European Network of Expertise for Rare Pediatric Neurological Diseases

nEUroped

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ENRAH Founder and Secretary General
Alternating Hemiplegia of Childhood, AHC

- Onset in infancy (up to 18 months)
- Episodes of Hemiplegia involving either side of the body and episodes of bilateral hemiplegia
- Other paroxysmal disturbances including tonic/dystonic attacks, nystagmus, strabismus, dyspnoea and other autonomic phenomena
- Developmental delay and neurological abnormalities choreoathetosis, dystonia and ataxia
- Normal MRI findings
AHC

- very rare
- a complicated migraine”, a “rare form of epilepsy” or a “movement disorder”?
- chronic and debilitating
- unknown cause (s)- no genes identified (not yet)
- no effective treatment (s)
- no management guidelines
AHC (in 2002):

- AHC PO – France (AFHA), Italy (AISEA) and USA
- A Yahoo Group of families (AFHA)
- PO’s Scientific Committees
- International Workshops (Rome, Seattle, Paris)
- Few published clinical studies on single cases
- Case reports on treatments and outcomes
- Genetic research (the Netherlands, Italy and USA) is hampered by the lack of sufficient well characterized patients
- An International Database started in the US
- An Italian/AISEA database and blood bank of AHC cases from Italy
European Network for Research on AHC

- Set up in 2003 by parents in Vienna, Austria
- Involves:
  - AHC Patients/Families and POs
  - AHC Treating Neurologists
  - Researchers
  - Anybody who can contribute
- 9 countries at the start,
  17 in 2008
FP6 Project  *ENRAH for SMEs (2005-2007)*

Proposal and Project Coordination: ENRAH

**Objectives:**
- Establish the Network
- Set up a European AHC Patient Registry
- Involve SMEs in the Network and the FP6 - extend the Network

**Participants:**
- 10 clinical and research centres + 3 POs
- 9 EU countries

**Grant:** 358,000 Euro’s, 100 % funding
ENRAH for SMEs Main Achievements

✓ a Network of Clinical and Research centers of AHC expertise in Europe
✓ a European AHC Patient Registry – validated 157 case records
✓ Best Practice Guidelines for the Development and Use of the ENRAH Registry
✓ Raised awareness on AHC among health care providers, researchers and patients
ENRAH for SMEs  Follow up 1

✓ A Network of Patients and Clinical and Research centers of AHC expertise ------and related disorders

Extended ENRAH

Network of Expertise on Rare Pediatric Neurological diseases nEUroped
ENRAH for SMEs Follow up 2

✓ a European AHC Patient Registry
  - One data collecting centre per country
  - Identify patients with possible diagnose (role of the POs and families)
  - Data collection Forms in five languages
  - Informed consent Patients in the country language
  - Data entry on line in English – CPS smart cards
  - Personal data removed- unique coding number
  - Software- subcontracted (20% of the total budget)

  157 cases (1-54 years) in one year!

Data Review and Analysis??—A funding gap after the end of a project!
Source of the records in the ENRAH Registry

Number of shared records

EU Country

FR | GE | ES | IT | NL | B | CZ | UK
ENRAH REGISTRY 2007

Registered AHC cases/1 mln population in EU countries

prevalence*

EU country

FR  IT  GE  ES  UK  CZ  NL  B/FL
ENRAH REGISTRY 2007
Patient’s Age distribution (2-54)

Incidence*: 1 in 20,000 births
ENRAH REGISTRY 2007
Males/Females

MALE

FEMALE
## AHC Diagnosis

(49.15-0.25) 3.25 Years average

### Diagnosis in Years after birth

<table>
<thead>
<tr>
<th>Country</th>
<th>Av. time Diagnosis</th>
<th>Av. Time of characteristic Symptoms</th>
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</thead>
<tbody>
<tr>
<td>FR</td>
<td>3.5</td>
<td>0.8</td>
</tr>
<tr>
<td>IT</td>
<td>4.0</td>
<td>0.5</td>
</tr>
<tr>
<td>DE</td>
<td>3.8</td>
<td>0.6</td>
</tr>
<tr>
<td>ES</td>
<td>2.5</td>
<td>0.5</td>
</tr>
<tr>
<td>UK</td>
<td>3.0</td>
<td>0.5</td>
</tr>
<tr>
<td>CZ</td>
<td>3.7</td>
<td>0.6</td>
</tr>
<tr>
<td>NL/BE</td>
<td>4.0</td>
<td>0.5</td>
</tr>
</tbody>
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ENRAH for SMEs Follow up 3

- Raised awareness on AHC:
  - new research: first positive clinical results in five AHC patients - support research
  - raised expectations and false hopes among families and POs? - “do something good for the patients”

--- Initiated by the ENRAH partners + New Partners
--- Application for the May 2007 call PHP
--- Positive Evaluation September 2007
--- nEUroped Start 24 April 2008
nEUroped co-funding

- Total budget 1,250,000 Euro’s
- 60 % co-funding by the PHP
- 13 partners from 10 EU countries: HCL (FR), CUNI (CZ), ENRAH (AU), UCL (UK), UNIBO (IT), EURORDIS (FR), GCPA (BE), AISEA Onlus (IT), MEDEA (IT), LUMC (NL), HSJD (ES), KSLjubljana (SI)
- 16 collaborating partners
- Main Partner – ENRAH, AU
- Change of the Main Partner – HCL, FR
  - 60% Co-funding for PO/NGO’s (and for new MS) in the rare disease diseases field is clearly a challenge
To improve diagnosis, management and dissemination of information for rare nervous system disorders in children characterized by paroxysmal attacks

- Alternating Hemiplegia in Childhood
- Narcolepsy in Children
- Rare Surgically Treatable Epileptic Syndromes
  - Cerebellar hamartomas
  - Hypothalamic hamartomas
  - Landau-Kleffner syndrome and related disorders
  - Sturge-Weber syndrome
  - Rasmussen syndrome

TO ANSWER QUESTIONS THAT REALLY MATTER TO PATIENTS
Rare nervous system disorders in children characterized by paroxysmal attacks

- expressed in early childhood
- chronic and long life
- under-recognized and misdiagnosed
- mistreated because of poor diagnosis and/or poor knowledge on their natural evolution or, anecdotal treatment strategies (medical or surgical)
- under researched with no clear concept on their pathophysiology
- with a, often, devastating impact on quality of life
- lacking established appropriate clinical management guidelines
### nEUroped Specific Objectives

<table>
<thead>
<tr>
<th>Disease</th>
<th>AHC</th>
<th>Narcolepsy in children</th>
<th>RSTES</th>
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</thead>
<tbody>
<tr>
<td>Objectives</td>
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<tr>
<td>Building up a Platform: Establish the Network and Integrate Patients</td>
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<td>Identify main research and health care and social needs of selected diseases: Questionnaires data collection, Survey Patients, Registries</td>
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<td>Data Review and Analysis Develop &amp; Disseminate Guidelines</td>
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<td>Ensure highest ethical standards</td>
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nEUroped
Project structure

WP2 Dissemination

WP1 Coordination

WP3 Evaluation

WP4 Network

WP5 Integrating Patients

WP7 Registries

WP6 Reviewing

WP8 Guidelines

WP9 Ethics
Integration of Patients in *nEUroped*
Leading Partner Eurordis

- Mapping of existing resources
- Set-up six European patient mailing lists
- Establishing of European Patient Networks for AHC and Narcolepsy in Children
- Two consecutive workshops for each of the Patient Networks
- Surveys among the Patient Networks – on quality of life and ethical issues
- Discussion of the drafts management Guidelines
Main outcomes of nEuroped

- Earlier diagnosis of these diseases
  (narcolepsy average delay in diagnosis 15 years)
- Improved knowledge and management of these diseases
- Critical mass of patients and researchers for collaborative and sustainable European research in the field of rare paediatric neurological diseases
- Registries as tool for research
Registries as tool for research

Effort

Research and Knowledge on the Disease

Time
More information and contacts

www.neuroped.eu

Thank you!