TRIAL TO REDUCE IDDM IN THE GENETICALLY AT-RISK (TRIGR)
http://www.trigr.org/

Description of Project

- The overall primary objective of this multi-center, international study is to determine whether weaning to a casein hydrolysate formula during the first 6-8 months of life in place of cow's milk based formula reduces the incidence of autoimmunity and type 1 diabetes in genetically susceptible newborn infants. This study was undertaken to confirm data derived from a human pilot study in Finland which was based on evidence from rodent models. The current study is taking place at 62 sites in 14 countries, including the United States and Canada.
    - The first specific aim is to determine whether weaning to the casein hydrolysate reduces the frequency of diabetes predictive autoantibodies by the age of 6 years in subjects with risk-associated HLA genotypes who have a first-degree relative with type 1 diabetes.
    - The second aim is to determine whether weaning to a casein hydrolysate reduces the cumulative incidence of clinical diabetes in subjects with risk-associated HLA genotype and an affected first-degree relative over a 10-year follow-up period.
    - The study requires the recruitment of 6,200 newborn infants for HLA screening of cord blood in order to recruit 2,800 infants who will be randomized to a weaning diet of either a casein hydrolysate formula or a standard cow milk formula.
    - This trial is the first international double-blind randomized nutritional intervention study for the primary prevention of type 1 diabetes.
    - Subjects will be followed during and after a 6-8 month intervention period for 6 and 10 years during which serologic markers are measured and the development of diabetes will be recorded. Recruitment is carried out during an approximately 2.5-3 year period in the United States (six centers), Canada (14 centers), 11 European countries and Australia.

Accomplishments

- The Data Management Unit (DMU) for TRIGR has established an entirely web-based data management system for world-wide study management, including study monitoring, data entry and quality assurance reporting. It has the capability of receiving and storing many different types of data, including clinical, genetic, dietary, and immunological data. Online desktop videoconferencing capability exists for education and coordination of study management.
- The first European child was registered and randomized on May 8, 2002, and the first North American one on June 11, 2002. As of May, 2004, 2,104 mothers of prospective subjects have been registered, and 746 babies eligible by HLA criteria have been enrolled, comprising 45% of those babies with their HLA genotyping results available. This figure is the predicted proportion eligible. Of the 2,104

mothers, 446 were registered in the United States. Of the 746 eligible babies in TRIGR, 140 have been enrolled in the United States.

- Establishment of TRIGR laboratories:
    - HLA typing laboratories have been set up in both Finland and Pittsburgh to serve Europe and North America, respectively.
    - A TRIGR CORE laboratory has been established in Helsinki for analyzing cow milk antibodies and for appropriate storage of serum samples for subsequent assays of diabetes-associated autoantibodies.
- Nutritional Advice Booklet:
    - The ICC in Helsinki, in collaboration with dietitians from Europe and North America, has produced an internationally acceptable parent training booklet and nutritional questionnaires organized as computer forms translated into the languages required and verified.
- Five abstracts have been submitted to three different scientific meetings.

Future directions

- Complete recruitment within 2 years;
- Perform mechanistic and ancillary studies;
- Unravel the complex potential mechanisms of islet cell autoimmunity and how these may be influenced by dietary proteins;
- Assess the potential role of enteroviral insults and of nutritional influences in the newborn diet, other than cow's milk, on a observational basis by interacting with the TEDDY Consortium wherever possible;

Material to be made available to researchers

- Material could be available to the scientific community after the completion of the 10 year follow-up of the study subjects after submission of the appropriate requests to the TRIGR Study Group.

Participants

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Academy of Finland
Finnish Diabetes Association
Canadian Institutes of Health Research
European Foundation for the Study of Diabetes
European Union
Juvenile Diabetes Research Foundation
Netherlands Diabetes Foundation
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Participating Institutions

TRIGR is comprised of 62 centers in Canada, the United States, Europe and Australia. For a complete listing of cities that have a participating institution, please visit http://www.trigr.org/centres.html.