

Association Between Type I Diabetes and Haemophilus Influenzae Type B Vaccination: Birth Cohort Study

The temporal association between *Haemophilus influenzae* type b (Hib) vaccination and the development of type I diabetes in Finland was studied. The risk of type I diabetes was compared among 3 Finnish birth cohorts: those born within 24 months before the Hib vaccination trial (ie, historical controls); those vaccinated at 3 months of age and with a booster at 14 to 18 months of age; and those vaccinated only at 24 months of age. The unvaccinated cohort included 128,936 children; the 2 vaccine-eligible cohorts totaled 116,352 children. No significant differences were found at any time during the 10-year follow-up in risk of type I diabetes between the children born before the vaccination period and those vaccinated at the age of 24 months only (risk ratio 1.01; $P=0.228$). The difference in the risk between children vaccinated first at the age of 3 months and those vaccinated only at the age of 24 months also was not statistically significant (risk ratio 1.06; $P=0.545$). The authors conclude that "based both on randomized design and on the use of historical controls," it is unlikely that Hib vaccination or its timing is related to type I diabetes in Finnish children.

Karvonen M, et al. *Br Med J* 1999;318:1169-1172.

Editor's comment: *Insulin-dependent diabetes mellitus (IDDM) has been increasing in Finland over the last 3 decades. In children under 14 years of age, there has been a 2% to 5% per year increase, with a prevalence of 45/100,000 reached in 1996. This incidence is perhaps one of the highest in the world. During this*

period, children also were given an increased number of vaccines, including Hib immunizations. However, this study provides ample evidence that the concomitant expansion of Finland's childhood immunization program, at least in regard to Hib, is not responsible for the increased incidence of IDDM. The temporal association between the 2 variables does not seem to indicate that there is a cause-and-effect relationship. Unfortunately, the media, including a major segment on "ABC World News" on September 25, 1998, have reported on the alleged association between Hib vaccine and the development of this disease. I wish that the report by Dr. Karvonen and colleagues would receive equal time so that the public would not be needlessly concerned. The beneficial effects of Hib vaccination are well proven, and it would be unjustified to restrict vaccination because of potential adverse consequences that have not been proven to exist.

In addition, other studies have found no increase of type I diabetes in association with various vaccines used in childhood, including measles, BCG, and pertussis vaccines.

Fima Lifshitz, MD

Blom L, Dahlquist G. *Diabetologia* 1991;34:176-181.

Dahlquist G, Gothefors L. *Diabetologia* 1995;38:873-874.

Heijbel H, et al. *Diabetes Care* 1997;20:173-175.

Parent M-E, et al. *Diabetes Care* 1997;20:767-772.

Cow's Milk Formula Feeding Induces Primary Immunization to Insulin in Infants at Genetic Risk for Type I Diabetes

Insulin autoantibodies (IAAs) often appear as the first sign of islet cell autoimmunity in prediabetic children. Because cow's milk contains bovine insulin, the authors followed the development of insulin-binding antibodies in children fed with cow's milk formula. Bovine insulin- and human insulin-binding antibodies were analyzed by enzyme immunoassay (EIA) and IAAs were analyzed by radioimmunoassay (RIA) in 200 infants carrying *HLA-DQB1*0302* but no protective alleles. These children participated in a Finnish population-based birth cohort study. Based on the prospectively registered information, the first 100 infants (group 1) enrolled in the study who were exposed to cow's milk formula before age 12 weeks and the first 100 infants (group 2) enrolled in the study who were exclusively breast-fed for longer than the first 12 weeks of life were selected for the present study. Also studied were 11 children from the 200 infants who had developed at least two diabetes-associated autoantibodies, 98 children with newly diagnosed type I diabetes, and 92 healthy children. The authors reported that the amount of IgG antibodies binding to bovine insulin was higher at age 3 months in infants who were exposed to cow's milk formula than in infants who were exclusively breast-fed before and at 3 months of age (median, 0.521 vs 0.190; $P<0.0001$). The antibodies binding to bovine insulin cross-reacted with human insulin. None of these infants tested positive for IAAs. The levels of bovine insulin-binding antibodies declined in both groups at age 12 and 18 months; in the 11 children with at least two diabetes-associated autoanti-

bodies, the levels increased during the follow-up period ($P<0.0001$). IgG antibodies correlated with IgG2 antibodies binding to bovine insulin ($r=0.43$, $P=0.004$) and IAAs ($r=0.27$, $P=0.02$) in diabetic children, but not in healthy children.

The authors concluded that cow's milk feeding is an environmental trigger of immunity to insulin in infancy that may explain the epidemiologic link between the risk of type I diabetes and early exposure to cow's milk formulas. This immune response to insulin may later be diverted into autoaggressive immunity against beta cells in some individuals, as indicated by these findings in children with diabetes-associated autoantibodies.

Vaarala O, et al. *Diabetes* 1999;48:1389-1394.

Editor's comment: *Many studies have linked cow's milk consumed by infants to subsequent diabetes. The association is*

Please Send Correspondence to:

Robert M. Blizzard, MD
University of Virginia, The Blake Center
1224 West Main Street, 7th Floor, Suite 701
Charlottesville, VA 22903