I.B.AHC – Biobank and Clinical Registry for Alternating Hemiplegia of Childhood
www.ibahc.org

A national Registry and Biobank Based Network for the Research and the Care of the patients affected by Alternating Hemiplegia of Childhood

Maria Rosaria Vavassori[1]; Filippo Franchini[1]; Elisa De Grandis[2], Michela Stagnaro[2], Marcella Gherzi[2], Livia Pisciotta[2], Melania Giannotta[3], Mariateresa Bassi[4], Fiorella Gurrieri[5], Danilo Tiziano[5]

Background

Alternating Hemiplegia of Childhood (AHC) is a very rare neurological disease (1 affected individual in 1 million), characterized by early onset, recurrent episodes of hemiplegia affecting alternatively both sides of the body, occurrence of paroxysmal phenomena such as tonic and dystonic attacks, seizures, oculomotor and autonomic disturbances. The disease causes also chronic and progressive deficits, motor, sensory and intellective.

The AHC is a highly chronically debilitating suffering with deleterious effects on the quality of life of the affected patients and of their families.

A.I.S.EA, the Italian Patient Association for AHC, was created in 1999 with the main goals to support the families, spread the knowledge about the disorder, promote and support the research.

In 2004, the **service I.B.AHC - Biobank and Clinical Registry for AHC**, was activated, thanks to a project funded and coordinated by A.I.S.EA, in close collaboration with its Scientific Committee, the appointed professionals for its management, some genetic labs for the research and the diagnostic testing, and the treating physicians of the participating patients.

The I.B.AHC service is respectful of the privacy of the patients and of their right to the information about the research projects using their samples and data.

The I.B.AHC service is open to all the research groups, national and international, for any research project related to AHC, provided that it is scientifically valuable and non duplicated.

Recently, the genetic cause of AHC has been identified, thanks to an international research in which the availability of the I.B.AHC service played an important role for the confirmation of the results, by providing a large, non duplicated and validated case-series.

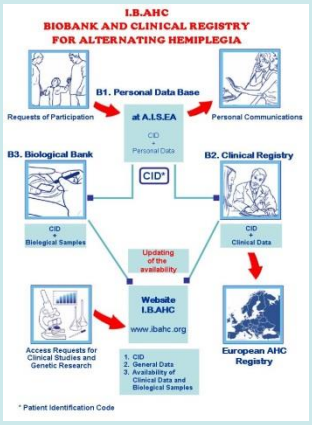
Acknowledgments

A.I.S.EA wants to thank the members of its Scientific Committee, its advisors, the I.B.AHC appointed managers, the collaborating genetic labs and all the treating physicians of I.B.AHC, for their active participation to this important project.

Many thanks to the Azienda ASL – Ospedale Maggiore, Bologna that hosted the first version of the Clinical Registry and to the Scientific Institute E. Medea, Bosisio Parini (LC) that is hosting the Biobank.

A special thank to the members of the Ethic Committee of the Institute E. Medea for their participation to I.B.AHC and for their precious advise to the association.

Architecture



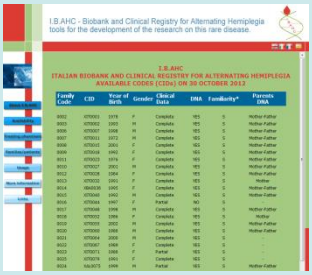
The I.B.AHC Architecture
The three repositories B1, B2 and B3 are physically separated but logically joined by means of the CID, the Patient Identification Code

The service I.B.AHC is composed by three coordinated repositories:

B.1 Personal Database - managed by A.I.S.EA. It contains the personal data of the patients and the link between such data and the related CID, the anonymous, numeric code used to reference the information kept in the following two repositories.

B.2 Clinical Registry – managed by the Data Managers appointed by A.I.S.EA: currently, Dr. Elisa De Grandis (Child Neurology Unit - G. Gaslini Institute, Genoa) and Dr. Melania Giannotta (Child Neurology Unit - Maggiore Hospital, Bologna). The Registry is an on-line secure database **https://dbonline.ibahc.org**, containing the clinical data, the video recordings and the photographs of the participating patients, to be used for clinical and therapeutic studies. All these data are identified only by the CIDs.

B.3 Biobank – managed by the Biobank Manager appointed by A.I.S.EA: currently Dr. Maria Teresa Bassi, Laboratory of Molecular Biology, Scientific Institute E. Medea (LC). It contains the biological samples of the participating patients (DNA, RNA and cellular lines) and of their parents (DNA only), to be used for genetic research. The samples are identified only by the CIDs, and processed and stored in the Biobank according to the specific **I.B.AHC Standard Operating Procedures (SOPs)**.



The updated availability in the Biobank and in the Clinical Registry is displayed on the **I.B.AHC Public Website www.ibahc.org**
Also the list of all the research projects that have been granted the access to the I.B.AHC service is published, as well all the forms for the enrolment of the patients and the application for the researchers.

Protocol

The I.B.AHC protocol consists of the following steps:

1. **Enrolment of the patients, their parents and their treating physicians**
A.I.S.EA collects the consent forms from the participating patients and parents and from their treating physicians, for the processing of their data (Italian National Law 30.06.2003 Nr 196). A **CID** is assigned by A.I.S.EA and notified to each participant. Only A.I.S.EA can communicate personally with the participants.

2. **Collection of the Clinical Data and the Blood Samples**
The treating physicians receive from A.I.S.EA an access code to login to the on-line Clinical Registry and enter the data of their patients with the support of the Data Managers.
With the collaboration of the treating physicians, also the blood drawings are organized and the samples, labelled by the CIDs, are sent to the Biobank.

3. **Access to I.B.AHC**
All research groups can request to use the I.B.AHC Biobank and the Clinical Registry, for studies and research projects related to AHC, by filling the **I.B.AHC Usage Request Form** and sending it to A.I.S.EA. The request is evaluated by the Scientific Committee of the association and by A.I.S.EA, within the following 30 days.
A **Material and Data Transfer Agreement (MDTA)**, with all the terms and conditions for the use of the biological samples and clinical data, must be signed by the research group before accessing I.B.AHC. Also diagnostic tests can be performed by the genetic labs collaborating with A.I.S.EA, using the samples in the I.B.AHC Biobank, upon request of the patients and their treating physicians.

4. **Discussion of the diagnosis**
At least once a year, A.I.S.EA organizes a video-session, during which the treating physicians can present their new AHC cases, to discuss and classify their clinical pictures together with the Scientific Committee of A.I.S.EA, and to validate their diagnosis, in case it is not confirmed genetically.

5. **Restitution of the results**
The general results of all the research projects accessing the I.B.AHC service are shared within the scientific community through publications. According to the conditions stated in the MDTA, A.I.S.EA enters the individual results in the I.B.AHC Clinical Registry to be used by any future research; the association also organizes the communication of their results to the patients together with their treating physicians, when necessary through a proper genetic counselling.

Results

At present, I.B.AHC contains the complete clinical documentation and the biological samples of more than 45 patients. Several clinical studies and genetic research projects have effectively used the I.B.AHC Biobank and the Clinical Registry in the past years, both in Italy and abroad.

The **I.B.AHC Consortium** has been created, including the AISEA staff, the appointed professionals, some advisors from the AISEA Scientific Committee, the laboratories collaborating with A.I.S.EA for the diagnostic testing and for the genetic research, and the treating physicians of the patients in I.B.AHC.

The I.B.AHC Consortium is member of the international network for the research on AHC, thanks to which some mutations in ATP1A3 were identified as the major cause for AHC (Heinzen et al., 2012). All the patients in I.B.AHC were included in this research; the results of their molecular testing and a proper genetic counselling were provided to the patients by the I.B.AHC laboratory participating to the research.

The I.B.AHC Consortium is now contributing to the **international study of the genotype-phenotype correlation**, as a further step of the research towards the development of an effective treatment for AHC.

Moreover, the active involvement of the treating physicians, the sharing of all the information collected in I.B.AHC and the dissemination of the information produced by the research accessing I.B.AHC, led to the establishment of a **national multidisciplinary network** for the diagnosis, treatment, rehabilitation and assistance to the people affected by AHC.

Conclusions

The I.B.AHC service is proving effective not only in the support to the research of a cure for AHC, but also in the development of a better care for the patients, in terms of better diagnosis and a better health and social assistance.

The main involvement of A.I.S.EA guarantees the sustainability of the project and the safeguard of the rights of the patients to the privacy and the information.

Contacts

Rosaria Vavassori
Coordinator
info@ibahc.org

Filippo Franchini
Project Manager
franchini@ibahc.org

I.B.AHC
Biobank and Clinical Registry for Alternating Hemiplegia of Childhood
www.ibahc.org

I.B.AHC is a project designed, funded and coordinated by

A.I.S.EA Onlus
Italian Association for Alternating Hemiplegia of Childhood
www.aisea.org

1. A.I.S.EA Onlus, Italian Association for Alternating Hemiplegia of Childhood www.aisea.org; 2. Department of Child Neuropsychiatry, Scientific Institute G. Gaslini, Genoa; 3. Department of Child Neuropsychiatry, Hospital Maggiore, Bologna, Italy; 4. Department of Molecular Biology, Scientific Institute E. Medea, Bosisio Parini (LC), Italy; 5. Institute of Medical Genetics, Catholic University, Rome, Italy.