

# **Capacity Building and Patient Network Integration into nEUroped**

## **nEUroped Extended Network Meeting Pre-Conference Workshop Report**

**9.30-17.00**

**November 21<sup>st</sup>, 2010**

On Sunday 21, November members of the nEUroped Extended Network including the Patient Network (patients and parents identified across Europe concerned with Alternating Hemiplegia, Narcolepsy and Rare Surgically Treatable Epileptic Syndromes (RSTES), project partners and other interested Extended Network members were invited to attend the pre-conference workshop focused on the roles of patients and clinicians in nEUroped and how nEUroped can be further developed to meet patient needs and interests in addressing rare paediatric neurological disease. This meeting marked the 2<sup>nd</sup> face-to-face meeting of patient groups and parents identified by the European Organisation for Rare Diseases (EURORDIS).

### **Specific Workshop Objectives**

The specific objectives of this workshop were to continue the integration and empowerment of patients affected by rare paediatric neurological diseases by having their input and involvement in nEUroped by:

- presenting the status of nEUroped outcomes
- building the capacity of patients to understand the basic principles of patient registries and discuss the specific role of patient groups in the nEUroped registry
- breaking out into disease specific groups to foster communication between patient groups and professionals on current and future expectations of the nEUroped consortium.

### **Workshop Programme**

Workshop objectives were addressed by a diverse programme including:

- A. Introductions by the EURORDIS and their role in integrating patients into the project, the European Network for Research on Alternating Hemiplegia (ENRAH) and their role as initiators of nEUroped and the Good Clinical Practice Alliance (GCPA).
- B. A Capacity Building on Patient Registries: Definitions, Benefits, Pitfalls and Patient Involvement by Jeanne-Helene di Donato, 3C-R consulting
- C. A presentation of an example of a patient-led registry and biobank: IBAHC Biobank and Clinical Registry for Alternating Hemiplegia Biobank and Clinical Registry for Alternating hemiplegia coordinated by the Italian Patient Association for Alternating Hemiplegia (AISEA)
- D. A general presentation of the project's progress and plenary discussion on how to best integrate patient needs and expectations, Alexis Arzimanoglou, Hospices Civil Lyon

- E. Presentations on the progress by disease specific Working Group leaders in the project (Alternating Hemiplegia - Brian Neville; Narcolepsy - Sona Nevsimalova; RSTES - Alexis Arzimanoglou)
- Discussion on proposed Care Management Guidelines
  - Sharing of experiences to receive patient input into nEUroped and their future expectations for involvement in the consortium

## Achievements

- A. Patients were introduced to EURORDIS' role in the nEUroped project. As an umbrella rare disease organisation, EURORDIS is experienced in identifying and creating relationships with patient support groups their members and families, identifying their needs and expectations as related to their disease and ensuring that these needs and expectations are understood by all other project stakeholders and integrated into the projects activities. EURORDIS is also in charge of setting up platforms for communication within disease specific patient communities either through mailing lists or larger online patient communities.

ENRAH, through previous European Commission funding, is an established network of patients, parents and researchers concerned with Alternating Hemiplegia for which specific objectives included:

- Pragmatic identification of patients with Alternating Hemiplegia across Europe
- Identification of researchers and small to medium sized enterprises interested in progressing research in the field
- Raising awareness of the disease in Europe
- Providing accurate information for patients and caregivers when it exists

This preliminary work serves as the basis for continued networking at the European level among all stakeholders concerned with Alternating Hemiplegia via the nEUroped project.

- B. Patients were presented with the basic definitions of the nEUroped patient registry as an on-going, exhaustive system of data collection of patients with epileptic, narcoleptic or hemiplegic paroxysmal attacks via Centres of Expertise across Europe that treat a steady number of patients with Alternating Hemiplegia, narcolepsy and rare RSTES. Beyond collecting data, the nEUroped registry will increase knowledge on the diseases included, support further research by pooling data in order to achieve a sufficient sample size for epidemiologic and clinical research and perhaps one day constitute a key instrument in allowing drug surveillance and supporting health service planning for patients affected with these rare paediatric neurological diseases.

The Patient Network and other workshop participants were also presented with the reality that although very thorough and effective research infrastructures, patient registries are tools that require significant time and financial investment and thorough planning to meet the needs of all stakeholders involved. As such, collaborative efforts to establish, manage and derive outcomes from patient registries are paramount in a network such as nEUroped which above all integrates the expectations of patients and their families.

- C. Participants of the Workshop were presented with an example of a registry (and biobank) established, managed and maintained by a patient organisation.

A. S. I. EA Onlus, the Italian Association for the AHC, was created in 1999 with the mission to support families affected by Alternating Hemiplegia, spread knowledge about the disease, and promote and support research. Since its inception, the association decided that the best way to achieve this objective, was to make clinical data and biological samples available and easily accessible to research groups. In 2004, the I.B.AHC (Italian Biobank and Clinical Registry for Alternating Hemiplegia) was by the association A.I.S.EA Onlus, on behalf of its patients, to physicians and researchers interested in carrying out studies and research projects on Alternating Hemiplegia in Childhood (AHC).

I.B.AHC is composed of two main repositories, the Clinical Registry and the Biological Bank, designed to gather, organise, store, and share the biologic material (DNA, RNA, Cellular Lines) and the clinical data of the patients affected by AHC.

The diagnosis of all the cases entered in the I.B.AHC Biobank and Clinical Registry are validated by the Scientific Committee of A.I.S.EA Onlus and by the treating physicians of the participating patients.

More specifically, the objectives of I.B.AHC are:

1. To support the scientific research of the causes of AHC and of an effective treatment, by making available the medical and scientific data and the biological material of a large number of validated cases to any research group presenting a written request
2. To facilitate the definition of new research lines and the start of new large-scale collaborating projects, through the sharing of the clinical information and the biological material and of the results of the studies using them,
3. To develop the knowledge of AHC and a better diagnosis and care for the patients, by making available the clinical history (evolution of the symptoms, effectiveness of the drugs ...) of the entered cases and by networking all the involved expertises (researchers, clinicians, patients, rehabilitation therapists, public institutions ...)

Currently, 35 cases are available, complete with clinical data and biological samples.

- D. Participants were briefly presented with the original objectives of the nEUroped registry:
- Creation of one common registry for Alternating Hemiplegia, Narcolepsy and RSTES – diseases with the common symptom of paroxysmal events
  - Identification of centres of expertise across Europe able and willing to enter data into the registry

An open discussion centered on three questions regarding the needs, expectations and involvement of patient groups, patients and their families. The discussion began in a plenary format with the following general conclusions.

1. *What are the patient expectations for the development, future management, and future use of data collected in the nEUroped registry?*
  - a. To identify patients across Europe and centralise general knowledge about their treatment and care

- b. Opening of the network to new specialist centres interested into contributing data
- c. To establish better communication and collaboration across the medical community
- d. To be consulted on request to use registry data
- e. To guarantee continuation and sustainability of the registry through long-term funding plan

Participants feel that currently not enough research to improve care and treatment for rare neurological paediatric diseases is being done. It is expected that the registration of patients and their outcomes in the nEUroped registry will lead to better existing knowledge on the causes and effective care and treatments. Patient groups expect all specialised centres across Europe who follow patients with these rare neurological syndromes will be invited to contribute to the registry and that once collected data will be openly available to all interested research teams. Patients groups expect to be notified of all requests to analyse registry data. Finally it is expected that a solution to sustain the registry should be developed and agreed upon.

2. *How can patient groups contribute to the success of the nEUroped registry?*

- a. Agree to participate
- b. Help recruit other patients
- c. Communicate its existence to health care professionals interested in entering and eventually using data
- d. Enter data themselves and propose self reporting data components
- e. by recruiting patients and clinicians to participate
- f. contribute to the sustainability of the network once European Commission funding has ended.

3. *What are the challenges, hindrances, to full patient participation in the nEUroped registry and project?*

- a. Lack of collaboration between experts scattered across Europe and subsequent fragmentation in research
- b. Lack of clarity for future sustainability of the registry
- c. Need for regular communication back to patients on the progress and outcomes to maintain their motivation to take part
- d. Need to develop standardized informed consent forms

It was signaled that the fact that the registry is structured **around the common symptom of paroxysmal attacks rather** than diseases may make it difficult for patients, parents and patient groups to know that they can contribute.

**The uncertainty of the sustainability of the nEUroped registry results in the hesitation of some patients and parents in contributing their data.**

E. Participants separated into three disease-specific groups to discuss:

- discuss draft management guidelines
- to discuss progress in the project as a whole and specifically on any advances in Narcolepsy
- to continue discussion around the questions above

Summaries of break-out sessions are included in Annex 1.

## Indicators

A total of **48 participants** registered for the Preliminary Workshop of the Extended Network meeting on November 21<sup>st</sup>. Of these participants, 24 parents, patients or patient representatives representing the 15 patient groups listed below attended:

European Network for Research in Alternating Hemiplegia (ENRAH)  
Associazione Italiana Narcolettici – Narcolepsy, Italy  
Associazione Italiana per la Sindrome di Emiplegia Alternante (AISEA) – Alternating Hemiplegia, Italy  
Landau Kleffner Syndrome, Norway  
Alternating Hemiplegia, Ireland  
Association Française de Narcolepsie-cataplexie et Hypersomnie – Narcolepsy, France  
Narkolepsie Deutschland e. V. – Narcolepsy, Germany  
Nederlandse Vereniging voor Narcolepsie – Narcolepsy, Netherlands  
Association Française de l'Hémiplégie Alternante – Alternating Hemiplegia, France  
Alternating Hemiplegia Support Group – Alternating Hemiplegia, UK  
AHC Association of Iceland – Alternating Hemiplegia, Iceland  
ALTERNERENDE HEMIPLEGI Danmark – Alternating Hemiplegia, Denmark  
Asociación Española del síndrome de la Hemiplejía Alternante – Alternating Hemiplegia, Spain  
Epilepsy HERE - Help, Education, and Research for Epilepsy - Epilepsy, UK  
Sturge-Weber Foundation - Sturge Weber UK

In addition, 22 participants from nEUroped project partnering institutions and five additional interested individuals from the paediatric neurological scientific community attended the workshop. Additionally, 2 new members of the nEUroped Extended Network registered to participate in the workshop.

## Recommendations

### Survey on Patient Needs

Include the input of patient groups on the structure and content of surveys on patient needs to best encourage feedback and guarantee that feedback is useful. Is the tool appropriate in asking the right questions, can the answers to these questions give feedback onto the daily needs of patients? Surveys should be streamlined to allow for easier translation and back translation or only allow responses in English given the centralisation of results by national patient groups in their native language.

### Survey on Ethical Issues

The survey on ethical issues should be finalised and distributed to the patient network and the larger extended network as soon as possible. Ethical guidelines drafted before the beginning of data collections should incorporate responses from this survey.

### Guidelines

Feedback from the patient perspective should be considered in the final publication of existing care management guidelines for Narcolepsy and Alternating Hemiplegia. Care management guidelines for RSTES should still be drafted and circulated for feedback from the patient perspective before final validation and publication.

### Registry

More regular updates on the specific progress of the development of the registry should be communicated to the Patient Network, including the latest request to prolong the nEUroped project and a precise plan for sustainability.

### Overall Integration of Patients in the Project

Integration of patients in the project through formal collaboration has led and will continue to lead to:

- Identification of patients not necessarily followed by specialists in this network
- Evaluation of patient needs and expectations
- Education and training for patients
- Identification and recruitment of patients or health care professionals
- Governance of registries and the network overall
- Contribution to items to be documented in registry such as patient satisfaction indicators and quality of life data
- Contribute to ethics board for project activities such as development or review of informed consent forms
- ...amongst many other beneficial points of collaboration

Successfully involving patient groups should bring win-win situation for all stakeholders: patients, health professionals, health authorities and industry by expanding the network and encouraging centres in other countries in Europe to join; by improving the quality of networking activities by ensuring that the needs of patients are directly reflected; and ultimately by improving progress in the knowledge diagnosis care research and treatment of Alternating Hemiplegia, Narcolepsy and many rare epileptic syndromes.

### **Conclusions**

Patients appreciate physically getting together to meet and discuss and have the opportunity to interact with nEUroped project partners but also with other professionals and patient representatives outside the project interested and motivated in networking.

Understanding the technical aspects and medical concerns on what should be included in a registry is still limited. Theoretical guidelines for how this should be best done and how patients can be involved was proposed by an external consultant, but how these principles are being or can be applied to the nEUroped registry remains uncertain as a global presentation of the status of the nEUroped registry was not presented during the Pre-conference workshop as planned. During break-out sessions, the WG leader of the group did present the status of the registry with examples of data fields related to narcolepsy included in the registry template. Patients, parents and representatives present in this group were very assured by this presentation.

There is a general disappointment from the parent/patient perspective that there are significant delays in the project and more worrisome the source of the delays that seem to be related to:

- 1) A lack of efficient coordination of stakeholders
- 2) A lack of commitment from the core project partners and willingness to open to other interested clinicians/researchers
- 3) A lack of a concrete plan on how to accomplish delayed objectives and how to continue networking beyond the proposal for sustainability
- 4) A lack of recognition for a harmonised consent form and its implementation in Centres of Expertise in the nEUroped network

Patient groups involved in nEUroped have an intimate knowledge of their diseases as well as of the barriers to research and access to medical and social services, enabling them to bring a different insightful and creative perspective and dedication. The effective participation of patient representatives has the potential to redefine innovative research, the highest standards of management guidelines and the most efficient healthcare pathways for greater quality, efficacy and cost effectiveness of care.

**Annex 1**  
**nEUroped Extended Network Meeting Pre-Conference Workshop**  
**Disease-specific Breakout Sessions**  
**15.30 - 17.00**  
**November 21<sup>st</sup>, 2010**

**Alternating Hemiplegia Working Group**

**Led by Brian Neville**

**1. What are the principle needs of children with specific neurological diseases regarding research?**

Comments that were made on the “Draft guidelines for the management of alternating hemiplegia”:

- **Should the name of the condition “Alternating Hemiplegia of Childhood” lose the childhood part of it?**

*The group agreed that it can be misleading and it can cause problems when the children enter adulthood within the social systems of various countries.*

*There could be a problem with discarding the “childhood” part because most of the associations have websites that have the AHC in it and also most of the information already out there refers to Alternating Hemiplegia of Childhood.*

- **There was a question about the drugs, Flunarizine being the first on the list of drugs that have worked, could we have a list of other drugs that have worked and also a list of drugs that should not be used?**

*The list could be split in two, the preventive and the rescue drugs.*

- **Nutrition, not all AHC children have a problem with nutrition,**

*Prof. Neville said that the guidelines are referring to height and weight issues.*

*AHC children should eat regularly!*

*Perhaps there should be a research on the nutrition of AHC children?*

*Parents need to be aware that some AHC children need to eat between episodes*

- **Neuropsychologist has helped a 17 year old girl in Denmark with anger issues – something that others should be aware of. This has helped teenagers cope with adulthood without using prescribed drugs.**

- **Is there anything to support that magnesium helps AHC patients?**

*It is not known.*

*Some of the above questions could be at the end of the guidelines as future research questions*

*There was a discussion about other drugs that could be used like new generation migraine drugs.*

*Add to the guidelines that occupational therapists and physical therapists are normally used to help the AHC children.*

- **How do we record the episodes and information that we experience throughout the years? Do parents keep records?**

*History for some parents shows that in the first years there is a lot of data recorded but as time passes the records get less attention perhaps because the records are not being used?*

The Italian association introduced a software "Daily report of crisis" that will be available on the bio bank website in January 2011. This software can be used to record the episodes.

It is a really good tool that parents and specialists can use. The result would be an information bank that could be used for research. This way there would be a reason for the parents to continue to record data because it will be used in the future to help solve the AHC mystery.

There was a discussion about that the record should be closely related to the US record that is already being used, that way exchange of records would be made simpler.

- That the information that has been discovered is available
- That the medical community is communicating among themselves all around the globe

## **2. Which kinds of research would patients and their families wish to see prioritised within nEUroped?**

- *Research that focus on the basics of AHC, what triggers episodes? What is the core cause of AHC?*
- *Research that help with daily standard of living for the patients.*
- *Research that will lead to the discovery of a drug that can stop the episodes entirely.*

What are the challenges, hindrances, to full patient participation in the nEUroped project?

- If patients are going to participate in the project the patient will have to be sure that the information will be used for research that are driven to solve the AHC mystery or help with the daily standard of living.
- Patients will have to have access to the information and be able to withdraw their information if they feel that it is not used in the right way.
- There will have to be a consent form.
- The registry will have to be updated regularly
- The registry should be open for other researchers that have the aim to help AHC patients.

- Patients or patient associations should know if a researcher is asking to get access to the registry.
- Patients will have to be sure that the committee that is in charge of nEUroped is working with the best interest of the patients in mind.
- Patients would have to be sure that other countries that are not now a part of the registry can be a part of the registry and will also be able to use the information that is in the registry for research.

**3. What are the challenges, hindrances, to full patient participation in the nEUroped project?**

- If patients are going to participate in the project the patient will have to be sure that the information will be used for research that are driven to solve the AHC mystery or help with the daily standard of living.
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- There will have to be a consent form.
- The registry will have to be updated regularly
- The registry should be open for other researchers that have the aim to help AHC patients.
- Patients or patient associations should know if a researcher is asking to get access to the registry.
- Patients will have to be sure that the committee that is in charge of nEUroped is working with the best interest of the patients in mind.

## **Narcolepsy Working Group**

**Led by Sona Nevsimalova**

Comments on the draft care management guidelines were incorporated into the final version in which guidelines on pharmacological therapy were revised to include:

*Owing to possible adverse effects (skin and subcutaneous tissue reactions and psychiatric complication), however, European Medicines Agency (EMA) does not recommend it (since June 2010) in children. Based on the experience of using modafinil in children over the past two decades, the initial dosage varies according to age between 50-100 mg/day in the morning, the therapeutic dosage between 100-300 mg/day divided at morning and noon dosage. Modafinil can be co-administered in children with other stimulants to enhance the alerting effect of either drug alone.*

The group reached a consensus that major obstacles in Narcolepsy included:

- delays or incorrect diagnosis, a lack of consensus on diagnostic methods at the European level
- a need to raise awareness of the diseases profile to receive better support from the medical and socio-medical community (including social workers, teachers and other carers for children with Narcolepsy)
- to better educate primary care physicians on the diagnosis, care and treatment of the diseases
- to raise awareness of the need for clinical trials and post-market authorisation surveillance of existing drugs.

More specifically, the benefits of using of Modafil in children (following recent recommendations) is unclear and one aim of the registry maybe to further clarify the most beneficial treatments for narcoleptic disorders in children with the least adverse effects.

Participants expressed their disappointment in the limited nature of elements included in the registry and expected that more qualitative investigation of the real life needs of patients and families. Participants expressed that research focusing on social/scholastic/quality of life issues would be valuable since little information is available about these aspects for children and their families living with narcolepsy.

**Rare Surgically Treatable Epileptic Syndromes Working Group**  
**Led by Alexis Arzimonoglou**

No Guidelines for the management of RSTES have been drafted.

Participants began with a general discussion of the status of the nEUroped Patient Registry.

To meet ethical standards it was suggested that this was started by an approach to the clinicians in the main paediatric centres in the European Union to report their findings supporting diagnosis of a small number of rare neurological conditions in childhood. These would be maintained in a Register with central custodians who would receive requests to have access thereto. It was also suggested that there should be a supplementary bank of biological resources to supplement the register for research purposes. The parents of patients whose details were to be included in the register would be approached by clinicians to give written formal consent to the details of their children being included in the register and for any biological material to be submitted to the biobank.

The extent to which support groups should be able to submit data was a point of discussion within the main meeting but in the smaller breakout session on Rare Surgically Treatable Epilepsy Syndromes (RSTES) the process of submission of information by clinicians to registry was accepted and the role of the support groups would be publicise the existence of the registry to parents and academics and assist the neurologist in obtaining completed permission templates.

1. The session was asked to consider what are the principal needs of children with RSTES regarding research?

It was accepted that the needs for research were driven by the rarity of the individual conditions and that they would need to be directed to either improvements in treatment or improvements in quality of life.

Earlier diagnosis was also signalled as a principle need.

2. Which kinds of research would patients and their families wish to see prioritised within nEUroped ?

These were felt to be those likely to lead to early improvements in treatment rather than those of a purely academic nature.

Research leading to improved diagnosis and earlier diagnosis were supported.

With regards to Sturge Weber syndrome specifically, patients and families wish to see some investigation into the benefits of taking a small daily dose of aspirin.

3. What are the challenges, hindrances, to full patient participant participation in the nEUroped project?

There may be a reluctance on the part of some patients/parents to engage with others or to take part in research projects. Many will have other children and will have to balance the needs of the whole family

Overcoming patients' apathy was also noted as an obstacle. As such, persuading patients and patient groups to take part in such projects by disseminating information about the project and how to become involved is important.