

Enrollment Still Open for Largest Worldwide Study of Type 1 Diabetes

Expectant mothers who meet the criteria are encouraged to enroll.

BY LAURA SUAREZ, MANAGING EDITOR

Currently the largest international study, the Trial to Reduce Insulin-dependant diabetes in the Genetically at Risk (TRIGR), is in the process of enrolling expectant mothers whose offspring may be at a high genetic risk for type 1 diabetes.

TRIGR is aimed at reducing the incidence of type 1 diabetes in children. Noticed as early as the 1980s, exclusively breastfed babies with a high genetic risk for type 1 diabetes seemed to develop the disease at a slower rate than babies who were bottle fed, said Margaret A. Franciscus, RN, BSN, in an interview with *DIABETIC MICROVASCULAR COMPLICATIONS TODAY*. Ms. Franciscus is the North America TRIGR study coordinator. "Researchers decided to start looking at the first foreign proteins that are introduced to babies. These are intact cow milk proteins found in infant formulas."

PILOT STUDY IN FINLAND

TRIGR began as a pilot study to determine the association between infant formula consumption and the development of type 1 diabetes. Initiated in Helsinki, Finland, from 1999 to 2000, principal investigator Professor Hans Akerblom and colleagues confirmed results from a rodent study suggesting that mice fed a hydrolyzed formula – formulas that break down cow milk protein into smaller molecules – versus a standard weaning formula developed diabetes at a lower rate.

The current randomized trial will include children from more than 70 centers worldwide (Tables 1, 2 and 3), with six in the United States and two in Germany, and will again test the hypothesis that hydrolyzed infant formulas lower the risk of type 1 diabetes in children with a predisposed risk of developing the disease.

"When babies are breastfed the mother digests the

Investigators are urging practitioners to encourage patients who fit the study criteria to enroll in TRIGR.

milk, whereas if you give them a bottle of milk it is intact protein," said Dorothy Becker, MBBCh, North America principal investigator of TRIGR, at the American Medical Association (AMA) Media Briefing, Diabetes: Understanding and Advancements. Investigators believe that larger intact cow milk proteins may cause destruction of beta cells and trigger diabetes in those with a predisposed risk.

Because TRIGR is the largest study of its kind, investigators are urging practitioners to encourage patients who fit the study criteria to enroll. In addition to current pregnancy, the child-to-be-born must have a first-degree relative with type 1 diabetes. Only infants born after 35 weeks with antibodies predisposing type 1 diabetes will remain valid study participants. Enrollment began in May 2002 and will continue until the late spring/early summer.

INITIAL ENROLLMENT

Although 1,637 babies who fit the study criteria are currently enrolled, Dr. Becker said that the study aims to enroll 2,052 who are genetically susceptible to type 1 diabetes. This means that more than 6,000 pregnant women would need to initially enroll in the trial. Over 4,300 women have already enrolled. Barbel Aschemeier, MPH, nurse coordinator at Germany's two enrolling centers (Berlin and Hannover), said that approximately

TABLE 1. NORTH AMERICAN PARTICIPATING TRIGR CENTERS (21)

Canada (15)		United States (6)
Calgary, Alberta	Regina, Saskatchewan	Los Angeles
Edmonton, Alberta	Saint John, New Brunswick	New York
Halifax, Nova Scotia	St. John's Newfoundland	Pittsburgh
Kingston, Ontario	Saskatoon, Saskatchewan	Ponce, Puerto Rico
London, Ontario	Toronto	Seattle
Montreal	Vancouver, British Columbia	Saint Louis
Ottawa, Ontario	Winnipeg, Manitoba	
Quebec City, Quebec		

Source: trigr.epi.usf.edu/centres.html

70 women have enrolled each year at the centers; she hopes to enroll 70 more by the deadline.

"Families should have time for careful consideration prior to their final decision regarding trial participation," Ms. Aschemeier told *DIABETIC MICROVASCULAR COMPLICATIONS TODAY*, in an interview. People who agree to participate through the German centers attend an "information talk" where a TRIGR physician and nurse explain the study. Through these talks, which according to Ms. Aschemeier are relaxed, participants can feel confident about their decision to participate.

"The benefit of this study is not directly applicable for the population suffering of type 1 diabetes," she added. "Hopefully the outcome of this will be beneficial for the general population, in short, to reduce the incidence of type 1 diabetes."

"If [the study] works, the big picture is that maybe we could decrease – if not prevent – diabetes around the world," Dr. Becker said at the AMA media briefing. She is from the division of endocrinology, diabetes and metabolism, department of pediatrics, Children's Hospital of Pittsburgh, University of Pittsburgh School of Medicine.

Participants have the option to breastfeed their babies for the first 6 months of the study, however they are then randomly assigned to one of two formulas to use for 2 additional months (standard cow's milk-based formula or hydrolyzed formula [Nutramigen, Mead Johnson, Evansville, Ind]). If mothers do not wish to initially breastfeed, they are randomly assigned to one of the formulas for 6 months.

PRESENCE OF ANTIBODIES

Infants will then be followed for 10 years to assess the difference in type 1 diabetes development between the standard formula group and the hydrolyzed formula group. Investigators from the United States, Canada, Europe and Australia will look for the earliest immunological signs of type 1 diabetes in the bloodstream, particularly the presence of antibodies specific to the onset of diabetes. If the investigators' hypothesis is correct, it may be possible to decrease or eradicate the rate of type 1 diabetes with a hydrolyzed infant formula. Preliminary results will not be known for another 2 to 3 years.

"If indeed it is true that if something as simple as the formula could be changed to help babies that are at risk for type 1 diabetes – to either prevent it or delay progression – it would have an enormous effect economically and socially on the world," said Ms. Franciscus. "The impact would be absolutely tremen-

TABLE 2. AUSTRALIAN PARTICIPATING TRIGR CENTERS (3)

Newcastle, New South Wales
Randwick, New South Wales
Westmead, New South Wales

Source: trigr.epi.usf.edu/centres.html

TABLE 3. EUROPEAN PARTICIPATING TRIGR CENTERS (46)

Czech Republic (5)	(Finland cont'd)	Italy (2)	Spain (2)
Brno	Kuopio	Rome	Baracaldo-Vizcaya
Ceske Budejovice	Lahti	Cagliari	Madrid
Olomouc	Lappeenranta		
Prague	Oulu	Luxembourg (1)	Sweden (10)
Usti Nad Ladem	Pori	Luxembourg	Boras
	Mikkeli		Gothenburg
Estonia (2)	Seinajoki	Netherlands (1)	Halmstad
Tallinn	Tampere	Rotterdam	Jonkoping
Tartu	Vaasa		Karlskona
		Poland (4)	Linkoping
Finland (15)	Germany (2)	Katowice	Norrkoping
Espoo	Berlin	Krakow	Orebro
Hameenlinna	Hannover	Lodz	Trollhattan
Helsinki		Wroclaw	Uddevalla
Hyvinkaa	Hungary (1)		
Jyvaskyla	Budapest		Switzerland (1)
Kotka			Zurich

Source: trigr.epi.usf.edu/centres.html

dous on people that have a family history of type 1 diabetes.

NATIONAL, INTERNATIONAL FUNDING

The \$25-million multinational trial is jointly funded by several national and international organizations including the National Institute of Child Health and Human Development, the Canadian Institutes of Health Research, the European Foundation for the Study of Diabetes, the European Union, the Netherlands Diabetes Foundation and the Juvenile Diabetes Research Foundation International. The study has received a superb priority score from the U.S. National Institutes of Health.

PARTICIPATE IN RESEARCH

"People are always saying 'When are they going to find a cure for type 1 diabetes?' But, if you don't help find a cure by participating in research, it will be longer and longer before we find one," Ms. Franciscus said. "You cannot wait and depend on other people to participate for you."

For general information, call 1-888-STOP-T1D (1-888-786-7813). For more information in the United States, visit www.trignorthamerica.org or call Margaret Franciscus at 412-692-5250 if you have patients who are interested in enrolling. For more information in Europe and Australia, visit trigr.epi.usf.edu or call Matti Koski, MSc at +358 9 191 25207 for enrollment. ■

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