Letter to the Editor

Concordance Between Twins for β-Cell Autoimmunity

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Charles Verge et al. (1) draw attention to the important observation that concordance between identical twins for β-cell autoimmunity is much higher than is overt diabetes. It is probable that the disease process in IDDM encompasses a wide spectrum of immune and metabolic changes that do not always lead to diabetes.

IDDM-associated immune changes can be identified in nondiabetic twins several years after the diagnosis of diabetes in their index twins (2). Verge et al. (1) identified IDDM-associated antibodies (to insulin, GAD, and ICA512) in 8 of 12 nondiabetic twins, while a study by ourselves identified IDDM-associated antibodies in 12 of 31 twins (to islet cell antigen, GAD, and the 37-kDa antigen) (3). It is unlikely that these antibodies are mere epiphenomena, since metabolic changes can also be identified; 4 out of 15 of the American twins had a first phase insulin response (FPIR) below the control range, as did 5 of 15 British twins (1,4). Other studies have demonstrated immune and metabolic changes in nondiabetic twins several years after the diagnosis of IDDM in their co-twins, including increased levels of activated T-cells, increased expression of CD45R0 cells, hyperproinsulinemia, and impaired glucose tolerance (2,5).

These autoimmune and metabolic changes may presage diabetes in nondiabetic twins of IDDM patients or reflect a process that stops short of clinical diabetes. Verge et al. (1) favor the former explanation, we favor the latter. Pairwise concordance rates from recent IDDM twin studies vary between 13 and 36%, i.e., the majority of twins have not developed diabetes (1,6–9). Verge's study was a prospective and not a cohort analysis, with twins being referred at different times (0.2–23 years) after the diagnosis of the index twin. The dramatic drop in IDDM-free survival in their series is based on the analysis of four cases, too small to be meaningful and rightly excluded from their summary. The only prospective cohort analysis of twins confirmed that the majority of twins referred as nondiabetic remain so (9). While some twins in all the series may develop IDDM many years after the index case (up to 40 years later in one of our cases), the majority do not; 94% in our series developed IDDM within 12 years of the index twin (9).

The fact that the process leading to IDDM may stop short of frank diabetes is important because it suggests that the destructive disease process can be modulated. By understanding this process we may be able to alter or stop β-cell destruction and even prevent diabetes.

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Received for publication 21 June 1996 and accepted 24 June 1996.

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