



HAEi Newsletter



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A Message from the President

Dear HAEi Friends

As you know, the world celebrates **hae day :-)** every May 16th.

On this very special day HAE advocates hold events that engage the general public and the medical community while raising funds to support programs designed to raise awareness of the need for (1) earlier and more accurate diagnosis, and (2) access to life saving medicines.

The number of **hae day :-)** events taking place throughout the world continues to increase every year as the voice of the global community strengthens and patient organizations unite around a common cause.

We are very excited about some of the events that have been planned for this year's **hae day :-)** and our next newsletter will include a full coverage of **hae day :-)** 2014!

As you already know, the 2014 HAE Global Conference will take place 15-18 May in the Washington, DC metropolitan area (USA). In addition to our regular newsletter topics we provide a brief overview of the conference agenda in this newsletter.

Warmest regards and happy **hae day ;-)**!

Anthony J. Castaldo
President, HAEi

HAEi on Facebook

The HAEi group page on Facebook has continued to grow and it now has close to **975** members. Sign up at <https://www.facebook.com/groups/172320032283/> to receive updates on HAE developments around the globe.




**HAE
GLOBAL
CONFERENCE
WASHINGTON DC
15-18 MAY
2014**

We are looking forward to welcome an amazing **450** delegates this week in Washington DC for the 2014 HAE Global Conference.



450 Expected to Attend the 2014 HAEi Global Conference

Over 450 delegates have signed up for the HAE Global Conference (Washington D.C. Metro Area 15-18 May 2014) making it the largest worldwide gathering of HAE patients that has ever been organized. We succeeded in breaking the record established at the inaugural worldwide conference in Copenhagen, Denmark in 2012! Over 30 countries will be represented as we welcome delegates from Argentina, Australia, Austria, Belarus, Brazil, Canada, China, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Israel, Italy, Japan, Macedonia, Malaysia, Mexico, Netherlands, New Zealand, Norway, Pakistan, Poland, Portugal, Romania, Russia, Spain, Sweden, Switzerland, United Arab Emirates, United Kingdom, Venezuela, and the United States of America.

With a focus on “Setting New Standards”, the 2014 HAE Global Conference will provide HAE advocates from all over the globe with an opportunity to (1) assess the state of HAE care in their countries and (2) interact and collaborate with colleagues to design strategies for making improvements. The active participation of the delegates will lead to invaluable interactions between patients, the scientific/medical community, and pharmaceutical manufacturers.

The conference is designed to serve as an incubator for developing creative collaborations and innovative approaches to improving HAE care in the respective countries. Hopefully, every patient will be inspired by what they learn during the conference and will translate that knowledge and motivation into systematic action aimed at improving diagnosis and access to life saving HAE therapies.

An Intensive, Informative, and Motivating Conference Program

The conference will begin on Friday morning 16 May with a scientific session to be attended by HAE physician/researchers. The session will feature presentation by Dr. Jonathan Bernstein, Dr. Andrea Zanichelli, Dr. Hilary Longhurst and Dr. Marc Riedl. The scientific session will also include abstracts to be presented by

Dr. Christian Drouet, Dr. Alejandro Malbrán, Dr. Camila Lopes Verones, Dr. Yung Chyung, Dr. Timothy Craig, and Dr. Wolfhart Kreuz.

During the Friday morning there will also be a patient session with a “HAE Disease Primer for Patients and Care Givers”, presented and moderated by Mrs. Sarah Smith-Foltz and Mrs. Alejandra Menendez. For HAEi National Member Organizations the morning will also feature our “General Assembly”.

The conference general sessions will start after lunch on Friday afternoon with the official opening and key note presentations by HAEi President, Anthony J. Castaldo, Dr. Bruce Zuraw, Dr. Michael Frank, Dr. Henriette Farkas, and Dr. Aleena Banerji.

The proceedings on Saturday will focus on the importance of patient advocacy and will start off with reports on the status of HAE diagnosis and treatment from the national organizations in Argentina (and Latin America), Australasia, Germany, Japan, Macedonia, Poland, and United Kingdom. The Saturday session will include motivating talks from patient advocates: Frank J. Sasinowski from the National Organization for Rare Diseases will address “The Rising Power of the Voice of the Patient in Developing Medicine,” and Melissa Hogan from SavingCase will chronicle her journey in caring for her child who suffers from a rare disease called Hunter’s Syndrome, “An Advocate by Necessity: A Mother’s Story.” Dr. Marc Riedl will wrap up the advocacy portion of the Saturday session by providing a physician/researcher’s perspective on “The Importance of Patient Advocacy.” The day will also include an important presentation by Dr. Suzanne Wait from SHW Health Ltd. that provides a scientific evidence (based on the European Burden of Illness Study that HAEi helped implement) that HAE has an extremely negative impact on the lives of patients.

The HAEi Communications Manager will be covering all of the conference sessions and will provide HAEi friends with the highlights in our next newsletter.



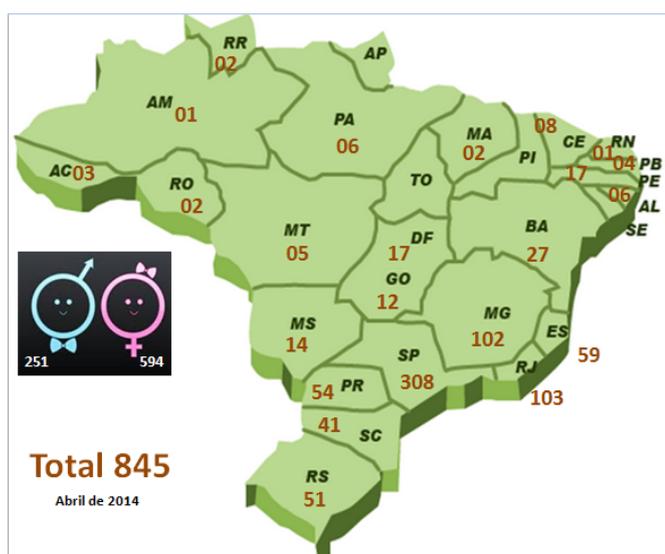
NEWS FROM OUR NATIONAL MEMBER ORGANIZATIONS AROUND THE GLOBE

Australasia (www.haeaustralasia.org.au)

The Australasian HAE organization held its third Annual Patient Meeting at the end of March. Dr. William Smith, a specialist in Clinical Immunology and Allergy at the Royal Adelaide Hospital, delivered an overview of HAE and the current treatments available. The organization's Medical Advisor, Prof. Connie Katelaris spoke about current and upcoming clinical trials and the need for a Patient Registry. Practicing Dietician Merryn Netting discussed the wide-ranging health benefits of a healthy balanced diet. Ryan Bogoyevitch delivered a presentation on how HAE impacts his life, school, friendships and family. The final speaker was Cameron Milliner, Associate Director Government Relations at Shire who spoke about the importance role that the patient advocacy group can play in educating government representatives on the needs of HAE patients.

Brazil (www.abranghe.org.br)

The Brazilian HAE Organization has just issued this map of the country, giving a brilliant picture of all registered HAE patients by April 2014:



Canada (www.haecanada.org)

On 26 April 2014 HAE Canada held a patient information evening in Saskatoon. Speakers included Dr. Tom Bowen,

Clinical Immunologist and Allergist, who spoke on HAE in Canada; and Dr. Karen Dallas of Saskatoon Health Region and Dr. Greg Peters of the University of Saskatchewan who addressed "Treatment of HAE Patients in Saskatoon and Saskatchewan."

Germany (www.angiooedem.de)

The German HAE organization will hold its annual gathering in Berlin 13 June 2014. The meeting is being organized in collaboration with the Charité and Healthcare at Home.

Mexico (www.haei.org/map/96)

Two years ago the first Latin American congress on HAE took place in Buenos Aires, Argentina. On 28 May 2014 the Latin American HAE world will meet again, this time in Vera Cruz, Mexico. The aim of this year's congress is to promote awareness of the disease in order to ensure early diagnosis. More information at <http://www.cicmundiales.com.mx>.



Spain (www.angioedema-aedaf.org)

The Spanish HAE organization held its General Assembly Meeting in Madrid on 5 April 2014. Among the speakers were Dr. Margarita López Trascasa from Hospital Universitario La Paz ("Commitment of patients in the study of angioedema"), Dr. Teresa Caballero Molina ("New classification of angioedema – Additional Study Results of Burden of Illness"), Dr. Nieves Prior ("Survey of Quality of Life in HAE"), and Dr. Maria Pedrosa ("HAE in children").





NEW PAPERS ON HAE

Below are summaries of HAE-related scientific papers published since our last newsletter.

“The prophylactic use of C1 inhibitor in Hereditary Angioedema patients undergoing invasive surgical procedures: a retrospective study” – *by G. Gavigan, University of Ottawa, Canada et al.*: Short-term prophylactic use of C1 INH was found to be effective at preventing post-procedure attacks in patients diagnosed with Type I HAE. (Allergy Asthma Clin Immunol., April 2014)

“Repeat treatment of acute hereditary angioedema attacks with open-label icatibant in the FAST-1 trial” – *by A. Malbrán, Hospital Británico de Buenos Aires, Argentina et al.*: The open-label extension phase of the For Angioedema Subcutaneous Treatment (FAST)-1 trial evaluated the efficacy and safety of repeated icatibant exposure in adults with multiple HAE attacks. Icatibant provided consistent efficacy and was well tolerated for repeated treatment of HAE attacks. (Clin Exp Immunol., April 2014)

“Postangioedema attack skin blisters: an unusual presentation of hereditary angioedema” – *by J. Wiesen et al., Cleveland Clinic, USA*: Describes a 36-year-old man with a history of HAE who presented with painful interdigital bullae secondary to an acute oedema exacerbation. Biopsy and cultures of the lesions were negative and they resolved spontaneously. It is important to highlight and recognize the development of edema blisters after resolution of a flare of HAE (only 1 previous case report), and hence avoid unnecessary dermatological diagnostic workup and treatment. (BMJ Case Rep., April 2014)

“Abdominal attacks and treatment in hereditary angioedema with C1-inhibitor deficiency” – *by E. Rubenstein et al., Boston Children's Hospital, USA*: HAE should be considered in the differential diagnosis of patients with recurrent discrete episodes of severe, unexplained crampy abdominal pain associated with nausea. (BMC Gastroenterol., April 2014)

“Upper airway edema in 43 patients with hereditary angioedema” – *by Y.Y. Xu, Peking Union Medical College Hospital, China*: Upper airway edema (UAE) occurs infrequently in HAE, but still results in significant morbidity and mortality. Clinical, laboratory, and genetic data were compared between 43 patients with HAE and 743 UAE attacks and those

without UAE and normal controls after ethics committee approval. Symptoms limited to the upper airway should be taken seriously. Dyspnea may be the only manifestation of UAE. UAE attacks most commonly start spontaneously and usually progress rapidly, as quickly as 30 minutes, from awareness of symptoms to maximum airway involvement. Patients with a positive UAE family history are predisposed to UAE attacks, and men appear to be more apt to develop asphyxiation than women. (Ann Allergy Asthma Immunol., April 2014)

“The influence of trigger factors on hereditary angioedema due to C1-inhibitor deficiency” – *by Z. Zotter et al., Semmelweis University, Budapest, Hungary*: The first stage of the study analyzed the data recorded by 92 subjects in their patient diaries over seven years. The second phase included 27 HAE patients, who had been completing the diary entry 'Trigger factors' every day for seven months whether or not they had experienced an attack. This analysis of the trigger factors explored, for the first time, their potential role in inducing HAE attacks. The findings might open new perspectives in extending the indications for edema-prophylaxis, and could contribute to a better understanding of the pathomechanism of HAE attacks. (Orphanet J Rare Dis., March 2014)

“Increased eNOS levels in hereditary angioedema” – *by M. Demirtürk, Istanbul University, Turkey et al.*: In this study, serum inflammatory cytokine levels and circulating endothelial cells collected from HAE patients during both acute attacks and asymptomatic periods were evaluated. These results suggest that an inflammatory response is not necessary to trigger HAE attacks. On the other hand, increased endothelial nitric oxide synthase (eNOS) levels might reflect a sustained hyperpermeability state in HAE patients. (Int Immunopharmacol., May 2014)

“The effect of weight on the efficacy and safety of c1 esterase inhibitor concentrate for the treatment of acute hereditary angioedema” – *by J.A. Bernstein, University of Cincinnati, USA et al.*: Despite the worldwide obesity epidemic, there have been very few studies investigating the influence of body weight on treatment dosing and outcomes in patients with HAE. The purpose of this analysis was to determine whether the standard weight-based dosing recommendation of C1 esterase inhibitor (C1-INH) concentrate (20 IU/kg) is adequate in HAE patients with a high body mass index. Treatment of HAE attacks with weight-based doses of C1-INH concentrate provided reliable

treatment response, regardless of body weight, in these patients with HAE. (Clin Ther., April 2014)

“Hereditary Angioedema with an Estrogen Trigger in a 12-Year-Old” – by *A.E. Mowat, Greenslopes Gynecology and Obstetrics Group, Brisbane, Australia and R. Kimble, Statewide Paediatric and Gynaecology Service, Queensland, Australia*: A 12 year old HAE sufferer failed to receive relief from her symptoms of angioedema with standard treatment. A trial of depot medroxyprogesterone acetate has resulted in resolution of her symptoms for the last 14 months. Although estrogens and progestins have been avoided in the management of HAE in the past, the reasons for this are based only on a small number of case reports. In this case, successful treatment with depot medroxyprogesterone acetate indicates that progestins, as an alternative management for estrogen-triggered HAE, certainly warrants further research. (J Pediatr Adolesc Gynecol., March 2014)

“Characterization of prodromal symptoms in a large population of patients with hereditary angio-edema” – by *M. Magerl, Charité-Universitätsmedizin Berlin, Germany et al.*: A questionnaire asking about the frequency, type and time of occurrence of prodromal symptoms, and the interval until the onset of an attack of HAE was sent to 808 German patients with HAE. Answers from 365 participating patients were analyzed. The results of this survey may aid the management of C1-HAE by recognizing that prodromal symptoms are of value in predicting the onset of an attack of angio-oedema and in diagnosing the condition. (Clin Exp Dermatol., April 2014)

“Endothelial cell activation during edematous attacks of hereditary angioedema types I and II” – by *E. Kajdácsi, Semmelweis University, Budapest, Hungary et al.*: This study demonstrates that ECs (endothelial cells) are activated during HAE attacks. The results might suggest the need for revising the knowledge on the pathogenesis of HAE-C1-INH and for reconsidering the role of ECs as a possible novel therapeutic target in patients with this disease. (J Allergy Clin Immunol., February 2014)

“Depression and anxiety in patients with hereditary angioedema” – by *A.S. Fouche, Penn State University, USA et al.*: The data as well as the literature support that depression and anxiety symptoms are common in patients with HAE and may be secondary to chronic disease burden, associated pathophysiologic features, or both. Treatment that addresses the psychosocial and mental health of HAE patients is critical for best practice. (Ann Allergy Asthma Immunol., April 2014)

News from Industry

From the *Shire* 2013 Annual Report: “Towards the end of the year, we announced a significant strategic acquisition of the high growth, rare disease biopharmaceutical company *ViroPharma* for approximately \$4.2 billion. The acquisition brought us a new growth-driving product, Cinryze, used for the prophylactic treatment for HAE, complementing Shire’s Firazyr, which is used for the treatment of acute HAE attacks. The acquisition also brought us other In-line and Pipeline assets. In addition to enhancing both Shire’s immediate and long-term growth prospects, the acquisition is also expected to bring significant cost synergies. (...) Firazyr sales growth (+102% compared to 2012) was primarily driven by the US market, where we continue to see both good growth in new patients and increased levels of repeat usage by existing patients.”

The U.S. Food and Drug Administration (FDA) has approved an expansion of the indication for *Dyax Corp.*’s Kalbitor (ecallantide), a peptide inhibitor of plasma kallikrein used in the treatment of acute HAE attacks, to include patients 12 years of age and older. With this approval, Kalbitor is the first and only subcutaneous therapy available to treat acute attacks of HAE in patients 12 years of age and older. Kalbitor is also the only therapy that is not purified from human plasma that has been approved to treat this patient group. The FDA approval of this label expansion for Kalbitor is supported by the results from two previously completed Phase 3 placebo-controlled clinical studies, known as EDEMA3® and EDEMA4® as well as the results of study DX-88/19, which was ongoing at the time of the original approval of Kalbitor. The efficacy and safety profile observed in pediatric patients 12 years of age and older is similar to the adult population.

“Kalbitor has an established track record in the HAE marketplace and this FDA approval for the expanded use in pediatric patients is an important achievement for both Dyax and the children and families who are affected by this disease”, said Gustav Christensen, President and Chief Executive Officer of Dyax. “We remain committed to providing access to novel therapeutics and first-class patient services to the HAE community.”



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](#)

or Communications Manager [Steen Bjerre](#). In addition, we invite you to submit articles on any topics that you believe would be of interest to other readers. We look forward to your comments and working with you on future newsletters.

HAEi is a global non-profit umbrella organization dedicated to working with its network of national HAE patient organizations to raise awareness of HAE.



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