
**Workshop 4: Strategies and Action Planning to Address Priority Areas ..... 65**  
**Closing Remarks ..... 70**

## **Executive Summary**

### **Introduction**

The 2009 Progress in Comprehensive Care for Rare Blood Disorders Conference was held November 13-15 in Mississauga, Ontario. This was the second conference of the Network of Rare Blood Disorders Organizations (NRBDO) since it was founded in 2004. The conference was attended by over 75 participants from Canada, the United States, and Europe including people with rare blood disorders, patient groups, medical experts, and blood services and industry representatives.

The conference's main objectives were to assess the progress made in different disease areas since the 2006 NRBDO Conference on Comprehensive Care for Rare Blood Disorders, examine effective patient registries and models of comprehensive care in Canada and abroad, and identify priorities and strategies for moving forward.

### **Development of Patient Registries**

Sessions on the first day focused on patient registries. Patient registries are used to gather data related to a particular disease or condition such as prevalence, patient demographics, and treatment modalities and outcomes.

Health informatics specialist Gavin Tong described the pivotal role of information technology in helping improve access to health services, enhance quality of care, and contribute to a more efficient and effective healthcare system. There are many initiatives underway in Canada and steady progress being made towards creating an integrated Canadian health information system.

Magda Melo of St. Michael's Hospital in Toronto outlined the key purposes and components of a patient registry. A registry can be developed for one or numerous purposes; for example, to study the natural history of a disease, determine clinical and/or cost effectiveness, measure or monitor safety and harm, and measure or improve the quality of care. Careful planning with well-defined objectives and clear policies and procedures on data collection and governance is essential.

Leading experts gave presentations on a range of national and international patient registries. Dr. Christopher Bredeson described the International Blood and Marrow Transplant Registry, which began as an observational database but now also supports assessment of risk factors and transplant outcomes, technology assessment, and clinical trials. Different people can benefit from a registry, and responsibilities can be shared effectively across multiple partners. However, operations and overall responsibility for the registry need be centralized in one place.

Jennifer Philippe of the OneMatch Stem Cell and Marrow Network gave an overview of the national donor registry, which strives to find stem cell and bone marrow donors matching patients in Canada, and the registry's linkages with international organizations and repositories. The registry data has also been useful in the development of recruitment strategies towards building a donor base that reflects the demographics and needs of the Canadian population.

Dr. Gerhard Kindle described the European Society for Immunodeficiencies Online Registry, which collects long-term patient data towards improving the diagnosis, classification, prognosis and treatment of primary immunodeficiencies. More than 200 primary immunodeficiencies have been identified but there are many knowledge gaps. The registry enables combined evaluation of genetic and clinical data, genetic and therapeutic trials within ESID, and research across centres.

Michael Bombara gave an overview of the Global Paroxysmal Nocturnal Hemoglobinuria (PNH) Registry created by Alexion Pharmaceuticals. The registry collects long-term data on clinical outcomes, quality of life, morbidity and mortality for patients with PNH, including long-term safety and effectiveness data from patients treated with the Alexion drug, eculizumab.

Dr. Anthony Chan described the Canadian Hemophilia Registry, which collects anonymized clinical data on patients with hemophilia and other inherited bleeding disorders. The registry helps promote research in hemophilia and other bleeding disorders. Dr. Bruce Ritchie then outlined the Canadian Hemophilia Assessment Resource Management Information System.

Dr. Maha Othman presented the Platelet type von Willebrand Disease (PT-VWD) Registry launched in 2006. PT-VWD is a very rare disorder that can be challenging to diagnosis because of its similarities to type 2B VWD. The PT-VWD Registry is a global study that is compiling DNA samples to determine whether this disorder is under- or misdiagnosed. Preliminary results show that many type 2B VWD and PT-VWD cases have been incorrectly diagnosed.

Heather Sutcliffe of Health Canada gave an overview of the Canada Vigilance Adverse Reaction Monitoring Program and the MedEffect™ Canada Initiative, and experiences in terms of data collection and management within the requirements of different legislative frameworks. This was followed by a presentation by legal expert Michael Power on the privacy, security and governance issues that must be addressed in patient registry development.

The day closed with a panel discussion on how to encourage the establishment of patient registries. Panelists emphasized the importance of being transparent about the registry objectives and data collection, having good governance practices and privacy policies, and ensuring that the registry's goals resonate with patients, physicians as well as researchers.

In terms of the NRBDO's goal to establish patient registries for rare blood disorders, there was consensus amongst the panelists that the ideal way forward would be to create one common national registry with individual modules for specific diseases. This would allow clinicians to both contribute data and derive information from the central registry, and also would facilitate international collaboration.

Development of a common registry also offers opportunities to leverage a broader range of expertise, stakeholders and funders than individual patient registries. However, given that the diseases have very distinct characteristics, there would inevitably be major challenges in terms of database programming. Still, there was overall support for developing a national registry for rare blood disorders with universal elements such as consent processes and data management and capacity to be adapted for specific disease areas and investigations.

## **Comprehensive Care for Rare Blood Disorders**

The second day focused on the progress being made towards the establishment of comprehensive care for rare blood disorders in Canada, lessons learned, and challenges moving forward.

Silvia Marchesin began with an overview of the vision for comprehensive care developed at the 2006 NRBDO conference. Foremost, there was consensus for the Network of Rare Blood Disorder Organizations, collectively, and its member organizations individually, to advocate with provincial/territorial governments for comprehensive care for rare blood disorders. Essential components of comprehensive care were identified—provincial/territorial designation, national patient registries, multidisciplinary care, defined core services delivered by a comprehensive care team, self/family administration of therapeutics, and standards of care, among others.

Sessions covered a wide range of comprehensive care programs in British Columbia, Alberta, Ontario and Quebec, Canadian treatment guidelines and standards of care, and international models of healthcare services for rare disorders.

Dr. Nancy Dower gave an overview of the Edmonton Rare Blood Disorders Program, which provides comprehensive care for all inherited bleeding disorders. The program encompasses education, treatment, multidisciplinary care, home infusion therapy, and transition from pediatric to adult health services. There are now over 800 patients registered in the program.

Dr. Jacques Hébert described the Quebec Primary Immunodeficiencies Network's goals to improve treatment for patients with primary immunodeficiency diseases and hereditary angioedema, and its successful efforts to advance home therapy. The physician group persuaded health authorities to switch patients from hospital-based to home therapy and from intravenous therapy to subcutaneous therapy, on the basis of the clinical benefits for patients and economic benefits for healthcare funders. Patients should be involved in decisions on treatment regimen.

Harriet Lyons described her journey towards being diagnosed with hereditary angioedema and progress in treatment and comprehensive care achieved over the past 20 years, including the development of a treatment protocol and access to new therapies through the Health Canada Special Access Program.

Dr. Robert Schellenberg spoke about the progress towards creating an adult clinic for primary immunodeficiencies and subcutaneous treatment for patients in British Columbia. Then Michael Whelan, a B.C. resident with primary immunodeficiency disease, described the significant impacts of intravenous immunoglobulin therapy and subcutaneous home therapy on his health and quality of life. He also shared some of the self-advocacy techniques he has developed to make sure that his healthcare providers understand his disorder and how it is managed.

Dr. Christine McCusker described how Montreal Children's Hospital came to establish a comprehensive care program for primary immunodeficiencies, including intravenous and subcutaneous home treatment options. For other hospitals and provinces interested in setting up home therapy for patients with primary immunodeficiencies, there are now a number of centres in Canada that can supply help, advice, protocols and information.

Dr. Bruce Mazer presented the Canadian guidelines on the use of immunoglobulin therapy for patients with primary immune deficiency, developed in 2009 by a national panel of experts convened by Canadian Blood Services and the National Advisory Committee on Blood and Blood Products. The guidelines aim to provide guidance on the complexities of diagnosis of primary immunodeficiencies and treatment with immune globulin therapy, and help standardize care.

Dr. Rena Buckstein spoke about the importance of practice guidelines and described the development of the Canadian consensus guidelines on the use of iron chelation to treat iron overload in patients with myelodysplastic syndromes. Then Dr. Yigal Dror described the comprehensive childhood bone marrow failure and myelodysplasia program at Hospital for Sick Kids and the importance of a multidisciplinary approach to treatment of these conditions.

David Page of the Canadian Hemophilia Society spoke about the development of standards of care for hemophilia and other inherited bleeding disorders, which was driven by patient needs and best practices. Dr. Robert Klaassen then described the pediatric to adult care transition programs for sickle cell disease and hemophilia at Children's Hospital of Eastern Ontario and Ottawa General Hospital.

Dr. Isaac Odame presented the recently developed Canadian treatment guidelines for patients with thalassemia, which aim to ensure that clinical practice in Canada is up to date with current evidence-based best practices. The guidelines set out the multidisciplinary team and services that should be accessible to people with thalassemia and treatment steps from diagnosis to laboratory evaluation, initiation of transfusion therapy, monitoring for iron overload, and chelation therapy.

Dr. Edmund Jessop gave a keynote presentation on the organization of comprehensive care for patients with rare conditions in England. The main services are medical procedures, disease management and diagnostics, provided at a small number of specialist centres in England. The core principle is that with very rare conditions, volume drives excellence; health professionals need to see a high volume of patients in order to develop strong diagnostic and practical skills, which are key to managing the unusual presentations and complications of very rare diseases.

## **Moving Forward**

While progress has been made in different disease areas and parts of Canada, there are ongoing challenges that need to be addressed to advance comprehensive care for rare blood disorders. The final day consisted of plenary workshops in which participants discussed strategies for advocacy and collective action, and opportunities for collaboration among patient groups, health professionals and other specialists, industry and government. The key priorities identified were:

- Develop relationships with all levels of government.
- Ensure continuation of the Network of Rare Blood Disorder Organizations.
- Identify expertise and resources to advance comprehensive care and patient registries.

- Advocate for support and funding.

The next steps towards advancing comprehensive care for rare blood disorders include:

- Publicize already established comprehensive care centres throughout Canada.
- Promote awareness of the NRBDO among health authorities, professional and patient organizations, and by engaging media.
- Engage federal/provincial/territorial representatives in discussion on the benefits of comprehensive care for rare blood disorders.
- Develop physician and patient brochures on diagnosis and treatment of rare blood disorders.
- Develop standards of care by disease group based on the comprehensive care model.
- Create a registry of specialized clinics and expert clinicians that can provide guidance or referral services.

The next steps towards advancing the development of patient registries include:

- Establish an NRBDO patient registry working group to examine existing models and determine the best way for patient groups in Canada to proceed.
- Involve physicians/specialists in the development of patient registries and identify physician champions who can help lead the way.
- Involve experts from other disciplines (information technology specialists, health informatics specialists, security and privacy experts, etc.).
- Develop a strategy to obtain funding for development of patient registry, operations, administration and maintenance.

It is vital to continue the momentum towards improving care and establishing comprehensive care for individuals with rare blood disorders in Canada. Moving forward, collaboration and partnership with the medical community, government and industry, will be critical.

## **Friday, November 13 – Patient Registries**

### **Opening Remarks**

**Conference Co-Presidents: Michel Long, Program Coordinator, Canadian Hemophilia Society  
Tina Morgan, President, Canadian Immunodeficiencies Patient Organization**

The 2009 Progress in Comprehensive Care for Rare Blood Disorders Conference was held November 13-15 by the Network of Rare Blood Disorder Organizations (NRBDO). Conference Co-President Michel Long welcomed more than 75 participants from across Canada and the United States, United Kingdom and Germany. This was the second national conference of the NRBDO since the coalition of patient groups came together in 2004 to work towards access to comprehensive care for Canadians with rare blood disorders. The three-day meeting drew a broad range of participants and international experts: people with rare blood disorders, patient groups, physicians, epidemiologists, researchers, and blood services and industry representatives.

Conference Co-President Tina Morgan set out the objectives of the conference:

- Examine Canadian and international comprehensive care models.
- Establish the foundations for the development of national patient registries.
- Share experiences and best practices towards achieving the common goal of comprehensive care for people with rare blood disorders throughout the country.

The conference's overall aim was to provide information to support patient organizations in their work to raise awareness about the need for comprehensive care for rare blood disorders, advocate for treatment, and develop initiatives for better care.

The first day focused on patient registries, which are important to advancing comprehensive care for rare blood disorders. Patient registries help quantify how many people are affected with a particular disorder, provide prevalence estimates, define demographics, measure treatment outcomes, and facilitate research.

### **Objectives of the Day**

**Co-Chairs: Dr. Bruce Ritchie, Association of Hemophilia Clinic Directors of Canada  
Silvia Marchesin, Aplastic Anemia Myelodysplasia Association of Canada**

Patient registries help advance treatment, education and research related to rare blood disorders, and monitor the use and safety of blood products—therefore, they are key to setting up comprehensive care for rare blood disorders in Canada, said Dr. Bruce Ritchie. The objectives of the first day were to examine models of comprehensive care, strategies for developing national registries, and ways that patient organizations and clinicians can move forward with registry development. The potential benefits of information technologies and related challenges and issues such as privacy and security would also be explored.

## **Session 1: Primer On Health Informatics**

**Gavin Tong, Director, Gordon Point Informatics, Ltd.**

Gavin Tong gave an overview of how health informatics in Canada has evolved over the past 30 years, current initiatives related to electronic health records, and some considerations for the development of an effective national patient registry for rare blood disorders.

Health informatics is a multidisciplinary field that brings together health sciences, management sciences, and information sciences to obtain better health information and achieve better health outcomes. Health information has primary and secondary uses:

- Primary use information is used directly by physicians, clinics and hospitals in the provision of care at the patient level (e.g., patient profile, medical history and treatment products).
- Secondary use information is used by governments, researchers and advocacy groups towards improving the delivery of care at the healthcare system level.

Canada's Health Informatics Association (COACH) was established in 1975 as the Canadian Organization for the Advancement of Computers and Health. Its main objectives are to advance the use of information technology in the Canadian health system to improve health care; it has been a strong supporter of electronic health records.

The terms “electronic health records,” “electronic medical/patient records,” and “personal health records” are often used interchangeably due to some common characteristics. In general, they are complete, up-to-date records with medical information on individual patients such as physician visits, hospital visits and stays, diagnostic imaging and laboratory test results, immunizations and prescribed medications.

However, from the health informatics perspective, there are important distinctions:

- Electronic health records refer to records collected within a health information system and network (e.g., pan-Canadian registry) that provide information on the health of Canadians.
- Electronic medical records refer to patient records localized in hospitals or doctors' offices.
- Personal health records refer to paper or electronic health records kept by patients.

There has been steady progress over the past decade towards the creation of an integrated pan-Canadian network of electronic health record systems. Canada Health Infoway (CHI), a government-funded organization established in 2001, has played a pivotal role in establishing pan-Canadian health records. Canada Health Infoway works with federal, provincial and territorial governments to help them build electronic health information systems. The main goal is to establish an electronic health record information system in Canada that links clinics, hospitals, pharmacies and other points of care so that healthcare providers, with specific

permission from patients, can access electronic health records in order to make informed decisions about their treatment.

Canada Health Infoway provides health informatics expertise and guidance, while the provincial and territorial ministries of health are responsible for the actual development and implementation of electronic health records. Its most powerful contribution has been the development a basic blueprint for a pan-Canadian Electronic Health Record Infostructure. Its key components are:

- Ancillary data and services such as outbreak management and public health reporting.
- Health information data warehouse containing anonymized information that may be accessed and used for research purposes such as comparative statistical analysis.
- Electronic health records data and services such as shared health records and drug information, and diagnostic imaging and laboratory services.

The ultimate goals and benefits of a national electronic health information system are improve access to health services, enhance the quality of care, ensure patient safety, and contribute to a more efficient and effective healthcare system.

In closing, Gavin Tong offered this advice on how to get started with planning and developing a patient registry: “List the top 10 questions to answer, determine what is core and what is not. Once you know the questions, you can come up with novel ways to capture answers. Over time, though, the questions start to evolve—and therein will lie the challenges of trending to more meaningful questions.”

## **Session 2: What Is A Registry?**

**Magda Melo, Research Manager, Observational Epidemiological and Qualitative Research Unit, Applied Health Research Centre, St. Michael's Hospital, Toronto**

The Applied Health Research Centre at St. Michael's Hospital in Toronto provides support to researchers at the hospital and throughout Canada by helping them coordinate clinical trials and multi-centre studies, and develop patient registries. Magda Melo described the purpose of a patient registry, issues related to planning, and basic elements and good practices for developing and evaluating a patient registry.

It is important to differentiate “registry” from “patient registry.” A registry generally refers to the recording or registering of data and the record itself, as in a database. The definition of patient registry is much more precise. A patient registry is an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition or exposure, and that serves one or more pre-determined scientific, clinical or policy purposes.

### **Planning A Patient Registry**

1. Articulate the purpose(s). A registry can be developed for a single or multiple purposes:
  - Study the natural history of a disease
  - Determine clinical and/or cost effectiveness
  - Measure or monitor safety and harm
  - Measure or improve the quality of care
2. Determine whether the data are already being collected elsewhere. (Is it accessible? Can relevant data be extracted from electronic health records or health insurance data?)
3. Determine whether a registry is the most appropriate means. Consider adapting a registry or linking to other relevant data sources (including piggybacking onto other registries).
4. Identify the stakeholders. The primary stakeholders are those who require the data, create and fund the registry; and the secondary stakeholders, are those who would benefit from the knowledge produced or be impacted by the results but they are not instrumental in establishing the registry. Examples of stakeholders include:
  - regulatory authorities
  - product manufacturers
  - healthcare service providers
  - payer or commissioning authorities
  - patients and/or advocacy groups, treating physician groups
  - universities or professional societies
5. Define the scope of the registry. This should include planned representativeness of the target population and characteristics of data to be collected.
6. Assess feasibility and likelihood success.

## Registry Design

When designing a patient registry, it is important to define its specific objectives, structure and the process for data collection. In addition, ensure that the registry effectively addresses the important questions through the appropriate outcome analyses.

- **Scope of Data**
  - Size (number and complexity of data points, enrollment of investigators and patients)
  - Setting (hospital, doctor's office, pharmacy or home)
  - Duration (period and length of time to collect and analyze data)
  - Geography (local, provincial, national or international)
  - Financing (costs depend on the amount and complexity of data collected)
  - Richness of clinical data
  - Scientific rigour of certain outcomes
- **Core Data Set**

Core data are the “need to know” data in order to address central questions. Non-core data are “nice to know” speculative fields that are useful for generating and exploring hypotheses. It is important to avoid collecting large amounts of data of limited value.
- **Patient Outcomes**

Primary and secondary endpoints need to be identified early in the design phase of the registry; this will guide the selection of the data set. It is also important to establish methods to ascertain the principal outcomes, diagnostic requirements and level of data validation.
- **Target Population**

Define the population to which the findings of the registry are meant to apply. The definition should be consistent with established guidelines and standards within the therapeutic area.
- **Registry Team**

A registry involves: clinical experts, epidemiologists, biostatisticians, data collection and management specialists, legal/privacy experts, quality assurance specialists, project manager.
- **Funding**

The cost of a registry is determined by the scope of the registry, the rigour of data collection, and whether an audit is required. Other factors include the projected life of the registry and/or its long-term sustainability. Potential sources of funding include: government, foundations, professional societies, industry, and health plan providers.
- **Governance**

Governance refers to guidance and high-level decision-making, including concept, funding, execution, and dissemination of information. Functions to consider include:

  - Executive or steering committee (financial, administrative, legal/ethical and scientific decisions; direction of the registry)
  - Scientific (database content, clinical research, epidemiology and biostatistics)
  - Liaison (large registries)
  - Adjudication (review and confirm outcomes)
  - Data Safety Monitoring Board
  - Data access, use and publications

Sponsors and participants should have an understanding of the proposed lifespan of the registry, who owns the data, and where data will be stored. It is also important to plan for transitions to continue the registry functions after the original funding sources have expired.

It is important to plan how to deal with requests from investigators seeking to access registry data to perform analyses for the purpose of submitting abstracts to scientific meetings and developing manuscripts for peer-reviewed journal submission. Some registries have processes in place to deal with data access requests, such as scientific and publications committees. These committees evaluate research proposals before access to data is granted. They may also have processes that require review of manuscripts before they are submitted to journals to ensure that the interpretation of the results of the registry takes into account the limitations of the data.

## **Session 3: Examples of Current Registries**

This session presented an overview of a range of national and international patient registries and their benefits and limitations, and challenges related to funding, governance and data privacy and security. The objective was to identify the best practices and elements for the development of a registry framework for Canadians with rare blood disorders.

### **Observations on the International Blood and Marrow Transplant Registry**

**Dr. Christopher Bredeson, Director, Hematologic Malignancies, Professor of Medicine, Medical College of Wisconsin, Milwaukee, USA**

Patient registries are very useful and valuable towards improving both individual patient care and overall health care for specific chronic diseases and conditions, said Dr. Christopher Bredeson. He shared some observations on successful outcomes from the International Blood and Marrow Transplant Registry (IBMTR) and lessons of practical relevance to current and future efforts to develop patient registries.

#### ***Purpose and Objectives***

The International Blood and Marrow Transplant Registry is based at the Center for International Blood and Marrow Transplant Research (CIBMTR), in Milwaukee, Wisconsin. It collects and monitors outcome data on people with diseases who undergo bone marrow transplant or blood stem cell transplant procedures. The registry is an observational database mainly for the purpose of research rather than to affect policy or clinical practice.

#### ***Registry Design***

Different people can benefit from a registry depending on its focus and design; some of these groups are also potential sources of funding. Therefore, when developing a patient registry, it is important to think in fairly broad terms about what data would be useful and valuable to collect.

The primary purpose of the IBMTR Registry is outcome research. Its specific functions are:

- Maintain an international database of clinical information on recipients of autologous and allogeneic bone marrow and blood stem cell transplants.
- Collate basic data on the core set (registration data on all patients in member centres) and comprehensive data on a subset of patients for research purposes.
- Provide scientific and statistical support for analyzing the data.

The core set involves about 50 different fields of data, which were established following 2.5 years of negotiation by multiple countries. The subset research database is much more comprehensive, with about 5,000 possible fields.

When the registry was first set up in 1972, there were only two centres involved. By 1985, the registry had 200 centres and 1,000 blood and marrow transplant cases and had contributed to 35 articles and publications; that same year, it began to receive funding from the National Institutes

of Health (NIH). This was all achieved with one doctor as scientific director, one statistician, three data management specialists and one administrative assistant—which shows that an effective registry can be done without significant funding, Dr. Bredeson said. Today, there are 500 centres in more than 50 countries in the IBMTR registry, and 60,000 transplant cases.

The power of the IBMTR Registry lies in its capacity to be adapted to address new questions. Its uses have evolved over time from descriptive analysis to assessment of risk factors and transplant outcomes, technology assessment and, more recently, as part of clinical trials and in study design. “Start small and dream big, and you can get there,” he said.

Dr. Bredeson offered some lessons on developing a patient registry based on his observations of the successes of the IBMTR Registry.

1. **Ownership:** Starting a registry is not easily done by committee—there needs to be a chief scientific director and/or chief statistical director who will own the process and make a career of building the registry. The experience with the IBMTR was that the organizational structure evolved as more people became involved over time; today, there are elected members on the committees that drive the research process.
2. **Centralization:** A registry needs to be centralized in one place responsible for operations.
3. **Structure and Governance:** The CIBMTR, which oversees the IBMTR Registry, is a joint collaboration of the Medical College of Wisconsin and National Marrow Donor Program, with many different levels of oversight and guidance. These include a joint affiliation committee (medical college and patient representatives), advisory and executive committees, chief scientific director/chief statistical director, data management experts, working/steering committees, and consumer advocacy committee. A rare blood disorders registry could have working committees for different diseases or objectives (e.g., access to home administration).
4. **Collaboration:** Responsibilities can be shared across multiple centres and partners with different expertise so long as the roles are clearly defined.
5. **Funding and Costs:** Key considerations in developing and maintaining a registry include:
  - Type and amount of data
  - People and personnel
  - Infrastructure/operations
  - Data acquisition and ownership
  - Technology (paper vs. electronic)
  - Life cycle
  - Data access and use
  - Security and confidentiality

Depending on the aim, an existing registry or a registry proposal has the potential to attract different types of funding (philanthropy, industry grants and contracts, academic grants, federal contracts).

6. **Data, privacy and consent:** CIBMTR is required by law to obtain signed consent from all patients. All patient data is de-identified with many levels of security.

7. **Registry use and access:** It is important to make the registry useful to the centres that provide data. The patients and centres that provide the data own it and they allow registries to borrow it. This can be done through a mechanism that sends data back or allows the centres to access the registry to analyze their own data. This is valuable towards getting buy-in.
8. **Ethical/legal issues:** It is essential to be transparent about the registry structure, committee membership, decision-making process and funding sources.
9. **Data Validity:** Every centre and critical data elements need to be audited.
10. **Data Forms:** Technology in itself will not make a registry successful. Effort, energy and resources need to be invested into personnel. In the initial or short-term, paper data collection can be an effective and economic way to clarify questions.

For data collection, it is better to gather a smaller number of elements on every patient because trying to capture too many elements will result in big holes in data. “Form follows function—figure out your 10 questions and everything will evolve from there,” he concluded.

## **OneMatch Stem Cell & Marrow Network**

**Jennifer Philippe, Director, OneMatch Stem Cell & Marrow Network, Canadian Blood Services**

Jennifer Philippe described the OneMatch Stem Cell and Marrow Network, a Canadian registry of over 254,000 volunteer stem cell and bone marrow donors. It is operated by Canadian Blood Services and linked to the Héma-Québec blood marrow and stem cell donor registry.

### *Purpose and Objectives*

OneMatch works with 16 transplant centres across the country to find and match stem cell and bone marrow donors for patients in Canada.

- All volunteer donors must fill out a consent form. Their specific human leukocyte antigen (HLA) typing is determined using a blood test or buccal swab test.
- Each volunteer’s HLA typing is entered into the OneMatch database.
- Transplant centres send their requests and information to OneMatch, which conducts all donor searches and transmits information on possible matches back to the centres.
- The transplant physicians decide if they would like to proceed with any of the potential donors and notify OneMatch.
- OneMatch screens the donor candidates and oversees the logistical arrangements for the collection and transport of stem cell or bone marrow donations.

OneMatch is an accredited member of the World Marrow Donor Association (WMDA) and affiliated with 63 international bone marrow donor registries. This gives Canadian patients access to over 13 million donors registered worldwide. OneMatch is currently searching for matches for 817 patients in Canada and handling requests from centres in other countries seeking compatible donors for over 1,000 patients around the world.

### ***Outcomes from OneMatch***

Canadian Blood Services has recently begun using registry data for strategic recruitment. The 2006 Canadian Census showed that 1 in 5 Canadians are foreign-born. In examining the data, CBS found that about 28 per cent of the patients in the registry are of non-Caucasian ethnicities, while about 83 per cent of the donors are Caucasian. The majority of donors were females 45 to 50 years of age. This led to a recruitment strategy to attract more ethnic, male donors under age 40 towards building a donor base that reflects the needs of Canadian patients.

CBS is also working with the Aboriginal Nurses Association of Canada to develop a recruitment program. Registry data shows that less than 1 per cent of the donors are aboriginal, whereas there are seven aboriginal patients in Canada searching for matches. “Due to their ethnic uniqueness, the chances of finding a match elsewhere in the world are very poor. We were able to use the data gleaned from the registry to talk to the communities and do our recruitment,” she said.

Strategic recruitment has led to a great increase in donors. In 2008, almost 20,000 donors joined OneMatch, well over its target of 12,000. This was achieved using basic donor information in the registry. A targeted recruitment event in Toronto’s Chinese community aiming to register 200 new donors actually got 1,013 donors in just over four hours. “That’s the power of having a common repository that we can look at and determine where we need to go,” she said.

### ***Issues and Challenges***

Having a common repository has helped standardize the nomenclature and processes used across Canada. However, since transplant centres send information voluntarily, the data is not always consistent. Because OneMatch is accredited with WMDA, there are specific data that need to be tracked. Effort is put into achieving consensus with transplant centres. Keeping up with changes in technology is also a challenge.

## **European Society for Immunodeficiencies (ESID) Online Patient and Research Database**

**Dr. Gerhard Kindle, Centre of Chronic Immunodeficiency, University Hospital Freiburg, Germany**

Primary immunodeficiency diseases (PID) are rare disorders caused by genetic defects in the immune system. More than 200 different primary immunodeficiencies have been identified, however, there are still gaps in knowledge about their prevalence, said Dr. Gerhard Kindle. He gave an overview of the European Society for Immunodeficiencies (ESID) Online Patient and Research Database.

### ***Purpose and Objectives***

The ESID Online Patient and Research Database, (ESID Online Registry) was created in 2004 to collect long-term patient data towards improving diagnosis and treatment. It is an Internet-based database that can be accessed by registered users from participating centres and organizations. Administration and programming are based at the University Hospital Freiburg in Germany.

The main objectives of the ESID Online Registry are:

- Improve the diagnosis, classification, prognosis and treatment of PID.
- Determine disease prevalence.
- Gather long-term patient data to help determine the course of the diseases and possible effects of therapy.
- Enable combined evaluation of genetic and clinical data.
- Enable genetic and therapeutic trials within ESID.
- Enable research across centres.

There are currently 79 registered centres from across Europe as well as Russia, Turkey, Egypt, and Iran. So far, the centres have registered 10,263 patients within the 214 primary immunodeficiencies that are currently comprised in the ESID Database. However, there are many patients who have been diagnosed but not yet registered in the database, and presumably also many people who have not yet been diagnosed, Dr. Kindle said.

### ***Registry Design***

The European Society for Immunodeficiencies website ([www.esid.org](http://www.esid.org)) serves as the portal to the ESID Online Registry. The ESID database system itself is stored on secure servers at the University Hospital Freiburg and can only be accessed by registered users with a username and password. However, the website contains a “test version” of the ESID registry, which can be useful towards the development of registries in other disease areas.

The registry gathers many different types and levels of data for research and clinical purposes. The core dataset consists of general information on the patient including:

- General patient information
- Diagnosis and quality of life
- Treatment with immunoglobulin products and antibiotics
- Other medications and adverse event
- Laboratory values

The database also contains centre-specific modules (patient treatment information) and disease-specific modules (family history, immunizations, core and extended laboratory services and samples, biopsies and surgery). A mutation browser allows users to view information on specific genetic mutations and analogs in the database. Patient reports can be generated for clinical use. The database is designed with the capacity to add new diseases, modules and additional fields.

### ***Funding***

The ESID Online Database is currently funded in part by the Plasma Protein Therapeutics Association (PPTA), the German Ministry for Education and Research and the European Union through the European consortium on primary antibody deficiencies (Euro PAD Net).

## ***Issues and Challenges***

Key issues include: documentation (manpower, quality of data, frequency of documentation), data protection (legal/technical issues), different legislation (even within one country), and the separate ethics approval processes required for every centre.

## ***Outcomes***

Regularly updated statistics are posted on total number of patients registered, gender distribution, distribution of patients across the centres, and number of patients by disease registered at each centre. ESID also offers five publication awards (with a total sum of 15.000 € per year) to encourage the use of the registry data for research studies and publication of the results.

## **Alexion Global Paroxysmal Nocturnal Hemoglobinuria (PNH) Registry**

**Michael Bombara, Senior Director, Global Clinical Operations, Alexion Pharmaceuticals**

Paroxysmal nocturnal hemoglobinuria (PNH) is a very rare blood disorder due to a lack of certain immune proteins that help prevent red blood cell destruction. It has chronic, debilitating and life-threatening effects. Michael Bombara gave an overview of the Global PNH Registry.

## ***Purpose and Objectives***

The Global PNH Registry is an observational, non-interventional study created and sponsored by Alexion Pharmaceuticals to collect the following types of long-term data:

- Clinical outcomes, quality of life, morbidity and mortality data on patients with PNH
- Long-term safety and effectiveness data on patients treated with eculizumab (Soliris®)

In clinical trials, eculizumab was shown to reduce red blood cell destruction by 86 per cent and result in 92 per cent fewer thrombotic events and significantly improved patient quality of life.

The overall objectives of the Global PNH Registry include:

- Enhance understanding of PNH disease among physicians and patients including demographics, natural history and progression.
- Enhance the understanding of PNH treatment to inform clinical decision-making and improve patient outcomes.
- Serve as a global database on PNH for future publications.

## ***Registry Design***

Leading experts were engaged in the development of the PNH Global Registry, which was launched by Alexion in the fall of 2004.

- The registry is designed as a prospective, multi-centre, multi-national, observational study on patients with PNH treated with or without eculizumab.

- Patient data is entered at enrolment and approximately every six months thereafter.
- The registry is web-based—data is collected and submitted via electronic case report forms, though paper forms are available if necessary.
- Data collected minimally includes: demographics, medical history, PNH diagnosis, flow cytometry, symptomology, clinical outcomes, safety events, and pregnancy.
- The registry has a broad range quality of life measures including patient questionnaires translated into local languages and available in both paper and online formats.
- An external contract research organization is responsible for administrative activities, training (electronic case report forms, PNH registry materials and procedures), data management, payments, and site support.
- Centres must comply with ethics committees and competent authorities and have informed signed consent from patients. All data is de-identified to ensure patient confidentiality. All centres must provide required submissions. The submission process is country-specific.

### ***Issues and Challenges***

- Physician and patient enrolment – There is a need to identify leaders in the field and build a community of physicians and patients to improve the management of PNH.
- Amending natural history registry to include new regulatory interests – Data collection forms were revised based on results from the original registry to gather streamlined purpose-driven information only.
- Research capabilities and staff vary by type of practice and country – Centres are given the option to manage all activities or have Alexion provide a monitor to handle activities such as data entry.
- Availability or lack of eculizumab therapy globally – In order to be able to collect information on PNH and/or patients treated with eculizumab through other mechanisms, Alexion developed different versions of the protocol and case report forms.
- Privacy laws and ethics committees vary by country – This presents tremendous challenges. Templates were created specific to different regulations.

### ***Outcomes of the Global PNH Registry***

The U.S. Food and Drug Administration approved eculizumab (Soliris<sup>®</sup>) in March 2007, which was followed by EMEA approval in Europe in June 2007. Regulatory approval was obtained in Canada in January 2009, and in Australia in February 2009.

## **Canadian Hemophilia Registry (CHR)**

**Dr. Anthony Chan, Head of Hematology/Oncology Division, Department of Pediatrics, McMaster University, and Director, Hamilton-Niagara Regional Hemophilia Program**

The Canadian Hemophilia Registry (CHR) is a national registry that collects anonymized clinical data on patients with hemophilia and other inherited bleeding disorders. Dr. Anthony Chan of the Association of Hemophilia Clinic Directors of Canada (AHCDC) described the development of the registry and its evolution over the years.

### ***Purpose and Objectives***

Hemophilia clinic directors in Canada began discussing the development of a national patient registry in 1987 soon after the formation of the Canadian Hemophilia Clinic Directors Group (predecessor to the AHCDC). The registry's original objectives were to determine the number of patients with hemophilia A and B in Canada, and collect limited anonymous, comprehensive data on the patients. Dr. Irwin Walker of McMaster University developed the registry and was later allocated one-time funding through the AHCDC for further development.

The Canadian Hemophilia Registry was launched in 1988 and is owned and operated by the AHCDC. The registry was designed to:

- Document number and basic characteristics of patients with inherited bleeding disorders.
- Promote research on hemophilia.
- Preserve privacy by assigning "CHR numbers" to each individual.

### ***Registry Design***

- Clinics send anonymized data by mail, fax or e-mail to be input into the CHR.
- Registry data is stored and backed up on the hospital's private computer system and cannot be accessed from externally.
- Each patient is assigned a CHR identification number (an anonymous proxy ID). Patient names are not entered.
- Clinics are responsible for the accuracy of the data and tracking their patients.
- AHCDC returns individual CHR numbers and clinic list reports back to the clinics.
- AHCDC posts collated national-level data from the CHR on its website ([www.ahcdc.ca](http://www.ahcdc.ca)).
- Since its launch, the registry has been modified to permit updates to status designation and collect data such as HIV or HCV infection and causes of death.
- In addition, a VWD registry was integrated in 2001, followed by incorporation on the Rare Inherited Bleeding Disorders Registry in 2002.

## ***Funding***

The registry was maintained without funding for many years. “The registry’s success and longevity are the result of lots of goodwill from many people who volunteered time and expertise, particularly Dr. Walker, and the 24 hemophilia treatment clinics across Canada that provide the data,” Dr. Chan said. As of 2009, due to Dr. Walker’s professional commitments on other projects, the AHDCDC has started to provide \$8,000 for a data entry assistant.

## ***Governance***

The registry is overseen by an AHDCDC committee and McMaster University Research Ethics Board. Any AHDCDC member can make recommendations on registry changes or enhancement, which are put forward for approval by members at the AHDCDC Annual General Meeting.

## ***Outcomes of the Canadian Hemophilia Registry***

The registry documented 652 hemophilia patients infected with HIV (82 per cent of regularly treated patients) and 1,174 hemophilia patients infected with hepatitis C (90 per cent of regularly treated patients) in the 1980s. The data provided a basis to advocate for compensation and assistance programs for patients who received contaminated blood products. Blood products have been safe from HIV since 1985 and from HCV since 1988.

In closing, Dr. Chan offered the following advice for developing a successful patient registry:

- Define a clear purpose and identify specific, useful objectives.
- Design a simple, user-friendly registry.
- Provide centres and participants with feedback and access to the data.
- Cultivate strong relationships with centres and their staff.

## **Canadian Hemophilia Assessment Resource Management information System (CHARMS)**

**Dr. Bruce Ritchie, Hematology/Oncology Division, Department of Medicine, University of Alberta**

The Canadian Hemophilia Assessment Resource Management Information System (CHARMS) is a national electronic database that tracks blood products and clinical data on people with inherited bleeding disorders. Dr. Bruce Ritchie gave an overview of its development.

CHARMS was established in 1993 by the Association of Hemophilia Clinic Directors of Canada (AHDCDC) to track the use of blood products and clinical outcomes—it is different from the Canadian Hemophilia Registry, which tracks patients with bleeding disorders. In Canada at any given time, about 70 per cent of the product inventory for bleeding disorders is stored in patients’ homes. However, the products don’t get used right away, therefore it is essential to track products in case of recall.

CHARMS consists of a network of identical computer systems in 26 adult and pediatric hemophilia clinics across Canada, linked to a central database called CentrePoint. It collects data

on blood product distribution, clinical outcomes, adverse events, and genotyping. There are different modules on clinical outcomes, nursing, consent on clinical research using CHARMS, and adverse events reporting. Physiotherapy and genetics modules and a module to track blood products through barcodes are being developed.

Clinics export anonymized electronic data to CentrePoint, which is based at McMaster University and protected by the Hamilton Health Sciences Centre firewall. The database collects aggregate data; information is pseudo-anonymized (patients are given an anonymized ID number that is traceable by administrators). CentrePoint transfers summary data to AHDC, Canadian Blood Services, Héma-Québec, Health Canada, the provincial/territorial governments, Public Health Agency of Canada, Quebec Blood Secretariat, and manufacturers.

Governance is carried out by a multidisciplinary committee involving AHDC and Canadian Hemophilia Society representatives, patients, nurses, physiotherapists, physicians, and Canadian Blood Services and Héma-Québec representatives. CHARMS is funded mainly by Canadian Blood Services and Héma-Québec, with additional support from the Public Health Agency of Canada. The overall operating budget is about \$270,000 per year.

CHARMS has been a very important and useful tool for recalls and withdrawals of blood products by enabling the AHDC to promptly identify patients that received specific lot numbers. The AHDC is in the process of renewing the CHARMS program and revamping the database to a web-based program. Key issues include renewal (open source vs. proprietary approaches), privacy, security, and networking. A privacy plan for CHARMS with a privacy officer, privacy statement and policy, and privacy impact assessments needs to be developed.

### **The Platelet type von Willebrand Disease (PT-VWD) Registry**

**Dr. Maha Othman, Professor, Laurentian University – St. Lawrence College, and Adjunct Assistant Professor, Department of Anatomy and cell Biology, Kingston, Ontario**

The Platelet type von Willebrand Disease (PT-VWD) Registry Project was launched in 2006 at the Queen's University Molecular Hemostasis Laboratory. The project is funded by the Canadian Hemophilia Society. Dr. Maha Othman, principal investigator, gave an overview of the disease, challenges related to diagnosis and early results from the registry.

Von Willebrand Disease (VWD) is the most common type of bleeding disorder and is caused by a problem with the von Willebrand factor (VWF) gene. Platelet type von Willebrand disease is a very rare bleeding disorder that is closely similar to type 2B von Willebrand disease (type 2B VWD). But with PT-VWD, the genetic defect is in platelets rather than VWF. Common features of PT-VWD are frequent and severe nosebleeds and excessive bleeding following tooth extraction, tonsillectomy and other surgical operations.

PT-VWD is a challenge to diagnose because it is very similar to type 2B VWD. The methods of diagnosis are phenotypic testing, which analyzes platelet-VWF interaction, and genotypic testing, which uses DNA analysis to definitively confirm the platelet gene defect.

## ***Purpose and Objectives***

It is critical to make a proper diagnosis of type 2B VWD because it impacts the treatment decisions and treatment costs. The PT-VWD Registry Project was created to investigate two main questions:

- Is PT-VWD truly rare or under diagnosed?
- How many cases are being misdiagnosed as type 2B VWD cases?

Given the rare nature of these types of VWD, it is by necessity a global study. The project is compiling cases diagnosed as type 2B VWD or PT-VWD. DNA samples from around the world are sent to the Queen's University Molecular Hemostasis Laboratory for analysis. A specimen is first analyzed for the VWF gene mutation, which positively signifies type 2B VWD. If it tests negative, it is then analyzed for the platelet GP1BA gene, which confirms PT-VWD.

## ***Outcomes from the PT-VWD Registry***

- Genetic analysis shows that some cases diagnosed as type 2B VWD are actually PT-VWD.
- To date, only 44 cases of PT-VWD (18 families) have been diagnosed worldwide. Four PT-VWD genetic mutations have been identified.
- So far, the study has followed up on 86 cases including 37 Canadian cases. Genetic analysis confirmed type 2B VWD in 45 per cent but 20 per cent were found to be PT-VWD and 25 per cent were negative for both.
- Of the 37 Canadian cases, genetic analysis identified 18 cases of type 2B VWD, 2 cases of PT-VWD and 10 cases that were negative for both. Additional cases in Canada that have not yet been registered with the PT-VWD project.

Information on the PT-VWD Registry is available at [www.pt-vwd.org](http://www.pt-vwd.org).

## **Canada Vigilance Adverse Reaction Monitoring Program and Database**

**Heather Sutcliffe, Director, Marketed Health Products Safety and Effectiveness Information Bureau, Health Canada**

Heather Sutcliffe joined the meeting by teleconference. She gave an overview of the Canada Vigilance Adverse Reaction Monitoring Program and the MedEffect™ Canada Initiative, and shared some of the experiences at Health Canada in terms of data collection and management within the requirements of legislative frameworks (Food and Drugs Act, Canada Health Act, Official Languages Act, and Privacy Act).

The Canada Vigilance Adverse Reaction Monitoring Program is part of Health Canada's post-market surveillance activities. Its main activities are information collection, processing and assessment, and signal detection. Health Canada requires mandatory reporting of adverse events by manufacturers and voluntary reporting by patients and physicians as the adverse events occur.

The main purpose of the program is to detect signals (signs of a possible causal relationship between an adverse event and a health product that was previously unknown or incompletely documented). The program also tracks adverse events occurring in other countries to the same products with the same combination of active ingredients that is marketed in Canada.

The Canada Vigilance Adverse Reaction Monitoring Program has seven regional offices that coordinate the collection of data from physicians and patients. Their key functions are:

- Collect reports, review for completeness, and follow-up with reporters
- Initial data entry into the Canada Vigilance electronic database
- Provide guidance and feedback (i.e., acknowledgement letters) to the reporters
- Increase awareness of the program among health professionals and patients in each region

Reports can be submitted online or by fax, mail or calling a toll-free number—all of these collection methods must incorporate privacy and confidentiality.

The program collects adverse reaction reports on pharmaceutical drugs, biologics, radiopharmaceuticals drugs, natural health products, and cells, tissues and organs. The amount of data collected has increased over the years. In 2008, there were 20,360 domestic reports; about 65 per cent consisted of mandatory reporting by manufacturers and 35 per cent was voluntary reporting by health professionals and patients. About 70 per cent of the adverse events were considered serious (i.e., causes death or life-threatening reaction, requires hospitalization or medical intervention).

When data is released, caveat statements are included explaining the limitations of data: for example, cause/effect relationships have not been established in the vast majority of reports submitted; and data representing only a small proportion of suspected adverse reactions are reported to the program, therefore cannot not be used to estimate the incidence of adverse reactions.

MedEffect™ Canada is an umbrella initiative launched in 2005 to better communicate health product safety information and increase awareness of adverse reaction reporting. It provides centralized access to product safety information and industry guidance on the MedEffect website and the Canadian Adverse Reactions Newsletter. Key features include:

- Standardized terminology for data classification, retrieval, presentation and communication of medical information
- Sharing of data internationally using consistent data coding and assessment
- Standardized electronic transmission of medical information
- Training of academic researchers on medical terminology for regulatory activities

Patient registries are useful tools for the surveillance of patients and products. Health Canada does not establish or fund registries but a variety of registries exist that have been developed by stakeholders including manufacturers and the Canadian Institute for Health Information (CIHI). Health Canada is currently developing the Progressive Licensing Project, which will include

regulatory requirements for post-market commitments depending on the information available in the pre-market phase by manufacturers.

## **Session 4: Privacy, Security, Ownership and Governance Issues**

### **Michael Power, Barrister & Solicitor**

Privacy, security and information management are paramount issues when collecting patient health information, said Michael Power. He outlined some of the patient concerns, privacy requirements and legal challenges surrounding patient registries.

When developing a registry, it is important to carefully consider and protect patient privacy in the following areas:

- Communication, transportation, storage and display of personal health information
- Remote electronic monitoring of patients
- Data sharing in patient care, public health surveillance and health research
- Electronic communication between and amongst patients and providers

Patients are concerned about the privacy and security of their health information regardless of whether their data is de-identified and anonymized or not. The main fears are that disclosure of their health information would lead to undesirable consequences such financial loss, social stigma, and discrimination, Power said. The concerns include:

- Commercial misuse of data: Use of medical data to deny or restrict insurance coverage, credit or other financial benefits; or for unsolicited marketing.
- Government misuse of data: Use by government agencies for secondary purposes (e.g. employment); or use for national security or law enforcement purposes.
- Criminal misuse of data: Fraud or identity theft resulting in financial or other harm due to security breaches, inadequate privacy policies or data leakage.
- Data quality: Data corruption or loss.

The following privacy and security elements need to be addressed when developing a registry:

- Identity management services
- Accurate identification of system users
- User registration, access and control
- User support
- Consent and notification management services
- Identity protection services (de-identify and re-identify patient health information)
- Encryption services (both “at rest” or “in motion”)
- Data integrity services (e.g., digital signatures)
- Audit services to monitor access and use
- General security-related IT services (e.g. data back-up, archiving and destruction)
- Registry lifecycle (ensure proper storage or disposal of data when it ends)

When developing patient registries, it is important to carefully consider the technology options and put in place procedures and policies for protecting patient health information—trust and confidence of patients is paramount, he concluded.

## **Session 5: Panel on How to Encourage the Establishment of Patient Registries**

**Panelists: Dr. Christopher Bredeson, Janina Kon, Michael Bombara, Magda Melo, Michael Power, Dr. Maha Othman, Dr. Gerhard Kindle, Dr. Anthony Chan**

Patient registries are crucial to the improvement of treatment and care for people with rare disorders and thus a primary goal shared by the members of the Network of Rare Blood Disorders Organization, said Co-Chair Silvia Marchesin. At this point in time, the Canadian Hemophilia Society is the only member organization with a patient registry. For this session, a panel of experts was asked to highlight key steps towards the establishment of patient registries. This was followed by plenary discussion on challenges and strategies for moving forward.

### **Dr. Christopher Bredeson, Medical College of Wisconsin, Milwaukee, USA**

- Keep it simple: Don't try to gather too much data on all the patients. A good approach to data collection is "comprehensive parsimony." For all the patients, just collect the basics.
- Get patients involved early: With rare diseases, patients are the driving force for both the registry's development and its success. The outcomes require patient participation (e.g., tracking products, reporting events).
- Reward the contributors to the registry: Find a way to reward the individuals who participate at the local level, those who provide and input the data for the registry. For academics, key rewards are the opportunities to participate on research committees and publications and attend conferences. It is important to also reward data managers and statisticians with similar opportunities.

### **Janina Kon, Streamline Counsel Inc., Vancouver, British Columbia**

- Be transparent about the data being collected: Make sure patients are aware of what data will be collected, the purposes of the information and how it will be used. Make sure the consent forms and notice forms are properly worded and appropriate to populations.
- Put in place good governance practices and privacy policies: Communicate who will be responsible overall for the collection and disclosure of the information (e.g., privacy officer) and provide means for people to easily contact that person.

### **Michael Bombara, Alexion Pharmaceuticals**

- Clearly define the purpose of the registry: Define the basis for the beginning and end of the registry, and the primary and secondary uses of the data collected. Make sure the physicians and patients understand how the data could be used.

- Think about others who might want to use the registry data: Privacy, consent and ownership are key issues. Pharmaceutical companies need data in order to make the next technological leap and develop new drugs and therapies, but often cannot access patient registries because of privacy and ownership issues. It is important to establish an appropriate structure and get proper consent from physicians and patients for the use of the data.

### **Magda Melo, St. Michael's Hospital, Toronto**

- Make sure the registry is meaningful to patients: The purpose of the registry must be meaningful to patients, who are the target population, and not just researchers.
- Protect patient privacy and confidentiality: The general public and patients worry about the confidentiality and security of their health information. Explain how their information will be kept private and secure. It is important to ease their minds; otherwise they will not agree to participate in the registry.

### **Michael Power, Barrister & Solicitor**

- Create a solid plan: The plan should set out the purpose of the registry, implementation costs, ongoing maintenance costs, funding, and possible sources of revenue.
- Plan for change management: Going from a non-registry to registry state involves a lot of change. There are many political and legal considerations for both supporters and registers.

### **Dr. Maha Othman, Laurentian University - St. Lawrence College, Kingston, Ontario**

- Focus on the value to patients: Make sure patients understand why it is valuable and important for them to be in the registry. For example, to improve scientific understanding and treatment of the disease, or track product safety.
- Engage and collaborate with physicians: Collaboration with primary physicians is critical. Provide information and support. For example, if the aim of the registry is diagnosis, provide for transportation of the blood or DNA samples.

### **Dr. Gerhard Kindle, University Hospital Freiburg, Germany**

- Don't try to do too much or get everything into the registry: Define and stay focused on the objectives. It is better to start with a small, dedicated set of questions than to try get everything possible into the registry. Try to answer the 10 most burning questions for the next five years.

### **Dr. Anthony Chan, Hamilton-Niagara Regional Hemophilia Program, Hamilton, Ontario**

- Gather and involve people with an interest in disease area: This is a particular challenge for rare blood disorders compared to bone marrow transplant or hemophilia, which already have established centres and networks of dedicated physicians and accurate methods for diagnosis. With many rare blood disorders, patients are scattered around the country and often lack

access to diagnosis and treatment. A key step is building a network of health professionals to work collaboratively towards comprehensive care.

## **Plenary Discussion**

Tom Bowen of the University of Calgary said it's discouraging that Health Canada has abdicated its responsibility for patient registries. "If they don't want to own them and be responsible for them, then at least they should fund them and put money into it." However, there's no need to reinvent the wheel if an appropriate registry already exists. He asked the panel if there are international laws that might prevent or deter Canadians from participating in registries based in another country. For example, how does the U.S. Homeland Security Act affect Canadian patient data stored on databases in the United States?

While it's useful to look at existing patient registries, it's important to ask whether the registry or entity has the same goals otherwise it may not be able to produce the information being sought, said Christopher Bredeson. A key challenge is that there is a shifting from research for the greater good to funded research—at the university level, research can't be simply a scientific pursuit anymore, the time has to be accounted for and the money has to follow.

The U.S. Patriot Act is a statute designed to facilitate law enforcement access to information without necessarily using normal due process, said Michael Power. In Canada, some jurisdictions have introduced amendments to their health information acts with respect to public sector holdings of personal information, specifying that the data must remain within the jurisdiction and that access from non-Canadian sources is not permitted. However, no such statutes apply to private sector entities—there is no legislation in Canada to prohibit the transfer of data on Canadian patients to private sector databases in the U.S. There is an enormous concern among Canadians about their data being subject to the U.S. Patriot Act. The fear is somewhat overblown but regardless raises political and emotional issues to address.

Michael Bombara said the key is to have appropriate consent from the patient on the data being collected, and explain how it will be anonymized and de-identified, so that physicians and patients feel more comfortable participating in the registry. For international registries, notice and consent forms need to be tailored to the legislation in each country. It is important to spell out the risks but that the sponsor will take all necessary precautions to protect the data.

David Page said the NRBDO is essentially made up of three types of patient groups—bleeding disorders, primary immunodeficiencies, and hereditary angioedema. The organizations share common goals in terms of establishing registries, comprehensive care, and home therapy for rare blood disorders. Canada does not have national PID or HAE registries but these exist abroad, and the Canadian Hemophilia Registry and CHARMS database are in the process of being revamped. He asked panelists which of the following strategies they would recommend:

1. Develop individual registries.
2. Develop individual registries that are linked to international registries.
3. Work together on one pan-Canadian registry for rare blood disorders with components for the different disease conditions.
4. Other strategies.

Christopher Bredeson recommended creating one common registry with a common structure whose content could be tailored for specific diseases. Responsibility and operations should be championed and centralized in one location and the expertise of different diseases can be distributed across the country to encourage synergy between the groups.

Maha Othman also endorsed the idea of working together on a national registry given the rare nature of the disorders. This would allow clinicians to both contribute data and derive information from the central registry, and also would facilitate international collaboration.

Gerhard Kindle said that developing a central registry or building on existing registries should be the first option. In terms of tackling political and emotional issues concerning international registry, it is useful to begin with a pilot study and get informed consent from patients including for the use or storage of data internationally.

Magda Melo agreed that a common registry is ideal because it would save costs, but noted that it will be an immense task to manage because the diseases are very different and therefore there will not be standard variables common to all diseases. However, the benefit of a common registry is the ability to leverage common stakeholders and funders.

Michael Power said that while there are many different variables for each disease, technology is capable of managing the data. From the implementation standpoint, one platform is the best solution because of the common technical support.

Michael Bombara also agreed, noting that clinicians in other areas are also working to establish a common IT platform and registry to enable collective research. He recommended that the patient groups work together to leverage expertise and funding for a national registry in order to bridge some of the research efforts and bring more value to the community.

Tina Morgan of the Canadian Immunodeficiencies Patient Organization said that since these are rare disorders, collecting data nationally might not be effective or sufficient enough if there are only a few patients with a particular disorder. Therefore, a registry for rare disorders needs to be international in scope so that research can be conducted in collaboration with other countries and vice versa. However, while the different disorders have some variables in common, there are also unique variables—trying to create a common database with many different purposes and interfaces will be an immense challenge.

It is essential to sort out with Health Canada what their plan is for phase 4 marketing of products, said Bowen. For rare disorders, it is critical to get drugs out as soon as possible—to do so, there needs to be a research base in Canada involving the participation of patients. Registries allow pharmaceutical companies to offer early introduction of new drugs to patients with rare disorders. A key benefit for Health Canada is that they will be promptly notified if there are adverse events or other problems related to the introduction of the drug.

If the new legislation proposed by Health Canada goes through, pharmaceutical companies will be compelled to do much more in terms of pharmacovigilance and phase 4 clinical trials, said

Co-Chair Bruce Ritchie. The Alexion Global PNH Registry shows that it can be done at arms length.

In terms of registry design, Bowen noted the need for international collaboration on rare disorders and having data formats that are exchangeable worldwide. He recommended importing or building on already established and successful platforms, and presenting the proposed registry to Health Canada before implementation to establish that it satisfies their requirements.

While international collaboration is important, the difficulty is that there isn't always consensus on the research questions, said Bredeson. To answer Canadian research questions, Canadian data needs to be collected, whether for tracking products and rare adverse events or for coordinating health care by telemedicine.

Different diseases will require different variables but a common registry can still provide the framework for basic elements such as patient consent, data collection and de-identification, governance practices, and privacy policies, said Ritchie. He suggested moving forward by trying to leverage a common platform that can be customized for specific diseases.

A key challenge is that physicians often have reservations about participating in registries because they are worried that findings will be concealed even if the pharmaceutical company has demonstrated 100 per cent ethical conduct, a pharmaceutical representative said. In addition, it's important for funders, clinicians and patients alike to know how long the registry needs to be in operation before they can expect results. Experts involved in well-established registries generally say that the true flowering of a registry does not occur for about 7 to 10 years. Kindle agreed, advising participants not to expect a lot of results after three years—results can be expected after about five years.

## **Day One Wrap-Up**

Co-Chair Bruce Ritchie summed up the first day, noting the excellent informative talks and discussions. Gavin Tong set the stage with a primer on health informatics and how the field has evolved in Canada. Magda Melo gave a thorough and comprehensive presentation on the definition of a registry and how to set one up. Then there were examples of registries in different disease areas and in other countries, which offered a range of different perspectives—national, international, patient, clinician, and pharmaceutical. Finally, participants discussed the legal, ethical and political issues related to registries, and strategies for moving forward.

## Saturday, November 14, 2009 – Progress in Comprehensive Care

### Objectives of the Day

The second day of the conference focused on the establishment of comprehensive care for rare blood disorders. The objectives were to appraise the NRBDO's vision for comprehensive care against the Canadian and international models that will be presented, and reach consensus on the key principles for comprehensive care for Canadians with rare blood disorders that the NRBDO should put forward to health policy decision-makers. The aim of the presentations was to illuminate the path for advancing the principles of comprehensive care for the various rare blood disorder groups.

### Session 6: Review of Recommendations from 2006 NRBDO Conference

#### Silvia Marchesin, Past President, Aplastic Anemia and Myelodysplasia Association of Canada

The Network for Rare Blood Disorder Organizations (NRBDO) was created in 2004 by national patient groups. The Network's key goals are to share best practices in healthcare delivery for people with rare blood disorders, work to further common interests and lobby for issues, and secure and maintain comprehensive care access for patients with rare blood disorders.

In 2006, the NRBDO held the Conference on Comprehensive Care for Rare Blood Disorders, which was attended by about 140 clinicians, nurses, researchers, healthcare professionals, patient organization leaders, and government and industry representatives. Comprehensive care for rare blood disorders and patient advocacy were identified as key priorities.

Silvia Marchesin, 2006 NRBDO Conference President, gave an overview of the vision for comprehensive care developed by participants at the 2006 meeting, and the motions passed towards achieving the Network's goals.

### Vision of Comprehensive Care for Rare Blood Disorders

- 1. Provincial/territorial designation:** Designated provincial/territorial programs and specialized centres are necessary to ensure that there is a dedicated budget and ensure sustained quality care.
- 2. National patient registries:** Registries promote high-quality, evidence-based medicine through the collection of data and support research into patient outcomes and improved therapies.
- 3. Self/family administration of therapeutics:** Switching from hospital-based to home therapy offers huge benefits to both the healthcare system and patients; hemophilia was vanguard of self-infusion revolution.

- 4. Patients, families and association involvement:** The patient and family are at the core of the comprehensive care team, while the patient association must be able to provide input and recommendations on service delivery.
- 5. Education of patients, families and healthcare providers:** Education is a continuous process. Education of patients and families is key to improved care and improved health. Education of healthcare providers about rare blood disorders, treatment and care is equally important.
- 6. Standards of care and portability:** Patients and their families must be free to move from place to place and from province to province and have access to consistent high-quality comprehensive care. National standards must be developed for all rare blood disorders to ensure that quality care is available to all patients throughout Canada.
- 7. Decentralization through outreach:** People with rare blood disorders are not confined to cities and urban centres. Treatment and services need to be provided in the home community; only highly specialized services requiring unique facilities should be centralized. A key function of the comprehensive care centre is therefore outreach.
- 8. Multidisciplinary care:** Comprehensive care treats the whole patient. Aggressive maintenance, early intervention and rehabilitation are essential to reduce the burden of disease. It is also important to anticipate and prevent physical, social, vocational and psychosocial problems, and provide assistance to the patient to lead as independent and normal a life as possible.
- 9. Defined core services:** The comprehensive care team should provide the following defined core services: diagnostic services, education, therapeutic services, nursing evaluation, genetic counseling, psychosocial evaluation and services, laboratory evaluation, and provision and monitoring of blood products and supplies, adverse reactions. And in addition: home/self infusion, women's issues, gynecology and obstetrics; allied medical specialist services; outreach; referral services; case management; program coordination and management; research; coordinated hospital and ER care.
- 10. Comprehensive care team:** The comprehensive care team consists of the patient, physician, nurse coordinator, social worker, and clerical staff. Other specialized services are available.
- 11. Program evaluation and accreditation:** Evaluation and accreditation should be conducted by qualified peers; based on measurable standards; conducted regularly; provide remediation; and entail consequences.
- 12. National collaboration among healthcare professionals and patient organizations.** Strong links between patient organizations and healthcare professionals are needed, among patient organizations such as the NRBDO, and at the national level among healthcare professionals, notably physicians and nurse coordinators, to facilitate standards of care, patient registries and research collaboration.

**13. Post-marketing surveillance include blood-borne pathogen surveillance.** A key role of a comprehensive care centre is to monitor for adverse reactions and conduct systematic blood-borne pathogen surveillance.

**14. Collaborative research:** To measure health outcomes and conduct research into improved therapies, a comprehensive care centre linked into a national network, with an integrated information system, is essential.

### **Motions Passed at 2006 NRBDO Conference on Comprehensive Care for Rare Blood Disorders**

**Motion 1:** The Network of Rare Blood Disorder Organizations, collectively, and its member organizations, individually, will advocate with provincial/territorial governments for comprehensive care for rare blood disorders. *(See above for the NRBDO's vision and recommendations on the components considered essential to comprehensive care.)*

**Motion 2:** The Network of Rare Blood Disorder Organizations recommends that Health Canada/PHAC, CIHR, Provincial and Territorial Health Ministries continue to support the work of the Network of Rare Blood Disorder Organizations.

**Motion 3:** The Network of Rare Blood Disorder Organizations recommends that The Public Health Agency of Canada establish a national working group to coordinate and support the development of national data base registries, including quality of life measures, for the rare blood disorder disease groups including, but not limited to:

- Primary immune deficiency
- Hereditary angioedema
- Rare blood disorders
- Hemoglobinopathies
- Bone marrow disorders
- Porphyria
- Hemophilia/bleeding disorders

And that Dr. Tom Bowen be mandated to represent the Network of Rare Blood Disorder Organizations for this initiative.

## Session 7: Progress And Lessons Learned In Canada

**Chair: Tom Alloway, Volunteer, Canadian Hemophilia Society, CHS Representative to the NRBDO**

### Edmonton Rare Blood Disorders Program

**Dr. Nancy Dower, Department of Pediatrics, Stollery Children's Hospital, Edmonton, Alberta**

The John Akabutu Comprehensive Centre for Bleeding Disorders in Edmonton provides diagnosis and treatment for all inherited bleeding disorders. Dr. Nancy Dower described the centre's evolution over the past 30 years.

The centre was founded in 1978 as a comprehensive hemophilia care clinic, following successful advocacy and lobbying efforts by the Canadian Hemophilia Society's Alberta Chapter. The program was based on an integrated healthcare delivery model for hemophilia developed in the 1970s, which became standard of care in Canada and worldwide.

The main features and benefits of the comprehensive hemophilia care program include:

- **On-demand and preventative treatment:** The comprehensive care approach leads to better health and treatment outcomes for patients and result in better outcomes.
- **Home infusion program:** Home treatment allows patients to self-infuse treatment promptly rather than having to go to the clinic, resulting in fewer ER and hospital visits.
- **Multidisciplinary care:** Treatment is provided by a core team made of a hematologist, nurse, dentist, physiotherapist, and orthopedist.
- **Annual clinic check-ups:** Annual assessment by the multidisciplinary team is efficient and less time-consuming than separate appointments with different hemophilia specialists.
- **Adjacent pediatric and adult care clinics:** The Stollery Children's Hospital is located within two blocks of the University of Alberta Hospital—this proximity fosters interactions between the pediatric and adult teams and eases patient transition from pediatric care to the adult clinic.

The clinic initially had about 80 patients with hemophilia but the number of patients has grown substantially over the years as services expanded to include other inherited blood disorders.

The Edmonton Rare Blood Disorders Program aims to provide comprehensive care for people with inherited blood disorders. This encompasses education, treatment, prevention of complications, home therapy, and transition from pediatric to adult health services. There are now over 800 patients registered in the program. Most patients live in Edmonton and the surrounding region, but the centre also provides services to patients from northern British Columbia and central Saskatchewan.

Good progress has been made through the introduction of home infusion therapy, subcutaneous immunoglobulin therapy, and red blood cell exchange.

- **Home infusion therapy:** Patients with hypogammaglobulinemia are treated with frequent infusions of immunoglobulin—home infusion therapy allows them to manage their own treatment and also decreases healthcare costs. Patients who enroll in the home therapy program are assessed in clinic by a hematologist and receive individual training on self-infusion. The hypogammaglobulinemia program was started in August 2006 and now has 92 patients enrolled, 72 of whom are now on subcutaneous immunoglobulin. Patients must sign a contract agreeing to infuse 5-7 days a week and keep a home treatment log.
- **Subcutaneous immunoglobulin therapy:** Treatment with subcutaneous immunoglobulin therapy prevents severe infections and reduces mild infections. For patients with hereditary angioedema (HAE), on-demand or preventative home treatment is more convenient and potentially life-saving. The HAE program started in 2000 and now has 53 patients on home infusion with C1 esterase inhibitor. Patients must sign a consent form and keep weekly infusion records (product and lot number, injection site, volume, adverse events).
- **Sickle cell anemia clinic:** The sickle cell anemia comprehensive care team consists of a hematologist, nurse practitioner, pulmonologist, neurologist, social worker, pain service nurse practitioner, and neuropsychologist. There are currently 35 pediatric patients with sickle cell anemia. A major challenge across Canada is that the majority of patients are new immigrants and refugees, and therefore the “backbone” of the program is education. After initial assessment, parents return for one-on-one training and educational resources are provided. Teenage patients are taught about sickle cell disease and introduced to the nurse for the adult program, in preparation for their transition to the adult clinic, which is located in same hospital complex.
- **Red blood cell exchange program:** Red blood cell replacement reduces chronic fatigue and pain, and helps prevent crises. There are currently 18 adult patients with sickle cell disease in the Edmonton Rare Blood Disorders Program, 7 of which are on red blood cell exchange. There is also a thalassemia patient and a hemoglobin-Alberta patient.

Current challenges include registry and data management, and concerns related to the stability of funding and possible cutbacks in the future.

### **Quebec Primary Immunodeficiencies Network**

**Dr. Jacques Hébert, Centre hospitalier de l'Université Laval, Centre de recherche en allergie de Québec, Réseau québécois de cliniques d'immunodéficience**

The Quebec Primary Immunodeficiencies Network is a physician group that works to improve treatment for patients with primary immunodeficiency diseases (PID). Dr. Jacques Hébert of Centre hospitalier de l'Université Laval spoke about the advantages of home therapy for patients and for healthcare authorities, the network's main goals, and its progress in advancing home therapy for their patients despite lack of proper funding thus far.

The network currently involves 26 physicians based at immunology clinics within three hospital centres: McGill University, Université de Montréal and Université Laval. Its main goals are to:

- Improve the diagnosis and treatment of primary immunodeficiencies.
- Introduce new treatment options such as home therapy for hereditary angioedema patients.
- Develop protocols for therapies and follow-ups.
- Implement a national registry.
- Establish teaching program.

The network approached health authorities with a proposal to switch primary immunodeficiency patients from hospital-based to home therapy, and from intravenous therapy to subcutaneous therapy. The case for home therapy was made on the basis of the clinical benefits for patients and economic benefits for healthcare funders.

Intravenous immunoglobulin therapy (IVIG) is the “Pump Method” and involves a syringe pump or driver, which is used to infuse the drug dose weekly as described in the product monograph. The main advantages of intravenous home therapy are:

- Convenient and well tolerated by most patients
- Ability to give large volumes per infusion and intermittent dosing (every 21-28 days)

Subcutaneous immunoglobulin therapy (SCIG) is the “Push Method” and involves using a syringe to inject smaller doses of the product more frequently—the weekly dose is divided over a number of treatment days (daily, every 2-3 days, 5 days per week, etc.) The main advantages of subcutaneous home therapy are:

- No venous access required
- Slow administration and gradual absorption reduces severe headaches and other adverse events
- Maintains more consistent IgG levels, and eliminates low troughs
- Clinical efficacy recognized, with annual rate as expected
- Excellent safety profile

The economic benefits for subcutaneous home therapy are supported by a number of studies that have been done in Canada and abroad:

- Studies in the U.S. and Europe comparing the cost of hospital-based IVIG therapy to home-based SCIG therapy have shown that home therapy is notably less expensive than hospital treatment.
- A 2008 report by the Canadian Agency for Drug and Technologies in Health estimated healthcare savings of \$9 million per year if 75 per cent of PID patients on IVIG are switched to SCIG, and savings of \$700 per patient annually because supplies for subcutaneous therapy (syringes) are less expensive than for intravenous therapy (syringe pump and tubing).

Additional benefits from the patient point of view include independence from pumps and worry about their reliability, and simpler and faster administration. Input from patients should be considered when choosing a regimen.

As of November 2009, there were 160 primary immunodeficiency patients in the province of Quebec. About half the patients are on IVIG therapy, and half are on SCIG therapy. Patients are trained on how to self-administer IVIG or SCIG therapy and keeping a treatment log.

There are about 25 patients with hereditary angioedema in Quebec, five of whom are on intravenous home therapy, and an additional patient from Moncton, New Brunswick.

The network's next challenge in terms of advancing home therapy for patients with primary immunodeficiencies is to get regional blood banks on board to serve as repositories where patients can go every two to three months to get their requisite supplies, he concluded.

### **Patient Perspective: Progress in Comprehensive Care for Hereditary Angioedema**

#### **Harriet Lyons, hereditary angioedema patient, Ontario**

Harriet Lyons described her journey towards being diagnosed with hereditary angioedema (HAE) and progress in treatment and comprehensive care achieved over the years.

Lyons was initially diagnosed about 20 years ago as having an allergy to aspirin due to face swellings. She was advised that if she ever felt funny in the throat, she should get to an emergency doctor immediately. At the time, she did not experience swelling very often, so she subsequently took a trip to Thailand, where she stayed in very remote places.

All went well for four days until she woke in the night to find a bump in her throat, which she thought might be an insect bite. She proceeded to take antihistamines and gargled with mouth wash but the swelling did not go away. She woke up Thai neighbours to take her to the nearest hospital, where she was admitted and given a room. Several hours later, the swelling in her neck was severe and she could not talk. She walked to the nursing station and woke the nurse. At that time a doctor took her to surgery room and inserted a trachea while she was still conscious. She woke up in the ICU, the windows and doors were wide open allowing animals to enter. She could not lie down so the nurses kindly brought her pillows that were inflatable beach toys. Lyons was then airlifted to Bangkok; during the flight both lungs collapsed. She was admitted to BNH Hospital and spent a week on life support in ICU and two weeks on a ward before returning to Canada.

Upon her return home, she set about looking for information of her symptoms. Her search led her to Dr. Paul Keith at McMaster University, who shortly after diagnosed her with hereditary angioedema. Through the Internet, she came in contact with Jeanne Burnham, Peggy Adomitis and Dr. Tom Bowen and together they decided to start the Canadian Hereditary Angioedema Society (CHAES). The organization had about 100 patient members and worked tirelessly with physicians to develop consensus on treatment. The group also formed a network with other HAE organizations, and held a meeting with researchers and doctors from across Canada and around the world. CHAES later folded; however, thanks to the efforts of Dr. Tom Bowen and Tina

Morgan, the HAE patients have joined up with CIPO. Being part of the NRBDO family is also very meaningful, she added.

The treatment for allergy when she was initially diagnosed with HAE consisted of antihistamine, epinephrine, prednisone, and danazol. Over the years, treatment and access to drugs has improved:

- A protocol for HAE treatment was developed thanks to the efforts of the medical advisory board of CHAES and CHAES members.
- Patients now have access to C1 esterase inhibitor produced by CSL Berhing. It is provided through the Special Access Program.
- Patients also have access to a new medication called icatibant (Firazyr™) by Shire.
- Home treatment is in the works, which will give patients greater control and autonomy.
- C1 esterase inhibitor is now in the process of getting it approved.

However, there remain a number of issues:

- Emergency treatment has improved—however, McMaster University Hospital is closing the adult services in its ER, which will be only for children.
- Pain control is a key issue because physicians who have not heard about HAE treat patients requesting pain medicine with suspicion; sometimes unnecessary blood tests and x-rays are performed, which delays treatment.
- Patient education (e.g., symptoms and treatment) is thoroughly lacking.
- Quality of life is not addressed at all.

### **Proposal for A Coordinated Adult Primary Immune Deficiency Clinic in British Columbia**

**Dr. Robert Schellenberg, Head of Allergy and Immunology Division, St. Paul's Hospital, Vancouver, B.C.**

Dr. Robert Schellenberg spoke about the progress towards establishing an adult clinic for primary immunodeficiencies and subcutaneous treatment for patients in British Columbia, challenges related to current delivery of care, and the need for a provincial program to provide optimal care for patients with primary immunodeficiencies.

Pediatric clinics for primary immunodeficiency diseases (PID) have been in place for many years. PID was initially diagnosed only in children and those with severe cases often did not make it to adulthood. However, it is now understood that PID is a variable disorder that occurs in many forms. An increasing number of adults are being diagnosed with PID and experts estimate that many people remain undiagnosed due to lack of awareness and education about PID.

Prior to the 2006 NRBDO conference, a provincial healthcare working group presented the B.C. Ministry of Health with a proposal on establishing comprehensive care for patients with primary immunodeficiencies. The rationale for the proposal included the following considerations:

- Patient needs and desires
- Convenience and cost
- Concerns regarding infection exposure in hospital

- Communication and education
- Optimization and standardization of care throughout province
- Reduced demands on scarce resources

In 2008, Canadian Blood Services and the National Advisory Committee on Blood and Blood Products convened a national panel of experts to develop evidenced-based practice guidelines on the use of immune globulin therapy for primary immunodeficiency diseases. The main objective was to standardize the care of patients.

The national expert panel’s main recommendations are:

- Patients diagnosed with a primary immunodeficiency should have their care coordinated by a comprehensive care clinic or expert in the immune deficiencies.
- In terms of clinical efficacy and adverse events, there is insufficient evidence to recommend one formulation of immune globulin over another.
- In terms of clinical efficacy for reducing infections, IVIG and SCIG preparations have comparable results and should be considered equivalent.
- When deciding on route of administration, patient preference should be taken into account.

Challenges related to the current delivery of care for PID patients in B.C. include:

- Shared outpatient treatment facilities: In urban areas, medical short-stay units handle many different services. In smaller communities, patients go to the hospital ER for treatment.
- Scheduling problems/lack of resources: Some physicians are being told to limit the number of PID patients per centre. Patients are “bounced” because PID is seen as a low priority disorder.
- Increasing number of adult patients: Due to advances in treatment, more patients survive childhood and need adult care. There are about 5-10 new adult patients identified annually.
- Lack of standards of care and patient follow-up: Care is not standardized, adverse event reporting is suboptimal, and follow-up of PID patients tends to be sporadic.

The current priorities in terms of comprehensive care for PID patients are:

- Establish a provincial program for optimal management of PID patients.
- Develop training and support for subcutaneous immunoglobulin home therapy.
- Involve patients and the patient database in ethically approved research initiatives.

Although limited in resources (personnel for training and evaluation as well as equipment), St. Paul’s Hospital has initiated SCIG therapy for patients with poor venous access or severe reactions. There are now about 25 patients on SCIG home therapy.

The protocol for SCIG home therapy is:

1. Patients who fit the criteria for SCIG home therapy must sign a consent form in order to enroll.
2. The patient is trained in self-infusion and required to demonstrate proficiency in two weekly sessions.
3. If the patient is proficient, the hospital provides product and supplies for one month of

weekly home infusions.

4. The patient's technique and log sheets are reviewed at one month. Product and supplies for three months are the provided.
5. Follow-up care takes place every three months.

The B.C. Provincial Blood Coordinating Office has completed a SCIG guidelines document, which provides an important foundation for moving forward. The guidelines, patient handbook and other resources are available on their website ([www.pbco.ca](http://www.pbco.ca)).

Efforts are now focused on the formation of a business plan to the Ministry of Health for the creation of a primary immunodeficiency centre of excellence. Key areas that still need to be addressed include funding of therapeutic products and ancillary supplies, and provision of comprehensive care to peripheral communities.

### **Patient Perspective: From Intravenous to Subcutaneous Immunoglobulin Therapy**

#### **Michael Whelan, patient with primary immunodeficiency, British Columbia**

Michael Whelan described some of his experiences as a patient with primary immunodeficiency disease and the significant impacts of intravenous immunoglobulin therapy and subcutaneous home therapy on his health and quality of life. He also shared some of the self-advocacy techniques he has developed to make sure that his physicians understand his disorder and how it is managed.

Diagnosed in 1982, Whelan was started on intravenous immunoglobulin therapy a couple of years later. "Up until I started my treatments, I was pretty much a couch potato but I soon found my infection rate went down and my 'to do' list at home also went up," he said. He became more active and fit, shedding 50 lbs. gained over years of diminished physical activity.

"What's surprised me the most over the years, living in different places because of my job, is that a lot of family doctors don't know what primary immunodeficiency is. I've had more than one doctor take a step back from me when I told them about my condition," he said. "So I've developed a little fact sheet that I give to GPs and that has worked out well as I've changed communities."

Three years ago, he switched to subcutaneous immunoglobulin therapy. He received subcutaneous treatments in-hospital for a year before being allowed to switch to home administration. "When I first started, I found it really counterintuitive to be sticking needles into myself," He said. "But after few months, I got the hang of it and was able to move out of Vancouver metropolitan area." He now resides in Cranbrook in southeastern B.C. He visits his local blood bank every three months to pick up his treatment products.

Being on subcutaneous home therapy has given him greater independence to travel, too. "What's really impressed me is how portable the subcutaneous products are and how easy it is to take them through the airports both in Canada and the United States," he said. "I tell them ahead of time that I will be traveling with medication and I carry a letter from my doctor, and I've have had no hassle. So my life is better and I hope to stay on the subcutaneous a long time."

## Home Treatment for Children with Primary Immunodeficiency Diseases

**Dr. Christine McCusker, Director, Allergy and Immunology Division, Montreal's Children Hospital, McGill University Health Centre**

In 2004, the Montreal Children's Hospital became the first hospital in Canada to initiate subcutaneous immune globulin home therapy (SCIG) for a child with primary immunodeficiency disease. Dr. Christine McCusker described the first patient case and how it set the path for establishing the clinic's comprehensive care program with subcutaneous home treatment for children with primary immunodeficiencies.

The patient was a three-year-old girl from Sherbrooke, about two hours away from Montreal, diagnosed with agammaglobulinemia (an immune deficiency due to lack of gamma globulin in the blood plasma) following recurrent infections and hospitalization for intravenous antibiotic treatment. The patient was started on intravenous immunoglobulin (IVIG) replacement therapy at her hospital but complained of severe headaches and had unmanageable behaviour changes for at least two to three days after treatment. On one occasion, the severe headache caused her to have seizures. While IVIG therapy reduced infection frequency, the patient's adverse events and debilitation, which lasted for at least one week after each infusion, were significant disadvantages.

The patient was referred for a consultation at the Montreal Children's Hospital. At the time, the clinic had in fact been exploring how it could start a home treatment program for PID but there seemed to be a huge mountain of obstacles, Dr. McCusker said. "But now the problem was not about how to get a program started—I was faced with a suffering child."

The clinic proposed subcutaneous immune globulin therapy, which had just become available through the Health Canada Special Access Program. Studies have suggested that subcutaneous immunoglobulin therapy may have less systemic side effects than IVIG. The patient was put on a weekly dose of subcutaneous gammaglobulin and her adverse symptoms were completely resolved. She is now on home therapy under the supervision of her physician. "Once you have the push to start the program, it's really not that hard—it's really a matter of getting the political, medical and social will to move it forward," Dr. McCusker said.

Important considerations when developing a SCIG home therapy program include:

- Patient selection
- Ancillary equipment (pumps, syringes, swabs, incidentals)
- Blood bank logistics
- Nurse training/nursing staff to train patients in self-infusion
- Monitoring and record-keeping process for tracking infusions
- Periodic reassessments
- Program evaluation

Patient selection and screening is very important—some patients are not suitable for home therapy, and not all patients want home therapy. Patients who switch from IVIG to SCIG therapy go from one injection per month to one injection weekly or more depending on their age, size

and lifestyle. A big challenge in pediatrics is needle-phobia among children, and parents are often reluctant about giving injections because they feel like they must be hurting the child. It is therefore vital to give patients options and flexibility in their choices. Newly diagnosed patients are not given IVIG; they are put directly on SCIG therapy, which allows children to return home and to normalcy relatively quickly despite their diagnosis.

Monitoring and recordkeeping are essential. It is important to emphasize to patients that SCIG home therapy is a privilege rather than a right. Patient responsibilities include:

- Patients must keep a detailed log of infusions.
- Lot number, location of infusion and reactions must be recorded.
- Log must be signed by patient or family member.
- Logs are transmitted to the clinic for review regularly at the three-month visit.

Patient responses have been very positive. As part of ongoing program evaluation, children who switched from IVIG to SCIG were interviewed on their new therapy. The young patients talked about having lots of energy, being proud to learn to self-infuse, feeling more relaxed and happier because of having more home time, and how their parents were less stressed too.

A key issue is how to fund a home therapy program. At the Montreal Children's Hospital, the intensive ambulatory service is also responsible for outpatient IVIG therapy; this made it easier to secure support for a SCIG home infusion program. However, there are still ongoing issues about who will fund or pay for different aspects. An important principle is to not download costs to patients. "We're already taking away the cost of having a nurse give and supervise intravenous infusion, so there has to be a way to open an envelope so that patients will not be out of pocket."

For other provinces interested in setting up IVIG or SCIG home therapy for patients with primary immunodeficiencies, there are now a number of centres in Canada with such programs in place that can supply help, advice, protocols and information. In fact, until recently, several patients from Ottawa were enrolled in the Montreal's Children Hospital home therapy program due to lack of a pediatric immunologist in eastern Ontario. A physician at the Children's Hospital of Eastern Ontario has now initiated a home therapy program in Ottawa.

## **Canadian Guidelines for the Diagnosis and Treatment of Primary Immune Deficiency**

**Dr. Bruce Mazer, Head of Allergy and Immunology Division, Montreal Children's Hospital, Quebec**

Primary immune deficiency (PID) is a rapidly evolving field with over 100 genetic diseases now identified and associated with primary immune deficiency. Most primary immune deficiencies involve a lifelong diagnosis and lifelong treatment. Dr. Bruce Mazer spoke of the importance of correct diagnosis, treatment and follow-up care coordinated through a comprehensive care clinic, and gave an overview of recently developed Canadian guidelines for the diagnosis of primary immune deficiency and treatment with immunoglobulin therapy.

The Canadian guidelines on primary immune deficiency were developed by a national panel of experts brought together by Canadian Blood Services and the National Advisory Committee on Blood and Blood Products. The key purposes of the guidelines are to provide guidance on the

complexities of diagnosis of PID and treatment with immune globulin therapy, and facilitate and standardize the care of patients with primary immunodeficiencies. The guidelines are published in January 2010 in *Transfusion Medicine Reviews*, titled “The Use of Immunoglobulin Therapy for Patients With Primary Immune Deficiency: An Evidence-Based Practice Guideline.”

A patient who is suspected to have a primary immunodeficiency and need for immunoglobulin treatment requires assessment at a comprehensive care clinic. Correct diagnosis of primary immunodeficiency involves a set of precise, defined steps: complete blood count, quantitative immunoglobulins (IgG, IgA, IgM, IgE), B and T cell enumeration, functional tests of immune system (responses to childhood or other vaccines, e.g., diphtheria, tetanus, pneumococcus, influenza), and assessment of end organ damage.

Assessment of end organ damage is important because most individuals with primary immune deficiency have sinus, ear, pulmonary, gastrointestinal and/or skin complications. Diagnosis and immune globulin treatment cannot be based only on a patient’s recurrent infections and low immunoglobulin level—organ assessment is needed to determine if procedures such as pulmonary rehabilitation, sinus surgery or gastrointestinal decontamination are advised. Ancillary testing should also be done (urine analysis and other protein loss studies if applicable, B and T cell functional studies and genetic diagnosis if available).

Comprehensive care clinics are essential to providing coordinated and optimal care for people with genetic immune disorders. They fulfill several key functions:

- Guidance to physicians: Comprehensive care clinics allow immunologists to guide physicians on primary immunodeficiencies and treatment with immune globulin therapy, and keep them updated on the latest research and practices.
- Genetic diagnosis: The diagnosis of primary immune deficiency requires specialized testing which needs to be coordinated through a comprehensive care clinic.
- Genetic screening: Through genetic screening, immunologists can triage and test individuals with a higher risk of primary immunodeficiency. Early diagnosis and appropriate treatment give patients a better prognosis.

The Canadian Society of Allergy and Clinical Immunology (CSACI) is working to build a network based on the expertise and resources of individual centres across Canada, Europe and the United States, to advance genetic screening and proper evaluation of patients with primary immunodeficiency.

Children and adults diagnosed with primary immune deficiency should be followed at least once a year by an immunologist, regardless of where they live in the country. It is important to give patients the choice of the route of administration (i.e., intravenous or subcutaneous therapy) in order to make sure that they are compliant and properly treated.

The key to proper care of patients with primary immune deficiency is to investigate suspected cases early and get patients to a comprehensive care clinic for genetic diagnosis including analysis for identified gene defects that are treatable by immune globulins, or other options such as antibiotic supplements or bone marrow transplantation.

## Canadian Myelodysplastic Syndromes (MDS) Practice Guidelines

**Dr. Rena Buckstein, Co-Director, MDS Research Program, Sunnybrook Health Sciences Centre, Toronto, Ontario**

Myelodysplastic syndromes (MDS) are a group of blood diseases in which the bone marrow does not produce enough healthy blood cells, leading to progressive bone marrow failure. Dr. Rena Buckstein gave an overview of the importance of practice guidelines and the Canadian guidelines on the use of iron chelation to treat iron overload in patients with MDS.

Practice guidelines help ensure that patients get optimal care, especially when clinicians are faced with various levels of evidence on the treatment options. Key functions include:

- Keep clinicians up to date on current treatment and practices.
- Serve as a guidance document for clinicians in the face of pressure from media, patients or companies to change practices or use certain therapies.
- Guide clinicians who lack access to up-to-date publications or Internet resources due to geographic, economic or technological barriers.
- Help inform healthcare funding decision-making by Ministries of Health.

The hierarchy of evidence for clinical decision-making involves five levels (highest to lowest): meta-analysis, randomized controlled trials, cohort studies and comparisons, case series, and case reports. A systematic review also provides a high level of evidence. This involves a structured review of the literature with an explicit description of the search strategy (i.e., databases and types of publications searched) and the inclusion/exclusion criteria.

Key outcomes that should influence the development of treatment guidelines and policy are: survival, quality of life, and economic benefit (i.e., one therapy compared to another). Other outcomes that are sometimes considered include progression-free survival, toxicity and rates of hospitalization.

Practice guidelines can be developed to assist practitioners in treating patients, drive local institutional policies, or guide policies at a higher level. At the higher levels, practice guidelines can be developed by expert consensus opinion of professional bodies, government agencies, journal solicitation, or through the international Cochrane Collaboration ([www.cochrane.org](http://www.cochrane.org)).

The development of practice guidelines should:

- Include a systematic review.
- Clearly distinguish evidence from opinion.
- Provide some interpretation of the data (e.g., weigh outcomes, generalize to other populations, put in context with other therapies, reflect local funding and other realities).
- Provide principles for decision-making.

The key features to look for in practice guidelines are:

- Systematic review component
- Respected sponsoring agency
- Consultation and review process (i.e., solicit input from community practitioners about the validity of the conclusions and whether they would apply them in real life)
- Practical guidance for practice
- Similar/comparable practice context (i.e., similar types of patients)

Five years ago, there was very little information to guide decisions about whether an MDS patient should be chelated. While there was incontrovertible information on chelation in thalassemia and sickle cell anemia, the same level of evidence was not available for MDS. With base funding from Novartis, a group of 11 Canadian hematologists and experts in MDS was convened in December 2005 to investigate the following four critical questions:

- Why should chelation be used to treat iron overload in patients with MDS?
- Who should be chelated?
- When should chelation therapy be started?
- How should you chelate to treat iron overload in patients with MDS?

The questions were divided among four subgroups, which appraised the literature and the level of evidence available. The level of evidence was generally limited to very small phase 2 studies and retrospective case series; therefore the group's recommendations are consensus guidelines rather than an evidence-based review.

The Canadian Consensus Guidelines 2007 recommend iron chelation to prevent end-organ complications of iron overload and extend lifespan in MDS patients with low or low intermediate risk scores who are transfusion-dependent and have expected survival of more than one year, and in higher risk MDS patients who were BMT candidates. Treatment options are deferasirox (Exjade™) or deferoxamine (Desferal™) and should be given (when ferritin level is greater than 1000 or transferrin saturation level is 0 to 0.5).

The MDS Program at Sunnybrook now prospectively registers all MDS patients into its database with their informed and signed consent. The centre recently submitted a national grant proposal to CIHR to fund a national database that would collect prospective clinical data and quality of life data as a way of predicting response and toxicity to therapy.

## **Comprehensive Childhood Bone Marrow Failure And Myelodysplasia Program**

**Dr. Yigal Dror, Director, Marrow Failure and Myelodysplasia Program, Hospital for Sick Children, Toronto, Ontario**

Bone marrow failure syndromes and myelodysplastic syndromes (MDS) encompass a large range of inherited and acquired conditions, which commonly cause patients to have low blood counts because their blood does not produce enough cells in the bone marrow. Many of these patients have extra hematological complications and many of the disorders have a very high risk of cancer, which is why multidisciplinary collaboration is the best approach to treatment, said Dr. Yigal Dror who spoke about the program's objectives, and current status and gaps related to comprehensive care that still need to be addressed.

Treatment options include:

- Supportive care (lifelong therapy with transfusions, antibiotics, etc.)
- Immunosuppressive therapy
- Bone marrow stimulants (steroids, growth factors, others)
- Hematopoietic stem cell transplantation (HSCT)

Life expectancy is reduced for most bone marrow failure and MDS syndromes due to the disease-related or treatment-related mortality. Myelodysplastic syndromes (pre-leukemia) have a high rate of conversion to leukemia. The overall survival rate for children is about 50 per cent.

The establishment of the Comprehensive Bone Marrow Failure and Myelodysplasia Program in 2001 was based on the following rationale:

- Bone marrow failure and myelodysplastic syndromes are a rare, unique and complex group of disorders with major needs.
- These disorders require a high level of expertise of healthcare professionals.
- A significant number of patients are treated at large institutions such as Sick Kids.
- A dedicated program will promote standards of care and opportunities for advancing research and education in the field.

The program's main objectives are:

- Become recognized regionally, nationally and internationally as a center of excellence.
- Promote clinical research and education.
- Advocate for the disorders at the local, provincial, national and international levels.
- Collaborate with other health care professionals at the regional, national and international levels.
- Partner with disease associations to set priorities and address general patient and family-related challenges.

The Bone Marrow Failure and Myelodysplasia Program at Sick Kids Hospital is the only pediatric program of its kind in Canada, and one of the largest in the world. It is recognized as a Centre of Excellence in research and clinical care in pediatric MDS by the International MDS Foundation.

The program provides a framework for clinical care, research and education. The core clinical team is made up of physicians, nurses, a social worker, pharmacist and dietician, lab coordinator, lab technician, clinical research coordinator, and students/trainees. Supplemental services are provided by additional consultants (genetics, endocrinology, gastroenterology, orthopedics, cardiology, otolaryngology, ophthalmology, neurology, nephrology, urology, psychiatry).

There are currently about 170 patients with acquired and inherited marrow failure syndromes and/or MDS in the program.

## **Standards of Care for Hemophilia**

### **David Page, National Executive Director, Canadian Hemophilia Society (CHS)**

David Page of the Canadian Hemophilia Society (CHS) gave an overview of the standards of care for hemophilia and other inherited bleeding disorders developed by a multi-disciplinary group and published in 2007.

In 2004, the AHCDC created a multidisciplinary working group including health care professionals and patient representatives to develop standards of care for inherited bleeding disorders driven by patient needs and best practices. The impetus for this included:

- A 2001 U.S. study showing that hemophilia patients on home therapy who were followed at an HTC had 90 per cent less hospitalization for bleeding complications.
- A 2000 U.S. study showing a significant higher mortality rate for patients who were not treated at an HTC compared to those followed at HTCs.
- Recognition that levels of care and access to comprehensive care varied across Canada.

The Canadian Comprehensive Care Standards for Hemophilia and Other Inherited Bleeding Disorders were presented in 2007 at an AHCDC/CHS Medical and Scientific Symposium, and subsequently adopted by all four professional groups (physician, nursing, physiotherapy and social work) and the CHS.

The standards focus on the structural and resource requirements necessary for a hemophilia treatment centre to effectively provide comprehensive care, and its functions and responsibilities. The key purposes of the standards of care are to:

- Assure equitable access and quality evidence-based care across Canada.
- Establish a reference for future advances and needs.
- Establish a focus and unifying force for health professionals of various disciplines.
- Promote discussion and research regarding optimal ways to deliver care.
- Provide the basis for design of clinics, for accreditation, audit and evaluation.

The document is divided into three sections:

- Scope of care: Bleeding disorders to be addressed by an HTC, the required staff, administrative structure and responsibilities.
- Quality Measures: Expected activities of an HTC that contribute to the quality of both the individual centre and the Canadian HTC network.
- Therapeutic Services: Actions required of an HTC in the direct delivery of therapeutic services.

The key responsibilities of an HTC include:

- Comprehensive assessment of adults at least annually and of children semi-annually.
- Provide hospital ERs and family physicians with guidelines on diagnosis and treatment.
- Arrange for qualified 24-hour medical coverage and consultative services.
- Utilize clinical practice guidelines published by AHCDC and other expert bodies.
- Provide access to special hemostasis testing, genetic testing, and treatment.
- Educate patients and families on how to access emergency care and other services.
- Guide patients and families on how to cope with a chronic health condition.
- Provide prophylaxis to patients according to AHCDC recommendations and best practice.
- Provide a home therapy program to all appropriate patients and monitor effectiveness.
- Provide injection equipment and other supplies to patients free of charge.
- Provide management for patients with inhibitors.
- Be located in a facility that is readily accessible and within an ambulatory clinic to facilitate prompt assessment and treatment.
- Have or provide access an Emergency Department for treatment outside of regular hours.
- Educate other community professionals who provide services to patients.

In spring 2009, 23 of 25 centres participated in an anonymous, voluntary self-administered survey for HTCs based on the standards. Analysis of the results suggests that the standards are appropriate and realistic. The next steps include the creation of a voluntary external audit process, which is intended as a tool for assessment and advocating or negotiating with hospital administrators and ministries of health. The goal is to conduct the first audits of HTCs in 2010, followed by rollout of audit process across Canada.

A participant said that when developing guidelines for thalassemia, the patient group was advised to use the word “guidelines” instead of “standards” because of possible legal complications. She asked whether the CHS and AHCDC define “standards” and guidelines” differently. David Page said that clinical guidelines provide the nitty-gritty information such as dosage and therapy, whereas standards describe the range of services and functions of a comprehensive care clinic. Standards of care should not necessarily have legal implications but

rather set out the services and level of care that should be provided and expected at a comprehensive care centre, Dr. Robert Schellenberg said.

### **Transitioning from Pediatric to Adult Care in Sickle Cell Disease and Hemophilia**

**Dr. Robert Klaassen, Division of Hematology/Oncology, Children’s Hospital of Eastern Ontario, Ottawa**

Transition from pediatric to adult care involves different challenges for patients, families and healthcare providers, said Dr. Robert Klaassen. He described the organization of care for sickle cell disease and hemophilia in Ottawa and recent steps taken by the Children’s Hospital of Eastern Ontario (CHEO) and Ottawa General Hospital to facilitate the pediatric to adult care transition.

The transition from pediatric to adult care generally involves a “teen health gap” due to the different culture of care that exists in pediatric and adult hospitals.

The culture of care at a pediatric hospital is:

- Family-centred (parents directly involved in treatment decisions and consent process)
- Developmentally oriented (approach adapted for pre-school, school age teenage stages)
- Nurturing (high level psychosocial support)
- Interdisciplinary (physician works closely with pharmacist, physiotherapist and dietician)
- Flexible

In contrast, the culture of care at an adult hospital provides:

- Less flexibility due to much higher volume of patients
- Individual-based care (requires patient to be autonomous and independent)
- Disease-focused care
- Cognitive rather than nurturing approach
- Multidisciplinary

The focus of transitional care is to attend to the medical, psychological, social and educational-vocational needs of adolescents as they move from child-oriented lifestyles and systems. Great effort is made to try to provide seamless transition of care for patients.

Some of the challenges faced by patients shifting from pediatric to adult care include:

- Patients making the transition to adult care sometimes feel lost in the adult care milieu—in Ottawa, the children’s and adult centres are within very close distance but it still seems like a leap for patients.
- Patients must leave behind the medical team they’ve known for many years and see new healthcare providers in another setting.

- Although the patient information is shared, there will be knowledge gap in the receiving team.
- The emergency services and admissions at adult hospitals are very different, especially for sickle cell disease.

Some of the challenges faced by healthcare providers in the adult setting include:

- Time constraints
- Knowledge and comfort zone
- Resources and support staff are much more limited compared to the pediatric setting.

Some key features of the hemophilia and sickle cell programs in Ottawa include:

- Both comprehensive care programs are housed in the same complex.
- Patients are followed throughout childhood at CHEO.
- Adult investigations, emergency room visits and admissions are at one of the two adult hospitals (the Ottawa Hospital General campus or Civic campus).

The CHEO Pediatric Hemophilia Program is staffed by a dedicated hemophilia nurse and a backup nurse, dedicated physiotherapist, part-time data manager, dedicated social worker, and administrative support. Patients visit the clinic for check-ups every six months to be assessed by the comprehensive care team. Blood bank services and emergency care are also centralized. The adult hemophilia program at the Ottawa General Hospital is similar to the CHEO program, which allows for fairly smooth transition.

The number of patients in the CHEO Pediatric Sickle Cell Anemia Program has grown since the introduction of newborn screening for sickle cell in Ontario three years ago. It was an enormous challenge to get a dedicated sickle cell nurse and great to now have one in place, he said.

Until recently, Ottawa did not have an adult sickle cell program. There is now a dedicated hematologist at the Ottawa General Hospital who sees all adult sickle cell patients. The hospital is currently applying for funding for a dedicated sickle cell nurse for adults, and working to establish emergency room protocols for handling patients with sickle cell disease.

While far from being a model for comprehensive care, CHEO has made baby steps in right direction, but lot more needs to be done, Dr. Klaassen concluded.

## Canadian Thalassemia Treatment Guidelines

**Dr. Isaac Odame, Division of Hematology/Oncology, Hospital for Sick Children, Toronto, Ontario**

Thalassemia is a blood disorder due to a genetic defect that impairs the body's ability to make normal amounts of hemoglobin needed to produce healthy red blood cells. Patients are treated with regular blood transfusions. However, long-term blood transfusion therapy leads to iron overload—this is usually the underlying cause of lower survival rather than the disease itself. Dr. Isaac Odame described the development of Canadian treatment guidelines for thalassemia.

The Thalassemia Project Planning Group was formed in 2006 by the Thalassemia Foundation of Canada, the Anemia Institute for Research and Education, and thalassemia patients, caregivers and treaters. The group established a number of key goals:

- Improve overall health and quality of life for thalassemia patients.
- Provide comprehensive, multidisciplinary care for thalassemia patients.
- Implement current evidence-based best practices.
- Develop guidelines for healthcare professionals on the management of care for patients with thalassemia and their families.
- Empower patients.

A writing group was formed to examine the standards of thalassemia care in Europe and the United States and develop Canadian guidelines that reflect the best current practices. Guidelines developed by the U.K. Thalassaemia Society, published in 2008, provided a benchmark standard of care.

The writing group consisted of Dr. Isaac Odame as chair, research fellow Dr. Farzana Sayani, Dr. Molly Warner of Montreal Children's Hospital, Dr. John Wu of BC Children's Hospital, Durhane Wong-Rieger of the Anemia Institute for Research and Education, and writer/editor Kimberly Humphreys. The research fellowship was funded by Novartis.

“Treatment and care for thalassemia has improved over the years so it is important to make sure that clinical practice in Canada is up to date and based on evidence,” Dr. Odame said.

Development of the guidelines focused on three areas:

- Principles of thalassemia care and desirable goals for comprehensive care centres
- Guidelines on basic requirements of the centres
- Interventions and specific steps to implement individual guidelines

Following review by a panel of Canadian and international experts, the document *Guidelines for the Clinical Care of Patients with Thalassemia in Canada* was published in 2009.

The guidelines are intended as an educational tool for health professionals, patients and families. It provides comprehensive information on key aspects of thalassemia care:

- Components of comprehensive thalassemia care
- Management of thalassemia (transfusion support, iron overload and chelation therapy, hematopoietic stem cell transplantation, and psychosocial aspects of thalassemia care)
- Transition from the pediatric to adult care setting
- Complications of thalassemia (cardiac, liver, endocrine and bone complications, fertility and pregnancy issues and infection, dental or nutrition-related complications)

The guidelines also include a chart on “Staffing Recommendations for Satellite Clinics and Specialist Centres,” which sets out the multidisciplinary team members and services that should be accessible to people with thalassemia through specialist centres and satellite clinics. In addition, a treatment flow chart outlines the steps from diagnosis to assessment of indications for transfusion, laboratory evaluation, initiation of transfusion therapy, monitoring for iron overload, and chelation therapy.

These charts are useful information and advocacy tools that allow physicians, patients and patient groups to compare their circumstances to the recommendations in the Canadian thalassemia guidelines, Dr. Odame said.

A key challenge will be actual implementation of the guidelines to improve care for thalassemia patients, particularly for adults in the Toronto area. He urged patients and health professionals to use the guidelines to advocate for services at their institutions, and as a benchmark for gauging their progress or success towards providing comprehensive care for thalassemia.

Participants discussed the differences between the terms “standards” and “guidelines,” and whether the term used influences their impact and take-up within the medical community. The Thalassemia Project Planning Group was advised to use “guidelines” to avoid controversy but in practice there is no difference in terms of the goals, and the thalassemia guidelines are recognized to represent the broad view of experts in Canada and abroad, Dr. Odame said.

A participant noted that small centres with small numbers of patients are unlikely to be able to meet some standards, whereas they can use guidelines to work towards improvements or solutions. Dr. Robert Schellenberg said guidelines are useful for treaters but it is important for patient organizations to advocate for standards of care to be met.

## **Session 8: Models for Comprehensive Care**

**Chair: Riyad Elbard, President, Thalassemia Foundation of Canada**

### **Commissioning for Rare Conditions in England**

**Keynote Speaker: Dr. Edmund Jessop, Medical Advisor, National Commissioning Group For Highly Specialised Services, National Health Service (NHS), England, U.K.**

Dr. Edmund Jessop presented an overview of the organization and provision of comprehensive care for patients with rare conditions in England, provided by the National Health Service (NHS) through the National Commissioning Group For Highly Specialised Services. He also spoke briefly about the National Institute for Health and Clinical Excellence in the U.K., which provides guidance on clinical practice, technology appraisals and public health.

The National Commissioning Group For Highly Specialised Services coordinates treatment for about 50 very rare diseases. The main services are medical procedures, disease management and diagnostics. These services are provided at a small number of specialist centres in England. “Our core belief is that volume drives excellence,” Dr. Jessop said. “When it comes to very rare conditions, health professionals need to see a high volume of patients in order to develop strong diagnostic and practical skills—that’s absolutely key to managing all the unusual presentations and extra complications of very rare diseases.”

A key aspect of comprehensive care is the multidisciplinary team. The centralization of specialized services for rare conditions allows specialist centres to serve a greater volume of patients, and helps ensure that all team members see adequate numbers of patients. Patients benefit from the coordinated care. It is crucial to have specialist nurses to bridge the nexus between technology and humanity, Dr. Jessop noted. During consultations with their physician, patients are often intimidated or frightened by the information. Nurses play a critical role in patient education, follow-up and outpatient care.

The National Commissioning Group’s main functions are planning, funding and monitoring of highly specialized services for rare conditions.

- **Planning:** Proposals on the national commissioning of rare diseases are generally driven by recommendations from the profession. Professional consensus is a key factor in the decision to set up specialist clinics for a rare disease. The strongest driver though is clinical outcomes. Thus in addition to organizing specialized care, the National Commissioning Group also develops clinical standards which are used to assess hospitals, providers and clinics.
- **Funding:** About 99.5% of the NHS budget is allocated to the local and regional healthcare decision-makers. The National Commissioning Group is allocated the remaining 0.5% of the budget, which is about £500 million per year. The unit must therefore be very selective about the conditions that get coverage.
- **Monitoring Outcomes –** Four main types of clinical outcomes are monitored: mortality, symptom scores, biochemical markers, and quality of life.

- **Monitoring Access and Services:** Since specialized services for rare conditions are centralized at specialist clinics, it is essential to monitor access to services and epidemiology to make sure that patients in remote areas are not being under diagnosed or under treated. Services are also monitored through patient opinion, feedback from patient organizations and international peer review (international experts are periodically invited to evaluate select services).

Some of the issues and considerations related to centralizing services for rare conditions include:

- **Burden of Travel:** The key question is how often patients need assessment or treatment. Distance and travel are barriers if the patients need daily or very frequent care at a clinic, and therefore would be a strong deterrent to centralizing services for a particular condition.
- **Access –** In Europe, rare disorder is defined as 5 per 10,000, which is the same level as the orphan drug legislation. The NHS definition of very rare disease is 1 per 100,000, thus the services are focused on extremely rare conditions.
- **Commissioning:** Decisions on rare diseases covered under national commission need to take into account practical considerations such as administration and funding.
- **Cost of Drugs:** Rising drug costs and very expensive orphan drugs are persistent issues and there are concerns that they could eventually become difficult to afford and provide to patients.

The National Institute for Health and Clinical Excellence (NICE) was established in 1999 and provides evidence-based guidance on clinical practice, technology appraisal and public health. Technology appraisals are recommendations on the use of new and existing medicines and treatments within the NHS and apply to England and Wales. While NICE is sometimes viewed as an organization that aims to limit or deny access to treatment drugs, the principle is to ensure that the medicines are uniformly available, Dr. Jessop said. The decisions made by NICE are legally binding to induce uniform application of all cost-effective drugs.

Health technology appraisal involves two basic questions of health economics: How much does it cost? What does it do? NICE examines cost of treatment from several perspectives:

- **Cost-effectiveness ratio:** Cost and effectiveness compared to the next best alternative.
- **Incremental cost-effectiveness ratio:** Increase in health benefit associated with increase in cost, e.g., cost of treatment per life year gained.
- **Cost per quality-adjusted life year:** Measurement of cost in terms of quantity and quality of life, i.e., low cost per QALY is preferred to high cost per QALY.

Although NICE does not have a declared cost per QALY threshold, its decisions over the years (on more than 100 drugs to date) have tended to revolve around a cost per QALY threshold of £30,000. However, social value judgments are also made. For example, NICE has accepted a higher cost for the first effective treatment for motor neurone disease. In addition, it was recently advised by the government to allow a higher cost per QALY for end-of-life treatments.

Some ultra-orphan drugs cost well over £30,000 per QALY. For example, treatment for rare disorders such as paroxysmal nocturnal hemoglobinuria (PNH) and rare enzyme deficiencies such as Hunter Syndrome and Maroteaux-Lamy Syndrome cost around £250,000 yearly for an adult patient. These have not been appraised by NICE because the organization only assesses drugs that are specifically requested by a selection panel representing the ministers of health; about 10-15 therapies are assessed per year.

A key issue is whether treatment cost is construed in terms of total cost per disease, per access, or total cost per patient. Some treatments for rare disorders and rare enzyme deficiencies can cost around £300,000 per patient yearly. At a glance, the cost of treating these rare disorders can seem very expensive—but if there are hardly any patients with the disease, the total cost for treating the disease may not add up to that much relative to other conditions, Dr. Jessop noted. Eculizumab therapy for PNH costs £300,000 per patient, which translates into £30 million annually to treat PNH patients in England; by comparison, the NHS spends about £50 million annually on laxative therapies. “There are always political judgments involved in healthcare—and since this is taxpayers’ money, it is absolutely right that these decisions should be made by politicians as their elected representatives,” Dr. Jessop concluded.

## **Audit of Hemophilia Treatment Centres in the U.K. and Ireland**

### **David Page, National Executive Director, Canadian Hemophilia Society**

David Page described the U.K. accreditation and audit of comprehensive care clinics, which he experienced first hand serving as the patient representative auditor in the audit of hemophilia treatment centres in Ireland in 2008.

Audits of hemophilia treatment centres in the U.K. and Ireland are conducted based on the national service specification for hemophilia and other inherited bleeding disorders, developed by the U.K. Haemophilia Alliance in 2001. The main purposes of the service specification are to inform those responsible for commissioning hemophilia services (i.e., hospitals) of the standards of care that should be available for all patients with inherited bleeding disorders, and standardize high-quality hemophilia treatment across the U.K.

The specification’s uses include:

- Guidance to commissioners on standards of care for inherited bleeding disorders
- Basis for health professionals making the case for comprehensive care at their hospitals
- Audit tool for external peer review

The Irish National Haemophilia Council was established in 2004 and advises the Minister for Health on all aspects of care and treatment for hemophilia and inherited thrombotic diseases thrombosis in Ireland. It involves the representatives of the Department of Health, the Paying Authority, clinicians, and the Irish Haemophilia Society.

Ireland has three comprehensive hemophilia care centres; there are two separate adult and pediatric centres in Dublin and one pediatric and adult centre in Cork. Two audits have been conducted since the Council formed.

The first audit was carried out in 2006. The audit identified several issues related to care:

- Staffing deficiencies in Dublin (pediatric) and in Cork
- Infrastructure deficiencies in Cork
- Requirement for in-patient designated beds in Dublin (adult)

Furthermore, the lack of a patient representative among the auditors was identified as a deficiency of the audit process itself. The Irish Haemophilia Society was adamant that a patient representative must be included on future audit teams.

The second audit was conducted in 2008. As the audit approached, the Irish Haemophilia Society reminded health authorities that key deficiencies identified in the 2006 audit had not yet corrected, and the National Haemophilia Council cautioned senior health service staff and the Minister for Health that a poor audit report would be inevitable unless resources were made available to address them. In the days before the audit, newspaper articles focused on the different problems that had still not been corrected. This spurred action and funding to augment staffing and improve facilities was confirmed the day before the audit was to begin.

The 2008 audit team was made up of a physician, nurse and patient representative. David Page was selected as the patient representative auditor by the Irish Haemophilia Society and also served as external auditor. The auditors spent one day at each centre and their activities included:

- Audit of physical facilities
- Audit of services
- Discussion on patient needs
- Review of anonymous patient questionnaires
- Discussion on human resources
- Policies and procedures
- Discussion with individual staff

While there was initially a lot of reservation about the audits on the part of staff, they have now come to realize that it is a non-punitive process, and a tool that helps them improve their services. The 2008 audit report identified several different deficiencies, many of which have since been corrected.

A participant asked about the Irish National Haemophilia Council's scope of responsibility. David Page explained that the Council is a statutory body created to oversee national services for hemophilia and other rare blood disorders as well as thrombotic disorders. Thrombotic disorders are more common but require a lower level of care, so this allows centres to provide care to more patients and make the best use of the facilities and healthcare resources available.

## Session 9: Advocacy Workshop – Tools for Action

**Facilitator: Ron Rosenes, Canadian Treatment Action Council (CTAC)**

This workshop offered strategies and tools for effective advocacy. Facilitator Ron Rosenes began by sharing some of his personal perspectives based on close to 20 years' experience as an advocate for people with HIV/AIDS at the municipal, provincial and national levels.

There are five key principles of advocacy:

- 1. Be a voice for other people.** Systemic advocacy is directed at changing institutional policies and/or programs, and raising the public profile for a particular group. Advocates provide authoritative information based on what they hear from the communities they serve.
- 2. Do your research.** It is important to take the time to research different advocacy options, and identify key players, decision-makers, and potential supporters and opponents.
- 3. Respect privacy and confidentiality.** This is essential to advocacy and especially for patients, who often face stigmatization due to their medical condition. Two key questions are: Under what conditions would it be appropriate to share health information or identify an individual? What are the moral, professional or legal ramifications of sharing information?
- 4. Use the style you are most comfortable with.** Determine the target audience for the issue at hand (e.g., government, medical professionals, patients, the general public, industry). Identify strong advocates who can communicate and advance the issues with the target audience.
- 5. Create the environment to empower those around you.** It is important to also provide support to advocates including opportunities to develop their skills.

Participants were asked to describe some of their priorities for advocacy. They identified:

- Access to therapies and drugs
- Access to treatment for adults with thalassemia in Toronto and other areas
- Access to care in rural and remote areas
- Home therapy for patients with rare blood disorders
- Pain management
- Funding for comprehensive care clinics
- International knowledge transfer (e.g., best practices)
- Patient care in the ER
- Equal access to funding and treatment for similar disorders

These challenges are exacerbated by the different provincial/territorial healthcare systems across the country, said David Page of the Canadian Hemophilia Society.

Dotty Nicolas, past president of the Sickle Cell Association of Ontario, said that medical allies were instrumental to helping the patient organization achieve its goal to establish newborn screening in Ontario. Other key players were opposition MPs and the media.

The media can be effective but the story must be very compelling to get their attention, said Tina Morgan of the Canadian Immunodeficiencies Patient Organization. She also cautioned that the media tends seek the controversial angle of a story. It is important to establish trusted media contacts long before a crisis occurs. It is also essential for organizations to write effective press releases and make sure that there are strong advocates, spokespeople and experts readily available for interviews.

Another participant highlighted the important of establishing strong contacts within different levels of government and within industry. Participation in public health consultations and advisory committees are particularly effective. Health Canada can also be a partner in advocacy. It is important to cultivate relationships with politicians; election time is good for gaining their attention, interest and support, another participant said.

Riyad Elbard of the Thalassemia Foundation of Canada said a big frustration is that even when politicians say they will help, responsibility for funding and decision-making gets shifted back and forth between the hospitals and the Ministry. Ultimately, a document with recommendations may be produced but nothing gets implemented. Furthermore, unlike common diseases such as cancer, heart disease and stroke, rare blood disorders now get an ever-decreasing amount of overall funding.

Another participant recounted his involvement some years ago with organizations seeking funding to improve cancer care. Policymakers, ministers, deputy ministers and other politicians said that increased funding would require the groups to “get your act together.” Dozens of cancer organizations therefore formed an alliance focused on getting the federal government to establish a national cancer act and a national organization to coordinate cancer care. With major issues at a national level, it is better to work in a coalition, Rosenes said.

Tom Alloway said that he considers it a matter of courtesy to go to government officials first, but not to wait very long before talking to opposition critics. If it gets media attention, politicians will have to start addressing the questions. Rosenes said that when CTAC was developing its plan to gain access to a national catastrophic drug program, members realized that given the national importance of the issue, they couldn’t do it alone and needed to identify allies, which included committed senior civil servants at various provincial Ministries of Health.

The rural/urban divide is an immense challenge, a participant said. It is very hard for people in rural areas to access care and lobby for improved care. David Page noted that the guiding principle in the U.K. is that volume drives excellence. For rare disorders, policymakers must be convinced to set up designated provincial centres that provide support to rural areas—with so few patients, it’s necessary to centralize.

Overall, successful advocacy relies on having a strong plan for action that identifies the goals and objectives, key players and allies and their roles and responsibilities, timeframe, and communication and outreach strategies to reach the target audience. Collaboration, partnership and determination are also vital.

## Day Two Wrap Up

David Page noted the progress towards the NRBDO's vision of comprehensive care for people with rare blood disorders in Canada.

The Edmonton Rare Blood Disorders Program, which provides coordinated health services for over 800 patients with inherited blood disorders, is a model of success. Other regions are likely to have comparable numbers of patients with rare blood disorders whose management of care could be improved through comprehensive care programs.

The Quebec Primary Immunodeficiencies Network has been successful in advancing home therapy for patients with primary immunodeficiency diseases and hereditary angioedema based on cost-benefit analysis showing the advantages for patients and healthcare funders. Progress is also being made towards establishing a subcutaneous and intravenous immunoglobulin program in British Columbia and the creation of a primary immunodeficiency centre of excellence.

The newly developed Canadian guidelines on the use of immunoglobulin therapy for patients with primary immune deficiency will help improve diagnosis and treatment and standardize care. Similarly important are the Canadian guidelines on the use of iron chelation in patients with myelodysplastic syndromes and the treatment guidelines for thalassemia.

Important challenges that still need to be addressed include funding and resources for comprehensive care clinics and the development of patient registries, and funding for the NRBDO and its ongoing advocacy efforts. Key issues across all the disease areas include the need for dedicated physicians in certain parts of the country, varying availability and access to therapy options in different parts of Canada, and lack of follow-up care in absence of comprehensive care programs.

## Sunday, November 15, 2009 – Workshops

### Workshop 1: National Collaboration and the Role of Patient Organizations

**Co-Chairs: David Page and Tom Alloway, Canadian Hemophilia Society**

This plenary workshop focused on collaboration and the dynamics between patient organizations and medical professionals, industry and government. Five statements on collaboration were presented to participants for discussion.

**Statement 1:** “The interests of patient organizations and pharmaceutical companies often coincide; both want new and effective therapies to be approved and funded for use. Patient organizations and pharmaceutical companies can work together effectively and ethically towards this goal.”

While there is often cynicism that the pharmaceutical industry is mainly motivated by profit, the reality is that drug companies are making drugs that patients want and need so that they can live, a participant said. Patient groups and industry can work together effectively so long as the relationship is clear, transparent and supported by ethical policies.

When collaborating with pharmaceutical companies, it is important for patient organizations to diversify their base of support, another participant said. Support from government bodies like Health Canada or medical groups helps strengthen perception and integrity.

Keeping the relationship at arms length is really important, a participant said. Patient groups need to look at proposals from pharmaceutical companies very critically because they have different mandates. The relationship, roles and expectations must be clearly defined.

Pharmaceutical companies have a very important onus to protect their relationships with patient groups, said an industry representative. Therefore there are policies to ensure that interactions are ethical, for the protection of the organization as well as patient groups.

**Statement 2:** “In the long run, smart health solutions save money and lives. Patient organizations have a responsibility to present these smart solutions to health authorities.”

Patient groups play a critical role in advocacy with governments because physicians and pharmaceutical companies do not necessarily get heard in the same way, a participant said. Another participant emphasized that the need to have the backing of medical organizations, which is also important for outreach and buy-in within the medical community.

Smart solutions are not only about benefits to health—smart solutions are also good for society as a whole, said co-chair David Page. They contribute to less hospitalization, less absenteeism from school or work, and greater social integration. These benefits are hard to put numbers to but they are a critical aspect of smart solutions.

Rare blood disorder organizations across Canada need to work together on smart solutions for their common goals. Key issues include the fact that Canada does not have a definition for “rare disorder” or national policy framework for rare disorders. A pan-Canadian strategy is needed.

**Statement 3:** “When advocating for change in the health system, making an emotional appeal is more important than presenting convincing data.”

There was consensus among participants that emotional appeal helps rally public support but must be accompanied by convincing data. However, a particular challenge for rare disorders is that in some cases, limited data is available.

**Statement 4:** “Those who make waves with healthcare providers risk receiving inferior health care.”

A key role of patient organizations is advocacy, which sometimes involves making demands or complaints about patient care, a participant said. For individual cases, advocates serve as a buffer between the patient and health provider. But with rare diseases, it’s often easy to figure out the source of a complaint and this can cause tension between a patient and health provider.

Among patients, there is often a fear that their care will be compromised if they raise issues about treatment with their healthcare providers, a participant said. Another said self-advocacy depends very much on the individual patient’s comfort level with their healthcare provider. “I made waves and experienced good results, but many patients feel very vulnerable and reluctant to risk alienating whatever healthcare support they might have,” he said

There are clearly defined ethical guidelines on the provision of patient care that healthcare providers must follow, a participant said. Another noted that healthcare providers are responsible to provide emotional, spiritual and medical care. Professional bodies (e.g., college of physicians) investigate all complaints from patients, and healthcare providers who do not fulfill their responsibilities are reprimanded and/or have their licenses revoked.

On the other hand, there are patient groups that have made waves, raised hell and made a difference in Canada, co-chair Tom Alloway said. For example, HIV/AIDS advocates successfully fought for access to health and social services for gay men who contracted the virus. The Canadian Hemophilia Society fought on behalf of thousands of Canadians with hemophilia who were infected with HIV through the blood system and brought about the re-organization of the blood system in Canada. “Patient organizations as a group are capable of changing the system in Canada, if you’re organized and you put your mind to it, you really can do it,” he said.

**Statement 5:** “When patient organizations and physician groups work at cross-purposes or in an uncoordinated manner, governments invest resources elsewhere.”

There was consensus that when patient and physician groups are not aligned on healthcare needs and proposals, governments are able to ignore requests for funding and resources and invest elsewhere.

## **Workshop 2: Barriers, Challenges, and Shortcomings**

**Facilitator: Tina Morgan, President, Canadian Primary Immunodeficiencies Patient Organization**

This workshop looked at challenges related to establishing comprehensive care for rare blood disorders and developing patient registries. Conference Co-President Tina Morgan launched the plenary discussion by highlighting some of the challenges mentioned during the first two days.

Challenges related to comprehensive care for rare blood disorders include:

- Lack of follow-up in the absence of a comprehensive care clinic
- Poor pediatric to adult care transition
- Inconsistent access to treatment across Canada
- The need for home therapy for rare blood disorders

Challenges related to development of patient registries include:

- Registry design
- Funding and resources
- Access, consent, privacy and security

### **Plenary Discussion on Comprehensive Care**

Discussion focused on challenges related to knowledge and expertise, diagnosis, treatment options, specialist/centralized care, policy and funding.

Knowledge and Expertise:

- Sometimes a patient with a rare disorder may have advanced knowledge about the disease but the information may not be well received by their health providers.
- Natural history of disease is not always clearly understood.
- Lack of knowledge, expertise and proper diagnosis are critical challenges. It is important to connect with clinicians so that they are informed about the diagnosis and management of rare blood disorders and about newly emerging rare disorders.

Diagnosis:

- Blood work is sometimes insufficient for making an accurate diagnosis—in some cases, genetic, polymerase chain reaction (PCR) or tissue diagnostics is needed.
- Access to diagnostic services and specialized tests is a critical issue since proper diagnosis is essential in order to establish the appropriate treatment.
- Inconsistent funding of diagnostic services is a key issue—not all provinces pay for specialized testing.

### Treatment Options:

- Patients should be involved in treatment decisions and given the choice of intravenous or subcutaneous home therapy.
- Patients on home therapy must be properly followed at a comprehensive care clinic.
- Patients who require or opt for in-hospital treatment should be treated in ambulatory facilities instead of the emergency department, which can very chaotic.

### Specialist/Centralized Care:

- A key barrier is a lack of clinician expertise in the rare disorders—in some cases, there may be only one or two specialists in the country.
- Modern ways to connect patients to the specialists need to be explored. Options include telemedicine and telehealth.
- A directory of specialists in rare blood disorders in Canada would be useful to both patients and clinicians.

### Definition of Rare Disease:

- Canada does not have a definition for rare disease.
- The definition of rare disease varies worldwide. The European Commission on Public Health defines rare disease as one that affects 1 in 2,000 people. The United States defines rare disease as one that affects about 1 in 1,500 people. Rare diseases that affect fewer than 1 in 100,000 people are sometimes called very rare or ultra rare diseases.
- The definition used has implications on policy, funding and access to rare therapies and orphan drugs.

### Funding:

- There is a misconception that the provinces and territories are solely responsible for healthcare funding. In fact, the federal government can earmark funds in its health transfer payments for specific populations, diseases or treatments—for example, the human papillomavirus (HPV) immunization program initiated in 2007.
- The starting point needs to be the development of a federal policy framework with provision of funds to kick start comprehensive care programs in the provinces and territories. This is a key priority in terms of advocacy for rare blood disorders.
- Drugs and therapies for rare diseases can be very expensive. However, funding decisions should not be based only on cost-effectiveness and quality-adjusted life year. It is also important to look at the value, clinical effectiveness and benefits.
- Total cost of treatment per patient can be high. However, therapies for rare diseases are clearly effective and the total cost of treatment for a rare disease is relatively low and a very small part of the overall health budget.

## **Plenary Discussion on Patient Registries**

Discussion focused on registry design, physician/patient outreach, and funding and resources.

### Registry Design:

- Many different types of patient registries exist. The key question is whether to strive for a national registry for rare blood disorders, national registries for individual disorders, or provincial registries linked nationally.
- Key limitations of the provincial registry approach include different platforms and inconsistent scope of data, which affect the sharing of information and therefore the usefulness of data collected. Other drawbacks are high cost/low enrolment and multiplied costs (multiple databases and servers, administration and IT support).
- Key limitations of the national registry approach include data collection and management given the different characteristics of the rare blood disorders and differing needs and objectives.
- Key benefits of the national registry approach include consistent scope of data collection, which is important to developing better knowledge about natural history of disease, and greater capacity to make international linkages.
- Other important issues include consent processes and privacy policies, ownership and use of data, access and security, and registry maintenance, sustainability and lifespan.

### Physician/Patient Outreach:

- Rare blood disorders affect a very small number of patients who are scattered across Canada. In the absence of coordinated and centralized care, a key challenge is finding patients who have or have not been diagnosed with a rare blood disorder.
- Outreach to both physicians and patients throughout Canada is essential.

### Funding and Resources:

- A fundamental challenge will be securing initial funding for registry design and development (hardware, software, initial set-up costs, and ongoing operating costs IT support) and long-term funding for registry operations (project management, administrative support and data entry).

Participants emphasized the importance of collaboration and common will among patient organizations, physicians, funders and other stakeholders in order to move forward with the establishment of comprehensive care and patient registries for rare blood disorders.

## **Workshop 3: Priority Areas Needing Action**

**Facilitator: Winnie Leung, Thalassemia Foundation of Canada**

This workshop engaged participants in small group discussions on the top priorities for action. Four groups formed to discuss and identify three or four priority areas, then reported back to the plenary. The groups all identified priorities as being in the following four main areas:

- Further development of comprehensive care for rare blood disorders
- Development of patient registries
- Continuation of the NRBDO
- Advocacy and education

### **Comprehensive Care**

- Further development of comprehensive care clinics
- Pediatric to adult care transition programs
- Medical outreach for patients in peripheral and remote communities
- Access to treatment, multidisciplinary care and specialized diagnostic services
- Access to self-administration of products (home therapy) when appropriate
- Development of treatment guidelines and standards of care
- Education and outreach for patients and health professionals.
- Opportunities for clinicians to network, consult and collaborate with their peers.

### **Development of Patient Registries**

- Registry design (common registry for all disorders vs. individual registries)
- Data management, access and ownership, consent and privacy, confidentiality
- Funding and resources for national patient registries

### **Continuation of the NRBDO**

- Continued funding for advocacy initiatives
- Ongoing collaboration among patient groups, health professionals, industry and government.

### **Relationships With Government**

- Provincial/territorial programs for rare blood disorders
- Funding for treatment and comprehensive care
- Definitions for “rare disease” and “orphan drug”

- Funding and legislation to improve access to orphan drugs

## **Workshop 4: Strategies and Action Planning to Address Priority Areas**

**Co-Chairs: Michel Long, Canadian Hemophilia Society, and Winnie Leung, Thalassemia Foundation of Canada**

The objective of the final workshop was to identify concrete strategies and actions to advance the vision of comprehensive care for rare blood disorders. Co-chair Michel Long explained that the plenary would break into four discussion groups to tackle one of the four priority areas:

- Development of patient registries
- Continued progress in comprehensive care
- Continuation of the Network of Rare Blood Disorder Organizations
- Relationships with government

Participants were encouraged to join the group that resonated most with their own particular knowledge and area of expertise. Their tasks were to:

- Identify strategies for advocacy, action and funding.
- Identify expertise and resources available and needed to move forward.
- Identify opportunities for collaboration among patient groups, physicians and allied health professionals, other specialists, as well as industry and government.
- Develop an action plan with specific roles, responsibilities and timelines if possible.

The groups would then report back on their proposed strategies, and the plenary would try to establish consensus on strategies for moving forward both as individual patient organizations and collectively as the NRBDO.

### **Group 1: Development of Patient Registries**

- **Investigate registry structure/framework:** Determine whether there would be an independent registry for each disorder or a single registry for all of the rare disorders. Other important issues include ownership and access, among others.
- **Involve physicians/specialists:** Patient registries rely on the participation of physicians and allied health professionals, who gather and provide data for the patient registries. Therefore, it is essential to consult and involve the medical community in the development of patient registries. Suggestions include: Present the registry concept at physician meetings, and identify physician champions already working with patient groups to help lead the way.
- **Involve other professionals:** Many other disciplines and professionals are key to the development and maintenance of patient registries. These include information technology

specialists, electronic health record specialists, security and privacy experts, etc. All can provide invaluable guidance and expertise towards registry development.

- **Funding:** Funding needs to be obtained for development of patient registry, operations, administration and maintenance.
- **Establish patient registry working group:** The purpose of the NRBDO patient registry working group would be to examine the existing patient registries and models, and make recommendations on how the members of the NRBDO can move forward individually or collectively to establish a patient registry. It is important to take into account that registries already exist for some of the disorders, and to consult those patient/physician groups about the idea of creating a national patient registry encompassing all the disorders.

Tina Morgan announced that the Canadian Immunodeficiencies Patient Organization found champions at this conference for the development of a registry for PID and HAE. Gerhard Kindle of the European Society of Immunodeficiencies will provide guidance on setting up a registry and some funding has been secured to move forward.

A participant questioned whether the NRBDO should be responsible for developing a common registry and whether it has the manpower and resources at board level to take on this initiative; perhaps individual registries should be developed by individual groups. Morgan said that this conference has brought together a wide range of experts and participants, providing a foundation for advancing comprehensive care and the establishment of patient registries. The NRBDO can continue to have a big impact in allowing this to occur.

The following option was proposed:

- Create an NRBDO Registry Working Group to investigate what would be needed to develop a common registry, and decide whether to work together on one common registry (i.e., collect basic demographic information on all the patients and a subset of data for different diseases), or develop individual registries with common variables so that data can be shared for research purposes. Data management and IT specialists should be consulted.

## **Group 2: Continued Progress in Comprehensive Care**

**Rapporteur: David Page, Executive Director, Canadian Hemophilia Society**

David Page presented the group's recommendations for how the NRBDO, individual patient organizations and individuals in general can work to advance progress in comprehensive care.

- **Publicize existence of already established comprehensive care centres:** A number of comprehensive care centres exist for a range of disorders throughout Canada, but there is not enough awareness of their existence and services.
- **Attend the Canadian Hematology Society Meeting:** Present about the NRBDO, and submit articles on the results from this meeting for publication in their newsletter.

- **Give talks at meetings of professional and patient organizations.** For example, the Canadian Immunology Society, Canadian Hematology Society and Canadian Hemophilia Society.
- **Presentations to Canadian Blood Services:** Promote awareness of the NRBDO, its goals and ongoing work towards comprehensive care through presentations to the CBS National Liaison Committee and provincial liaison committees.
- **Engage local media:** Local media have a greater interest in “human interest” stories than national media. Still, local coverage can trigger wider interest and lead to national coverage.
- **Engage federal/provincial/territorial representatives:** Write to MPs and MLAs and present them with the results of the NRBDO meeting. A summary will be sent to ministries of health, which were invited to the conference but did not attend.
- **Develop physician/patient brochures on rare blood disorders:** A key purpose is to provide physicians and patients with information on diagnosis and treatment as well as specialized clinics and clinicians that can provide guidance or referral services. This would likely involve developing individual brochures for different disorders or by disease group.
- **Develop standards of care by disease group based on the comprehensive care model:** Different groups are making progress in establishing standards of care using the comprehensive care model. As this model gets applied more and more, it is gaining recognition, validation and support.
- **Publish proceedings of this meeting in a medical journal:** For example, following the last NRBDO meeting, Canadian and international investigators collaborated to develop the “2007 International Consensus Algorithm for the Diagnosis, Therapy, and Management of Hereditary Angioedema,” published in *Annals of Allergy, Asthma & Immunology*.
- **Create a registry of expert clinicians:** A registry of expert clinicians would be a useful resource for members of the NRBDO seeking information for their own purposes or experts for referral (e.g., patients, media). It could be for internal use only.

Participants agreed with all of the recommended actions and had no further comments.

### **Group 3: Continuation of the Network of Rare Blood Disorder Organizations**

**Rapporteur: Tom Bowen, Clinical Professor of Medicine and Pediatrics, University of Calgary**

- **NRBDO Mandate:** The Network’s main mandate should continue to be comprehensive care for each of member diseases based on the hemophilia care model.
- **NRBDO Website:** Consider development of an NRBDO website with comprehensive and high-quality information about each of the diseases and to direct people to centres of excellence. The idea is to provide comparable, uniformly presented information on all of the blood disorders, post newsletters, and have links to the websites of the member organizations. However, this would be an expensive undertaking and requires funding.

- **NRBDO Conferences:** We specifically have meetings of representatives to the NRBDO on an annual basis; at least we get together and look at where we've been going. Continue to have NRBDO conferences to review and report on progress made and identify strategies to help implement comprehensive care.
- **NRBDO Structure:** Investigate whether to develop a more formal NRBDO structure given the progress to date and objectives moving forward.

Discussion centred on the pro's and con's of developing a more expansive NRBDO website. Silvia Marchesin questioned whether it is necessary to develop a website that encompasses all the disorders. In her view, having individual websites makes it clear that the organizations are different entities that have come together to work on common issues; therefore the current format, which provides links from the NRBDO website to the individual websites, is fine as is.

Tina Morgan said the proposal came about after a pharmaceutical representative mentioned not knowing that the NRBDO has a website, which is currently housed within the CHS website. The suggestion is to branch out so that NRBDO has its own separate website. Winnie Leung added that the current NRBDO website looks like a subset of the CHS site—having a main page or portal specifically for the NRBDO would help strengthen the coalition's presence.

Developing a separate NRBDO website would also reinforce the concept of comprehensive care for rare blood disorders, another participant said. The website could also provide useful information such as successful models for comprehensive care, clinical experts in Canada, and centres of excellence.

David Page said that the current NRBDO website could be improved rather than creating a new one, as there's no need to redo what each organization already has on their individual websites.

The following options were proposed:

- Keep the current website but create additional sub-sections and pages for topics (e.g., comprehensive care, registry development, guidelines and other resources) and disease area. Individual organizations can have their own pages with access so that they can update the information.
- Keep the current website but create a distinct NRBDO web address ([www.nrbdo.ca](http://www.nrbdo.ca)) and redirect it to the current site so that visitors can land directly on the NRBDO website rather than having to navigate through the CHS website.
- Discuss website re-structuring at the next NRBDO meeting, involving representatives from all the patient groups.

## Group 4: Relationships with Government

**Rapporteur: Danielle Pratt, Canadian Organization for Rare Disorders (CORD)**

- **Explicitly amplify the voice of NRBDO and its members:** Reach consensus on a Canadian definition of “rare disorders.” The NRBDO and its members were asked to support the definition put forward by the Canadian Organization for Rare Disorders (CORD), whether as a coalition or as individual patient organizations. Consensus and a consistent message across the organizations will help amplify their individual and collective efforts vis-à-vis government. The proposed date for a deliverable is before National Rare Diseases Day, February 28, 2010.
- **Support and attend World Rare Disease Day:** Events to raise awareness will be held on Parliament Hill, February 28, 2010. Patient organizations can get involved independently or in concert with other rare disease organizations.
- **Regularly follow up with MPs and other elected representatives:** Write letters and arrange to meet with MPs and provincial/territorial representatives to give a human face to the disease. Remind them of the goals and benefits of developing comprehensive care and patient registries, and what is needed to get there. Provide MPs with fact sheets and other useful information to pass on to the Minister of Health.
- **Identify champions to target the Minister of Health and Minister of Revenue.**

Michel Long noted that the recommendations focus largely on collaborating with CORD on advocacy initiatives, whereas the original focus was to examine building relationships with government in order to increase access to therapies and work towards orphan drug/catastrophic drug legislation—which could be achieved through a mechanism such as Rare Disease Day.

A participant from the group said the intent was to emphasize the need for all the rare disorder organizations to collaborate on common goals so that a unified voice is heard in Parliament. The message needs to be consistent and cohesive, and would be more powerful coming from the NRBDO than individual groups.

Silvia Marchesin asked whether the NRBDO is actually in a position to endorse the proposals or whether this should be done by the organizations individually. Long noted that a number of organizations are part of both NRBDO and CORD, and that if there is agreement among all NRBDO members, it would be possible to take a unified position in support of the recommendations.

The following option was proposed:

- Individual organizations should take the recommendations back to their members to discuss whether they support the European model and definitions of rare disorders. If there is agreement, the NRBDO can take a common position and communicate it to MPs through letters or advocacy campaign.

These recommendations will be brought forward to the next NRBDO meeting so that members can discuss whether they can be carried out, and identify strategies and areas of common interest for collaboration.

## **Closing Remarks**

Conference-Co-President Michel Long thanked everyone for their participation in the 2009 Progress in Comprehensive Care for Rare Blood Disorders Conference. He noted the broad representation of the rare blood disorders community at this conference including patient groups, medical experts, health information specialists and blood services and industry representatives. Continued collaboration is essential. A key priority will be to engage policymakers and obtain government support to move forward with comprehensive care for rare blood disorders and the development of patient registries.

He thanked all the members of the Network of Rare Blood Disorder Organizations for their active involvement. On behalf of the NRBDO, he thanked CSL Behring for sponsoring the 2009 Progress in Comprehensive Care for Rare Blood Disorders Conference and its ongoing support of the NRBDO.