



# Closing Remarks

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## Awards

Experts' lectures

Basic science

Therapies &  
Trials

Contraception &  
Oestrogens

Diagnosis  
Disease

Scoring &  
HRQoL

Trials

Cohorts,  
Centers,  
Organisations

Presentation by patient: words < tone < body language

The biannual workshop is this year 12 years old

Getting together clinicians, researchers, patients and industry –  
the real strength of this WS

Excellent location to convene

The first time 3 awards to be distributed

- “For HAE Patients”: congratulations to Michael M. Frank, USA
- “For HAE Research”: congratulations to Margarita Lopez Trascasa, Spain
- “Grant for Young Researchers”: the four grants goes to
  - Delphine Charignon, France (oral)
  - Dorottya Csuka, Hungary (oral)
  - Alberto López-Lera, Spain (poster)
  - Zsuzsanna Zotter, Hungary (poster)
- Thanks to the sponsoring industry



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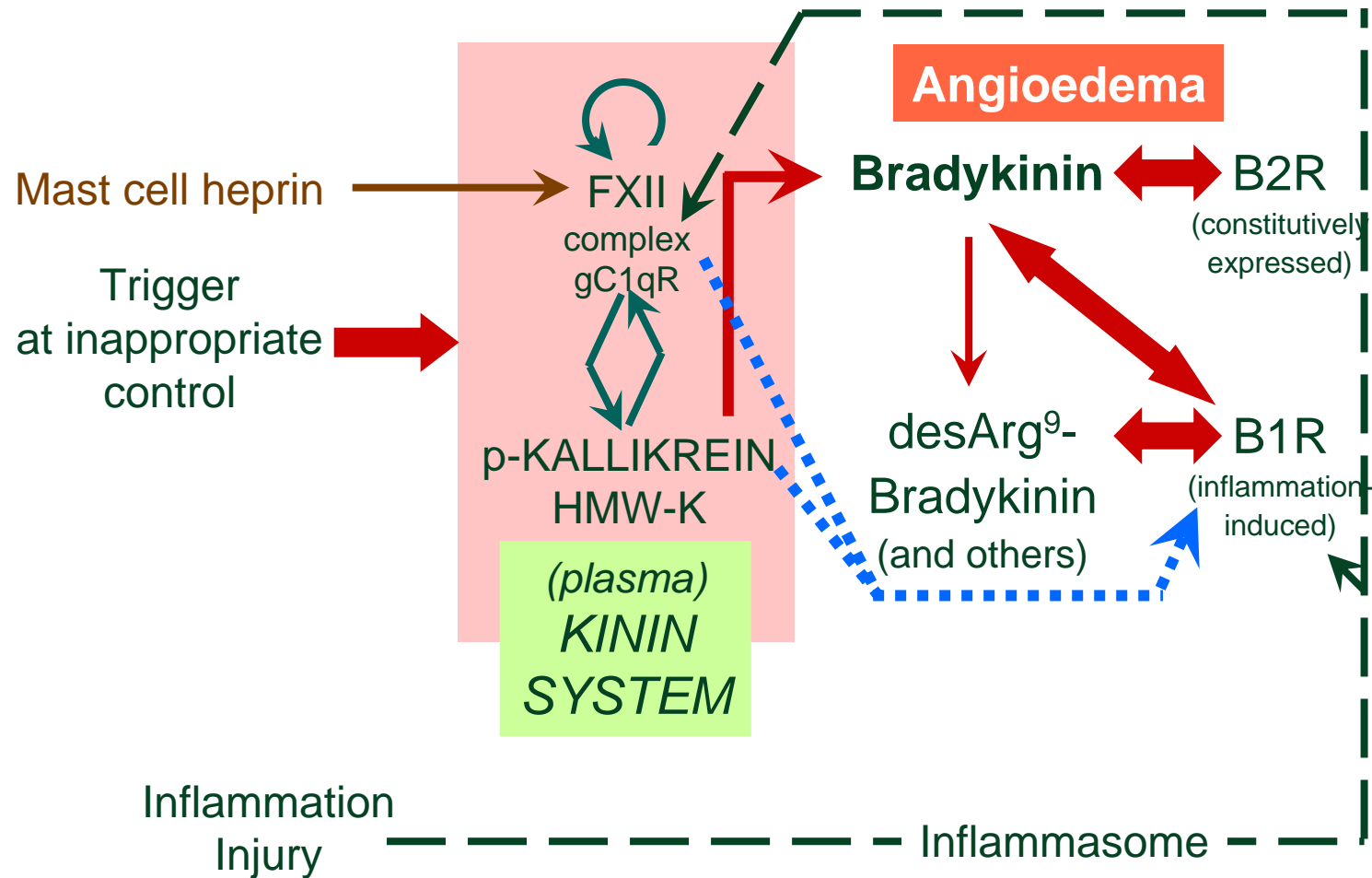
Disease

Scoring &  
HRQoL

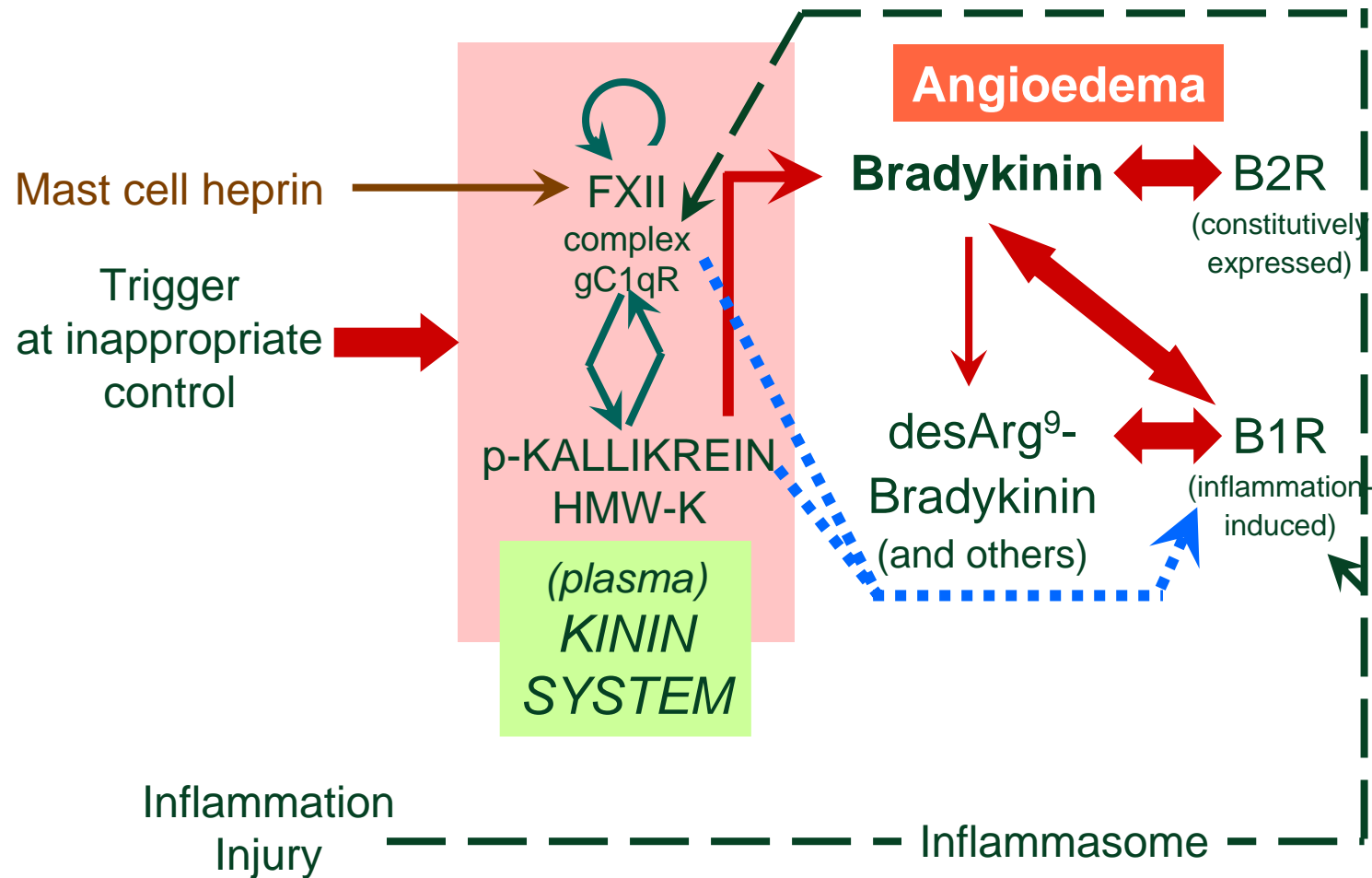
Trials

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- *T. Renné, Sweden:* Emerging functions of the plasma contact system for hereditary angioedema
- *F. Bossi, Italy:* New emerging roles for complement and kinin systems in angioedema episodes associated with C1-inhibitor deficiency
- *A. Kaplan:* Angioedema: Clinical and laboratory diagnosis
- Consequences
  - My decision → mainly skipping complement
    - C1-INH & disease: a protein of the kinin and not complement system; name inappropriate
    - FXII & disease: a lot might be learned



*Renné T:* Mast-cell derived heparin apparently can activate FXII  
*Bossi F:* HAE patient plasma can generate *in vitro* & *in vivo* B1R-reactive substances → to be characterized  
 → optimal protection on a receptor level by a cocktail of antagonists



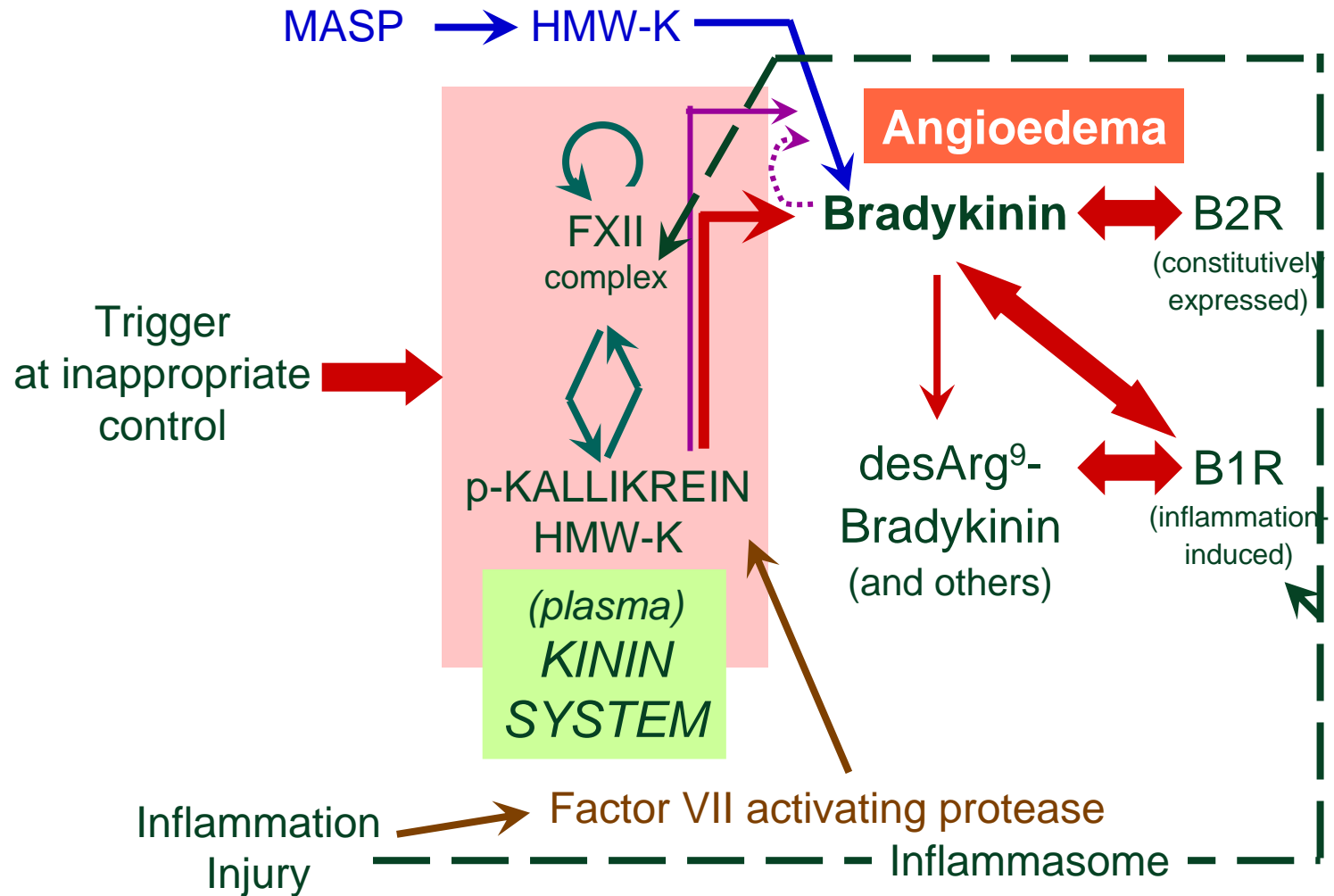
Localization and level of expression of B1R (and gC1qR) might be disease modifying factors! – in addition to

- genetic polymorphisms & protein isoforms
- hormonal conditions

EBNA1 and upper airway attacks



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*Bouillet L et al.* kallikrein directly and bradykinin indirectly can cleave VE-cadherin

*Dobó J et al.* FXIIa- & kallikrein-independent cleavage of HMW-K (in vitro)

*Stephan F et al.* FSAP a new target for C1-INH

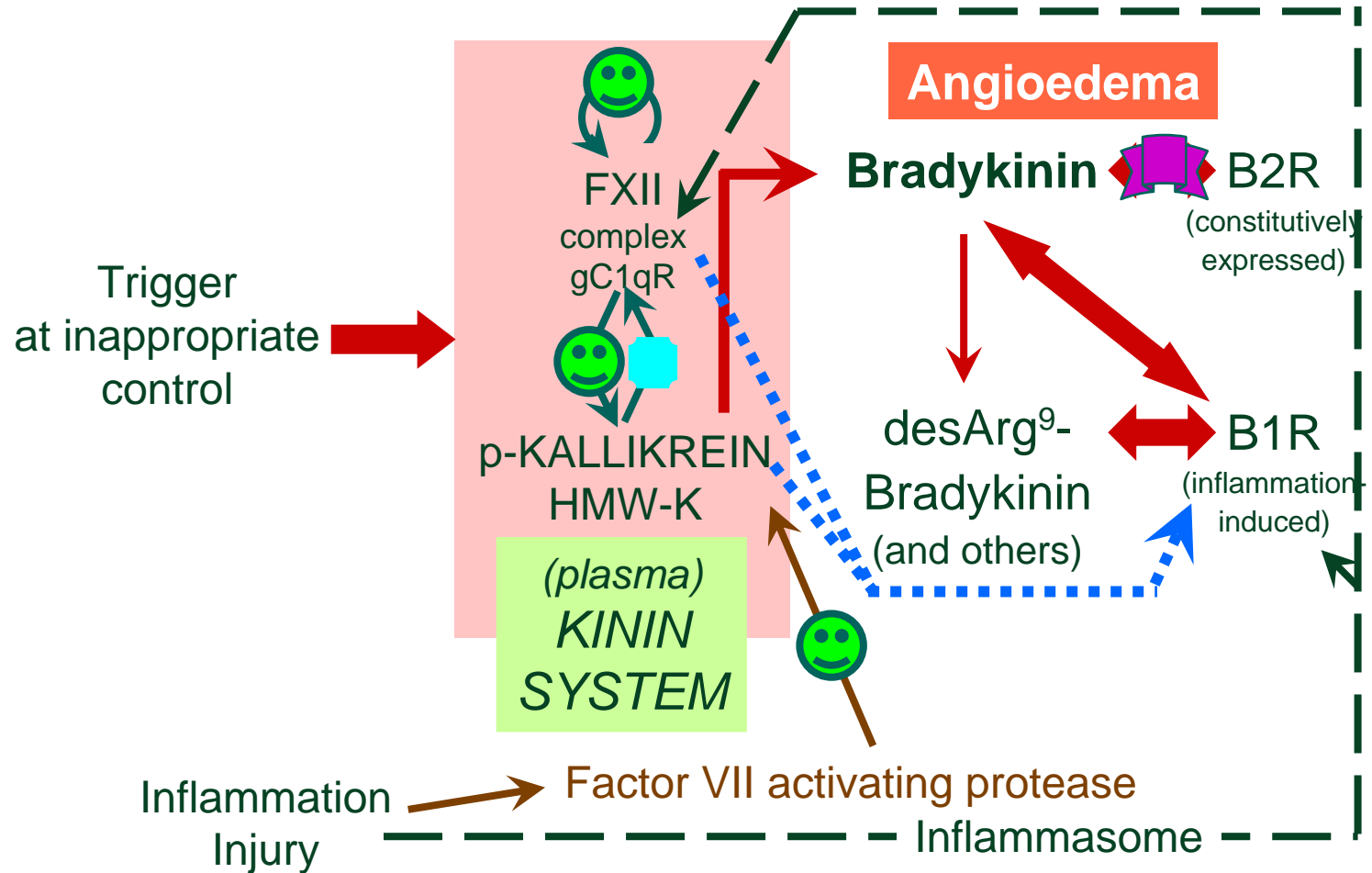


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- Overview: Inflammation, clot formation, clot lysis
- Analysis of rhuC1-INH data
- The minimal effective dose in circulation?
  - 0.35 U/mL sufficient; autoactivation of C1r prevented
  - new test
  - 0.7 U/mL C1-INH able to shut-off kininogen-cleavage completely
  - pdC1-INH and rhuC1-INH behaving more or less equally
- Heparin (polyanion) having an effect on inhibition by C1-INH of
  - C1r/s: yes
  - FXII: no
  - Kallikrein: no
- HAE-FXII
  - new: deletion in the proline-rich region of FXII
  - large cohort of patients studied in France



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*Inflammation: a 'boiling soup' might evolve; rarely, unexpectedly*

Self-administration: altering responsibilities e.g. for patients



Replacement by plasma-derived or recombinant C1-INH



B2R antagonist



recombinant plasma kallikrein inhibitor (US market only)





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*Aygören-Pürsün E et al. & Bork K et al.:* Surgery and trauma only in a minority of unprotected HAE patients induce an attack

pdC1-INH prophylaxis up to 1000 U is not able to prevent all attacks

pdC1-INH prophylaxis efficacious (2x pdC1-INH)



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## Contraception and HAE

- Progestin contraceptives are safe
  - Antigonadotropic progestins best
  - Side effects exist
    - Be careful when combining with danazol therapy
- Oestrogen pills: decrease in C1-INH (c,f) in healthy women
  - C1-INH specific activity (in-house test)
  - 50% mild decrease; reversible
- Oestrogen will remain a topic for all types of HAE



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## Overview by Dr. Kaplan

- DD of different types of angioedema, associated or not with urticaria
- ACE inhibitors
  - typically without urticaria
  - Polymorphisms / isoforms of APP; DPP, NEP
- C1-INH associated
  - no urticaria
- Idiopathic
  - mainly peripheral
  - rarely bowel syndrome
  - no upper-airway edema
  - response to therapy as DD
  - high-dose antihistamines can be effective (ca. 70% of cases)



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- Main problem today: HAE-unknown; lot of work
  - Oestrogen dependency highly variable
  - Attacks in pregnancy more or less?
  - Therapy: limited experience
    - Icatibant
    - Tranexamic acid
    - pdC1-INH prophylactic
- Emerging markers (hen or egg?)
  - Soluble extracellular part of VE-cadherin
  - Grenoble, F:
    - Reconstitution of proteases (quick), HMW-K (slow)
    - Kininogen breakdown
    - Kinin catabolism
  - MAb anti-XIIa
  - C4b/c (surrogate)
  - Cleaved HMW-K (HAE-unknown)
  - sE-selectin (inter-attack period); others?



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- To be done: adaptation of C1-INH functional assay e.g. chromogenic substrate assay for FXIIa inhibition
  - Proposal: always to mention which functional test was used
- Presently no 'simple' routine testing for parameters of the kinin pathway



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- Scoring - Not yet a new instrument
  - Gargnano meeting
  - Broadly based survey: experts (49) and patient's representatives (4); 19 countries
- HRQoL
  - SF-36v2
    - preliminary data
  - German effort
    - Prospective multi-centre naturalistic, prevalence based
    - Cultural aspect considered
    - C1-INH therapy; available; available on demand not available
    - Age; 4-7; 8-17, >18
    - (Cross cultural) field testing: coming



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- Registries – admirable activities in Latin America
- Activities by HAEi: HAE management in the EU
  - HAE Patient Advocacy Forum
  - Good evidence work
  - Web-based questionnaire supplemented by workshop; 11 European countries
  - No cure but optimal treatment
  - As always and everywhere in this world: awareness needs to be increased
- The HAE community is waiting another story from the girls!

# Music in the Air





# Music in the Air The Surprise





Dr. Kaplan this Sunday morning (22 May 2011)

- 1<sup>st</sup> time attending the WS
- Good, interesting young people
- Great science
- Good poster sessions

# Thanks



To the 'angyalkák' (the 'angels') /  
Goddesses

To George Füst "the father" of these  
meetings

To the 'backstage' (collaborators) of the  
'angels'; Diamond Congress Ltd

To the presenters

To the representatives of patient  
organisations

To the sponsoring companies





Have a safe trip home  
See you latest in two years