Project “Rare diseases”: Infant Botulism

Responsible: Lucia Fenicia
Senior Scientist - National Reference Center for Botulism - Centre for Food Quality and Risk Assessment – Istituto Superiore di Sanità – E-mail fenicia@iss.it

Infant botulism (IB) is the most recently recognized and in the US the most common form of botulism. In Italy IB was recognized in 1984 and results from a unique pathogenesis: ingested spores of Clostridium botulinum germinate, colonize the infant’s colon, where produce botulinum neurotoxin (BoNT). After the toxin is absorbed, binds to peripheral cholinergic synapses, causing flaccid paralysis. Knowledge of this intestinal pathogenesis resulted in the discovery of novel pathogenic strains of Clostridium baratii in USA and Hungary, and Clostridium butyricum in Italy producing botulinal neurotoxins and causing the clinical picture of IB. In particular in Italy 18% of IB cases is related to a strain of C. butyricum producing BoNT type E. Discovery of these strains enlarged the number of organisms known to cause “intestinal toxemias of infancy”, of which IB is the prototype. After the United States and Argentina, Italy has the third highest number of cases of IB. Twenty-four cases of IB occurred in Italy between 1984 and 2006. IB is included in USA National Organization for Rare Disorders as No 95.

The incidence rate of IB is low, but however it can be considered as underestimated for various reasons. Firstly, the disease is difficult to diagnose, especially because there is a wide spectrum of clinical manifestations. These are non-pathognomic and are not always present, and because the severity of the disease can vary greatly. In fact, the diagnosis is generally done by clinicians who are quite familiar with the clinical manifestations of IB and maintain a very high index of clinical suspicion, which probably occurs in the United States were about 100 cases are confirmed /year. The laboratory confirmation of suspected cases need a rapid and specific method to detect BoNT producing clostridia in clinical samples.

The only specific treatment for IB is BIG IV - Botulism Immune Globulin Intravenous –(Human) (commercialized as BabyBIG®), although not yet licensed in Italy it can be obtained from the CDC through Italy’s Medicines Agency importation procedures.

The National Reference Center for Botulism (NRCB) at the Istituto Superiore di Sanità (ISS) in Rome performs an active surveillance of the disease with laboratory confirmation of suspected cases, by performing additional microbiological analysis on clinical, environmental, food samples and by collecting clinical and epidemiological data regarding the patients. Further, data and informations from this activity have to be completed with other clinical aspects and spread to improve the knowledge and the management of IB in Italy.

The project will consider different aspects of IB so it will be structured in three WPs:

WP1: Educational program

The main objective is to improve the knowledge on the disease by training physicians (pediatricians, neurologists, and clinical toxicologists) to look out for the possible presence of IB cases and improving public awareness through a prevention program. In Italy knowledge should be improved by the standardization and dissemination of therapeutic protocols, including treatment with the specific drug, BIG IV, and other therapeutics measures.
Scientists of California Department of Health Service, Infant Botulism Treatment and Prevention Program will collaborated in the definition of the program of the training courses and will participate as experts in workshops.

**Scientific responsible for the WP1:**
Davide Lonati and Carlo Locatelli
Institute of Toxicology, Poison Center and National Toxicology Information Center, University of Pavia and Maugeri Foundation, Via Maugeri 10, 27100 Pavia, Italy, Phone: +39038224444 (Poison Center) (24-h), Phone: +390382556600 (Research Center), Fax: +39038224605, E-mail: cnit@fsm.it, website: www.cavpavia.it

**WP2: Molecular methods**

The aim of this WP is to develop rapid molecular biological methods (conventional and Real-Time PCR) for detecting BoNTs producing clostridia in clinical samples to obtain a rapid diagnosis of the disease.

**Scientific responsible for the WP2:**
Dario De Medici
Senior Researcher – Centre for Food Quality and Risk Assessment – Istituto Superiore di Sanità E-mail dario.demedici@iss.it

**WP3: NRCB Website on Infant Botulism**

This WP deals with the dissemination of collected data on clinical and microbiological aspects of cases. All the informations will be easily available on the Internet that could be consulted by all stakeholders.

**Scientific responsible for the WP3:**
Lucia Fenicia
Senior Scientist - National Reference Center for Botulism - Centre for Food Quality and Risk Assessment – Istituto Superiore di Sanità – E-mail fenicia@iss.it