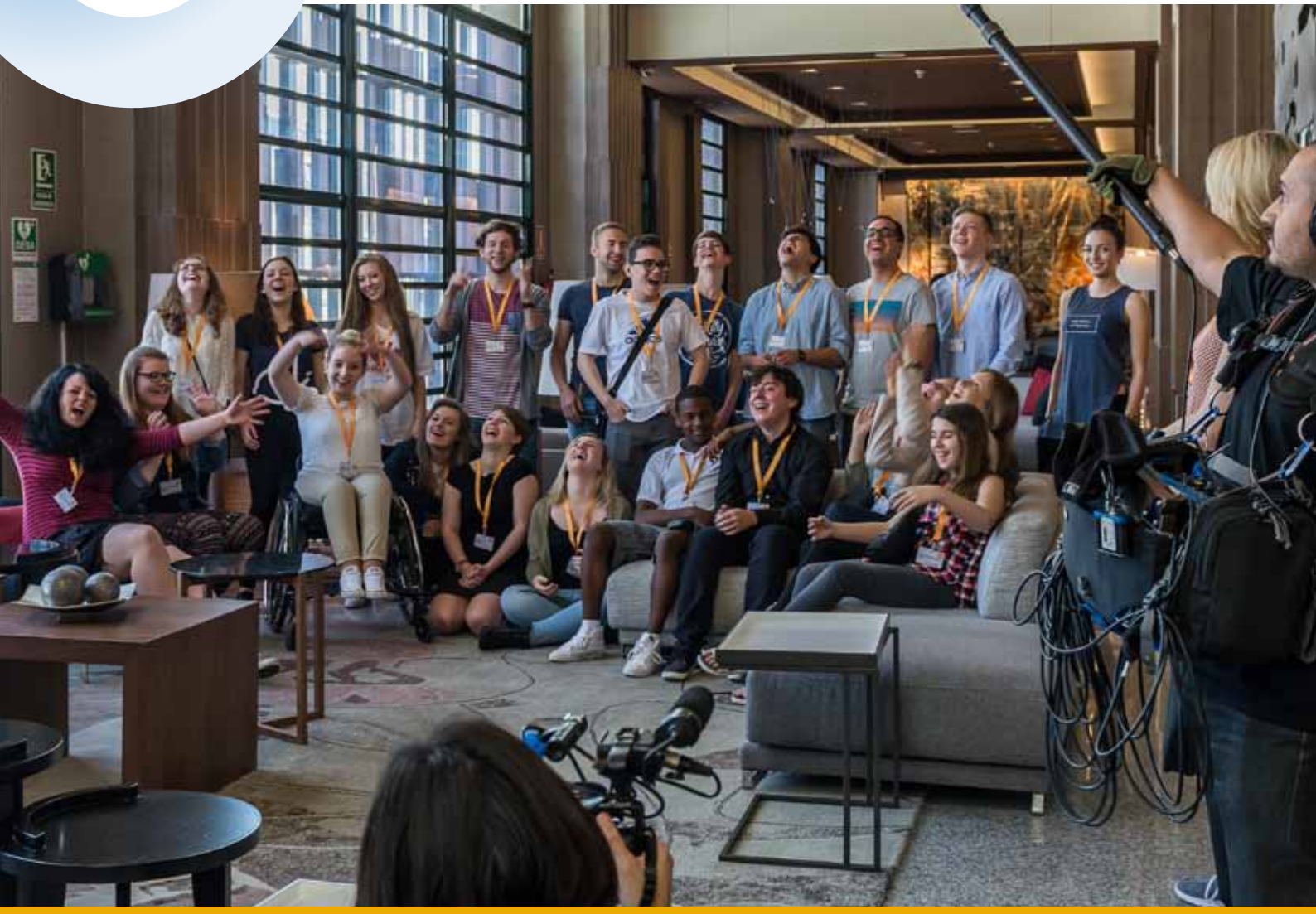
Issue 3 · June 2016

HAEi Newsletter



HAE Global Conference 2016

The third HAE Global Conference was record-breaking in a number of ways: The largest Scientific Program Committee, the largest number of participants (550+) and countries represented (50+), the largest number of keynotes, presentations and posters, the first HAE Global Conference with royal patronage – and an international gathering with a very successful youngsters' track.

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HAEi

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

HAEi Newsletter · Issue 3 · June 2016

Cover photo: From session in the Youngser's track during the HAE Global Conference in Madrid 19-22 May 2016.

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Dear HAEi Friends,

Unity, shared purpose, motivation for action, and hope for the future—these are the words that come to mind as I attempt to summarize what took place at the 2016 HAE Global Conference in Madrid. As you will read in the following pages, this gathering of 550 likeminded people from 50 countries—patients, caregivers, physician/scientists, and pharmaceutical industry representatives—created a unique environment for sharing ideas and aspirations. Indeed, the meeting rooms and corridors of the Madrid Marriott were filled with enthusiastic discussions covering vital topics such as the scientific frontiers of HAE research, challenges encountered in broadening access to HAE medicines, and the power of patient advocacy.

The upbeat and optimistic perspective that we all shared at the Global Conference emanated from the energy and accomplishments of 80 brave souls from 14 countries who joined us in Madrid right after celebrating **hae day :-)** by walking around 50 kilometers along the El Camino de Santiago in northern Spain. The feedback we received indicates that the conference achieved its ultimate objective because participants said they were inspired by what they learned and look forward to applying that knowledge and motivation into systematic action aimed at improving HAE patient quality of life in their home countries.

I would like to thank Sarah Smith Foltz, President of our host member organization—Asociación Española de Angioedema Familiar (AEDAF)—for inviting us to hold the 2016 HAE Global Conference in Spain and for taking care of the innumerable details that made the meeting and the Camino Walk such great successes. A special thank you is also in order for our Executive Director, Henrik Balle Boysen for his formidable organizational skills and tireless and professional approach to accomplishing the infinite tasks that enabled such a wildly successful gathering.

I wish you happy reading and good health!

Warmest regards,

Anthony J. Castaldo

President, HAEi


HAE
GLOBAL
CONFERENCE
MADRID
19-22 MAY
2016
Welcome

HAE Global Conference 2016

Every second year HAEi welcomes HAE patients, care givers, health care professionals, and industry representatives to the HAE Global Conference – the largest international gathering of its kind solely with focus on HAE topics. At the conferences the participants learn much more about HAE as they share experiences and knowledge in a friendly atmosphere conducted and driven by the patient community organized in HAEi.

The first HAE Global Conference took place in Copenhagen, Denmark in 2012, followed by Washington D.C., USA in 2014 and Madrid, Spain in 2016. The next HAE Global Conference is scheduled for May 2018.

The third HAE Global Conference was record-breaking in a number of ways: The largest Scientific Program Committee, the largest number of participants (550+ from more than 50 countries) the largest number of keynotes, presentations and posters, and the first HAE Global Conference with royal patronage.

The conference took place at the newly renovated Madrid Marriott Auditorium Hotel & Conference Center, conveniently located close to the Barajas Airport in Madrid.

While most of the conference attendees arrived in Madrid Thursday 19 May 2016, the HAEi Executive Committee as well as the HAEi Scientific Program Committee met in order to make the final preparations.

Continues on next page

Friday 20 May 2016

Scientific Program, part 1

Konrad Bork, Germany chaired the first Scientific Program session Friday morning. He is Clinical Professor of Dermatology at the University Medical Center in Mainz, Germany. He has served as president of the German Society of Angioedema Research since 1996 and has authored more than 350 articles in textbooks and peer-reviewed scientific journals. Prof. Bork opened this session under the heading *"Improving HAE Diagnosis"* and that was also the title of the keynote speech held by Prof. Marco Cicardi, Italy. He is Professor of Internal Medicine at Milan University and has had long interest in HAE: his research activity in this field has resulted in 150 scientific papers and he follows more than 600 patients with HAE. Prof. Cicardi focused mainly on identifying etiology, identifying pathogenetic mechanisms, identifying phenotypes, and stratifying phenotypes – and he concluded:

- C1 inhibitor deficiency, mutations in Factor XII and treatment with ACE inhibitors are diagnostic of specific forms of angioedema
- Evidence of histamine as the mediator distinguishes one form of acquired angioedema
- Two forms of angioedema are defined only by clinical picture and exclusion of specific diagnosis
- Markers to stratify angioedema patients are still only partially identified and need to be further refined

João Bosco Pesquero – Professor of Biophysics and Director of the Center for Research and Molecular Diagnosis of Genetic Diseases at the Federal University of São Paulo, **Brazil** – presented the first abstract of the day, titled *"Quantitation of large deletions and insertions in SERPING1 gene for the diagnosis of hereditary angioedema"*. Prof. Pesquero concluded that the technique was able to detect for the first time large deletions in the SERPING1 gene in Brazilian HAE patients not diagnosed by Sanger sequencing. These data highlight the importance of using this technique as routine laboratory in the HAE diagnosis.

In the second abstract of the morning **Maria Pedrosa**, who is Doctor in Medicine at Universidad Autónoma de Madrid in **Spain**, spoke about *"Expression of the disease in parents and encouraging counselling on early testing the offspring influence the delay in diagnosis in children with hereditary angioedema"*. She concluded that parents are more concerned with the diagnosis of the disease in the offspring if they are symptomatic. Encouraging counseling on early diagnosis has shown to be effective, giving parents the opportunity to be aware of the disease of their children and be ready for prompt and specific treatment.

Then followed the abstract "*Hereditary angioedema with normal C1 inhibitor: an Italian case series"* presented by Dr. **Maria Bova.** She is Medical Officer in the Internal and Emergency Medicine department at Villa Malta Hospital Sarno in Salerno, **Italy**. The study concluded that the prevalence in Italy seems to be lower than in other European countries. It further hyphotesized a disomogeneous geographical distribution of nC1-INH-HAE among European countries and that Italian patients with FXII-HAE appear to come from the same common ancestor. The study also confirmed that males with F12 gene mutation are asymptomatic.

Dr. **Camila Lopes Veronez** presented the fourth abstract with the title *"ACE inhibitor-induced angioedema caused by a rare mutation in Factor XII gene"*. She is in the Ph.D. program at Universidade Federal de São Paulo, **Brazil** with a main research interest within molecular biology of kallikreinkinin system and HAE. The study showed for the first time a special case of an asymptomatic FXII-HAE man presenting a rare mutation who developed angioedema without wheals at old age triggered by ACEi treatment. Considering the increasing number of patients presenting ACEi induced angioedema and the low penetrance of FXII-HAE, especially in male, the study suggests including the screening of F12 exon 9 in atients with angioedema episodes after ACEi.

Patient Program, part 1

Parallel to the first Scientific Program session there was a Patient Program session with focus on HAE Disease Primer for Patients and Care Givers. In this session **Sarah Smith-Foltz, Spain** and **Alejandra Menendez, Argentina** presented *"Essential HAE Facts for Patients and Caregivers"*.

Patient Program, part 2

The second part of the Patient Program session was reserved for the HAEi General Assembly 2016. In his report for 2014 **HAEi President Anthony J. Castaldo** focused on topics like the Global Conference in USA, the growth of the organization to 40 members, participation in HAE-related meetings in Romania, Japan, Australia, the Gulf Region, Mexico, and Germany, the sponsoring of two HAE research initiatives, and expanded communications with member organizations and other stakeholders.

As for the 2015 report the HAEi President spoke about issues such as the growth in the membership number to 51, a State of HAE Management Reports for Europe and Latin America, participation in nine national HAE meetings and regional workshops, the issuing of eight newsletters, advocacy at nine major international medical meetings, the planning for 2016 HAE Global Conference, launch of the HAEi Global Access Program as well as the launch of two new websites.

Following the General Assembly's approval of the two reports the **HAEi Treasurer Fiona Wardman** presented the financial report for 2014 and 2015. These were also approved by the General Assembly and **HAEi Executive Director Henrik Balle Boysen** could then proceed to the election of candidates to the Executive Committee.

Prior to the General Assembly **Peter Hermeling, Germany** had announced that he would not take another turn as Executive Committee member. Thus, a new representative had to be found for the empty seat – and at the same time four other members were up for election: **Sarah L. Smith Foltz, Spain, Alejandra Menendez, Argentina, Rachel Annals, United Kingdom**, and **Anthony J. Castaldo, USA**. They were all reelected while the General Assembly chose **Nils Berretz, Germany** as new member of the Executive Committee.

HAEi sends Peter Hermeling a warm thank you for the years he has contributed to the Executive Committee. It has been a pleasure having Peter on board – and HAEi wishes him – and his family – all the best for the future.

Scientific Program, part 2

Bruce Zuraw, who is Professor of Medicine at the University of California, San Diego, **USA** and Section Chief of Allergy and Immunology, chaired the second Scientific Program session. Dr. Zuraw's research interests center on inflammatory lung disease and HAE – and he opened this part the program titled *"Improving HAE Care"*. That was indeed also the topic of the keynote speech delivered by Dr. **Teresa Caballero**, who has worked as a senior consultant in allergy at Hospital Universitario La Paz in **Spain**, has a long-standing interest in HAE, and has authored numerous scientific publications on angioedema.

On comprehensive HAE centers Dr. Caballero said that recent government initiatives have focused on community and patient-centered 'integrated' care to ensure long-term affordability and to improve social and medical outcomes. The provision of specialist services for patients varies geographically, depending on availability of funding for high cost drugs as well as the location of major centers of expertise. Furthermore, she said that all patients should have timely access to a specialist immunology nurse, and that the specialist immunology nurse has a key role in supporting the patient and their family in the practicalities of living with HAE to achieve the best quality of life.

Continues on next page

Then spoke Dr. **Henry Li**, executive member of the Chinese-American Medical Society Mid-Atlantic Chapter, **USA**. He focused on *"The impact of androgen derivatives on male sexual hormone profile in man with HAE: A less mentioned long-term side effect"*. Dr. Li concluded that long-term use of androgen derivatives in male HAE patients demonstrated a strong trend of suppression of luteinizing hormone, sexual hormone binding globulin, and testosterone levels. Furthermore, Dr. Li said that the sexual hormone profile in male HAE patients could be affected by the use of Danazol or Oxandrone and that the changes usually are undesirable as potential clinical symptoms may include reduced sexual drive/function, oligospermia, and depression. Not all changes are reversible; some may require additional testosterone treatment.

The main clinical research interest of **Andrea Zanichelli** – an Adjunct Professor at the University of Milan, **Italy** – is in angioedema due to C1 inhibitor deficiency. He spoke about *"Criteria for HAE care/research centers: The experience of ITACA"*. The Italian network for C1-INH-HAE (ITACA) was established in 2012 and includes 17 referring centers. Standards to be qualified as an HAE care center are presence of a referring doctor, availability for routine visit and in case of emergency, possibility of performing diagnostic tests, collaboration with other specialist (dentist and gynecologist in particular), management of acute attacks (availability of specific drugs in Emergency Room and in case of procedures), accountability for home use of drugs (prescription, supply and registering beneficial and adverse drugs outcomes), educational programs for patients' self-administration/home therapy and for colleagues involved in the treatment of patients as well as official authorization to certify the disease. Patients are issued with a card reporting clinical characteristics of the disease, triggering factors, medications to avoid, and treatment options for acute attacks that might be useful in case of emergency. A physician can be contacted by phone 24 hours a day. Dr. Zanichelli stressed that patients should be linked with comprehensive care clinic programs bringing together clinical care, education and research.

Henriette Farkas is Professor of allergology and clinical immunology at the Semmelweis University in Budapest, **Hungary,** and she works as the director of the Hungarian Angioedema Center. In her presentation titled *"Hungarian Angioedema Center – Patient care and compliance"* she told about the center, established in 1996 by integrating an outpatient clinic, hospital background, a complement and genetics laboratory, and a patients' organization. Each year, the complement laboratory receives on average 750 blood samples from 680 patients with suspected or known C1-INH deficiency. Currently, 164 patients are registered with the center and 130 of these keep record of their disease events. However, 35 patients do not replenish their emergency medication for acute episodes and 20 patients do not attend periodic follow-up visits. Dr. Farkas concluded that comprehensive care centers are required for the management of rare diseases, whereas compliance is a prerequisite to ensuring good quality of life and safety for the patients.

Daniela Rivero Paparoni, Venezuela who holds a degree in medicine from Universidad Central de Venezuela and is currently working as Allergy Consultant in the Department of Allergy in Hospital Universitario La Paz in Madrid, Spain, was the last person on stage in this part of the Scientific Program. She spoke about *"Comprehensive management of fertilization, pregnancy and breastfeeding in female patients with hereditary angioedema with and without C1-inhibitor deficiency"* – and concluded that high-estrogen situations may aggravate the disease in female patients. Furthermore, she said that situations like fertilization procedures, pregnancies, and breastfeeding could be managed with on-demand/intermittent long-term prophylaxis with plasma-derived C1-INH concentrate.

Pictures by and of the participants kindly shared with HAEi and you.

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Scientific Program, part 3

The Scientific Program sessions closed with the poster presentations.

The Odyssey of HAE Patients: Medical Interventions in Patients with Hereditary Angioedema – by J. Hahn et al., Ulm University Medical Center, Germany

Knowledge about HAE is still limited. A couple of medical interventions in HAE patients could be avoided by limiting the odyssey: early and accurate diagnosis in accordance with the appropriate treatment. Even when HAE is diagnosed, avoidable procedures are performed due to widespread ignorance. On the other hand the line between right and wrong is a very thin one: HAE patients do also have appendicitis – in case of emergency and non-specific symptoms the doctor in charge must decide individually.

Pregnant women with angioedema treated with Berinert – by L. Bouillet, Grenoble University Hospital, France and National Reference Centre for Angioedema CREAK, France, et al.

Pregnancy is a critical period for women presenting angioedema and few data are available concerning the treatment of their attacks and their prophylaxis. To describe the clinical profile of pregnant women with angioedema treated with Berinert and their treatment modalities their data have been extracted from the COBRA registry, which has been set up 5 years ago to collect all available information concerning patients treated with Berinert in France. The study shows that the use of Berinert contributes to the safety of pregnancy by women presenting angioedema.

Compliance to therapy in Brazilian patients with Hereditary Angioedema (HAE): validating and applying a questionnaire – by A. A. Barbosa, School of Medicine do ABC, São Paulo, Brazil, et al.:

Compliance to treatment in patients with HAE seems to not only depend on how patients affirm to be committed or satisfied with the treatment. Adherence to treatment in patients with HAE seems to be proportionally related with clinical repercussions of the disease. A great difference between this Brazilian survey and international surveys are in the frequency of emergency services needed by the HAE patients. The majority of respondents affirmed not having the need of emergency services to control a sudden or episodic attack related with HAE in the last six months. The majority of the Brazilian HAE patients in this study stated to have a good understanding of the disease. The main discouraging factors to the treatment seem to be its high cost and/or no availability in the pharmacies and hospitals.

Hereditary angioedema in Slovakia – results from pilot study – by M. Jesenak, Comenius University in Bratislava, Slovakia, et al.

A national study about the number of HAE patients and their selected characteristics was performed through a questionnaire-based survey in out-patient clinics for allergy and clinical immunology. 87 living patients with HAE from 39 families were found; 15 already died due to laryngeal edema. 42 percent were without prophylactic treatment, while acute attacks were treated with danazol (30 percent), icatibant (26 percent), pd-C1-INH (22 percent), and rh-C1-INH (22 percent). The survey is still ongoing and the creation of a national HAE registry and a HAE patients' organization is planned.

Results from an interim analysis of a Ruconest treatment registry in Europe – by R. Hakl, St. Anne´s University Hospital, Brno, Czech Republic et al.

The Ruconest treatment registry provides real-world data on the treatment of 419 HAE attacks that is consistent with previous reports on the safety and efficacy of Ruconest therapy.

To what extend an availability of emergency treatment impacts HAE patients' everyday life? – by G. Porebski, K. Obtulowicz and E. Czarnobilska, Jagiellonian University, Krakow, Poland

We performed a standardized questionnaire asking for selected aspects of patients' life. It was conducted three

years before and six months after a recombinant C1-INH became available in Poland. The highest improvements were noted in the questions concerning patients' depression about the disease, an influence of HAE on their family and social life, and decision on parenthood in future. We observed how much availability of a drug improves patients' sense of security, but also we could demonstrate a distinctly positive influence on areas of patients' life indirectly associated with the disease.

HAE Australasia patient profile survey 2015 – by C.H. Katelaris, Western Sydney University and Campbelltown Hospital, Australia, and F. Wardman, HAE Australasia

Despite improvements in HAE management and better access to acute treatment, the burden of illness remains high and in particular, self-reported rates of anxiety and depression are significantly higher than in the general population. There is an opportunity for positive interventions to improve the mental health of people living with HAE.

The relationship between complement levels and disease activity in Japanese eight cases with hereditary angioedema caused by an inherited deficiency of C1-inhibitor (HAE-C1-INH) – by A. Fukunaga, Kobe University Graduate School of Medicine, Japan, et al.

The serum level of C1-INH, C4, and CH50 during symptom-free periods might be useful as a laboratory biomarker of HAE disease activity. Two elderly HAE-C1-INH Japanese patients with normal levels of C4 and CH50, confirmed by DNA analysis, have to-date not experienced HAE attacks.

Off-label subcutaneous use of 1500 IE C1-INH – a new approach for prophylaxis in HAE? A case report – by M. Nordmann, J. Hahn, T. K. Hoffmann and J. Greve, Ulm University Medical Center, Germany

Subcutaneous use of 1500 IE C1-INH seems to be easy and safe. In our case it showed similar effectiveness compared to the intravenous therapy. No adverse events could be noticed. The quality of life measured by the AE-Qol could be approved. By learning a self-application the patient gained independence. The results of this case seem promising, however bigger studies are needed to underline the findings.

Treatment of hereditary angioedema with C1 esterase inhibitor concentrate in pregnant women and pediatric patients: findings from the International Berinert Patient Registry – by I. Martinez-Saguer, Hemophilia Centre Rhine Main, Frankfurt-Mörfelden, Germany, et al.

Considered along with previously reported experience, the Registry findings confirm the safety of pnfC1-INH concentrate use across a range of doses for treating HAE in children and adolescents and for pregnant women before and during pregnancy.

Assessment of the cardio-cerebro-vascular and hepatic safety in patients with hereditary angioedema due to C1 inhibitor deficiency – by F. Perego on behalf of ITACA (Italian network for C1 inhibitor Hereditary Angioedema)

The aim of the project is to propose a national collaboration to relay on this unique series of patients to assess whether the causes of death, the risk for cardio-vascular events and hepatic neoplasm are different in C1-INH-HAE patients compared to the general population and whether long term AA change these outcome measures. The cardio-vascular risk is characteristically multifactorial and long term, thus it is difficult to calculate in rare diseases as C1-INH-HAE. In Italy, patients with this condition started to be diagnosed and systematically followed in specialized centers since early seventies. First in the world, HAE Italy now has created a network (ITACA) that recently published the largest series of C1-INH-HAE patients. Important finding in the paper is some evidence for lower life expectancy in the patients' population compared to the general population.

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Pictures by and of the participants kindly shared with HAEi and you.

Managing children with HAE – by M. Wiednig, Medical University of Graz, Austria

In families with a history of HAE, children should be screened early, as there are good options for prophylaxis. Danazol, however, should be avoided in girls. The on-demand therapy requires trained individuals for intravenous application. New drugs like Icatibant can improve quality of life of children and their parents because subcutaneous self-administration becomes possible.

What You Can't See Can Kill You: Mapping the Geography of HAE Throat Swells Using 3D Modeling – by I. Brunkan; Seattle, USA

Using 3D printing and advanced mathematical concepts, the degree of airway narrowing was calculated at multiple locations in the patient airway for various amounts of submucosal edema. The airway was modeled after a 16-year-old female HAE patient. By using 3D modeling, it was possible to demonstrate visually how the larynx swells during an HAE attack. Since the edema does not reabsorb immediately, it provides a compelling visual for HAE patients, urging them to treat as soon as they recognize the beginning of an attack. The study illustrates the importance of treating even small laryngeal edema early. The regions with smallest airway diameter are not seen or felt on a physical exam; therefore the most important terminent to treat should be the patient's description of their own symptoms, rather than clinical findings.

Hereditary Angioedema: An Unconsidered Disease – by S. Nieto, Instituto Nacional de Pediatría, Mexico City and Asociación Mexicana de Angioedema Hereditario et al.

Physicians should recognize the patient, understand the patient's major complaints and ask questions to explore their underlying causes, make a clinical diagnosis and the possibility of another diagnosis. Many healthy people have routine lab tests before surgery. In these cases, test results rarely make the surgery safer or change the surgery's outcome, but these "routine" lab tests do not discard that a patients has HAE. An alarming ignorance of this disease prevails in Mexico, which causes a late diagnosis and unnecessary deaths.

Efficacy of Recombinant Human C1 Esterase Inhibitor for the Treatment of Patients With Severe Hereditary Angioedema Attacks – by H. H. Li, Institute for Allergy and Asthma, Chevy Chase, USA, et al.

The data of the study support the efficacy of recombinant human C1 esterase inhibitor for severe HAE attacks as it reduced the time to the beginning of symptom relief compared with placebo. Data are consistent with results from a subanalysis of two double-blind, randomized, controlled phase trials with open-label extension phases that demonstrated a significant reduction in time to beginning of symptom relief with recombinant human C1-INH versus placebo in patients with severe attacks.

Creating an empowering space for patients and improving care through HAE patient advocacy in Japan – by B. A. Yamamoto and N. Kitano, Wakayama Medical University, Japan

In the Japanese context, the rare disease patient organization can nurture a unique space that allows for a shift in the dynamics of the physician-patients relationship from paternalism to shared power and responsibility. Through structured and unstructured activities, mutual participation is practiced. At the same time, new knowledge and social capital may be generated, which can translate directly or indirectly into improved patient quality-of-life and lower disease burden.

Triggers and Prodromal Symptoms of Attacks in Patients with Hereditary Angioedema: Results from an International Registry – by T. Caballero, Hospital La Paz Institute, Madrid, Spain, et al.

As of April 2015, 395 icatibant-treated patients with HAE type I/II were enrolled in the Icatibant Outcome Survey: 268 patients reported 697 historical attacks and 256 patients reported 1484 attacks during the survey. The most common triggers were emotional distress, change in estrogen levels and physical trauma, whereas the most common prodromes were tiredness and erythema marginatum. Understanding triggers and prodromes may help patients to better recognize attack onset.

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Learning self-intravenous administration in patients with HAE deficit C1 – by F. Sánchez Hernández, Almeria University, Spain

Intravenous self-administration courses have been shown to be a future option in the treatment of acute attacks in HAE patients, being able to reduce mortality. Success or failure of this treatment depends on knowledge and training skills of multidisciplinary teams that give courses.

Mutations in SERPING1 gene and clinical features of Brazilian individuals belonging to ten unrelated families with C1 inhibitor-deficient hereditary angioedema – by L.S.M. Maia, University of São Paulo, Brazil, et al.

Predominant symptoms of the studied patients are swelling of hands and face, followed by abdominal pain. Laryngeal edema was present in almost one third of the patients. New mutations, as well as previously described mutations in SERPING1 gene were identified as cause of C1-INH-deficient HAE in Brazilian patients.

C1INH-HAE. A web based poll on accessibility to acute attack treatments in Argentina – by A. Menéndez, HAE Argentina, and A. Malbrán, Unidad de Alergia, Asma e Inmunología Clínica, Argentina

A web based poll asking about accessibility to icatibant and pdC1-INH, self treatment, delay to treatment and coverage was compared with previous reports of 2008 and 2013. 75 percent of the patients have either pdC1-INH, icatibant or both, while 25 percent do not have access to treatment. In 2008, 3.4 percent had access. 26 percent self-injected, similar to 28.6% in 2013, though between studies widespread self-injection clinics have taken place. However, considering injections by proxy, home treatment reached 55 percent. Only half of the patients select to receive treatment early during the attack. 63 percent have full coverage, while 5 percent have no coverage at all and the rest only partial reimbursement. 31 percent of the families share one treatment dose of the medication, better than 36 percent in 2013. Efforts should continue to further improve accessibility and optimal management of HAE acute attacks to all patients.

The Application of the Knowledge to Action (KTA) Framework to Promote Uptake of the Canadian Hereditary Angioedema (CHAE) Clinical Practice Guidelines (CPGs) – by S. Betschel, University of Toronto, Canada, et al.

Clinical Practice Guidelines are considered an important knowledge translation tool aimed at informing clinical practice, yet their adoption is inconsistent. Furthermore, passively disseminating guidelines is not sufficient to ensure implementation and uptake. We applied the Knowledge to Action Framework to improve the implementability and uptake of the Canadian Hereditary Angioedema guidelines. We conducted two knowledge end-user workshops with guideline developers and HAE patients. Key barriers identified by both groups were the lack of knowledge of new HAE treatments, difficulty obtaining appropriate referrals to specialists and poor HAE management by emergency personnel. Patients raised concerns about their ability to self-manage and to maintain a good quality of life due to the unpredictability of onset, severity and frequency of attacks. Specific target audiences identified were patients/caregivers and emergency personnel. Knowledge translation interventions included presentations and workshops.

Recombinant Human C1 Esterase Inhibitor to Treat Acute Hereditary Angioedema Attacks in Adolescents – by J. W. Baker, Baker Allergy, Asthma, Allergy & Dermatology Research Center, Portland, USA et al.

Recombinant human C1 esterase inhibitor for acute attacks of HAE was efficacious in adolescents and normalized C1-INH levels in almost all individuals, an important attribute for therapy. It was well tolerated among adolescents with no new safety signals identified in this pooled analysis; data reinforce the benefits of recombinant human C1 esterase inhibitor for the treatment of acute HAE attacks in adolescents.

Pictures by and of the participants kindly shared with HAEi and you.

Self-administration of plasma derived C1 inhibitor for patients with hereditary angioedema: a learning experience – by M. Castiglioni and A. Zanichelli

41 patients and caregivers were trained for self-administration of plasma-derived C1-INH. 20 patients started self-administration, while two went on long-term prophylaxis TP with C1-INH. The patients reported improvement in quality-of-life when switched to home therapy with C1-INH. While on home therapy patients did experience decreases in hospitalization and absence from school/work. No side effects or injection-site complications were reported.

A nationwide survey of acquired angioedema due to C1 inhibitor deficiency in Italy – by M. Cancian on behalf of ITACA

99 patients with C1-INH-AAE and 983 with C1-INH-HAE were diagnosed by ITACA with a relative frequency of 1:10. Median age at diagnosis in C1-INH-HAE is 26 while in C1-INH-AAE is 64 since the late symptoms onset. Median delay in diagnosis in C1-INH-AAE is 2, shorter compared to >10 in C1-INH-HAE. C1q plasma levels are < 50 percent in 76 percent of patients while in C1-INH-HAE patients is between normal range.

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Patient Program, part 3

The third and last of the Patient Program sessions Friday contained presentations from 10 countries.

Argentina

Alejandra Menendez, President of **HAE Argentina**, said that 413 patients are registered with the organization and it expects that approximately 45 percent of all HAE patients in Argentina are diagnosed.

Interest among specialists has increased but general physicians and emergency doctors do not have a sound understanding of HAE. Patients are seen by allergists, immunologists and occasionally by gastroenterologists or dermatologists on a first visit. However, there are no HAE specialized centers in Argentina.

Patients keep medications at home as it is not available in the hospitals. They are encouraged to learn to self-treat at home avoiding delays and risks. All attack locations are eligible for treatment. Doctors encourage HAE patients to treat all attacks affecting their quality of life as early as possible. Available medications are Firazyr, Berinert, androgens, and tranexamic acid.

A survey conducted by HAE Argentina shows that 62 % have access to one of the modern treatments while 14 percent have access to both of them. There are huge diversity and inequality in access to Argentina's Health Care System as there are differences in regulations within each province. 65 percent of the patients have all reimbursement, while 35 percent still have to partially pay for the medication, making it impossible for these patients to follow an optimal treatment plan. 50 percent delay treatment to preserve medication for life threating attacks, while 80 percent reported difficulties or long delays in replacement of treatments. 57 percent are under home treatment – 22 percent self-treat at home, while 43 percent still go to a hospital for treatment.

HAE is not easily recognized in an emergency situation and modern HAE treatments is not available in hospitals. Also, carrying self-medication to hospitals raises concerns to those unfamiliar with HAE. The HAE Argentina recommendations to the patients are to learn to treat their attacks, to treat as early as possible, and to have an emergency plan in place.

As for the future of HAE in Argentina it is the aim of HAE Argentina to achieve universal, unrestricted access to modern treatments for all HAE patients, to have all modern treatments available, to coordinate a National Patient Register, and to have a national HAE care center.

Japan

President **Beverley Yamamoto** and Vice-President **Makiko Matsuyama** represented **HAE Japan**, stating that at this point 412 HAE patients have been localized. The estimated number of patients in the country is 2,500.

There is low awareness of HAE among health care professionals, leading to non-diagnosis and delayed diagnosia, and there is still a relatively low awareness of HAE in Emergency Centers. Only one product (Berinert) is licensed for HAE treatment, patients have little autonomy as treatment is in the hands of the physicians. 50 percent of the diagnosed patients are not using modern HAE treatments – and there is no HAE center of excellence.

HAE patients are reimbursed under Rare Disease Law, but there is a monthly limit depending on income of the person insured. There are restrictions to the use of Berinert for acute attack, based on the doctor's discretion. However, the Japan Complement Research Society has HAE guidelines. Rare diseases are a health priority in Japan.

Regarding the future of HAE in Japan the organization is working for accurate and timely diagnosis, management of HAE with effective medication that gives patients

autonomy and control, and engagement in national and international advocacy to improve treatments further. Also, HAE Japan hopes for collaborative approaches with physicians and industry (, eg. clinical trials, patient registry, surveys and patient research) as well as gaining a voice in rare disease advocacy space in Japan and wider Asia Pacific.

Brazil

In her presentation President **Renata Martins** of **HAE Brazil** said that 1,235 patients have been registered and that there are an estimated 4,116 patients in Brazil in total. The number of physicians registered with the organization is 390. In other words Brazil has many HAE specialized doctors – the problem is for the patients to reach them.

Regarding diagnosis only a few laboratories do the complete blood exam and as for genetic exams by researchers these are new and scarcely accessible. However, there has been great improvement in diagnosis over the last six years.

When it comes to long-term prophylaxis Brazilian patients have access to attenuated androgens (Danazol, Oxandrolone) and antifibrinolytics (tranexamic acid, epsilon-aminocaproic acid), while the available medication for short-term prophylaxis is attenuated androgens (Danazol, Oxandrolone), antifibrinolytics (tranexamic acid), and Berinert. Acute attacks can be treated with antifibrinolytics (tranexamic acid), Berinert, Firazyr and fresh-frozen plasma. Finally there are these products under no license: Attenuated androgens, Cinryze/Cetor, Ruconest, and Kalbitor.

Tranexamic acid, Oxandrolone, and Danazol can be picked up for free, but the production in currently suspended. In case of crisis the patient can have Firazyr or Berinert at home for self-administration.

USA

Janet Long, Executive Vice President of the HAE organization in **USA**, said that 3,904 HAE patients have been located so far and that the total number of patients could be more than 10,700.

In general, US physicians are only somewhat knowledgeable, but great progress has been made in the last 15 years. HAE patients are mainly cared for by allergists and immunologists, while the US HAEA Angioedema Center at UC San Diego provides expert care, education, and research. Patients get an accurate diagnosis through the center, a Medical Advisory Board of doctors, and a physician referral database. HAE patients are focused on achieving lifelong health and, like others with rare diseases, are encouraged to advocate for their own care.

HAE treatments licensed in the US are androgens, fresh frozen plasma, and modern HAE therapies (Cinryze, Berinert, Kalbitor, Firazyr, and Ruconest). Theatments are reimbursed via private insurances and most government insurances, while non-profit agencies help with premiums, co-pays, etc.

Self-administration is determined by the label, depending on what the FDA approves. HAE therapies are also available at hospitals, doctors' offices, infusion centers, and through visiting nurse care. Some insurance companies are moving toward limiting the number of doses per shipment as well as access to only one therapy.

In an emergency situation all patients should have access to at least two standard doses of an FDA-approved medicine for on-demand treatment of acute HAE attacks. However, HAE often still goes unrecognized by doctors in the Emergency Room. Thus, patients are encouraged to personally set up a plan with their Emergency Room in advance – if medication is available in the Emergency Room, or if patients carry it in themselves, it is usually administered promptly.

The plans and dreams for HAE in the US include greater patient identification, faster and more accurate diagnosis, increased awareness, legislative influence, improved therapies, and advanced research for a cure.

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Pictures by and of the participants kindly shared with HAEi and you.

Australia and New Zealand

The HAE patient population is expected to be 450 in Australia and 50 in New Zealand. At the moment 110 patients are known in Australia and 14 in New Zealand.

The **HAE Australasia** President **Fiona Wardman** and the New Zealand Representative **Olivia Worthington** said that immunologists care for HAE patients in both countries. There are knowledgeable doctors in major cities but general practitioners are lacking in knowledge and awareness of HAE. Accurate diagnosis is by blood tests, while HAE care is "hit and miss" depending on the doctor and hospital the patient attends.

In Australia Danazol, tranexamic acid, and Firazyr (some restrictions) is reimbursed, while C1 Esterase is soon to be reimbursed with restrictions in hospitals. For New Zealand Danazol, tranexamic acid, and Firazyr (some restrictions) is reimbursed, while C1 Esterase is in hospitals for some special use.

Some hospitals' Emergency Rooms with regular HAE patients recognize symptoms and treat patients as necessary. However, medication is not always available or administered promptly and often patients go through unnecessary tests and procedures.

It is the aim of HAE Australasia to find more patients in the region, to gain better access to all available HAE treatments, to create more awareness of HAE, and to have better education of medical professionals for quicker diagnosis.

Chile

President **Lorena Merino** of **HAE Chile** said that there are an estimated 360 patients in the country and that 48 have been diagnosed so far. There are no modern HAE medications registered in Chile with tranexamic acid as the only available solution. On top of that physicians don't recognize HAE and patients get adrenaline or corticosteroids, which are not specific HAE medications.

The main goal is having an HAE care center so that all HAE patients in Chile can improve their quality of life.

Canada

According to Board Member **Dianna Graves** and Regional Director **Bob Simon** of **HAE Canada** there are approximately 720 HAE patients in Canada, however only 253 have been located so far. Most patients are diagnosed and treated by specialists but there is currently no officially designated specialist center. Regional clinics are emerging as leaders in care and research, and in general patients feel fortunate to have treatment. Berinert and Firazyr is available for acute treatment, while Cinryze is available for long-term prophylaxis. Home and self-administration is common and medication is funded and available via provincial formularies and private insurance plans. Rare diseases are gaining traction with decisionmakers and becoming more of a priority.

As for emergency situations HAE is not well recognized and treatment is not always readily available. Emergency Rooms have HAE Protocols in place and HAE Canada is working with the pharmaceutical companies to educate Emergency Room staff. Also, HAE Canada has produced resource materials and developed an HAE app.

United Arab Emirates, Saudi Arabia, Qatar, Oman, Kuwait and Bahrain

Rashad Matraji, who is one of the newly appointed HAEi Regional Patient Advocates, gave an orientation on the situation in a number of countries in the **Middle East.**

In the United Arab Emirates there are five diagnosed patients and the registered medications are androgens and antifibrinolytics. Berinert is also available, however with a very limit access and it is not registered. Saudi Arabia has 100 patients and the registered medications are androgens, antifibrinolytics, and Berinert, while in Qatar there are four patients with access to androgens and antifibrinolytics. As for Oman there are two known HAE patients and here the registered medications are androgens, antifibrinolytics, and Berinert. In Kuwait there are four patients with access to androgens and antifibrinolytics. Finally there is Bahrain with one known patient and also here the registered medications are androgens and antifibrinolytics.

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There are no proper guidelines or procedure to be followed for diagnosis. As awareness is not that strong Rashad Matraji has arranged two workshops in the region.

If they have the patient's details on file some hospitals they have Berinert for emergency situations but this is very rare. The emergency response will therefore be to save life more than treating HAE.

As for the future of HAE in these countries Rashad Matraji said that everyone should have the right to a normal life, that medication should be available and registered, that there should be proper emergency response to treat attacks, and that medication should be reimbursed for non-nationals as there are large numbers of these in the countries.

United Kingdom

Chief Executive Officer **Laura Szutowicz** and Executive Officer **Rachel Annals** of **HAE UK** said that there are an estimated 1,500-2,000 HAE patients in the United Kingdom. The number of patients known to the organization is around 1,000 but there might be duplication – HAE UK is looking into that at the moment. Therefore one can make the reasonable assumption that HAE is hugely under-diagnosed, having to do with the fact that family history is often concealed but also due to misdiagnose, incorrect referrals, and the sporadic nature of the condition.

General practitioners will rarely see more than one HAE patient in their lifetime. Diagnosis tends to take a long time. As most of the 30 or so specialist immunology centers in the UK now also deal with allergy the majority of HAE patients should now be under immunology. The ideal referral would be from the general practitioners to the immunology centers but often it is via other specialties.

All HAE treatment in the UK is under socalled Specialized Commissioning, covering some 70 therapy areas. Treatment is directly funded by National Health Service. Many patients are successfully treated with low-dose androgens to prevent attacks. Home therapy is the 'Gold standard', however, there are still some clinicians that are unaware of the funding process. In come cases free service is not taken up and patients are only allowed 'one attack'.

HAE has strong advocate voices in Clinical Reference Groups and awareness amongst treating clinicians and specialist nurses is very high. However, patients frequently do not attend, there is lack of compliance or failure to engage – and they don't always understand the difference between treatments and need for soonest possibly action. Many patients hold supply of C1-INH and take it with them to the emergency department but due to delays, ignorance and 'it looks like an allergic reaction' HAE UK has introduced an A&E card and established an emergency phone line.

Among the future projects of HAE UK are updating of the website with a member area and a youth section, the first Scottish patient day 1 October and the annual patient day 19 November 2016 – and naturally continuing to raise awareness through media campaigns, HAE unit visits and meetings.

Germany

Stephanie Berretz and **Peter Hermeling** from **HAE Germany** estimated that 1,600-2,000 HAE patients are living in their country – and at the moment 300 are known to the organization.

As for HAE treatments androgens have never been licensed in Germany and since 2005 they have not been commercially available. Modern HAE medications include Berinert, Cinryze, Firazyr, and Ruconest – and they are all fully reimbursed. Berinert, Cinryze, and

Firazyr can be used for self-administration. All attacks can be treated all the time and being on home treatment is the patient's decision in dialogue with the doctor.

It still quite often happens that HAE is not recognized in the emergency room and that the patient is therefore misdiagnosed or mistreated with antihistamines and cortisone. Some doctors simply ignore the information given by the patients and use ineffective treatments. The HAE medications are not regularly available in smaller hospitals. This can lead to long waiting time for the patients if medication needs to be obtained from another hospital or pharmacy – and even worse if the doctor decides to use antihistamines, cortisone or wants to wait and see.

As for the plans for HAE Germany Stephanie Berretz and Peter Hermeling said that the organization wants to enable patients to be strong and educate patients to be independent, for instance trough self-infusion. In 2016 the focus is twofold: Encouraging the young patients through continuation of the HAErkules Project and getting more patients diagnosed.

The HAErkules Project was rolled out on hae day :-) in 2015 and the aim of the project is to have youngsters visit youngsters at their home. HAE Germany bear the travel cost for youngsters whose families are member of the organization and the exchange of youngsters is currently running in Germany, Austria and Switzerland.

The HAE Germany presentation ended with the video 'Find your way out of the labyrinth' with the young German HAE patient Nils Berretz. The German organization asked all participants to share the video on websites and YouTube in order to encourage everyone to learn self-administration and to request this treatment option.

Pictures by and of the participants kindly shared with HAEi and you.

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HAE Youngster Program

Friday also contained an all-day HAE Youngster Program. As you can see from the pictures the day included a number of activities and new strong ties were made across borders. Among other things the participants agreed to work on a HAE Youngsters Summer Camp – most likely somewhere in Europe – hopefully already for 2017.

Pictures by and of the participants kindly shared with HAEi and you.

General Session

Last on the packed Friday program was a General Session including the official opening of HAE Global Conference by HAEi Executive Director Henrik Balle Boysen as well as a keynote with the title *"Creative Advocacy for Expanding Access to Therapy"*, delivered by the HAEi President Anthony J. Castaldo.

The HAEi President used a mouse as a role model for HAE advocacy as it has helped scientists pinpoint the cause of HAE – but not least because the mouse that jumped into the jar of cream and kept on churning until the cream was turned into butter tells something important about advocacy: Keep churning and never give up. Talking about many recent HAE success stories – in for instance Mexico, Macedonia, Japan, and the Gulf Region – Mr. Castaldo said that the keys to successful advocacy are a passion for making things better and that it actually happens when you keep on churning.

Welcome Reception

There was, however, one more item on the agenda, as Friday ended with a Welcome Reception taking place in the Exhibit/Conference Foyer of the hotel.

Pictures by and of the participants kindly shared with HAEi and you.

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Saturday 21 May 2016

General Session, part 1

Saturday started out with the first part of the General Session. In their presentation *"HAEi 2016 Global State of Management of HAE"* the HAEi President and Executive Director informed about a 37 member organizations survey covering almost 10,000 patients and addressing a variety of issues related to the management of HAE in their respective countries.

Top three challenges:

1. Access to (including reimbursement for) modern HAE medications
2. The health and welfare of patients not on treatment
3. Lack of awareness of HAE in the country

One fourth have no access to modern HAE medication; androgens and/or antifibrinolytics are the only therapies available in the countries with no modern medicines – and two countries didn't even have access to androgens or antifibrinolytics.

In the vast majority of countries, modern HAE medication is used for acute treatment, not prevention. In countries where modern HAE therapy is available, self-administration is becoming a more common practice. Nevertheless, in seven countries that modern HAE medication has to be administered by a physician.

The survey shows that compliance with HAE guidelines remains a challenge as less than 15 percent of the countries reported that patients have two or more treatments of modern HAE attack medication on hand at all times. Only 14 percent reported that their HAE patients have an emergency plan and only 16 percent estimated that their patients have family members tested for HAE.

54 percent of the countries that reported that patients have access to modern therapy cited limitations on the use of the medicines such as life-threatening attacks only or abdominal and/or facial attacks only.

Well over half of the respondents indicated that availability and reimbursement to modern HAE therapies is not considered a priority by the healthcare authorities, governments, and/or payers.

An overwhelming majority stated that without access to a HAE medicine patients have a low or very low likelihood of success to live a 'normal' everyday life and fulfill their potential in school, at work, and in social life. In contrast, more than 80 percent stated that patients with access to medicine have a very high or high likelihood of success to live a 'normal' everyday life and fulfill their potential in school, at work, and in social life.

59 percent rated the physicians who treat HAE patients to have good or excellent HAE knowledge, while 73 percent rated the emergency room physicians and also the average physician's (including the family doctor's) HAE knowledge as poor or very poor.

Regarding the impact to unrestricted access to modern HAE medicine patients said that it would mean the start of a new life, that they can look for employment again and support themselves, that they can try and have a child before they reach menopause, that they would no longer have to fear untimely death, and that their children will not have to suffer as much as their parents have done.

This session also contained a presentation on *"HAEi Global Access Program"*, delivered by **Rob Britt**. He has a strong career history in the pharmaceutical environment beginning in sales and progressing to medical communications in both the domestic and international arena.

Then followed the second part of the country presentations, this time with six countries on stage.

Spain

Maria Arraiza, who is Regional Representative in **HAE Spain**, said that there should be some 1,000 HAE patients in the country of whom 312 are registered with the organization.

The knowledge of the general physicians about HAE is improving but it is still quite deficient, especially in emergency room situations. Allergists usually see HAE patients and there is no 'official' national reference center. Hospital Universitario La Paz in Madrid is the leading care center and Spain has an excellent group of 19 allergists who focus on HAE: the Spanish Study Group on Bradykinin-Induced Angioedema. The level of care varies from poor to excellent and mostly depending on geographical location, but generally speaking HAE patients receive good care compared to other rare diseases.

HAE treatments include androgens and to a lesser extent tranexamic acid while the modern HAE medications licensed in Spain are Berinert, Cinryze, and Firazyr. All medications are reimbursed under Spain's national healthcare system. Again, depending on geographical location and attending physician, the criteria differ, but the consensus is to allow patients to keep the modern HAE medications at home and learn to self-administer. The same is true of restrictions as in most cases there are none. Patients who are allowed to keep medications at home are required to report to their physicians all attacks and the number of vials used for each attack.

Emergency room treatment is the weak link of the chain, as more often than not emergency room doctors do not recognize HAE. Medication is available in only some hospitals and in some cases emergency room staff refuse to administer medication, even if the patient brings it himself/herself. HAE Spain has a telephone number and a Twitter account to receive urgent messages from anyone needing help in an emergency room situation.

Among the activities of HAE Spain are emergency cards, patient diaries, patient guidance booklets, regional workshops for patients and their families, and the launch of a new website. Most recently HAE Spain has worked to help prepare the HAE Global Conference as well as the Camino Walk.

Greece

Representative **Stavroula Labiri** from **HAE Greece** said that there are presently 120 HAE patients registered in the country and that there are expected to be a total of around 300.

In 40 percent of the patients the diagnosis of HAE was established only during the last five years and the overall delay of diagnosis is more than 16 years. There are seven confirmed deaths from laryngeal edema in Greece.

The doctors that usually treat HAE are allergists, immunologists or specialists within ear, nose and throat. In 2009 the Hellenic Society of Allergiology and Clinical Immunology an HAE registry with the aim to locate and register all HAE cases in the country. An awareness campaign started in 2010 in order for all allergists and allergy hospital departments in the country to be informed regarding HAE and it was gradually extended to addressing specialists in all fields involved in the diagnosis and treatment of the disease. However, the knowledge of the general physicians is still very poor – and there is no specialist center for HAE in Greece.

As rare diseases are not a priority in Greece, HAE is under-diagnosed with obvious implications for the treatment, the mortality and the deterioration of quality of life of the patients.

For long-term treatment only Danatrol and Transamin are available – and none of them are reimbursed. As for treatment of attacks Berinert is administered by hospitals and Firazyr is available for self-administration – and both are reimbursed.

Doctors in the emergency rooms do not recognize HAE and medication is not available, but patients must bring their own medication. Furthermore, the medical personnel is not trained to administer Berinert – patients or caregivers must give instructions.

The action plan of HAE Greece includes creating a national website, recruiting more members to the Facebook group, and collaborating with local HAE specialists to raise awareness among their co-workers. Also, the organization focuses on encouraging people to get tested, appointing one of the main hospitals in Athens as a HAE center, and to train patients to self-administer their medication.

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Serbia

Ivana Golubovic, who is President of **HAE Serbia**, opened her orientation by giving a few number on the situation in the country: The expected number of patients is 140 and at this moment 71 patients in 34 families have been located. Six have undergone tracheostomy and eight families have lost one or more family members to HAE.

At the Clinical Center of Serbia in Belgrade patients have access to Tranexamic Acid and fresh frozen plasma, while a clinical study is conducted with Ruconest. In local hospitals in Serbia patients can get Tranexamic Acid and to some extent fresh frozen plasma.

If an emergency situation takes place in Belgrade, the best thing to do is to call Dr. Sladana Andrejevic from the Clinical Center of Serbia as treatment is available while waiting in the emergency room or the intensive care unit. The situation is quite different in the rest of the country – here HAE Serbia characterizes it as wrongful treatment and violation of patient rights.

As for the future HAE Serbia is working on an HAE ID card as well as a national registry of HAE patients, further treatment possibilities in all of the country, distribution of educational materials, media outreach, and setting up a HAE network of medical specialists.

Kenya

Dr. **Erick Njenga Kimani** joined Patient Representative **Patricia Karani** on stage for the presentation of **HAE Kenya**. They anticipate around 940 HAE cases in Kenya but at this moment only five cases have been confirmed.

HAE currently has no government recognition and the knowledge among medical personnel is dangerously low. There is no specialist center for HAE in the whole country, nor are there HAE clinically trained medical personnel. Patients are seen by physicians and general practitioners in urban areas, clinical officers and nurses in rural areas.

Only androgens are licensed and treatment is not reimbursed by the national health insurance scheme or private insurance. There is no access to emergency treatments other than fresh frozen plasma. Indeed, rare diseases such as HAE are a major challenge due to limited clinical expertise, misdiagnose, cost, and logistics.

HAE Kenya is attended by three patients, Dr. Njenga, and the international support member from HAEA, Karen Baird. HAE Kenya is working on including HAE patients in Uganda and Tanzania with one confirmed case each.

Plans for the future include incorporating HAE Kenya as an NGO, expanding the Facebook page, publishing a booklet on life with HAE, conducting interviews with the media, and establishing a 'Aid my HAE'-campaign program to seek medical funds for individual HAE patients who are in need of financial assistance for their HAE therapy.

Other aims are to build a robust organization able to gain government recognition, access to life-saving medications in both public and tertiary referral hospitals, creation of a fund that will facilitate HAE treatment and training of medical personnel as well as enrolment of more HAE patients.

Turkey

In his presentation on behalf of **HAE Turkey** International Communication Manager **Ersan Sevinc** said that there are 491 HAE patients in the country but that the expectancy is up to 7,800.

Danazol and Transamine have had a license for prophylaxis for years, while Cetor has been licensed for acute attacks since 2010. It is possible to import Firazyr and Kalbitor – and thanks to the efforts of the Turkish HAE Working Group the government does not ask for an extra charge any more. Cetor has no indication for prophylaxis yet as negotiations between the Ministry of Health and the Turkish HAE Working Group is still

going on but it can be used with special permission. After education Firazyr can be used at home for some patients but there is no self-administration for C1-INH yet. Except major cities and some hospitals most hospitals doesn't have drugs for acute therapy; they have fresh frozen plasma instead. Once the diagnosis has been made, here are no restrictions for prescribing these drugs.

There are still some problems in the emergency rooms as most of the doctors do not recognize HAE and try to administer antihistamines or adrenalin. Also, most of the hospitals do not have Cetor, Firazyr, or Kalbitor – they would use fresh frozen plasma. Those who have the drugs may not administer them properly (dosing problems, medication errors, etc.).

The perception of HAE has been largely changed since the establishment of the Turkish HAE Working Group in 2009. Among the recent activities of HAE Turkey (established 2015) are the publication of educational materials for doctors, an HAE workshop, education for patients, patients' ID cards, public awareness in the media, cooperation with the Ministry of Health and a major insurance company as well as a new website under the HAEi umbrella.

Macedonia

Natasa Angjeleska is in charge of PR and Advocacy for **HAE Macedonia** and she said that there are presently 16 HAE patients diagnosed in her country, five of them newly diagnosed. The expected total is 60-70.

There is a limited number of physicians, nurses, and emergency room personnel with knowledgeable about HAE. Consequently, HAE Macedonia in 2014 organized a three-month educational HAE Caravan to seven cities. Also, the organization took crucial part in setting up rare disease lectures earlier in 2016, targeting doctors and students of medicine. Furthermore, HAE Macedonia organizes activities aimed at raising awareness among general public and in the media.

Specialist dermatologists and pediatrician immunologists are the two reference physicians in Macedonia. Patients referred to the dermatology hospital or the children's hospital in Skopje will be tested for HAE.

Presently, no HAE medications have been licensed in Macedonia and there are no reimbursement options if patients buy medicines. HAE medicines are available through a program for rare diseases: Ruconest and Berinert are available for adult patients, administered at the Dermatology Clinic in Skopje, while Berinert is available for children, administered at the children's hospital. In some occasions it is available for home-treatments as well. There are rigid restrictions for treatments as adult patients can only have six to eight vials per year, while children can only have two vials per month.

Rare diseases are not a priority question for the government but public pressure as well as a lot of debates and activities raised by the National Alliance of Rare Diseases has resulted in securing funding for rare diseases treatment through taxes on cigarettes.

HAE is usually not recognized by doctors in the emergency room. Adult patients should go to the dermatology hospital in Skopje to receive treatment with Ruconest and/or Berinert – and that is indeed also the case for patients who live outside the capital. There are situations where the hospital doesn't have vials and patients are left without treatment. Children can go to the children's hospital in Skopje to receive treatment with Berinert. In some situations this hospital will give Berinert for home-treatment by parents.

Among the future plans of HAE Macedonia are ensuring modern therapy options as well as home-treatment for all HAE patients, training of additional doctors, participation in research activities with doctors and researchers, and enhanced regional cooperation and joint activities. For instance HAE Macedonia is organizing a meeting for patients and doctors from the Balkan countries to take place in Skopje 17-19 June 2016.

Before the lunch break Prof. **Marc Riedl, USA** and Prof. **Markus Magerl, Germany** talked about *"Improving HAE Care"*. While Dr. Riedl is Professor of Medicine and Clinical Director of the US HAEA Angioedema Center at the University of California – San Diego and directing an active clinical research program focused on angioedema and immunodeficiency conditions, Dr. Magerl is Professor of Dermatology and Senior Physician at Charité - Universitätsmedizin Berlin, Germany, and focuses on mast cells, urticaria and angioedema.

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General Session, part 2

Then followed two more keynote speeches. Firstly **Mark Skinner** – the President and CEO of the Institute for Policy Advancement, a consulting company specializing in patient-centered healthcare and outcomes research – spoke about *"Experiences from Hemophilia and the Importance of Patient Advocacy"*. Secondly **Jacob Giehm Mikkelsen** – Professor at Aarhus University in Denmark and strongly involved in genetic engineering in relation to genetic therapies, genome editing for translational purposes, and disease modeling – delivered a presentation about *"Juggling with Genes for Cellular Modeling and Therapy of HAE"*. He and his 15-member research group work to create new insight into disease mechanisms causing HAE. Full understanding of the cellular mechanisms leading to HAE may affect not only attempts to develop genetic therapies, but also impact HAE drug development and treatment.

Before the HAEi President made the closing remarks, Prof. Zuraw headed a Patient/Physician Leadership Panel answering numerous questions put forward by the audience.

The Saturday concluded with a dinner – also at the hotel – but before that the delegates had an unique opportunity to take part in an advanced screening of the movie *"Special Blood"*, presented by the film instructor **Natalie Metzger**, USA an HAE patient herself.

Sunday 22 May 2016

Sightseeing Madrid

As in Copenhagen in 2012 and Washington D.C. in 2014 the HAE Global Conference ended with an optional four-hour sightseeing tour. More than 200 of the delegates took the chance to get to know some more about Madrid before going back to their home countries.

Sponsors for the HAE Global Conference

Once again HAEi was delighted to have the support from a number of leading pharmaceutical companies in the field of HAE. The organization wishes to thank these supporters for their contribution to this conference, which is greatly appreciated:

DIAMOND SPONSOR: Shire

GOLD SPONSORS: BioCryst Pharmaceuticals
CSL Behring

SILVER SPONSOR: Pharming Group NV/Sobi

BASIC SPONSOR: KalVista Pharmaceuticals

Pictures by and of the participants kindly shared with HAEi and you.

Raising awareness on the Camino

From 15 to 17 May 2016 80 people – the majority of them suffering from HAE – walked part of the legendary Camino de Santiago in northern Spain together.

Over three days they took close to 4,000,000 steps for HAE awareness. These brave souls – coming from Argentina, Australia, Brazil, Canada, Denmark, Hungary, Italy, Japan, Mexico, New Zealand, Spain, Sweden, USA, and Venezuela – joined forces and proved to themselves and others that obstacles are only there to be overcome. Indeed, if you want to – you can.

– I have heard that some of the HAE Camino walkers are planning to come back and do more steps for HAE – maybe already around **hae day :-)** next year. We absolutely encourage them to do so, says HAEi Executive Director Henrik Balle Boysen.

A lot of pictures from the AEDAF/HAEi Camino Walk as well as comments from the participants can be found on the HAEi Facebook page at

www.facebook.com/groups/172320032283.




Pictures by and of the participants kindly shared with HAEi and you.

Help us raise awareness

JOIN THE GLOBAL HAE WALK

The Global HAE Walk

Before **hae day :-)** 2016 quite a number of people told HAEi that they would really have liked to take part in the Camino Walk but were for one reason or the other unable to go. Therefore HAEi set up a website for a Global HAE Walk and encouraged everyone interested to participate. All they needed to do was to walk any distance they would like wherever they would like – on their own or together with others – and report the distance walked to the website. HAEi would then add these steps to those taken by the people doing the actual Camino Walk.

- It has been a delight to see how well this has caught on, literally all over the world. The campaign opened late April and ran all through May 2016, allowing people to enter as many walks as they would like, says HAEi Communications Manager Steen Bjerre:

- And there really has been a tremendous amount of HAE walking going on. Including the close to 4,000,000 steps taken during the Camino Walk we have registered more than 12,000,000 steps taken by individuals as well as by groups wanting to be part of the HAE awareness movement. With people walking in Argentina, Australia, Austria, Belgium, Brazil, Canada, Cyprus, Czech Republic, Denmark, France, Germany, Greece, Honduras, Ireland, Italy, Kenya, Luxembourg, Macedonia, Malta, Mexico, New Zealand, Peru, Russia, Serbia, Spain, Sweden, Switzerland, The Netherlands, Turkey, United Arab Emirates, United Kingdom, Uruguay, USA, and Venezuela there is no doubt that this became a truly international event – just like the HAE Global Conference.

You can see the final count of steps – as well as kilometers, miles, and number of participants – at

www.haei.org/steps

The results of the global HAE walk

12,510,628 steps taken in total

Last updated 1 June 2016

9,624	5,980	1,193	12,510,628
Kilometers	Miles	Participants	HAE Happiness Index (HAE-hi)

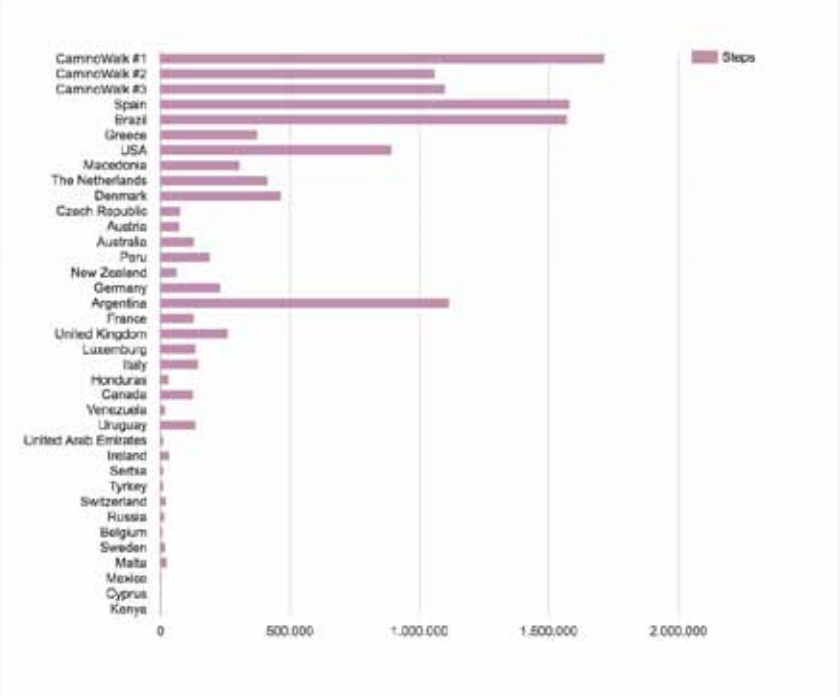
All these awesome people joined the global HAE walk and helped raising HAE awareness:

Show 10 entries Search:

date	name	walked in	participants	total steps	note
05/31/2016	Steen Bjarne	Denmark	1	6500	To and from meeting downtown
05/31/2016	maria isabel Rodriguez Otaño	Argentina	1	52000	
05/31/2016	patricia buscio	Argentina	1	52000	
05/30/2016	Lyn McGuigan	Australia	1	17160	Good health to all.
05/30/2016	Carlos A. Cano	Argentina	1	26390	
05/30/2016	Thereainna Moyses	Brasil	2	62400	
05/30/2016	Jane Sproat	United Kingdom	1	44628	
05/29/2016	Sarah SmithWEDAF	Spain	2	9100	
05/29/2016	Carlos A. Cano	Argentina	1	7670	
05/29/2016	Thereainna Moyses	Brasil	3	93600	

Showing 1 to 10 of 455 entries Previous 1 2 3 4 5 ... 46 Next

See where people walked



Let HAEi host your website

A growing number of national HAE organizations have their own websites with their own individual hosting solution. However, some of them would like to change hosting or altogether change the look and content of their websites. And others would like to just have a website at all.

- In order to accommodate any such national HAE organization we have established a system under the HAEi website allowing us to host national websites as well as provide them with templates for an individualized website – naturally all in their native language, says HAEi Executive Director, Henrik Balle Boysen.

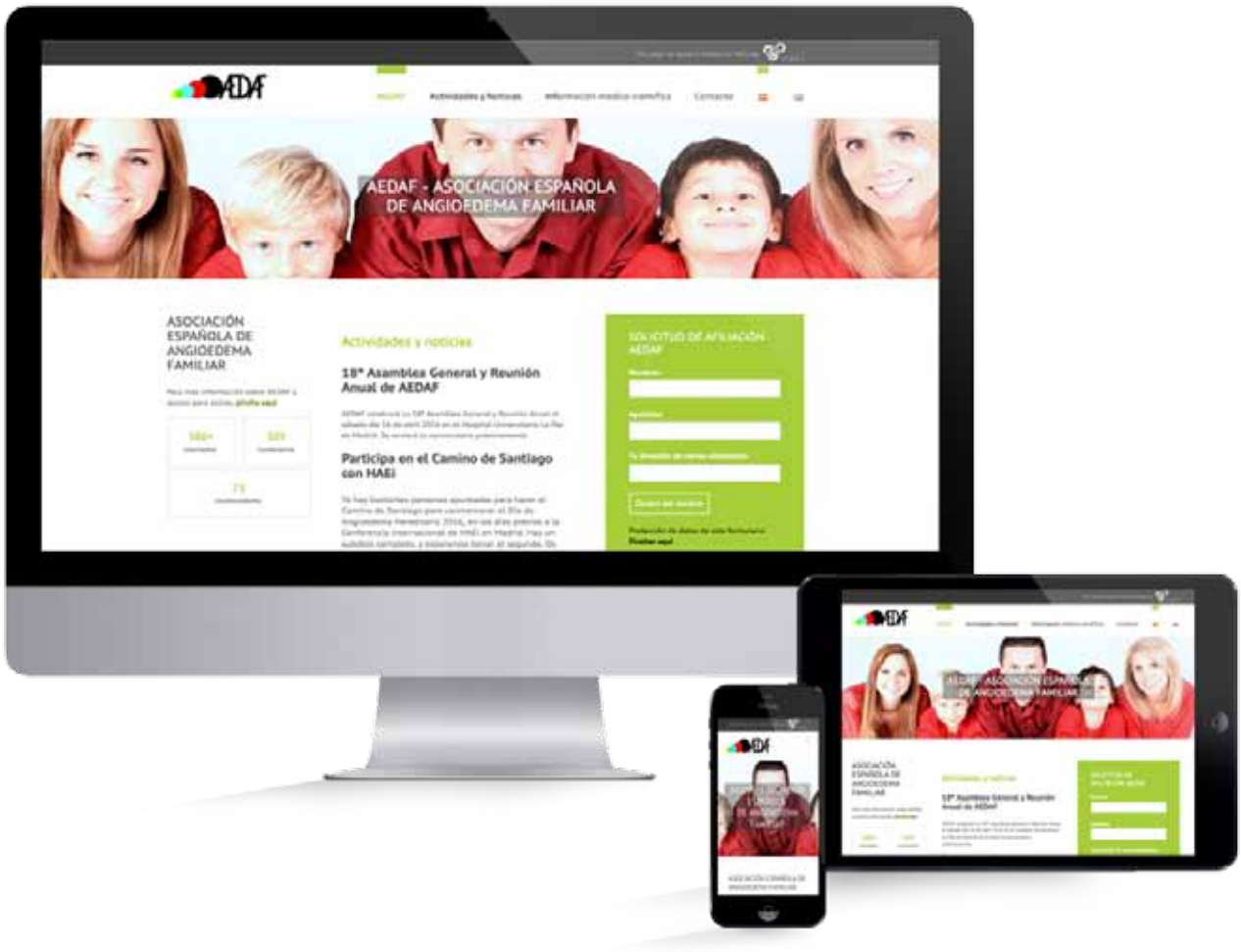
At this point national websites have been launched for Iceland, Kenya, Macedonia, Serbia, Spain, and Turkey – and HAEi is preparing a few more at the moment.

At www.haei.org/haei_countries you'll find an overview of all 52 countries registered with HAEi.

Link to national website hosted by HAEi

Link to national website

– and the national flags on the page link to the HAEi information on the specific country (national organization, care centers, hospitals, available medication etc.).



survey

Global HAE survey initiated to support patients and caregivers

On **hae day :-)** 16 May 2016 Shire initiated a global HAE survey to better understand the psychosocial impact the disease has on the daily lives of patients and caregivers. Shire plans to use the results to inform the development of patient-centered tools and programs to help improve communication about the condition with healthcare providers, caregivers and friends and families.

To access the survey, please visit

http://www.onepoll.com/menothaesurvey/

The survey is open until 29 July 2016.

HAEi supports this Shire initiative, as well as all bona fide research directed at improving the lives of patients.

HAE News from Around the Globe

Italy **www.angioedemaereditario.org**

7 May 2016 HAE Italy held the annual general meeting at the Crown Plaza & Hotel in San Donato Milanese, Milan. It was an excellent opportunity for physicians, patients and researchers to meet and share information about the latest medical-scientific news.

Patients were informed about the role of ITACA (the Italian Network for C1 Inhibitor Angioedema), a network of doctors that includes the 17 reference centers in Italy established under the aegis of HAE Italy and has surveyed the Italian patients diagnosed since 1973, a total of 963 subjects. The centers are evaluated according to the standards of diagnostic tests, the ability to manage emergencies and to apply the therapeutic indications. Prof. Marco Cicardi and his team participated in the national congress of the Italian Society of Allergy, Asthma and Clinical Immunology (SIAAIC) in Naples in April 2016), where they shared the final version of the register so that now each center will start to collect and process the data of the attacks. From the national congress a videoconference was recorded and posted on YouTube. The conference was chaired by prof. Cicardi, Dr. Maria Bova, Dr. Mauro Cancian, the president of the association Pietro Mantovano and the regional representative for the region Nunzia Del Prete. More interviews and videos can be found at

www.osservatoriomalattierare.it

In the annual general meeting Vice President Vincenzo Penna invited everyone to visit the new version of the website that is much faster and more user-friendly. It now includes all information in the medical-scientific, social and welfare fields. For people who travel to Italy there is also a good guide to get in touch with hospitals, angioedema specialists and patients if they need treatment or help. Please see

www.angioedemaereditario.org

United Kingdom **www.haeuk.org**

From the HAE UK CEO Laura Szutowicz:

Again our fundraisers have been very active with Rick Talbot donating even more money, this time raised at his 70th birthday party. Danny Owen cycled in the London Revolution, a two-day 185 miles around London, and Rose Joseph ran a coffee morning in aid of HAE UK as well as donating some proceeds from her cycle ride. We are so fortunate to have these brilliant supporters.

Two of our members have been very active in raising awareness about HAE; we tasked members with delivering posters we had prepared about HAE to their local GP and A&E department as a promotion for HAE day. We also encouraged members to offer to give short presentations at practice meetings and so on. June Cole, who is 'passionate about education', gave a lot of thought about what she wanted to say from a patients' perspective and found it very helpful in putting together a talk about this rare genetic condition, together with photos of her and her brother's swellings. She then set about researching the location of local GP practices and Practice Manager names, and looked for contacts at the local hospitals. Her own GP surgery were very receptive to meet and hear her talk about HAE from the perspective of a patient, to talk through about this rare genetic condition, and also show photos of swellings. Questions were asked and answered and the Practice Manager agreed to inform the other doctors and nurses

at their regular meetings as a topic of interest. June Cole says 'Showing the disfiguring photos of HAE had a real impact; a picture paints a thousand words, and really illustrated the impact these huge disabling, debilitating, disfiguring swellings have on a person's body and life; whereas simply just talking about HAE swellings does not sometimes get across the message of the huge swellings and potential life-threatening situation. It was picked up immediately how a laryngeal attack could appear to mimic anaphylaxis, and how important and potentially life-threatening HAE swellings are in the face and airways, and also in the abdomen. I feel lucky that 'my' GP Medical practice is now well versed with HAE in case another patient presents with similar symptoms and has not been able to obtain a diagnosis.'

Another brave speaker is Sheila Witts, who has AAE. She writes; 'Dr. Tarzi rang me on 19 May, and asked me if I would be prepared to talk to 120, 2nd year medical students at Brighton and Sussex medical school on the 27 May, on AAE, I've got to say I was very apprehensive. I am so glad I did, after Dr. Tarzi presented his Symposium about HAE, he introduced me to his students, my talk lasted about 1/2 an hour, the students all stood up and clapped. Dr. Tarzi asked if any one would like to ask any questions. At this stage I did advise I am deaf and wear hearing aids – and Dr. Tarzi repeated all their questions. Some of the questions asked: How long do the attacks last? How does AAE affect my life? How long was I in A&E? One student asked my husband how it affected him.'

Well done and a huge thank you to both of these ladies! Sadly there is still a huge lack of information about HAE in the wider medical community.

Rachel Annals and I wore our HAE UK T-shirts for the HAE Global Conference in Madrid, over 25 UK delegates were there and we had a fantastic meeting. The country presentations were fascinating and we realized how lucky we have been to come so far in the UK with a core of expert and clinicians and available treatments. Rachel was voted back on to the Executive Committee and so we hope that the UK perspective will assist in making HAEi an even greater force than it is already.

One of our projects this year was to select a 'Young Ambassador'. We had several very good applicants and after much discussion elected Alex Graham. She is an amazing representative for us; she was diagnosed at three years old and there is a long family history of HAE Type 1 with her mother and sister both having HAE. They have lost two family members to the illness, so from a young age Alex was aware that she was a bit different from all her friends. But her family always explained that HAE should never let it stop her from achieving everything she wanted in life. Alex is currently in the final year of Sixth Form studying Biology, Drama and Psychology. She was also School Prefect for year 10-11, and a member of School Council, which gave her the opportunity to attend meetings with the school management bodies to discuss points raised by the pupils. As a very sport-orientated person, Alex is County Sports Leader for Oxfordshire, helping young children of all ages and abilities across the county to get involved in activities out of their comfort zone. She finds the feedback from the children so motivating and satisfying, and as a firm believer in positive mental attitude she encourages people and shows them how self-respect, determination and discipline can enhance your wellbeing. She is also interested in martial arts and, although there were natural concerns for triggering attacks, Alex managed to train regularly and at 16 became a 1st Dan Black Belt in Shukokai Full Contact Karate. She now teaches youngsters (and adults – including her mother!) from five years old up to 60+, and achieved second place in combat and kata in the National Championships.

HAE UK sponsored Alex to attend the HAE Global Conference and she has come back absolutely bursting with ideas for our younger members. She is a great addition to our team.

We have set dates and venues for the Patient Day meetings; a Scottish meeting in Perth on 1 October 2016 for all those Scottish patients who tend to be unable to come to the patient day because of distance. The annual Patient Day is 19 November 2016 in Bristol and we are delighted that both Anthony J. Castaldo and Henrik Balle Boysen will be attending.

Continues on next page

Mexico **www.facebook.com/AMAEH.AC?fref=ts**

Celebrating: Just as previous years **hae day :-)** was celebrated in many ways around the globe – for instance in Mexico where patients, caregivers and healthcare professionals gathered for an event.

Video statement: Sandra Nieto, who is President of HAE Mexico, has produced a 20-minute long video on her HAE story. The video – in Spanish – can be found at

http://kortlink.dk/mdbw.

Austria **www.hae-austria.at**

HAE Austria will be celebrating the 10th anniversary of the national organization 3-4 September 2016.

Canada **www.haecanada.org**

Upcoming meetings: Patient meetings will be held during 2016 in Winnipeg and Victoria. Information on dates and venues will be posted on the HAE Canada website.

In the media: Leading up to the HAEi/AEDAF Camino Walk the Canadian patients Ken and Amanda Howlett were interviewed for a local newspaper as well as a local radio station. The printed interview can be found at http://kortlink.dk/mdaz.

Attack tracking app: HAE Canada has released a attack tracking app. The app allows patients to keep a journal about the regularity, duration, location and severity of their attacks; keep track of information about whether treatment was required for an attack including the impact of the attack on attendance at school or work and whether hospitalization was required; to take personal photos displaying the physical symptoms of the associated attacks; and to generate reports that can be printed or emailed to the health care professional. The app is available for free for iOS and Android users at www.haeattacktracker.com.

Japan **www.haej.org**

As mentioned in the last newsletter **hae day :-)** has been registered as an official day to be remembered with the Japan Anniversary Association. Recently HAEJ President Beverley Yamamoto received a certificate to recognize the anniversary day, here flanked by the patient Akio Mazusawa and Mr. Kase, the President of Japan Anniversary Association. Please see

http://www.kinenbi.gr.jp/mypage/897.

USA **www.haea.org**

Janet Long, Executive Vice President of US HAEA, writes:

More than 65 patients from the US HAEA traveled to Madrid, Spain for the 3rd HAE Global Conference. We made new friends from around the world and learned about how HAE patients live in their countries. Scientific presentations provided important HAE information and new HAEi regional patient advocates were announced. We already look forward to the 4th Global Conference in 2018.

18 US patients hiked the Camino, covering 50 kilometers, to Santiago de Compostela. The group enjoyed Spanish foods, the spectacular scenery and the wonderful company of fellow hikers from many other nations. Buen Camino!

Our HAE In-Motion® 5K races/walks have grown since the first event held last October, following the HAEA National Patient Summit. At the moment these events are scheduled across the US for 2016:

- Puerto Rico – 10 July 2016
- Chicago – 13 August 2016
- Cincinnati – 10 September 2016
- Rhode Island – 1 October
- San Diego – 15 October
- Atlanta – 22 October 2016
- Florida – November 2016

Each event is created by an HAE patient with the help of the HAEA and funds raised at all events will go toward research for a cure and the support of patient initiatives. Each 5k also offers the opportunity of raising HAE awareness. Read much more at http://5k.haea.org.

A community-wide HAE awareness campaign for this year's **hae day :-)** was all about how HAE does not have to hold you back. All HAEA members were invited to send in photos for the whole month of May to show off their "#myMove4HAE." Moves included skydiving, swash-buckling light sabers, hikes and motorcycle riding. Photos were shared on social media to spread HAE awareness.

One of the newest HAEA initiatives is the Brady Club – http://brady.haea.org – an online platform for kids with HAE and their siblings. Brady the Bear was named for Bradykinin, the mediator of HAE. He celebrates the HAEA's Year of the Youth! Another initiative is the HAEA Café, an online platform that facilitates webinars, connects patients to HAEA Patient Advocates in real time and provides HAEA news quickly and easily.

Also, we have created a new CME program for physicians – www.haeedu.com – based on our Medical Advisory Board's 2013 Recommendations for the Management of HAE.

Plans are developing for the 2017 US HAEA National Patient Summit. 2015's Summit success leaves big shoes to fill next year, but we are up to the task. Stay tuned!

Testifying before the Board: US HAEA Patient Advocate John Williamson has testified before the Texas Drug Utilization Review Board on behalf of HAE patients in the State who are receiving Medicaid. The US HAEA's objective was to maintain patient access to all available HAE medicines amidst concerns about cutbacks. The Review Board members were very pleased to hear from a patient and found John Williamson's testimony to be compelling. Right after hearing from him, the Review Board voted to maintain the current level of patient access to medicines.

Summer Camp: US HAEA is providing a summer camp experience on 18-21 August 2016, aimed at HAEA members ages 13-17 years. The camp takes place at Wesley Woods Retreat Center in Williams Bay, Wisconsin.

Review: The HAEA 2015 Year in Review is now available online – with a great overview of the year's successes, such as the National Patient Summit, the creation of the HAEA cafe, as well as research, **hae day :-)** updates and much more. Have a look at

www.haea.org/DOCS/YearInReview2015.pdf

Recruiting for study: The US HAEA Angioedema Center is currently recruiting for the Shire (formerly Dyax) HELP study, a placebo-controlled efficacy and safety study to evaluate a prophylactic treatment for HAE attacks. This research study is open to Type I or II HAE patients aged 14 and up. Participants will come to the clinic in San Diego approximately once every two weeks over the course of seven months to receive the study drug as two subcutaneous injections in the upper arm. 2/3 of all participants will be randomized to receive drug and 1/3 will receive placebo. Participants in the randomized portion of the study may be eligible to continue in an open-label treatment extension study. Modest compensation is provided for time dedicated to the study activities. Interested patients may call the Angioedema Center at 858-657-5350 for more information.

Germany www.angiooedem.de

At the HAE Global Conference in Madrid HAE Germany presented the awareness video "Escaping the labyrinth" that was produced by the German organization supported by CSL Behring. You can find the video at

www.youtube.com/watch?v=bMd7SJfWdCs.

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The Netherlands **www.hae-qe.nl**


Onbegrepen pijn

Leading up to **hae day :-)** 2016 the major Dutch newspaper De Telegraaf contained an article about a female HAE patient from The Netherlands. De Telegraaf is the largest Dutch morning newspaper with a daily circulation of more than 450,000.

Romania **www.haenet.ro**

13-15 May 2016 the Romanian Network for Hereditary Angioedema and the Romanian Society of Allergology and Clinical Immunology organized a HAE workshop in Bucharest, aimed at contributing to the implementation of a national program of the management of HAE. Reimbursement of some of the new treatment alternatives was the main aim on this approach.

Prof. Craig presented the latest WAO consensus on HAE management, while others were asked to highlight the current state of HAE management in their countries: Prof. Christiansen for USA, Prof. Bork for Germany, Prof. Cicardi for Italy, Prof. Varga for Hungary, and Dr. Reshef for Israel. In his presentation Prof. Cicardi paid special attention to the Italian HAE registry.

The situation regarding HAE reimbursement was summarized by Dr. Andrejevic from Serbia, dr. Valerieva from Bulgaria, and Mr. Jankovski from Macedonia, while the present situation as well as the perspectives in Romania was pointed out by the organizer, Prof. Moldovan. The future of health technology assessment of the new therapeutic alternatives in rare disorders was summated by Dr. Lorenzovici. The Romanian patients' voice was run down by Ramona Petran, the President of HAE Romania. Dorica Dan, who is President of the national alliance for rare diseases, was condensing the efforts made in the past years of this umbrella organization and the principles of the newly released reference centers ministry order in Romania. Participants agreed that a tight cooperation between experts, patients, authorities and pharmaceutical companies is of paramount importance in moving forward in building-up a cost-efficient national program of HAE management.

Professors Cicardi, Zuraw, Bork, Bernstein, and Farkas as well as Doctors Reshef and Suez were presenting in plenum state-of-the art and up-to-date lectures about angioedema phenotypes, the future of the angioedema, laryngeal attacks and asphyxiation in patients with HAE, emergency treatment of acute urticaria and anaphylaxis, diagnosis and treatment of HAE and drug-induced angioedema, and atopic dermatitis. Further international cooperation was planned along with a roadmap of homeland efforts to solve the urgent need for a comprehensive national HAE management program. A press conference ended the HAE workshop.

Spain **www.angioedema-aedaf.org**

Sarah Smith, President of HAE Spain (AEDAF), writes:

On 30 May 2016, AEDAF was present at the official presentation, in the Royal Academy of Medicine in Madrid, of "Angioedema", a book coordinated by Drs. Teresa Caballero and Rosario Cabañas of Hospital Universitario La Paz of Madrid. 43 collaborators have contributed to this excellent multidisciplinary publication on angioedema, which is meant to serve as a source of ongoing medical education and a guideline for the diagnosis and treatment of different angioedema types, and in particular bradykinin-mediated angioedema. The book will also be made available to physicians in Latin America. Shire Pharmaceuticals Ibérica has contributed part of the financing for this publication.

AEDAF held its 18th General Assembly and Annual Meeting on 16 April 2016. Aside from the normal business of the General Assembly, Dr. Teresa Caballero gave us an update on the new and future treatments for HAE and ongoing clinical trials, and Dr. Nieves Prior presented some results of several burden of illness and health-related Quality of Life surveys.

Finally, AEDAF would like to thank all the participants from Spain and the rest of the world who took part in the HAEi/AEDAF Camino Walk and the HAE Global Conference in Madrid – in our opinion two very successful and unforgettable events.

Global Advocacy Work

Recent events

22-25 April: HAEi met in ***Manila, Philippines*** with the President and a member of the Board of Directors of the Philippine Society of Rare Disorders (PSOD) to discuss the objectives, scope, and milestones of a potential HAEi Development Development Grant aimed at (1) raising HAE awareness among the medical community and (2) identifying patients and physicians interested in forming a HAE group.

23-25 May: HAEi joined patient groups representing hemophilia, Alpha 1 Anti-trypsin, and Immune Deficiencies at a Plasma Users Group (PLUS) meeting in ***Lisbon, Portugal***.

11-14 June: HAEi participated in EAACI 2016 in ***Vienna, Austria.*** During the conference HAEi was part of the task force working on an updated version of the WAO Guidelines for treating HAE.

16-20 June: HAEi participated in the HAEi Balkan Regional Workshop, which took place in ***Skopje, Macedonia.***

Upcoming events

2-4 September: HAEi will participate in the 10th anniversary celebration for HAE Austria in ***Vienna, Austria***.

12-18 September: HAEi will take part in the annual meeting of Australasian Society of Clinical Immunology and Allergy (ASCIA) at ***Goldcoast, Australia***. ASCIA offers a great opportunity to meet with physicians from all over the Asian continent.

18-21 September: HAEi will participate in the Third HAWK Consensus Conference in ***Gargnano, Italy***.

20-22 September: HAEi will take part in the Bradykinin Symposium in ***Berlin, Germany***.

28-30 September: HAEi will participate in a conference that includes allergist/dermatologist specialists from Southeast Asia. The meeting, taking place in ***Bangkok, Thailand***, will prominently feature HAE and will include a session with patients. We hope this meeting leads to establishing a patient group in Thailand.

News from the Industry

6 May, 2016

"We are currently working through the start-up activities for the APeX-1 trial of BCX7353 for prevention of angioedema attacks in HAE patients and are targeting the end of the year to report results," said Jon P. Stonehouse, President & CEO of **BioCryst Pharmaceuticals, Inc.** "In addition, we are conducting a Phase 1 clinical pharmacology study in healthy volunteers to determine if we are able to meaningfully increase exposure and get to a twice-daily oral dosage form of avoralstat. We expect to report results from this study this summer."

(Source: BioCryst)

16 May, 2016

Pharming Group N.V. supports the Fifth Annual International Hereditary Angioedema Day, **hae day :-)** taking place on 16 May 2016 and aiming to raise awareness around HAE.

As part of its global commitment to improving the lives of patients with HAE and their caregivers, Pharming participates in the HAEi Global Access Program initiative as well as in several multi-country studies and projects aimed at improving patients' quality of life.

"HAE is a complicated disease that can sometimes take many years to diagnose. As frequently indicated by experts, HAE has many different faces. For this reason, **hae day :-)** is an important event, which raises awareness of this serious condition and helps to ensure that patients are diagnosed earlier and treated safely", said Dr Sijmen de Vries, CEO of Pharming Group NV. "At Pharming, we have been collaborating with the HAE community since 2000. We are delighted to support this year's fifth anniversary of **hae day :-)**. We are very proud of the difference in patients' and their families' lives that we can make together with HAEi and its local affiliates".

"HAEi is excited to celebrate the 5th anniversary of **hae day :-)"**, said Henrik Balle Boysen, Executive Director of HAEi. "We are pleased that over the years **hae day :-)** events have fostered increased awareness about this debilitating and potentially fatal condition. We are confident that **hae day :-)** 2016, along with other supportive initiatives, will continue the momentum towards more timely diagnosis and improved access to life-saving therapies".

(Source: Pharming)

Continues on next page

CSL Behring

16 May, 2016

CSL Behring joins the global HAE community today in recognition of the fifth annual **hae day :-)**, an initiative led by HAEi along with the support of its national member organizations.

CSL Behring is a proud supporter of **hae day :-)** and to continue its partnership with HAEi. CSL Behring **hae day :-)** activities will take place globally and locally and include:

- Global participation in the "Send a Smile" and the virtual "Global HAE Walk" social media events
- Local awareness-raising events at CSL Behring offices and manufacturing plants, and at CSL Plasma collection centers
- Sponsorship of the US Hereditary Angioedema Association (HAEA) 5K run/walk series, HAE In Motion. Seven events will take place throughout the year, aiming to raise awareness and improve the quality of life of those afflicted with HAE.
- Collaboration with the German HAE patient association to raise association to raise awareness of HAE through a new, sponsored video, "Wege aus dem irrgarten" (or "A way out of the maze"), that draws attention to the often long ordeal to diagnosis and treatment.
- A BioBlog feature post, "World hae day :-) – Many Faces, One Family," written by HAEi executive director, Henrik Balle Boysen.
- Collaboration with national patient associations to raise awareness and emphasize the importance of family screening in HAE patients.

CSL Behring is also a Gold Supporter of the 2016 HAE Global Conference in Madrid, Spain. This conference gives CSL Behring the opportunity to deliver on its promise to improve care and enhance patients' lives by connecting with physicians and patient representatives to discuss on how to raise awareness and access to therapies. The sponsorship also helps supports travel grants to bring patients to the conference.

(Source: CSL Behring)

PHARMING

19 May, 2016

From the **Pharming Group N.V.** financial report for the first quarter ended 31 March 2016:

- During the quarter we initiated sales of Ruconest in the countries, which Pharming now commercializes directly, in Germany, Austria and the Netherlands. These countries had proved very difficult for our partner SOBI prior to 2015 when we agreed to take them back. We are encouraged by feedback so far and look forward to building on this.
- The Q1 result show that the change to strategy is now bearing fruit and the sales growth of Ruconest is more pronounced from March onwards, with more patients starting to switch to Ruconest in all our major markets. In addition to the new sales in our own territories, SOBI continues to do well in Eastern Europe. We have also seen requests for Ruconest from new patients through the HAEi Global Access Program conducted with the HAEi, the International Patient Organization for C1-Inhibitor Deficiencies, in association with Clinigen Group plc. The "HAEi GAP" program provides access to Ruconest for eligible patients with HAE who currently do not have access to effective medication to treat acute attacks of the disease, such as certain Gulf states and much of Africa. In Colombia, our partner Cytobioteck continues to make progress, and has represented Ruconest at the recent HAE conference and seminar there.
- We continue to make good progress in our efforts to develop our pipeline to produce the next generation of therapies. Our first program lead has been optimized and the second is under way. We will be announcing the details of these programs and the timetable of their clinical development in the next few months.
- Late in the quarter, the European Commission adopted the CHMP recommendation to include the treatment of HAE attacks in adolescents and to remove the requirements for rabbit IgE testing that previously formed part of the EU label for Ruconest. The CHMP also noted that the importance of favorable effects of Ruconest is further supported by the continued availability of supply of Ruconest (produced by

recombinant technology) in comparison to supply from blood donor plasma that may vary, and that as it is not a blood derived product Ruconest carries no potential risk of exposure to blood-borne pathogens.

- Our clinical Phase II randomized, double-blind, placebo-controlled study of Ruconest in prophylaxis of HAE continues on track and we remain on track to announce the preliminary results of this trial by the end of June/ early July.

(Source: Pharming)

19
May, 2016

KalVista Pharmaceuticals supports the third HAE Global Conference in Madrid, Spain. Andrew Crockett, KalVista's CEO, said: "KalVista is delighted to support the HAE Global Conference, which aligns with our mission to provide oral treatments for HAE patients. We believe that an oral plasma kallikrein inhibitor provides a more convenient way to manage HAE and improve quality of life."

(Source: KalVista)

16
June, 2016

Carbylan Therapeutics, Inc. and **KalVista Pharmaceuticals Ltd.** have entered into a definitive share purchase agreement pursuant to which the shareholders of KalVista will become the majority owners of Carbylan.

David Renzi, President and CEO of Carbylan stated: "We are optimistic that KalVista's pipeline and strong leadership team, together with the combined company's cash resources, will enable the company to reach significant milestones in KalVista's pipeline."

Andrew Crockett, KalVista's CEO said: "This transaction allows us to continue the development of our potentially best-in-class plasma kallikrein inhibitor platform, and rapidly advance our programs in HAE, bringing much-needed treatments to patients. We are in a very strong position to drive the growth of the combined company, and achieve the full potential of our therapeutic pipeline."

The proposed transaction is expected to close late in the third quarter or early in the fourth quarter of 2016.

(Source: KalVista)

HAEi

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

HAEi Worldwide

Currently you will find HAE member organizations in 52 countries:

North America (2): Canada, United States of America

Central America and Caribbean (3): Costa Rica, Mexico, Puerto Rico

South America (8): Argentina, Brazil, Chile, Colombia, Ecuador, Peru, Uruguay, Venezuela

Europe (28): Austria, Belarus, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Macedonia, Norway, Poland, Portugal, Romania, Serbia, Slovenia, Spain, Sweden, Switzerland, The Netherlands, Ukraine, United Kingdom

Middle East (3): Israel, Turkey, United Arab Emirates Africa (1): Kenya

Central Asia (1): Russia

South Asia (1): India

East & Southeast Asia (3): China, Japan, Malaysia

Australia/Oceania (2): Australia, New Zealand

You will find much more information on the HAE representations around the globe at www.haei.org. On our World Map you will find contact information for our member organizations as well as care centers, hospitals, physicians, available medication, and clinical trials.

The information on www.haei.org is being updated as soon as we receive fresh data from the national member organization.

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.

Corporate Information

HAEi is officially registered as a non-profit/ charity organization in the Canton of Vaud in Switzerland. The registered address is:

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1006 Lausanne
Switzerland

Corporate Registration Number:
CHE-160.474.141

Bank Connection:
UBS Nyon, Switzerland

EUR Account:
IBAN: CH06 0022 8228 1117 3360 T
SWIFT/BIC: UBSWCHZH80A

USD Account:
IBAN: CH54 0022 8228 1117 3361 Z
SWIFT/BIC: UBSWCHZH80A

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