Available online at www.sciencedirect.com
SCIENCE DIRECT®
Transfusion and Apheresis Science 29 (2003) 205–214
TRANSFUSION AND APHERESIS SCIENCE
www.elsevier.com/locate/transci

Management of hereditary angioedema: a Canadian approach

Tom Bowen [a,b,*], Jacques Hebert [a,b], Bruce Ritchie [b], Jeanne Burnham [a], Mike MacSween [b], Richard Warrington [b], William Yang [a,b], Andrew Issekutz [b], Nick Karitsiotis [c], Nancy McCombie [c], Tony Giulivi [c]

[a] *The Canadian Hereditary, Angioedema Society (CHAES)/ Société d'angioédème héréditaire du Canada (SAHC), Canada*
[b] *Medical and Scientific Advisory Committee, CHAES/SAHC, Canada*
[c] *Health Canada/Sante Canada, BSS-HCAID Centre for Infectious Disease Prevention & Control, Population & Public Health Branch, Canada*

Abstract

C1 esterase inhibitor (C1-INH) deficiency is a rare disorder that lacks consensus for diagnosis therapy and management. Recognizing that Canada is behind the European approach to this disorder, we have formed the Canadian Hereditary Angioedema Society (CHAES)/Société d'angioédème héréditaire du Canada (SAHC) to foster knowledge of this disorder in Canada and to advance care of patients with this disorder in Canada. We here present a review of treatment of this disorder in Canada including prevention of angioedema events and use of replacement therapy and present an algorithm for diagnosis therapy and management of C1-INH deficiency in Canada for discussion at our International Conference on Hereditary Angioedema to be held in Toronto, Canada, October 24th to 26th, 2003.

C1 esterase inhibitor (C1-INH) deficiency presents in congenital or acquired forms. There have been described three variants of hereditary angioedema (HAE): HAE I with low C1-INH protein and function [1,2] (85% of cases; autosomal dominant); HAE II with normal protein but low function [1,3] (15% of cases; autosomal dominant); and a newly described estrogen-dependent inherited form of HAE with normal protein and function [4,5] (?% of cases; found only in females; X-linked dominant or autosomal dominant with reduced penetrance). Acquired angioedema (AAE-I) is most frequently associated with B-cell lymphoproliferative as well as T-cell lymphoma, multiple myeloma, myelofibrosis, Waldenström macroglobulinemia, monoclonal gammopathies, rectal carcinoma, essential cryoglobulinemia, erythrocyte sensitization, livedo reticularis, cold urticaria, lupus anticoagulant, and infection with *Echinococcus granulosis*. AAE-II is not associated with any specific disorder but is associated with autoantibodies directed against C1-INH. Acquired angioedema has been seen with ACE inhibitor use and with some B-cell malignancies. Patients with HAE may experience recurrent soft tissue swellings, intestinal swellings and abdominal pains, and life threatening swellings of the airway. The incidence of HAE is estimated at 1:10,000 to 1:50,000. Risk of dying from airway obstruction is not clear but deaths from this complication if left untreated are not uncommon [1]. There have been

* Corresponding author. Address: University of Calgary and University of British Columbia, 705 South Tower, 3031 Hospital Dr. NW Calgary, Alta., Canada T2N 2T8. Tel.: +1-403-283-8291; fax: 1-403-283-8255.
E-mail address: tbowen@pol.net (T. Bowen).

1473-0502/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.transci.2003.08.009

recent deaths in Canada in the past three years and this pointed to the need for a better understanding of this disorder in Canada and support for a Canadian algorithm for approaching this disorder. Learning from the European experiences from Italy, Germany, Hungary, USA and Argentina, Jeanne Burnham organized a group of Canadians interested in advancing the standard of care for HAE in Canada and from this grew the Canadian Hereditary Angioedema Society (CHAES)/Société d'angioédème héréditaire du Canada (SAHC) (established 2001; Website: www.haecanada.com).

CHAES/SAHC organized a Medical and Scientific Advisory Committee (MSAC) and the Society held its first annual meeting in conjunction with its MSAC July of 2002 in Calgary, Alberta, Canada. It was recommended that a consensus approach to diagnosis therapy and management for HAE in Canada be sought and working with Health Canada, non profit patient groups, professional societies and industry groups, we organized an international meeting for Toronto that was to be held on April 25th to 27th, 2003. Unfortunately, that meeting was cancelled because of SARS and has been rescheduled for Toronto, Ontario, Canada on October 24th to 26th, 2003 (see Appendix C—meeting agenda).

To better understand the scope and nature of this disorder in the Canadian consortium thought that the development of a Canadian data base registry for HAE would be helpful. Working with Health Canada, and using models from the Canadian Hemophilia Society and the Association of Hemophilia Clinic Directors of Canada (AHCDC) including their data base registry concepts (CHARMS) and their hemovigilance approach, it was decided to establish a network of clinics in Canada with an interest in diseases that have some common care considerations: a clinic network for primary immune deficiency (PID), hereditary angioedema (HAE), and rare blood disorders (RBD; not covered by other data base registries). Health Canada and the PID section held its first meeting in Calgary on July 25th, 2003 to establish a Canadian PID data base registry (in collaboration with NIH and the Immune Deficiency Foundation, IDF), to start organizing the network of clinics and to set up pilot clinic groups.

Modeling after the AHCDC experience, the group has decided to incorporate a clinic directors group and this process is underway. There will be a separate steering committee for each of the PID, HAE, RBD clinics to oversee the data base registry for the group (coordinated through Health Canada). It is intended that the steering committees will foster a common hemovigilance protocol [7] for all patients regularly receiving blood-related products and facilitate development of vein-to-vein traceability for all blood products including fractionation products for such patients in Canada (in collaboration with AHCDC, the Anemia Institute for Research & Education, the Canadian Apheresis Group, Canadian Blood Services, and Hema-Quebec) (See Line Chart—Canadian Clinic Network—Fig. 2). It is hoped that patients within these groups will be offered full genotype characterization upon entry to the data base registry and that there will be annual storage of blood samples for hemovigilance surveillance. Research and Development in these three patient groups will become a benefit through this registry. It is expected that the clinic directors will publish an annual report available to the public which will provide an overview of numbers of patients with these disorders, products received, outcome analyses including clinical outcomes (including therapy risks, benefits, side effects and event outcomes treated and untreated).

CHAES/SAHC has been working towards harmonization in these goals with the European and American initiatives and we look forward to a common more global approach for HAE including common registry data points and promotion of research. Health Canada and the clinic directors group will work to prevent duplication of activities, minimize overlap of efforts, and work towards exchange of data base registry data in an unlinked fashion with the international groups including efforts by the NIH, USA HAE, EU HAE, ESID and the like. Through collaboration, resource expenditures will be minimized and patient care benefit maximized.

To facilitate a Canadian Consensus approach to the diagnosis therapy and management of HAE, participants in the Canadian HAE Conference have been asked to present their clinic's or country's algorithms for HAE management including sugges-

tions to answer the questions included in Appendix A. The Algorithm that will hopefully be completed and proposed for implementation will then need validation. It is hoped that the network of clinic directors will adopt the proposed algorithm and test this through a clinical protocol that would need development and testing. The proposed approach to diagnosis therapy and management for HAE in Canada is included in Appendix B and is in Draft Form for presentation at the Canadian Consensus Conference to be held in Toronto, Ontario, Canada on October 26th, 2003.

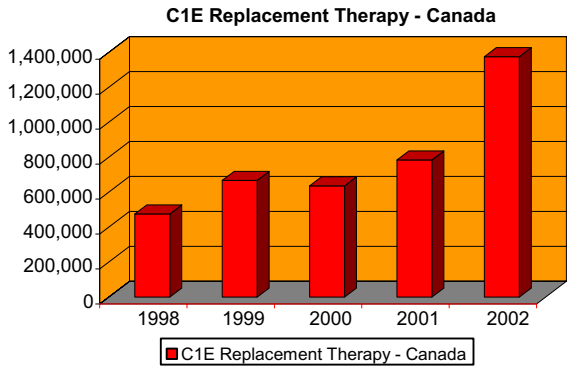

Fig. 1. Utilization graph.

In Canada, blood products are provided without charge to the patient and are funded through an interprovincial funding government program. There is a central distribution system through Canadian Blood Services for 9 of the 10 provinces or Hema-Quebec in Quebec so national statistics are available for fractionation blood products. C1-INH replacement therapy has been available in

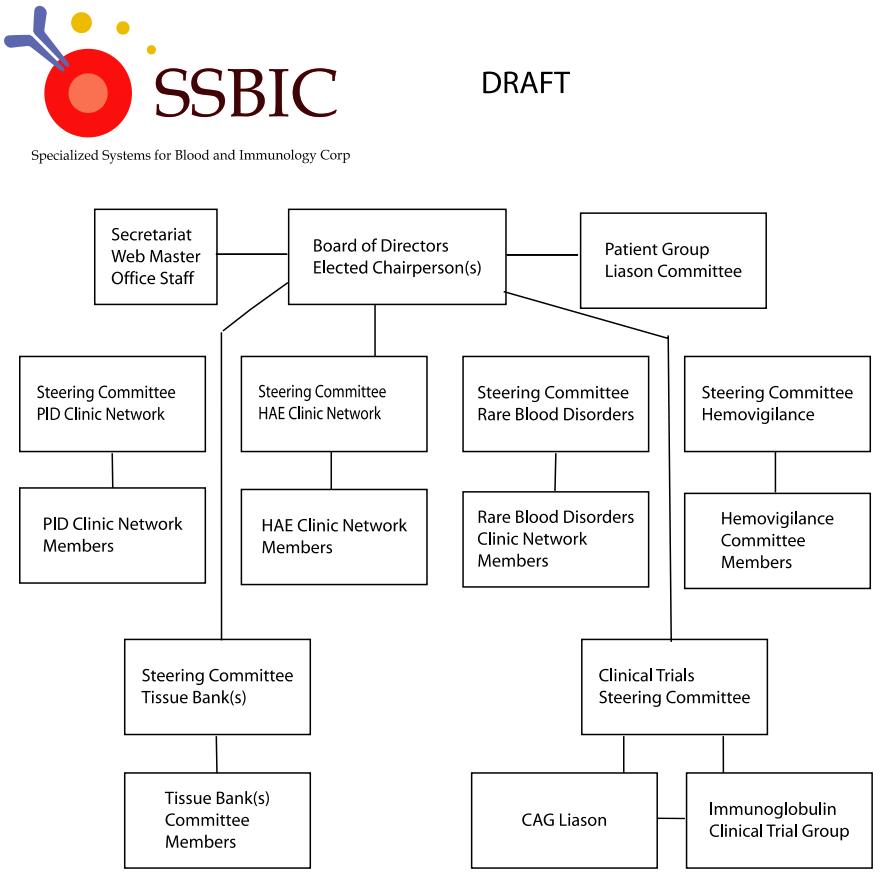

Fig. 2. Clinic network line diagram.

Canada under the Special Access Program of Health Canada with no licensed C1-INH replacement product being available to date.

Initially, the Baxter product was available and utilized until their removal of their product from the Canadian market in June of 2002. Since then, we have used the Aventis Behring product, Berinert P^{R}. No comparison in safety-efficacy has been done. We now transfuse about one million units of C1-INH product per annum (see Fig. 1, compiled by Mathias Haun and Heather Hume from Canadian Blood Services and Francine Decary from Hema-Quebec) but have not had a program in place to track the safety-efficacy profile. It is our intention to implement a clinic network consensus algorithm for therapy and track the safety-efficacy sometime in the next year. We have no laboratory in Canada to measure C1-INH autoantibody levels and hopefully this will develop over the next year as well. As with Factor VIII utilization data, C1-INH utilization figures will greatly change when inhibitors develop or other acquired situations develop. Overall, C1-INH replacement therapy has tripled over the past five years and currently is running about 30,000 units per million population in Canada (about 32 million population). We have no explanation for the jump in C1-INH replacement therapy in the past year and part of the role of a clinic network will be to provide such insight. Patients and physicians are becoming more aware of the availability of the C1-INH replacement therapy and this could explain the increase. With the incidence of HAE estimated at 1:10,000 to 1:50,000, we estimate there are somewhere between 600 and 3000 HAE patients in Canada. This would give a current utilization rate between 300 and 1700 C1-INH units per patient per year, the equivalent of one infusion per patient per year. Drs. Cicardi and Zingale report from their clinic in Milan that their patients receive an average of 3.85 infusions per year for laryngeal edema, 7.93 infusions per year for abdominal edema, and 1.57 infusions per year for cutaneous edema [6]. One would predict therefore that there will be further increase in the utilization of C1-INH replacement therapy and close monitoring of utilization will be necessary and clear guidelines developed for Canada.

Because C1-INH replacement therapy is a blood product, we believe vein-to-vein tracking should be in place for product recall and for tracking of transmission of infectious agents known and emerging and to monitor event outcome and adverse events. Health Canada has introduced a National Transfusion Transmitted Injuries Surveillance System in Canada. Their goal is "to carry out surveillance and targeted research leading to risk assessment to enable reduction in the risk of transfusion/transplantation related blood-borne pathogens and injuries in Canada". To this end, they are assisting in the creation of data base registries for the PID, HAE, and RBD clinic networks to facilitate tracking of transfusion transmitted injuries including for the HAE group of patients. The clinic networks will model the Canadian hemophilia experience and will parallel the Canadian Hemophilia Assessment and Resource Management information System (CHARMS) and the AHCDC setup and reporting. Similar to their system, the HAE clinic network will report transfusion transmitted injuries as part of a standardized hemovigilance program. It is hoped that the Hemophilia hemovigilance program will be the standard used for the HAE, PID, and RBD clinics in Canada [7].

Regular prophylaxis for HAE has been with tranexamic acid or Danazol currently with Stanozolol used in the past but not now readily available in Canada. Only the occasional patient takes regular C1-INH replacement therapy as regular prophylaxis. Surgical prophylaxis has been with Danazol or C1-INH replacement therapy depending on the type of procedure. Therapy of angioedema events consists mostly of C1-INH replacement therapy in dosage between 500 and 1500 units with usual dose 1000 units (two vials) (approaches 15–25 units/kg/infusion). The occasional patient receives home care self administration. This is also not the norm but the clinic network intends to explore this option further. Patients have the option of traveling with C1-INH replacement therapy including out of country. This is also not commonly used and is not the norm but again the clinic network is assessing this option further. Standards for home care preventative and therapeutic use of C1-INH replacement therapy will be formulated by the clinic network. It

is intended that vein-to-vein tracking of C1-INH product will be implemented but is currently not in place. We hope to establish a Canadian Centre for HAE genotyping over the next year.

We hope that the EU HAE group is developing an international algorithm, approach to diagnosis therapy and management for HAE and we appreciate the significant input that our European, American, and International Colleagues have provided and continue to provide in standardizing data base registries and approaches to management of HAE in Canada. We hope to collaborate with the EU data base registry initiative utilizing similar data points to allow data exchange. We appreciate the participation of our international colleagues in our Canadian HAE International Meeting and Consensus Discussion being held in Toronto, Ontario, Canada on October 23rd to 26th, 2003 in conjunction with the Canadian Hematology Society and with the support of the following groups, agencies, sponsors and partners: Health Canada/Sante Canada, Health-Care Acquired Infections Division; Canadian Institutes of Health Research (CIHR) Institute of Infection and Immunity; Canadian Clinic Network for Primary Immune Deficiency, Hereditary Angioedema, and Rare Blood Disorders; Canadian Hereditary Angioedema Society (CHAES)/ Société d'angioédème héréditaire du Canada (SAHC); Canadian Immunodeficiencies Patient Organization (CIPO); Canadian Hematology Society (CHS); Canadian Apheresis Group (CAG); Anemia Institute for Research & Education (AIRE); Canadian Blood Services (CBS), Hema-Quebec (HQ); Canadian Society of Allergy and Clinical Immunology (CSACI), University of Calgary (U of C); Canadian Society for Immunology (CSI); Canadian Organization for Rare Disorders; Aventis Behring; Baxter; Bayer; Dyax. We look forward to formulating a Canadian algorithm at our consensus portion of our International HAE meeting to be held at this October Toronto meeting (draft for discussion—see Appendix B).

We hope the establishment of an HAE data base registry and clinic network will improve the care for Canadians with HAE. May we always remember: ''It can be done—It must be done for the sake of our patients''.

Acknowledgements

The authors wish to thank Mathias Haun and Heather Hume from Canadian Blood Services and to Francine Decary from Hema-Quebec for compiling the data on C1-INH utilization for Canada.

Appendix A. Questionnaire to participants

I. Diagnosis:
   1. At what age do you first screen for HAE if the family history is positive?
   2. For diagnosis, do you measure both functional and protein levels routinely? C4 level? What % of your patients have a normal C4 when well, between attacks? Do you have access to molecular diagnosis?

II. Childhood management:
   3. What is your approach to HAE event prevention and event management in the prepubertal child? What are your indications for or criteria for using preventative pharmacotherapy? What is/are your drug/s of choice?
   4. When do you use inhibitors of fibrinolysis? Which agent do you use and what dose and frequency? Do you use this for prevention as well as treatment?
   5. Do you use ever use androgens in this setting? If so, for treatment, prevention, or both? What dose?
   6. What monitoring do you do for the androgen therapy? Liver functions? Bili? Lipid profile? Abdominal liver spleen ultrasound? How often?
   7. Do you use C1 inhibitor replacement therapy in children? Would this be first line? Second line? Third line? Do you have a consent form for this blood product?
   8. What do you use for preoperative prophylaxis in the childhood setting?
   9. During adolescence, do you use oral contraceptives to control menstrual irregularity or cramping and if so which OCP with what doses of estrogen progesterone have you found safe and effective?

III. Adult management:
10. What is your approach to HAE event prevention (including surgery) and event management in the adult? What are your indications for or criteria for using preventative pharmacotherapy? What is/are your drug/s of choice?
11. Do you use inhibitors of fibrinolysis in adults? Which agent do you use and what dose and frequency? Do you use this for prevention as well as treatment?
12. When do you use androgens in the adult setting? Males? Females? For treatment, prevention, or both? What dose? Do you start high, induce remission, and wean down to lowest dose to control symptoms or start low dose and increase as needed to obtain control? How long to wait for effect before increasing the dose? Which androgen do you use? What monitoring do you do for the androgen therapy? Liver functions? Bili? Lipid profile? Abdominal liver spleen ultrasound? How often?
13. Do you have access to licensed or special access C1 esterase replacement therapy? What are your indications for use? Prevention? Therapy? What dose? Do you have to have failed other therapies first? Is this therapy first line? Second line? Third line? Do you have a consent form for this blood product? Do you use this for abdominal episodes or just for life threatening episodes? Who pays for the product?
14. What oral contraceptives have you found safe and effective? What dose of estrogen? Progesterone?
15. Do you have a line diagram or algorithm for diagnosis, therapy, management of HAE?

Appendix B. Draft answers—Canadian HAE treatment draft consensus

I. Diagnosis:
1. If the family history is positive for HAE: propose—screening can be done at any time, but usually from one year of age unless infants with a family history are symptomatic.
2. For diagnosis: propose—measure both functional and protein C1-INH levels and screen with C4. C4 may be normal between attacks but this is uncommon (estimated incidence 1:450—Dr. Marco Cicardi, personal communication)—Diagnosis can be confirmed by molecular diagnosis but this is not routinely available—we hope to establish a Canadian Centre for HAE genetic typing in the next year and hope to relate response to prevention and treatment to genotype and phenotype.

II. Childhood management:
1. For HAE event prevention and event management in the prepubertal child: propose—if more than two disabling attacks per month, then tranexamic acid 75 mg/kg/day for prevention and treatment of mild attacks. C1-inhibitor replacement for severe attacks—15 units/kg/infusion—repeat if progressing or poor response at 1 h. As for all blood products, consent should be obtained prior to use. A standardized consent form should be designed.
2. Attenuated Androgens: rarely first line therapy—if used, then Danazol—10 mg/kg/day for prevention—Androgen monitoring: proposed—six monthly bilirubin, alkaline phosphatase, ALT, lipid profile (three monthly for children during first year of therapy)—annual abdominal liver spleen ultrasound.
3. During adolescence, hormonal therapy should be used with caution. Need recommendation on hormonal therapy if indicated—progestational agent.

III. Adult management:
1. Event prevention (including surgery): propose—if disabled more than 5 days per month, then attenuated androgens—Danazol 400–600 mg/day for 1 week prior to surgery—general prevention—400–600 mg daily for 1 week then wean 100 mg/day once weekly till at 200 mg daily and then wean 50 mg/day once weekly until breakthrough or until 50 mg daily—50 mg daily

minimum dose—if more than six attacks per year, then increase the dose to reinduce remission and then wean again to higher dose than previous—Androgen monitoring: proposed—six monthly bilirubin, alkaline phosphatase, ALT, lipid profile—annual abdominal liver spleen ultrasound.

2. Antifibrinolytics: less effective than attenuated androgens—propose—tranexamic acid orally—for attacks, 1 g every 4 h—for prophylaxis, 1 g three times daily.
3. C1-INH Replacement therapy: not currently licensed in Canada—available in Canada through Health Canada Special Access Program—Propose—for Prevention—rarely indicated—For therapy—mild to moderate attacks—500 units (one vial; 7.5 units/kg)—severe attacks—15 units/kg/infusion—repeat if progressing or poor response at 1 h. As for all blood products, consent should be obtained prior to use. A standardized consent form should be designed.
4. Oral contraceptives—use with caution trying to avoid estrogen—progestational agents may be acceptable for some.

Appendix C. Meeting agenda

Canadian Hematology Society/Société Canadienne d'Hematologie

Canadian Hereditary Angioedema Society/Société d'angioedème héréditaire du

Canada International Conference on Management of Hereditary Angioedema and Canadian Clinic Networking Launch for: Primary Immune Deficiencies, Hereditary Angioedema, and Rare Blood Disorders

October 24th to 26th, 2003, Toronto, Canada

Radisson Plaza Hotel Admiral, Harbourfront

Partners/Sponsors:

Health Canada/Santé Canada

Canadian Institutes of Health Research (CIHR) Institute of Infection and Immunity

Specialized Systems for Blood and Immunology (SSBI)

Canadian Hematology Society (CHS), Canadian Apheresis Group (CAG)

Canadian Hereditary Angioedema Society (CHAES)

Canadian Immunodeficiencies Patient Organization (CIPO)

Canadian Blood Services (CBS), Héma-Québec (HQ)

Canadian Society of Allergy and Clinical Immunology (CSACI)

University of Calgary (U of C), Canadian Society for Immunology (CSI)

Anemia Institute for Research & Education (AIRE)

Aplastic Anemia and Myelodysplasia Association of Canada (AAMAC)

Aventis Behring, Baxter, Bayer, Dyax

This event is an Accredited Group Learning Activity as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada. Physicians may claim up to 17.0 h under Section 1.

Canadian Hematology Society/Société Canadienne d'Hematologie

Canadian Hereditary Angioedema Society/Société d'angioedème héréditaire du Canada

Specialized Systems for Blood and Immunology

Canadian International Conference on Management of Hereditary Angioedema

Friday, October 24th

Morning Symposium: Complement for the Hematologist

Chairperson—Dr. Armand Keating, CHS President Elect

8:30	Introduction—Dr. Gail Rock, CHS President
8:30–8:45	Introduction—complement disorders including hereditary angioedema—Canadian perspective Dr. Tom Bowen, Canada
8:45–9:25	Complement cascade and deficiency states: genes to animal models and up to man Dr. Alvin Davis III, USA
9:25–10:05	Human complement disorders excluding hereditary angioedema Dr. Jerry Winkelstein, USA

10:05–10:45	Human complement disorders—hereditary angioedema—kinins, bradykinins, kallikrein interactions Dr. Bruce Zuraw, USA
10:45–11:00	Refreshment break
11:00–12:30	Abstract presentations—CHS Lunch

Afternoon Symposium: Launch of the SSBI Canadian Clinic Network for Primary Immune Deficiencies, Hereditary Angioedema, and Rare Blood Disorders

Chairpersons—Dr. Jacques Hébert, Dr. Tom Bowen

13:15–13:50	Experience of the IDF NIH PID data base registry & collaboration Dr. Jerry Winkelstein, IDF, USA
13:50–14:25	The Canadian Apheresis Group registry experience—collaborative IVIG study proposal(s) Dr. Gail Rock, Canada
14:25–15:00	International hereditary angioedema data base registry Dr. Marco Cicardi, Italy
15:00–15:15	Refreshment break
15:15–15:50	The Canadian Hemophilia Clinic Group experience—collaborative hemovigilance protocol proposal Dr. Bruce Ritchie, Canada
15:50–16:25	Canadian PID, HAE, rare blood disorders data bases and registries national transfusion transmitted injuries surveillance system (TTISS) in Canada—a review Health Canada proposals Dr. Antonio Giulivi, Canada
16:25–17:00	SSBI—clinic launch summation discussion—so what now? Where Now? Website—physician discussion patient management—next meeting? Dr. Tom Bowen, Jacques Hébert, Bruce Ritchie, Antonio Giulivi—Canada
17:00–18:30	Annual Meeting: Canadian Hematology Society
17:00–18:30	Annual Meeting: Specialized Systems for Blood and Immunology Annual Meeting and Elections: Canadian Hereditary Angioedema Society

Saturday, October 25th

Canadian International Conference on Management of Hereditary Angioedema

Morning Session: Chairpersons: Jeanne Burnham/Denise Ommanney

8:15–8:30	Introduction & Welcome—Jeanne Burnham, President, CHAES Dr. Tom Bowen and Dr. Jacques Hébert, MSAC, CHAES
8:30–9:15	The complement cascade—HAE—overview Dr. Alvin Davis, USA
9:15–10:00	Kallikrein inhibitors—USA HAE experience Dr. Bruce Zuraw, USA
10:00–10:15	Nutrition break

Chairpersons: Dr. Richard Warrington, Denise Ommanney

10:15–10:45	Estrogen-dependent inherited angioedema Dr. Karen Binkley, Canada
10:45–11:30	Role of antifibrinolytics in HAE Dr. Bruce Ritchie, Canada
11:30–12:15	Hormones and HAE Dr. Lorenza Zingale, Italy
12:15–13:00	Lunch

Afternoon Session: Chairpersons: Dr. Bill Yang, Harriet Lyons

13:00–14:00	The Italian experience—European initiatives Dr. Marco Cicardi, Italy
14:00–14:45	The Frankfurt HAE experience Dr. Emel Aygoren-Pursun, Dr. Inma Martinez, Dr. Wolfhard Kreuz, Germany
14:45–15:30	The German HAE experience—European initiatives Dr. Konrad Bork, Germany
15:30–15:45	Nutrition break

Chairpersons: Dr. Bruce Ritchie, Suzanne Benoit

15:45–16:30	The Hungarian HAE experience Dr. Henriettte Farkas, Dr. Lillian Varga, Hungary
16:30–16:45	The Quebec experience Dr. Jacques Hébert, Canada
16:45–17:00	Day summary and introduction to Consensus Conference Dr. Tom Bowen, Dr. Jacques Hébert, Canada
	Banquet

Sunday, October 26th

Canadian Consensus Conference on the Treatment of HAE

09:00–09:20	DX-88 and HAE; a developmental perspective Dr. Anthony Williams, Dyax
09:20–09:50	Safety and efficacy of pasteurized C1 inhibitor concentrate (Berinert® P) in hereditary angioedema: a review Dr. Jean De Serres, Aventis Behring
09:50–10:30	Round table discussion and discussion of algorithms for the diagnosis, therapy and management of HAE International speakers from Friday and Saturday sessions, clinic physicians and staff members, HAE patients
10:30–10:45	Nutrition break
10:45–11:45	Consensus document discussion All
11:45–12:00	Closing discussion and summary—what next? Dr. Tom Bowen, Dr. Jacques Hébert, Dr. Bruce Ritchie, Jeanne Burnham

Scientific Program Committee/Comité du Programme Scientifique

Dr. Tom Bowen (Chair)
Jeanne Burnham (CHAES president)
Tina Morgan (CIPO president)
Dr. Jacques Hébert
Dr. Gail Rock
Dr. Armand Keating
Dr. Bruce Ritchie
Dr. Bruce Mazer
Dr. Richard Warrington
Dr. Mike MacSween
Dr. Bill Yang
Dr. Alvin Davis
Dr. Antonio Giulivi

You are never given a dream without also being given the power to make it true. (Richard Bach, Writer)

Imagination is more important than knowledge. Knowledge is limited. Imagination encircles the world. (Albert Einstein 1879–1955, Physicist)

References

[1] Agostoni A, Cicardi M. Hereditary and acquired C1-inhibitor deficiency: biological and clinical characteristics in 235 patients. Medicine (Baltimore) 1992;71:206–15.
[2] Donaldson VH, Evans RR. A biochemical abnormality in hereditary angioneurotic edema: absence of serum inhibitor of C'1-esterase. Am J Med 1963;35:37–44.
[3] Rosen FS, Alper CA, Pensky J, Klemperer MR, Donaldson VH. Genetically determined heterogeneity of the C1 esterase inhibitor in patients with hereditary angioneurotic edema. J Clin Invest 1971;50:2143–9.
[4] Binkley KE, Davis Jr AE. Clinical, biochemical and genetic characterization of a novel estrogen-dependent inherited form of angioedema. J Allergy Clin Immunol 2000;106:546–50.
[5] Bork K, Barnstedt SE, Koch P, Traupe H. Hereditary angioedema with normal C1-inhibitor activity in women. Lancet 2000;356:213–7.
[6] Cicardi M, Zingale L. How do we treat patients with hereditary angioedema? Transfus Apher Sci, In this volume, 2003; doi:10.1016/j.transci.2003.08.001.
[7] Ritchie BC. Tissue archives to track blood borne pathogens in people receiving blood products. Transfus Apher Sci, In this volume, 2003; doi:10.1016/j.transci.2003.08.010.