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Multiple autoantibodies as predictors of Type 1 diabetes in a general population

To the Editor: Autoantibodies have been widely used to predict the development of Type 1 diabetes [1]. Most studies have been carried out on first-degree relatives of Type 1 diabetic patients [2, 3, 4] who are at a 10 to 15-fold higher risk of developing the disease than people in the general population. However, approximately 85% of all patients who develop Type 1 diabetes do not have an affected family member.

To evaluate the predictive value of autoantibodies in a general population, we screened 9698 Florida school children, who were between 5 and 18 years of age, for islet-cell autoantibodies (ICA). Informed consent was obtained from all subjects under a protocol approved by the institutional review board at the University of Florida. We followed 3854 of these children for 6 to 12 years for the subsequent development of Type 1 diabetes.

DOI 10.1007/s00125-003-1123-7
Received: 3 February 2003 / Revised: 3 February 2003
Published online: 11 June 2003

At the initial screening, 55 children were ICA positive. These children were then tested for autoantibodies to insulin, GAD, IA-2 and IA-2β. Of the 55 children positive for ICA 13 also had antibodies to insulin, 18 to GAD, 13 to IA-2 and 8 to IA-2β (Fig. 1). Of the 55 ICA-positive children, 11 progressed to Type 1 diabetes. Of these 11 ICA-positive children, 6 had autoantibodies to insulin, 10 to GAD, 9 to IA-2 and 7 to IA-2β. During the course of the study, only one ICA-negative child developed Type 1 diabetes.

Table 1 shows the autoantibody profiles of the 11 ICA-positive children who developed Type 1 diabetes. All had multiple autoantibodies at the initial screening. Clinical disease developed 3 months to 10 years later.

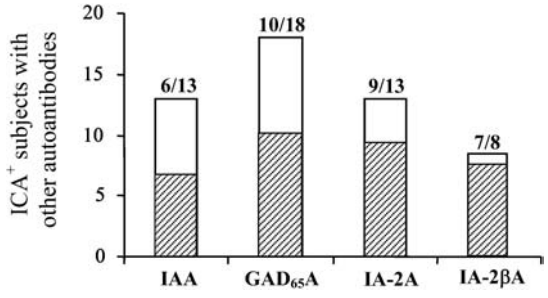

Fig. 1. Autoantibodies in 55 ICA-positive subjects. Shaded areas show number of subjects who progressed to Type 1 diabetes in the presence of each of the autoantibodies

Table 1. Autoantibody profile of children progressing to Type 1 diabetes

Subjects	Age (years/months)[a]	Sex	Autoantibodies					Time to Onset of Diabetes (years/months)
			ICA	$GAD_{65}A$	IA-2A	IA-2βA	IAA	
1	7/7	M	+	+	–	–	–	4/4
2	7/5	M	+	–	+	+	+	4/3
3	7/9	M	+	+	+	+	–	1/2
4	10	F	+	+	+	+	+	3/6
5	13/5	F	+	+	+	–	–	6/8
6	15/6	M	+	+	+	+	–	7/1
7	7/9	M	+	+	+	+	+	6/2
8	9/5	F	+	+	+	+	+	0/3
9	7	F	+	+	–	–	–	6/8
10	8/4	F	+	+	+	–	+	2/0
11[b]	9/8	F	+	+	+	+	+	10/1

[a] Age when samples were collected
[b] Initially autoantibody negative, but became autoantibody positive 3 years later

Of the 44 ICA-positive children who did not progress to diabetes, 36 had only ICA and none of the other autoantibodies. These children showed normal first-phase insulin release curves as evaluated by intravenous glucose tolerance tests. The remaining 8 ICA-positive children had at least one other autoantibody and showed abnormal first phase insulin release curves suggesting that they were at increased risk of eventually developing Type 1 diabetes.

Taken together with other reports [5, 6, 7, 8], our study shows that with ICA alone, the risk of developing Type 1 diabetes is low, whereas with more than one autoantibody the risk of developing Type 1 diabetes in a general school population is high. These findings on 3854 school children add further support to the concept that multiple autoantibodies are good predictive markers for Type 1 diabetes not only in first degree relatives, but also in a general population.

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