

Concordance for Islet Autoimmunity among Monozygotic Twins

TO THE EDITOR: The risk of type 1 diabetes among the monozygotic twins of patients with type 1 diabetes is reported to be as low as 30%; this percentage is usually based on the ascertainment of data at a single time point.¹⁻³ Less is known about the cumulative incidence of islet antibodies and diabetes among twins followed over time.^{4,5} We analyzed the long-term risk of islet autoimmunity and type 1 diabetes in a cohort of twins of patients with type 1A diabetes as defined by the American Diabetes Association criteria (95% of the twins with a prediabetic condition who were initially discordant for diabetes were islet autoantibody–positive before diabetes developed). Eighty-three monozygotic twins without diabetes were prospectively followed for antibody expression (i.e., GAD65, ICA512, insulin, and cytoplasmic islet-cell antibodies),⁵ progression to diabetes, or both for up to 43.8 years (mean, 12.8; median, 8.5; range, 0 to 43.8). Twins were identified at the Joslin Diabetes Center and the Barbara Davis Center for Childhood Diabetes and through the Diabetes Prevention Trial–Type 1 Diabetes.

As shown in Figure 1, by 60 years of age, the cumulative incidence of diabetes among monozygotic twins who were initially discordant for diabetes was 65% (95% confidence interval [CI], 39 to 91), and persistent autoantibody positivity, type 1 diabetes, or both had developed in 78% (95% CI, 61 to 95). Among 32 autoantibody-positive monozygotic twins, the risk of diabetes was 89% (95% CI, 72 to 100) within 16 years after the first positive antibody test. Because we

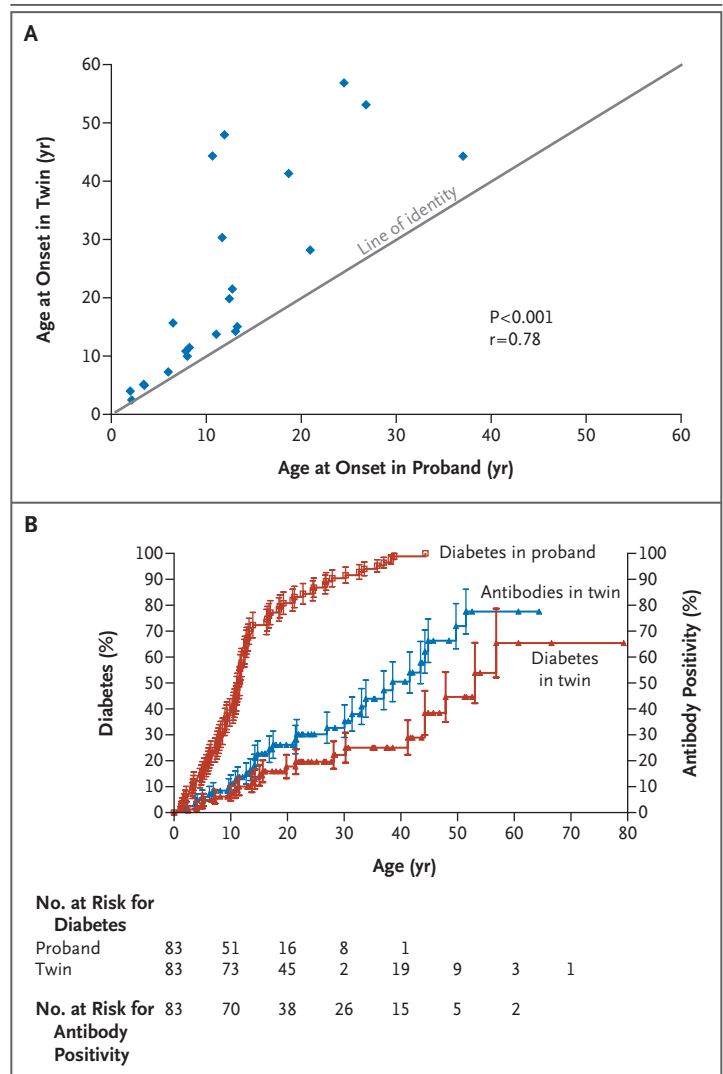


Figure 1. Progressive Development of Anti-Islet Autoimmunity and Diabetes.

Panel A shows the correlation between the age at the onset of type 1 diabetes in the probands and in their monozygotic twins. The line of identity shows the values if diabetes developed in a proband and his or her twin at the same time. In the nine monozygotic twin pairs with a twin in whom diabetes developed before 10 years of age, there was a close correlation in the age at onset ($r = 0.78$, $P < 0.001$), whereas if diabetes developed in the twin after 10 years of age, there was greater variability in the ages at onset between the twin pairs, with the age at onset differing by more than 30 years in many twin pairs ($r = 0.55$, $P = 0.05$). Panel B shows the cumulative incidence of diabetes among the probands and the cumulative incidence of diabetes and autoantibody positivity according to life-table analysis in the twins who were initially discordant for diabetes. Kaplan–Meier estimates of progression to diabetes and anti-islet autoimmunity according to age are shown. Survival analyses of progression to diabetes in patients (proband) and in their monozygotic twins who initially did not have diabetes are indicated by the red lines ($P < 0.001$). Progression to anti-islet autoimmunity (i.e., development of positive anti-islet autoantibodies, diabetes, or both) in the monozygotic twins of patients is indicated by the blue line. The numbers of patients still followed at each time point are shown. I bars denote 95% confidence intervals.

studied only monozygotic twins who were initially discordant for diabetes, and a subgroup of twins before 1992 was not assessed with more recently available biochemical autoantibody assays (GAD65 and ICA512), the rates of progression to autoantibody positivity shown in the figure are probably underestimates.⁵

We conclude that with prospective long-term follow-up, both autoantibody positivity and diabetes frequently develop in monozygotic twins of patients with type 1 diabetes, even if the twins were initially discordant for diabetes. We believe that, at least in studies of autoimmune disorders, estimates of the concordance rate for diabetes among monozygotic twins should include long-term follow-up.

Maria J. Redondo, M.D., Ph.D.

Joy Jeffrey, B.S.

Pamela R. Fain, Ph.D.

George S. Eisenbarth, M.D., Ph.D.

Barbara Davis Center for Childhood Diabetes

Aurora, CO 80045

george.eisenbarth@uchsc.edu

Tihamer Orban, M.D.

Joslin Diabetes Center

Boston, MA 02215

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