Trial to Reduce IDDM in the Genetically at Risk

Autumn 2004

TRIGR Newsletter

Mikael Knip
Professor of Pediatrics
Deputy Principal Investigator, M.D.

WHY IS THE INCIDENCE OF CHILDHOOD TYPE 1 DIABETES INCREASING IN THE DEVELOPED WORLD?

Recent data indicate that the incidence of type 1 diabetes is increasing in most industrialized countries, at least among children under the age of 15 years. E.g. from Finland we have data showing that the incidence rate has risen from 12/100,000 children in 1953 up to 54 in 2003 implying that the incidence has increased 4.5-fold over a time period of 50 years. One may ask whether such a change reflects a true increase in lifelong disease rate or is due to disease presentation at a younger age. A Swedish survey tried a few years ago to find an answer to this question and reported that there was no significant increase in incidence among people under the age of 35 years over a 16-year time period from 1983 to 1998. The average age at diagnosis dropped, however, during that time period by 2.5 years among boys and by 1.5 years among girls, resulting in an increased incidence among those under the age of 15 years. A similar preliminary analysis in Finland indicates that there has been a significant increase in incidence in the age group under the age of 30 years over a 30-year period, but that the increase has been steeper among those younger than 15 years of age. This suggests that we witness in parallel an increase in disease rate and disease presentation at an ever younger age. Both these phenomena indicate that the diabetogenic pressure related to environmental factors and life style has increased in the developed countries after World War 2.

An open question is why type 1 diabetes is becoming more frequent among children. At this point of time there is no generally accepted explanation to this development. The situation is very similar to that seen in relation to asthma and other allergic disorders, which are like type 1 diabetes immune-mediated diseases. Also those disorders have become more and more common among children over the last 50-60 years.

The hygiene hypothesis has gained quite substantial support as a tempting explanation to the increasing rate of allergic disorders. The hypothesis postulates that the decrease and change in microbial exposure seen in the industrialized countries over the last half a century due to increased standard of hygiene has resulted in a situation, where the immune system has to start to look for new stimuli as a consequence of the decreasing frequency of microbial infections. This may trigger immune responses targeting either foreign environmental substances to which individuals are exposed through air or food or the organism's own tissues, such as the insulin-producing cells in the pancreatic islets. It is highly unlikely that there is only

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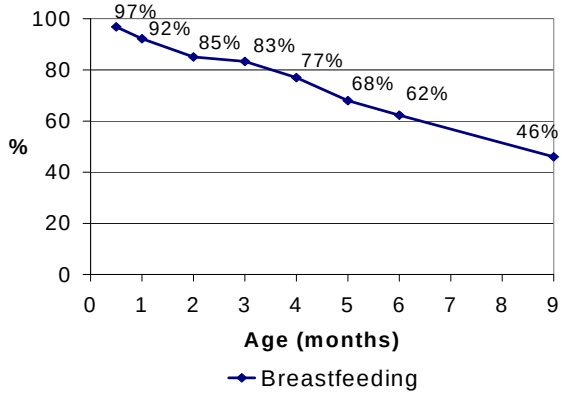
one reason to the increasing rate of type 1 diabetes and allergic disorders. Most likely there are a series of interacting factors contributing to this phenomenon. In some, so far unknown way these factors must be related to the increased prosperity and changes in lifestyle that have occurred over the last 50 years in the developed countries.

The increasing incidence rate of type 1 diabetes emphasizes the importance of identifying means to reduce the risk of the disease. TRIGR represents such an attempt, and if the early nutrition intervention studied in TRIGR turns out to have an effect on the risk of type 1 diabetes, as all of us do hope, that will represent a breakthrough in how the risk of type 1 diabetes could be reduced. Accordingly the families taking part in TRIGR give their own valuable contribution to the work aimed at finding safe and effective ways of decreasing the risk of this disease. From that point of view all of you represent true heroes in everyday life.

BREASTFEEDING NEWS - RESULTS FROM FINLAND

We are interested in how well breastfeeding is implemented among the TRIGR families. Therefore we have analyzed data from dietary interviews from 162 Finnish TRIGR babies who were born before the end of year 2003. Here are some results showing that breastfeeding is going well!

At 2 weeks of age almost all of the TRIGR babies were breastfed. As shown in the figure below breastfeeding declined slowly with age. At 3 months of age 83% were breastfed and at 6 months of age 62%. At 9 months of age almost half of the children were still breastfed.



There is still very little research information about the course of breastfeeding among mothers with type 1 diabetes. Diabetic mothers may experience difficulties in starting breastfeeding. However, a previous study showed that there was no significant difference in the amount of breast milk between diabetic mothers and mothers without diabetes. When we look at the duration of breastfeeding among the Finnish TRIGR mothers, it seems that mothers with type 1 diabetes breastfeed for a shorter period than mothers without diabetes. Among Finnish mothers included in this analysis, 60 mothers had type 1 diabetes and 102 did not have diabetes. At 9 months from delivery, 34% of the diabetic mothers and 53% of non-diabetic mothers were still breastfeeding. When we get more data from all the TRIGR countries, we can take a more detailed look at this issue.

Liisa Vähätalo
M.Sc. Research Assistant

Sonja Bärlund
M.Sc. Nutrition fellow

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TRIGR statistics

Our target in the TRIGR trial is to screen altogether 4516 children and our estimation is that 2032 randomized children should continue in the study after genetic HLA screening. By the end of September 2004 we are over half way trough and the study is on schedule. So far 2748 mothers have been registered and 2375 children randomized. Out of the randomized children 1021 continued in the study after the genetic screening. Somewhat more subjects were HLA ineligible and for several children we are still waiting for the HLA results.

		Randomized Children				
Region	Registered Mothers	Total	*Ineligible Children	HLA Results Not Available	HLA Ineligible	HLA Eligible
North America	1309	1096	31	59	541	465
Europe and Australia	1439	1279	17	29	675	556
	2748	*2375*	*48*	*88*	*1216*	*1021*

*Child does not fulfil participation criteria

Families in the study

The family history of the children who are continuing in the study at the end of September 2004 is presented in the table below. We have a little bit more families participating where the mother is affected by type 1 diabetes than families where the father is affected. Families with the mother affected are 482 and families with the father affected are 351. At the moment 140 families are participating where a sibling of the subject is affected by type 1 diabetes. In some families more than one family member has type 1 diabetes.

	Family Member With Type 1 Diabetes				
Region	Mother	Father	Sibling	More Than 1 Family Member	Total
North America	236	133	73	23	465
Europe and Australia	246	218	67	25	556
Total	*482*	*351*	*140*	*48*	*1021*

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The Principal Investigator of the TRIGR project, Emeritus professor Hans K. Åkerblom was promoted to the *Doctor of Medicine Honoris Causae* degree of the Medical Academy of Wroclaw on September 30, 2004. The degree was bestowed on him due to his achievements in furthering research on childhood diabetes in Poland and incorporating Polish type 1 diabetes research centers into international research efforts to prevent the disease. The ceremony took place in the magnificent "Aula Leopoldina" of the University of Wroclaw in connection with the opening of the academic year.

On the left you see the best motivation source we have. We are very grateful to all of you families who are in our trial, and we do hope that you are as keen as we are to reach our common goal.