



# HAEi Newsletter



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## A Message from the President

Dear HAEi Friends,

This newsletter is solely dedicated to providing the global HAE patient community with a relatively brief summary of what transpired during the 8th C1 Inhibitor Deficiency Workshop held in Budapest, Hungary in late May. As you will see from the excellent overview prepared by HAEi Communications Manager Steen Bjerre and HAEi Executive Director, Henrik Balle Boysen, the workshop provided the medical/scientific community with an opportunity to share groundbreaking ideas on the biochemical aspects of HAE.

Nevertheless, this meeting as well as the 7 workshops that preceded it, was not only about unlocking the remaining biochemical secrets of the HAE pathophysiology. One could not help but get the sense that the organizers, Dr. Farkas and Dr. Varga, as well as the physician/scientists and industry participants, have a deep compassion and concern for patients and go to work every day to help find ways to improve our lives.

We would like to congratulate Dr. Farkas and Dr. Varga for arranging yet another very interesting meeting. The global HAE patient community is forever grateful to these remarkable leaders for organizing these valuable biannual scientific workshops that, from the outset in Visegrad in 1999, featured something that no other such medical meeting had ever done - welcoming patient participation with open arms.

Please remember to save the date for the next HAE Global Conference, which will take place 15 to 18 May 2014 in Washington DC Metro Area, USA. We will keep you posted about the details for this conference and also keep you informed when registration is open.

Again, please do not hesitate to contact Steen at [s.bjerre@haci.org](mailto:s.bjerre@haci.org) or Henrik at [h.boysen@haci.org](mailto:h.boysen@haci.org) if you have any questions regarding the content of this newsletter.

Warmest regards to all,

Tony Castaldo  
President, HAEi



From left Olena Mykal, Sarah Smith-Foltz and Alejandra Menendez (all three from the HAEi Executive Committee) enjoying the conference.



Organizers Henriette Farkas and Lilian Varga with Istvan Nagy, President of the Hungarian Association of Angioedema Patients

## Background

It has been 50 years since Donaldson and Evans published their findings, demonstrating that the deficiency in C1 inhibitor (C1-INH) is the root cause for certain forms of HAE. Since then, medical science has come a long way in broadening the understanding of HAE genetics and pathophysiology, but there are still many unanswered questions. Over 250 people from about 30 countries gathered at the 2013 C1 Inhibitor Deficiency Workshop to explore the remaining HAE-related scientific mysteries and discuss a variety of issues related to treatments and patient care.

## Workshop Overview

The workshop began with an official opening by Ildiko Horvath, Head of the Hungarian Health Policy Department, and the presentation of a “For HAE Patients” award to Henriette Farkas and Lilian Varga. Attendees then heard two very interesting lectures by Francois Marceau, Centre de Recherche en Rhumatologie et Immunologie CHU de Quebec, Canada (“Bradykinin receptors:

Agonists, antagonists, expression, signaling and adaptation to sustained stimulation”), and Coen Maas, Laboratory of Clinical Chemistry and Hematology, University Medical Center Utrecht, the Netherlands (“The protease storm of angioedema”).

The second day was jam packed with fascinating topics and started off with a lecture by Peter Gal, Institute of Enzymology at the Hungarian Academy of Sciences in Budapest, entitled “Activation and regulation of the lectin pathway of the complement system”. The day included a variety of lectures on Non-conventional Diagnostics, Genes and Cascades, and The Attack in the Limelight. There was also a session that featured the presentation of 18 posters.

The third day opened with the presentation of an award “For HAE Research” to Dr. Allan Kaplan, USA. Dr. Kaplan then delivered a fascinating lecture that addressed a variety of important biochemical issues related to the HAE pathophysiology. This day, too, was filled with captivating presentations on the topics Sorting Things Out: HAE-FXII, Management Fine-tuned, and

Angioedema Avalanche. There was also a poster session featuring 17 presentations.

The program of the final day of the workshop featured lectures under the headings The Shades of Freedom and Living with HAE Around the World. Finally Peter Späth from the Institute of Pharmacology, University of Bern, Switzerland summed up the workshop, and four young scientists were awarded grants to support their ongoing HAE-related research.



Celebrating the 50<sup>th</sup> anniversary after the publishing of Donaldson and Evans' findings on HAE



Allan Kaplan and Marco Cicardi eagerly waiting to get the microphone from Avner Reshef



## Highlights from lectures delivered by physician/scientist groups throughout the world

**Brazil:** Genetic screening has been performed on 17 subjects from 12 unrelated families. Of the 11 different mutations identified, 6 were not previously identified in mutation. Although the HAE population in Brazil is likely to number 4,000, only 572 patients had been identified as of 2012. (Camila Lopez Veronez, Department of Biophysics, Federal University of Sao Paulo, Brazil).

**USA:** Historically, the most commonly used HAE prophylactic treatment has been attenuated androgens (AA). The effectiveness of AA in preventing attacks is variable. Clinical trial evidence demonstrates the effectiveness of Cinryze for long-term prevention of HAE, even in patients who have been on AA with variable degree of control. (Bruce L. Zuraw, University of California, USA/San Diego VA Healthcare, USA)

**Denmark:** Half of the patient population practice home therapy and, in this group, the average number of acute hospital visits has been reduced by 84% (Anette Bygum, Department of Dermatology and Allergy Centre, Odense University Hospital, Denmark)

**United Kingdom:** Overall, Ruconest (recombinant C1-INH) is effective and well-tolerated; it has the potential to improve outcomes in HAE. (A.L. Mason, Department of Immunology, Barts Health NHS Trust, United Kingdom)

**USA:** Ecallantide (Kallikrein inhibitor) appears effective for pediatric patients 9-17 years of age and is associated with a rapid

time to near-complete symptom resolution. (Mark Davis-Lorton, Winthrop University Hospital, USA)

**Germany:** The risk for asphyxiation due to laryngeal edema is higher among patients who are not (1) adequately informed about the danger of laryngeal attacks, (2) trained about emergency treatments, and (3) aware of the importance of early administration of therapy. (Konrad Bork, Department of Dermatology, University Medical Center, Johannes Gutenberg University, Germany)

**Israel:** Prodromes (early signs and symptoms) in HAE are more common than has been previously reported and a majority of patients are able to predict their attacks. (Avner Reshef, Department of Allergy, Immunology, and Angioedema Center, Sheba Medical Center, Israel)

**Germany:** Self-administration can successfully be introduced for the majority of patients, even for some children and adolescents. Self-administration decreases the time to treatment and the severity of the attack; avoids unnecessary pain and increases quality of life; and increases the ability to work or to attend school. (Karin Andritschke, Rhine-Main Haemophilia Centre, Germany)

**South Africa:** HAE remains a clinical challenge in this country. Although the expected number of patients is about 1,000, only 43 patients are documented. Patients are treated with Danazol or tranexamic acid. At this point, there is no HAE patient organization. (Bernd Rosenkranz, Division of Pharmacology, Department of Medicine, Stellenbosch University, South Africa)



Jonathan Bernstein giving his lecture on HAE patients' experience with short term prophylaxis



Anthony Castaldo presenting the poster on HAEA's role as an important partner in a longstanding effort to improve patients' quality of life

**Latin America:** The access to laboratory diagnosis and therapy is restricted in all countries, with more profound problems regarding drugs and assistance for HAE attacks. The author proposed a plan for action that includes a registry of identified cases, HAE educational programs, laboratory support with reference centers, and access to prophylactic and acute attack treatment. There are likely up to 57,000 HAE patients in Latin America. (Anete S. Grumach, Outpatient group of recurrent infections and Laboratory of Immunology, Faculty of Medicine ABC, Brazil)

**Sweden:** A retrospective patient survey shows that patient's quality of life does not appear to improve during the period in between acute attacks when the patient is not experiencing symptoms. (Patrik Nordenfelt, County Hospital Ryhov, Sweden)

**Greece:** 104 patients belonging to 36 families have been registered. HAE has moderate to severe consequences in the quality of life of 74% of the patients. (Anastasios E. Germeris, Department of Immunology & Histocompatibility, University of Thessaly, Greece)

## Highlights from posters presented during the workshop

**Switzerland:** A questionnaire answered by 94 patients revealed: The delay in diagnosis for patients with de novo mutations (no family history) is 15 years; patients in Switzerland use Danazol for long term prophylaxis; half of the patients use therapy only on demand, predominantly C1-INH concentrate. (Urs Steiner, Spitalnetz Bern, Switzerland)

**Hungary:** The severity of HAE is greater in patients who experienced symptoms early in life. In addition, women aged 20 to 40 years have more severe symptoms than men of similar age. (Nora Veszeli, 3rd Department of Internal Medicine, Semmelweis University, Hungary)

**Hungary:** Long-term treatment with Danazol has a mild virilizing effect. However, this side effect has not led to the

discontinuation of Danazol therapy in female patients. (Zsuzanna Zotter, 3rd Department of Internal Medicine, Semmelweis University, Hungary)

**Slovenia:** A national network of access points has been set up in 7 Slovenian emergency departments. A logistical plan to assure sufficient stocks of acute episode HAE medicines as well as a system for recording each patient's consumption of medicine and treatment outcomes has been developed. (Maja Jost, University Clinic of Pulmonary and Allergic Diseases Golnik, Slovenia)

**USA:** Breakthrough attacks for patients on C1INH prophylaxis are of shorter duration and are less severe than attacks suffered by patients not on this form of therapy. (Jennifer Schranz, ViroPharma Inc., USA)

**Europe:** Observational data from the Icatibant Outcome Survey registry show that early treatment with icatibant reduces the duration of attacks and the time to attack resolution. (Priscila Valente de Freitas, Department of Dermatology and Allergy Center, Odense University Hospital, Denmark)

**Germany:** 18 HAE patients were trained to self-administer IV HAE medicines by experienced specialist nurses. This training was successful in almost all patients. (M. Magerl, Department of Dermatology and Allergy, Charité – Universitätsmedizin Berlin, Germany)

**Hungary:** Short-term prophylaxis is justified in acquired C1-INH deficiency, just as it is in the hereditary form. (Kinga V. Köhalmi, 3rd Department of Internal Medicine, Semmelweis University, Hungary)

**Hungary:** Ruconest is effective and generally well-tolerated as a therapy for cutaneous and/or abdominal HAE attacks. (Erika Szabo, 3rd Department of Internal Medicine, Semmelweis University, Hungary)



## THE BACKGROUND:

It has been 50 years since Donaldson and Evans published their findings, demonstrating that the deficiency in C1 inhibitor (C1-INH) is the root cause for certain forms of HAE. Since then, medical science has come a long way in broadening the understanding of HAE genetics and pathophysiology, but there are still many unanswered questions.

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## HAEi presentations

HAEi and its member organizations were involved in the scientific lectures as well the poster presentations:

**HAE patient experience with short term prophylaxis – responses to an on-line questionnaire survey (survey conducted by HAEA):** A small percentage of HAE patients report experience with short term prophylaxis for surgical/medical procedures. Notwithstanding the short-term prophylaxis therapy, 42 percent of these patients still required on demand treatment for a procedure-related attack. This finding supports current recommendations for short-term prophylaxis before surgical/medical procedures with ready availability of on demand treatment for any breakthrough attacks. (Jonathan A. Bernstein, HAEA/University of Cincinnati, USA)

**Practicalities and barriers to HAE self-administration therapy – discussions from an international HAE expert meeting (HAEi represented by Executive Director Henrik Balle Boysen):** The international HAE expert panel recommends that all HAE patients should be considered for self-administration because this therapeutic option ensures early treatment and can be life-saving. Nevertheless, self administration may not be suitable for certain patients, and the degree of support required to ensure success varies from patient to patient. Standardized training, experienced training staff, a 24-hour helpline, and individual disease management programs could encourage further expansion of self-administration. (Christine Symons, Derriford Hospital, United Kingdom)

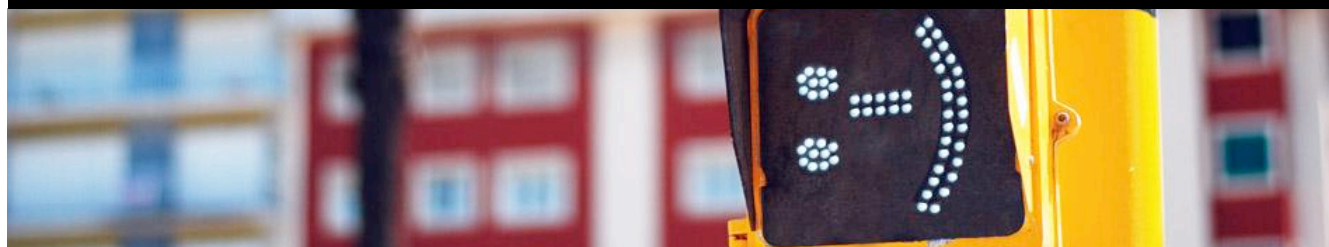
**The building blocks for an effective patient group advocacy program:** Patient Advocacy leaders from throughout

the globe know from experience that the journey required to (1) establish an effective HAE organization and (2) gain access to and reimbursement for medicines can be long, frustrating, and full of obstacles. Nevertheless, nothing will ever happen unless patient advocates start the process of “clearing the path” establishing an energetic and well-organized HAE advocacy and awareness program in their respective countries. (Executive Committee HAEi, presented by Alejandra Menendez)

**Health status utility weights for HAE attacks and in between attacks (HAEi represented by Executive Director Henrik Balle Boysen):** The cross-sectional HAE Burden of Illness Study of Europe indicates that HAE may cause considerable burden even in between attacks. (Emel Aygören-Pürsün, Department of Pediatrics, Pediatric Hematology, Oncology, Hemostaseology and Cardiology, University Hospital, Johann Wolfgang Goethe University, Germany)

**The HAE burden of illness study in Europe – a conceptual model of patients’ impacts (HAEi represented by Executive Director Henrik Balle Boysen):** HAE has wide-ranging short- and long-term physical and emotional impacts on patients’ lives. The conceptual model from the HAE Burden of Illness Study in Europe can be used to inform and improve clinical management of HAE. (Anette Bygum, HAE Centre Denmark, Department of Dermatology and Allergy Centre, Odense University Hospital, Denmark)

**A cross-sectional questionnaire survey to assess physician’s approach to short-term prophylaxis in HAE patients (survey conducted by HAEA):** Short-term prophylaxis of HAE patients undergoing minimally invasive or invasive surgical/medical procedures was most effective in patients with a history of trauma induced swelling. The best



outcome was realized using a combination of short-term prophylaxis with on-demand therapy readily available for any breakthrough attacks. (Jonathan A. Bernstein, HAEA/University of Cincinnati, USA)

**The US HAE Association – an important partner in a longstanding effort to improve patients' quality of life:** An organized and highly motivated patient organization that partners with interested physician/researchers and industry can be a powerful force in driving programs, activities, and research that improve patient quality of life. HAEA has 4,300 members and an experienced and devoted group of 16 staff members. (Anthony Castaldo, HAEA/HAEi)

## International HAE Nurses' Organization established

The 8th C1-INH Deficiency Workshop saw the birth of a new organization. Following a scientific lecture on the nurses' aspect on patients living with HAE, Iris Leibovic from the Allergy, Immunology and Angioedema Center at Sheba Medical Center in Israel informed the audience about the founding of HAE-INO, an international organization for nurses working with HAE patients.

HAEi is thrilled that there is now a nurses' organization with a clear and strong focus on HAE and we look very much forward to cooperation with HAE-INO.

## Budapest 2015 and HAE Global Conference 2014

The next C1-INH Deficiency Workshop will take place in Budapest, Hungary in 2015. In the meantime,

patient organizations, scientists, health care professionals, and industry will have an opportunity to meet in spring 2014 at the 2nd HAE Global Conference. This conference will take place in Washington DC Metro Area, USA around haeday :-)

More information on the global conference will be available on our websites [www.haei.org](http://www.haei.org) and [www.haeday.org](http://www.haeday.org), Facebook page [www.facebook.com/haeday](http://www.facebook.com/haeday), Twitter account [www.twitter.com/haeday](http://www.twitter.com/haeday), and Youtube channel [www.youtube.com/haedaychannel](http://www.youtube.com/haedaychannel).

## Further reading

Certain abstracts and lectures from the Budapest meeting will be published in the Journal of Angioedema – see [www.journalofangioedema.com](http://www.journalofangioedema.com).

## Your feedback is very welcome

Please let us know what you believe should be included in future newsletters. You can do that by providing feedback to Executive Director Henrik Balle Boysen at [h.boysen@haei.org](mailto:h.boysen@haei.org) or Communications Manager Steen Bjerre at [s.bjerre@haei.org](mailto:s.bjerre@haei.org). In addition, we invite you to submit articles on any topics that you believe would be of interest to the readers of this newsletter. We look forward to your comments and working with you on future newsletters.



HAEi is a global umbrella organization dedicated to raising awareness of CI inhibitor deficiencies around the world. It is a non-profit network of national HAE patient organizations.

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HAEi - International Patient Organization for C1 Inhibitor Deficiencies



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Tim Craig with Henrik Balle Boysen (middle) and Steen Bjerre (left)