Relationship Between Dairy Product Consumption and Incidence of IDDM in Childhood in Italy

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OBJECTIVE — To test the hypothesis that the consumption of dairy products, including fluid cows' milk and cheese, is related to the incidence of insulin-dependent diabetes mellitus (IDDM), we correlated incidence rates in children 0–14 years of age with cows' milk and cheese consumption in nine regions of a single country, Italy.

RESEARCH DESIGN AND METHODS — Data on the incidence of IDDM were derived from the only nine Italian regions where primary and secondary sources of ascertainment were available for 1991. Data on fluid cows' milk and cheese consumption in the corresponding year in each region were obtained from the National Institute of Statistics.

RESULTS — The correlation between fluid milk consumption and incidence of IDDM in Italy was 0.84 ($P < 0.004$, Poisson regression analysis). Cheese consumption was not related to IDDM incidence.

CONCLUSIONS — The results indicate that there is a relationship, even in a single country, between dairy product consumption and the incidence of IDDM that is confined to fluid milk consumption. Cows' milk may contain a triggering factor for the development of diabetes, but the high incidence of IDDM in Sardinia and in other countries worldwide cannot be explained simply by the quantity of fluid cows' milk consumed.

Insulin-dependent diabetes mellitus (IDDM) is caused by destruction of the insulin-secreting islet cells, possibly mediated by an immune process (1). This immune process is thought to be induced by the interaction of genetic and environmental factors (2). The nature of the environmental factors is unclear, but recent evidence indicates that early exposure to dairy products may be important (3). The hypothesis that exposure to dairy products may cause IDDM derives from epidemiological studies, supported by evidence from animal models of diabetes, which have implicated both bovine albumin and casein (4,5). Recent meta-analysis of case-control studies indicated that the incidence of IDDM could be reduced by 40% if cows' milk was eliminated from the diets of children during their first 3 months of life (6). There is a strong linear correlation between the incidence of IDDM in different populations worldwide and their fluid cows' milk consumption (7). To define the relationship between consumption of dairy products, including the quantity of fluid cows' milk and cheese, and the incidence of IDDM, we studied their correlation in nine regions of a single country, Italy.

RESEARCH DESIGN AND METHODS

— We considered data for 1991 on the incidence of IDDM in children 0–14 years of age and on cows' milk and cheese consumption in families in nine regions of Italy. Data on incidence of IDDM were obtained from registries of all new cases diagnosed in those <15 years of age. Nine Italian regions were chosen because they were the only regions where data on IDDM incidence had primary and secondary sources of ascertainment. These 9 of the 20 Italian regions cover the north, center, and south of Italy and its islands. Incidence data for IDDM in children 0–14 years of age in four regions (Lombardy, Lazio, Sardinia, and Sicily) were derived from EURODIAB Subarea A study (8). Data from the regions Marche (9), Liguria (10), Abruzzo (11), and Campania (12) were previously published and vary between $5.3 \cdot 100{,}000^{-1} \cdot \text{year}^{-1}$ for Campania (lowest incidence) and $30.2 \cdot 100{,}000^{-1} \cdot \text{year}^{-1}$ for Sardinia (highest incidence). Finally, data from Piedmont were kindly given by Dr. Bruno

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Received for publication 15 April 1994 and accepted in revised form 13 July 1994.

IDDM, insulin-dependent diabetes mellitus.

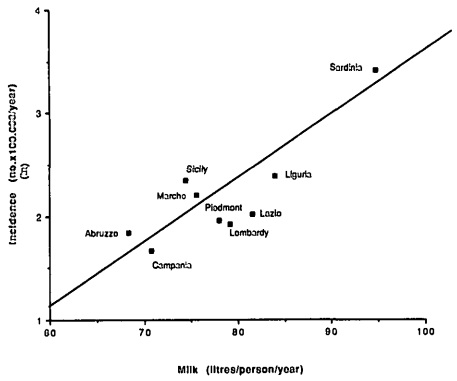

Figure 1—*The correlation between IDDM incidence (children 0–14 years of age) and fluid cows' milk consumption in nine Italian regions ($P < 0.004$, Poisson regression analysis).*

and colleagues and collected using the same sources of ascertainment described elsewhere (13). Data on fluid cows' milk and cheese consumption per person in the corresponding year for each region were derived from ISTAT (National Institute of Statistics, Italy) (14). These data were collected by means of diet histories using standardized interviews taken from 34,000 families in each region.

RESULTS— Figure 1 shows the association between cows' milk consumption per person and the incidence of IDDM in children 0–14 years of age in 1991 in nine different regions in Italy. The correlation between milk consumption and the incidence of IDDM was statistically significant (correlation coefficient, 0.84; $P <$ 0.004, Poisson regression analysis). The incidence of IDDM in Sardinia was substantially higher than that in other Italian regions. Cheese consumption in the nine regions did not correlate with either milk consumption or with the incidence of IDDM.

CONCLUSIONS— Epidemiological studies relating disease incidence with environmental factors may be biased as a result of genetic and environmental differences between populations (2). In addition, methods for estimating both disease incidence and exposure to environmental factors may differ among different populations. To limit these biases and to further define the proposed relationship between the consumption of dairy products and the incidence of IDDM, we studied these factors in a single population. Our results from the Italian population confirm a strong relationship between fluid cows' milk consumption and IDDM incidence. This correlation in a single country (Italy) is consistent with a linear regression model previously described and based on worldwide incidence data (7). That model was derived from a number of countries worldwide, but Italy was not included. However, it should be pointed out that Sardinia has an incidence rate of $30 \cdot 100{,}000^{-1} \cdot \text{year}^{-1}$, which is similar to that in Finland, but the milk consumption in Sardinia ($94.8\ \text{l} \cdot \text{person}^{-1} \cdot \text{year}^{-1}$) is substantially lower than that in Finland ($>200\ \text{l} \cdot \text{person}^{-1} \cdot \text{year}^{-1}$) (15). Thus, the relationship between the quantity of cows' milk consumption and IDDM incidence is not a simple one and probably involves other factors. To further define this relationship, we compared, for the first time, the disease incidence with a dairy product other than fluid cows' milk, namely, cheese. We found no relationship between cheese consumption and IDDM incidence.

We conclude that the relationship between dairy products and IDDM incidence is confined to the quantity of fluid cows' milk consumed and can be detected even within a single population.

References

1. Muir A, Schatz MD, Maclaren NK: The pathogenesis, prediction and prevention of insulin-dependent diabetes mellitus. *Endocrinol Metab Clin North Am* 21:199–219, 1992
2. Tajima N, Matsushima M, La Porte RE: Population studies. In *Causes of Diabetes*. Leslie RDG, Ed. Chichester, U.K., Wiley, 1993
3. Virtanen SM, Rasanen L, Ylonen K, Aro A, Clayton D, Langholz B, Pitkaniemi J, Savilahti E, Lounamaa R, Tuomilehto J, Akerblom HK: Early introduction of dairy products associated with increased risk for insulin-dependent diabetes mellitus in Finnish children. *Diabetes* 42:1786–1790, 1993
4. Karjalainen J, Martin JM, Knip M, Ilonen J, Robinson BH, Savilahti E, Akerblom HK, Dosch H-M: A bovine albumin peptide as a possible trigger of insulin-dependent diabetes mellitus. *N Engl J Med* 327: 302–307, 1992
5. Elliott RB, Bibby N, Reddy S: Casein peptide precipitates diabetes in the non-obese diabetic mouse and possibly humans. In *Genetic and Environmental Risk Factors for Type I Diabetes (IDDM)*. Laron Z, Karp M, Eds. London, Freund, 1992, p. 57–62
6. Gerstein HC: Cow's milk exposure and type I diabetes. *Diabetes Care* 17:13–17, 1994
7. Dahl-Jorgensen K, Joner G, Hanssen KF: Relationship between cows' milk consumption and incidence of IDDM in childhood. *Diabetes Care* 14:1081–1083, 1991
8. Green A, Gale EAM, Patterson CC for the EURODIAB Study Group: Incidence of childhood-onset insulin-dependent diabetes mellitus: the EURODIAB ACE study. *Lancet* 2:905–909, 1992
9. Cherubini V, Cantarini M, Ravaglia E, Bartolotta E: Incidence of IDDM in the Marche Region, Italy. *Diabetes Care* 17: 432–433, 1994
10. Mazzella M, Cotellessa M, Bonassi S, Mulas R, Caratozzolo A, Gaber S, Romano C: Incidence of type I diabetes mellitus in the Liguria region, Italy: results of a prospective study in a 0- to 14-year age-group. *Diabetes Care* 17:1193–1196, 1994
11. Verrotti A, Chiarelli F, Tumini S, Blasetti A, Altobelli E, Marzan M, Morgese G: WHO Diamond Study: epidemiologia del diabete tipo 1 in età pediatrica in Abruzzo negli anni 1990, 91, 92. In *Atti IX Congresso Società Italiana Endocrinologia e Diabetologia Pediatrica*. Milan, Italy, CSH, 1993, p. 128
12. Prisco F, Iafusco D, Palumbo F, Sagliocca L, Vicedomini D, Boccia C, Amodeo BM, De Felice E, Stoppoloni G: Incidenza in Campania del diabete mellito tipo I in

soggetti di età <14 anni nel triennio 1989–1991. *Diabete* (Suppl. 1):190–191, 1992
13. Bruno G, Merletti F, Vuolo A, Pisu E, Giorio M, Pagano G: Sex differences in incidence of IDDM in age group 15–29 yr: higher risk in males in Province of Turin, Italy. *Diabetes Care* 16:133–136, 1993
14. Istituto Nazionale di Statistica (ISTAT): *I consumi delle famiglie nell'anno 1991*. 28: 476–479, 1992
15. Muntoni S, Loddo S, Stabilini M, Stabilini L, Muntoni S. Cow's milk consumption and IDDM incidence in Sardinia. *Diabetes Care* 17:346–347, 1994