The Hereditary Angioedema Center
Experience in the United States

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University of California, San Diego
• Evaluation/Diagnosis
• Optimization of Management Plans
• Collaboration with local MDs and specialists
• Dynamic over time
• > 250 physicians treating HAE in U.S.
• ~85% Allergy/Immunology
• > 70% of U.S. patients managed by physician who had experience with <10 HAE patients
• Wide range of variable treatment patterns; inconsistency with consensus guidelines
• Only about 50% of first-degree relatives screened for C1INH-def...
Benefits of HAE Expert Physician Involvement

- National referral centers or networks
- Collaborative care with local physicians
- Optimal patient education regarding condition and treatment options
- Iterative process to adjust/adapt treatment plan over time
The US HAEA Angioedema Center at UC San Diego, in partnership with the US Hereditary Angioedema Association, aspires to improve the lives of angioedema patients throughout the world. We strive to provide comprehensive and collaborative care for individuals with angioedema conditions with state-of-the-art diagnostic tests and techniques, the latest available therapeutic modalities, a full range of patient support programs, and cutting-edge translational research in angioedema.
Angioedema Center: Where Does It Fit?
The US HAEA Angioedema Center: A Collaborative Effort

- Vision and impetus from Anthony Castaldo
- Negotiations with the University of California, San Diego
- Recruitment of Physicians
- Outreach to Donors
- Collaboration from Medical Advisory Board
- Building the Center
- Developing staff expertise
- Development of shared vision and mission for the future
The Angioedema Center Model

- Expert & experienced staff
- Utilization of full range of RX options
- Basic, clinical, & translational research
- Adequate clinical & lab resources

Patient

Courtesy of B. Zuraw
Clinical Operations: Designing the Patient Experience

• **High-touch personal approach**
  – Office design
  – Scheduling
  – Travel assistance/funding
  – Medical record collection
  – Physician Consultation
  – Nursing support
  – Prescription authorization
  – Implementation of management plan
  – Collaboration with local physicians
  – In-person/teleconference/remote follow-up
Patient Experience

- **Staffing Model**
  - UCSD
    - Nurse Navigator
    - Clinical Nurses
    - Administrator/Visit authorizations
    - Medical Assistant/Medication authorizations
    - Clinical Study Coordinator
  - US HAEA
    - Health Advocates
    - Patient Advocates
Patient-Centric Care

• Physician consultation – 90 minutes
• Nursing support – knowledgeable regarding condition, medications, self-administration
• Shared-decision making - discussion of all treatment options available to determine optimal individual management plan
Patient and Family Education

- US HAEA resources, development of educational modules
- Family testing
  - Angioedema Clinical Epidemiology Testing (ACET): 46 untested first-degree relatives of confirmed HAE-C1INHdef patients
  - 30% confirmed to have C1INH deficiency (Age range 2-60)
  - 64% of newly diagnosed relatives were symptomatic with a mean angioedema attack rate of 2.5 episodes/month

Ried MA, Allergy Asthma Proc, 2015
## Individualized HAE Treatment Plan

### Treatment of Attacks

<table>
<thead>
<tr>
<th>Effective emergency treatment</th>
<th>Laryngeal Attacks</th>
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<tbody>
<tr>
<td>should be given as soon as possible to arrest the attack. There are several effective therapies available, including:</td>
<td>Because of the risk of asphyxiation during a laryngeal attack and because the effective medicines can take 30-60 minutes to begin to work, physicians should be prepared to emergently intubate the patient or perform a cricothyrotomy.</td>
</tr>
</tbody>
</table>

1. **C1-inhibitor concentrate by IV injection:**
   - 20 U/kg (Berinert), or
   - 1000 U (Cinryze), or
   - 50 U/kg (Ruconest) [max 4200 U]

2. **Icatibant (subcutaneous inj):**
   - 30 mg in 3 ml (Firazyr)

3. **Ecallantide (subcutaneous inj):**
   - 30 mg, 3x1ml (Kalbitor)

### Laryngeal Attacks

- Signs of impending airway obstruction include stridor, inability to swallow, and change in the voice. The airway may be significantly distorted and these procedures should be performed by an expert.

### Additional information

**Online:** [www.haea.org](http://www.haea.org)


I'm worried that healthcare has become too impersonal, doc.

Nonsense... just relax and lie back on the barcode scanner.
Patient Care Statistics

- Over 700 patient evaluations for angioedema; ~200 HAE patients

- 95% patients from United States: 35 states

- Patients from Canada, Mexico, Central America, South America, Asia, Africa
Research at the US HAEA Angioedema Center

• Clinical studies of investigational drugs for HAE
• Translational and diagnostic studies
  – HAE with normal C1INH
• Patient focused projects
  – HAE and stress
  – HAE and diet
• Recently establishment of US HAEA Research Network for collaborative research efforts
US HAEA Research Network
Patient Registries to Study Rare Diseases

6,000 – 10,000 HAE I/II

??? HAEnlC1INh

HAE Registry

Internet

Investigators

Patients
US HAEA Registry

- Established February 2005 with GeneLogic and Genetic Alliance
- 909 US HAEA members signed up
  - 801 are active enrollees
  - 3187 DNA samples
  - 821 serum samples, 647 Buccal samples
  - 538 Past medical history, 839 general medical, 1,436 Attack Event and 2,868 completed
- May 2012: migrated to custom MySQL database
- October 2016: Centered at UCSD
  - Chromogenic assays and sequencing projects planned
Hereditary angioedema with normal C1 inhibitor function: Consensus of an international expert panel

Bruce L. Zuraw, M.D.,¹,² Konrad Bork, M.D.,³ Karen E. Binkley, M.D.,⁴ Aleena Banerji, M.D.,⁵ Sandra C. Christiansen, M.D.,¹,⁶ Anthony Castaldo, M.P.A.,⁷ Allen Kaplan, M.D.,⁸ Marc Riedl, M.D.,⁹ Charles Kirkpatrick, M.D.,¹⁰ Markus Magerl, M.D.,¹¹ Christian Drouet, Ph.D.,¹² and Marco Cicardi, M.D.¹³

Allergy Asthma Proc 33:S145–S156, 2012
HAE Normal C1INH: Clinical Studies

Mechanisms and Pathophysiology

Controlled Trials to Determine Safety and Efficacy in a Specific Population
Blood Drawing – The Key to Success

- Extensive interactions between staff and lab to develop optimized protocols for drawing research blood samples
Critical Efforts for Continued Progress

- **Scientific registries**
  - Response to therapies
  - Genetic investigations
  - Long-term safety data

- **Government and regulatory advocacy efforts**
  - Secure access and coverage of effective treatment

- **Research**
  - Development of diagnostic assays
  - Clinical Data on special populations: pediatrics, elderly, pregnancy
  - Developing next generation of HAE treatments
  - Quality of Life improvements
  - Pharmacoeconomics
Educational Efforts

• Clinical rotations for students, residents, fellows
• HAE CME Program to regional medical societies
• Peer-to-peer discussions
• Implementation of “Visiting Scholars” curriculum for physicians
Improving HAE Management

- Efficient and effective acute treatment of attacks for every patient
- Appropriate use of prophylactic treatment
- Minimizing treatment burden
- Maximizing patient activity and function
- Improved understanding of disease mechanisms (genetics, mediators, triggers): Scientific registries
- Improve diagnostic capabilities
- Studies to investigate new treatments for improved clinical outcomes
- Offer comprehensive education for patients, families, health care providers
Current state of hereditary angioedema management: A patient survey

Aleena Banerji, M.D.,¹ Paula Busse, M.D.,² Sandra C. Christiansen, M.D.,³,⁴ Henry Li, M.D.,⁵ William Lumry, M.D.,⁶ Mark Davis-Lorton, M.D.,⁷ Jonathan A. Bernstein, M.D.,⁸ Michael Frank, M.D.,⁹ Anthony Castaldo,¹⁰ Janet F. Long,¹⁰ Bruce L. Zuraw, M.D.,³,¹¹ and Marc Riedl, M.D., MS³,¹¹

Before and after, the impact of available on-demand treatment for HAE

Authors: Christiansen, Sandra C.; Bygum, Anette; Banerji, Aleena; Busse, Paula; Li, Henry; Lumry, William; Davis-Lorton, Mark; Bernstein, Jonathan A.; Frank, Michael M.; Castaldo, Anthony; Long, Janet F.; Riedl, Marc; Zuraw, Bruce L.

Source: Allergy and Asthma Proceedings, Volume 36, Number 2, March/April 2015, pp. 145-150(6)
Improved Patient-Reported Outcomes

Christiansen, Allergy Asthma Proc. 36:213, 2015
Effects of Improved HAE Care


![Graph showing the effects of improved HAE care]
Indications of Success

• Improved diagnostic accuracy
• Access to effective medication
• Rational use of HAE-specific drugs
• Increased self/home-administration; reduced hospital visits
• Increased referrals from payors
• High patient satisfaction scores
• Need for more rigorous outcome measures; cost-effectiveness, quality of life
Questions, Suggestions, Recommendations.....

always make new mistakes

(esther dyson)
THANK YOU