TEDDY – The Environmental Determinants of Diabetes in the Young: An Observational Clinical Trial

William A. Hagopian, Åke Lernmark, Marian J. Rewers, Olli G. Simell, Jin-Xiong She, Anette G. Zeigler, Jeffrey P. Krischer, and Beena Akolkar

- Type 1 diabetes mellitus (T1DM) is a common pediatric disease. In some parts of the world (like Scandinavia), it is more common than in other areas, and we're not completely sure why.
- T1DM is caused in part by a person's genetics. The most important genes that are known to increase the risk T1DM are called HLA genes.
- Based on previous studies, we know that there are also environmental causes for T1DM, but we are not very sure what they are or how they work.
- In six study centers throughout the United States and Europe, newborn children were tested for their HLA genes. Those children who have HLA genes with a higher risk of getting T1DM were asked to be followed by the TEDDY Study.
- As of 2006, many children are being followed by the TEDDY Study and the study is going very well.

Environmental factors in the development of Type 1 diabetes

Hui Peng and William Hagopian

- Previous studies have shown that type 1 diabetes mellitus (T1DM) is caused half by genetic factors and half by environmental factors.
- If we could find the environmental causes of T1DM, we could then avoid them and potentially reduce the prevalence of T1DM in very simple ways.
- There are likely to be many different environmental causes which cause T1DM, some more important than others.
- Many studies have suggested some environmental causes of T1DM, including infections, early diet, nutrient deficiencies, stress, and others.
- These studies were not able to conclusively prove which of these factors cause T1DM, and a study like TEDDY is needed to see which factors are most important.

The Environmental Determinants of Diabetes in the Young (TEDDY) study: study design

The TEDDY Study Group

and

The Environmental Determinants of Diabetes in the Young (TEDDY) Study

The TEDDY Study Group

- Most of our understanding of type 1 diabetes mellitus (T1DM) comes from studies of people with T1DM or relatives of those with the disease. However, 85-90% of people who get T1DM have no family history of the disease.
- The TEDDY Study was designed to follow children with and without a family history of T1DM to understand what environmental factors contribute to the disease. Children in the study will be followed very closely from birth to 15 years old.
- Data collected in the study will include collection of medical information, blood samples, stool samples, drinking water, diet records, and measurements of psychological stress.
- The TEDDY Study Group predicts that T1DM will be linked to early infections, differences in the timing of food introduction, certain vitamin deficiencies, immunizations, certain characteristics of drinking water, exposure to pets and other allergens, excessive weight gain, and increased stress.
- While some aspects of the data analysis will occur while the study is ongoing, much of the major analysis will not begin until all of the data has been collected.

Trans-Atlantic data harmonization in the classification of medicines and dietary supplements: A challenge for epidemiologic study and clinical research
Susan Moyers, Rachel Richesson, Jeffrey Krischer

- In studies like the TEDDY Study, it is important to be able to accurately record what types of medications and dietary supplements our subjects take.
- Currently, there is no internationally standard way of collecting this data, as various different databases use different definitions for what a medication or a dietary supplement is.
- The TEDDY Study has decided to use the RxNorm database to classify the medications taken by our subjects.
- There is no database for dietary supplements which fit the needs of the TEDDY Study, so instead we have created our own database which we have modeled after RxNorm.
- If internationally recognized standards for collecting this information arise, the TEDDY Study is ready to convert to these new standards.

Achieving Standardized Medication Data in Clinical Research Studies: Two Approaches and Applications for Implementing RxNorm
Rachel L. Richesson, Susan B. Smith, Jamie Malloy, Jeffrey P. Krischer

- The Pediatric Epidemiology Center (PEC) at the University of South Florida is the computerized data center for the TEDDY Study as well as the Rare Disease Clinical Research Network (RDCRN), a collection of about 50 individual studies.
- The TEDDY Study and the RDCRN both need to record what medications people take, but these studies have different ways of doing it.
- RxNorm is a computerized index of medications, describing active ingredients, brand names, and doses of all medications.
- The TEDDY study is only interested in recording the active ingredients of medications. The PEC has developed numerical codes for RxNorm's list of active ingredients in a way that is easy for the TEDDY Study staff to use.
- Some studies in the RDCRN are interested in active ingredients of medications only, while others are interested in doses of medications as well. The PEC has developed a way for RDCRN staff to search RxNorm in a way that is tailored to their needs.

Harmonization of Glutamic Acid Decarboxylase and Islet Antigen-2 Autoantibody Assays for National Institute of Diabetes and Digestive and Kidney Disease Consortia

Ezio Bonifacio, Liping Yu, Alastair K. Williams, George S. Eisenbarth, Polly J. Bingley, Santica M. Marcovina, Kerstin Adler, Anette G. Zeigler, Patricia W. Mueller, Desmond A. Schatz, Jeffrey P. Krischer, Michael W. Steffes, and Beena Akolkar
Published in *The Journal of Clinical Endocrinology & Metabolism* in 2010

- Islet autoantibodies are commonly used in type 1 diabetes mellitus (T1DM) research to identify those who are at risk of getting the disease. In the TEDDY Study, we measure the levels of three autoantibodies in the blood of our subjects.
- The TEDDY Study has two labs which perform these measurements, one in the United States and one in Europe.
- These two labs did not always agree on whether or not a sample tested positive or negative for these autoantibodies.
- The two labs standardized their measurement procedures and re-calibrated the way they report their results so that they performed their measurements in the same way.
- After this harmonization, the two labs get much more similar results when determining if a blood sample tests positive or not for islet autoantibodies.

Accelerated progression from islet autoimmunity to diabetes is causing the escalating incidence of type 1 diabetes in young children

Anette-G. Zeigler, Maren Pflueger, Christiane Winkler, Peter Achenbach, Beena Akolkar, Jeffrey P. Krischer, Ezio Bonifacio
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- Type 1 diabetes mellitus (T1DM) is becoming more prevalent each year.

- BABYDIAB is a German study which is set up very similar to the TEDDY Study. BABYDIAB started following children 15 years before the TEDDY Study began.
- This paper compares relatives of type 1 diabetics (called first degree relatives or FDRs) in BABYDIAB to German FDRs in TEDDY. All of the children used in this publication tested positive for islet autoantibodies before the age of four years old.
- Children in the two studies began testing positive for islet autoantibodies at the same rate. However, autoantibody positive children in the TEDDY Study went on to develop T1DM more rapidly than those in the earlier BABYDIAB Study.
- These results indicate that the nature of T1DM in young FDR children has changed in recent years. It appears that in Germany, young, autoantibody positive children are more likely to rapidly progress to T1DM than in years past.