

Growth of Children Before Onset of Diabetes

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OBJECTIVE— To examine the growth of children before the onset of diabetes.

RESEARCH DESIGN AND METHODS— Heights before diagnosis, expressed as SDS, of each diabetic child identified from the diabetes register and of two age- and sex-matched control subjects were obtained from records of routine examinations performed at 3.5, 6, 11, and 13 yr. The heights of their siblings, with control subjects, also were obtained.

RESULTS— Diabetic children were considerably taller than control subjects before diagnosis (0–1 yr before diagnosis SDS 0.82 ± 0.26 vs. 0.16 ± 0.14 , $P < 0.05$, $n = 24$; 1–2 yr before diagnosis SDS 1.02 ± 0.17 vs. 0.16 ± 0.14 , $P < 0.001$, $n = 30$; 2–3 yr before diagnosis SDS 0.97 ± 0.23 vs. 0.04 ± 0.20 , $P < 0.005$, $n = 16$). At more than 3 yr before diagnosis, the diabetic children were not significantly taller than control subjects (SDS 0.8 ± 0.2 vs. 0.27 ± 0.13 , respectively; $n = 33$). The siblings of the diabetic children were no taller than control subjects.

CONCLUSIONS— Diabetic children, but not their siblings, were taller than control subjects before diagnosis, suggesting growth-inducing metabolic changes may precede the onset of clinical diabetes by at least 3 yr.

Diabetic children are taller at diagnosis than control subjects (1–3). The only study to examine the growth of children before the onset of diabetes suggested (slightly at variance with the previous studies) that the growth velocity of diabetic identical twins is reduced beforehand compared with their nondiabetic twins (4). The aim of this study was to examine the growth of children before the onset of diabetes and to compare the heights of the sib-

lings of diabetic children with control subjects, with height measurements from school health records.

RESEARCH DESIGN AND METHODS

Diabetic children were identified from the Leicestershire Diabetes Register, which includes all IDDM children ≤ 14 yr of age diagnosed in the county. Ascertainment is checked against the records of hospital consultants, community diabetic liaison nurses, patient

associations, local general practitioners, and response to local press advertisements. Heights at diagnosis were obtained from hospital case notes. Heights before diagnosis were obtained from Leicestershire Health Authority computerized school health records. Children's heights were measured routinely at 3.5 yr of age by a general practitioner and at 6, 11, and 13 yr of age in school by a community pediatrician. The heights of the next two sex-matched nondiabetic subjects born on the same day were selected as control subjects. No control group for the heights at diagnosis was selected. Only measurements from routine medical examinations of white subjects were used. Details of the children's siblings were obtained from a previous study in which the families on the register were interviewed by a diabetic liaison nurse. Heights of siblings and matched control subjects were obtained as described above. Heights were measured with a Microtoise (KabiVitrum Growth Service) and are expressed as SDS calculated from the Tanner and Whitehouse growth charts with a KabiVitrum growth computer (5). Results are means \pm SE, and comparisons were made with the Mann-Whitney test.

RESULTS— Of 115 eligible white children on the register since 1981, when computerized records of heights began, 79 (40 boys, 39 girls) had one or more heights before diagnosis recorded. The mean age at diagnosis was 10.30 ± 0.43 yr. The heights at diagnosis of 53 subjects were obtained, and 103 heights before diagnosis were obtained. One height before diagnosis was available in 56 cases, two heights before diagnosis were available in 22 cases, and 1 child had three heights recorded before diagnosis.

The heights of the children before the onset of diabetes are given in Table 1. The heights of those < 9 yr old at diagnosis compared with those ≥ 9 yr old at diagnosis and of boys compared with girls are shown in Table 2.

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SDS, STANDARD DEVIATION SCORE; IDDM, INSULIN-DEPENDENT DIABETES MELLITUS.

Table 1—Height SDS of children before onset of diabetes and control subjects (2 for each diabetic patient)

YEARS BEFORE DIAGNOSIS	N	SDS		P
		DIABETIC CHILDREN	CONTROL SUBJECTS	
AT DIAGNOSIS	57	0.72 ± 0.15		
0–1	24	0.82 ± 0.26	0.16 ± 0.14	<0.05
1–2	30	1.02 ± 0.17	0.16 ± 0.14	<0.001
2–3	16	0.97 ± 0.23	0.04 ± 0.20	<0.005
>3	33	0.80 ± 0.20	0.27 ± 0.13	NS

Of the 79 children studied, detailed family histories were available in 60 cases, and 55 had ≥1 full sibling. Details of 96 height measurements of 58 siblings were available. The heights of the diabetic children, their siblings, and the control subjects in each age-group are given in Table 3. There was no significant difference in height between siblings and control subjects at any age.

CONCLUSIONS— These results suggest that children who become diabetic are considerably taller than control subjects for at least 3 yr before the onset of clinical diabetes. Previous studies have been criticized for their selection of control subjects (4). The use of height measurements taken at routine school medical examinations in this study enabled us to select well-matched control subjects. The children's heights were measured by different observers and this is a potential source of error. However, any error probably would apply equally to the control group, which was carefully matched. A retrospective analysis of the children's postal code, which correlates closely with social class, revealed no difference between diabetic children and control subjects. Several height measurements were missing; however, the proportion missing was similar in the diabetic, sibling, and control groups, and the selection of control subjects ensured that it was unlikely the missing measurement introduced any bias between the groups.

The relative height of the chil-

dren appeared to reach a maximum 1–2 yr before the onset of diabetes and then fall off. This decline may be due to the development of glucose intolerance and other metabolic abnormalities inhibiting growth immediately before the onset of clinical diabetes. The cause of the increase in height before the onset of diabetes is unknown. If it is due to the same genetic or external factors that trigger the onset of IDDM, it would seem likely that

siblings might also be affected. These results suggest that the siblings of diabetic children are no taller than control subjects. These findings are similar to those of Songer et al. (2), who reported that only the siblings of diabetic children aged 5–9 yr at diagnosis were taller than control subjects.

The findings of this study are consistent with the hypothesis that the increase in height may be due to growth-inducing metabolic changes preceding the onset of clinical diabetes. Islet cell antibodies can be detected many years before the onset of clinical diabetes, suggesting a long prodromal period (6). Several metabolic abnormalities may precede the onset of hyperglycemia. Hyperinsulinemia, which stimulates growth, may occur in the prodromal stage (7). Growth hormone excess also occurs in diabetes and theoretically might occur before the onset of clinical diabetes (8). Whatever the cause, the results of this study suggest that, in the search for the cause for diabetes in chil-

Table 2—Height SDS before onset of diabetes in children <9 yr old at diagnosis compared with children ≥9 yr old at diagnosis and girls compared with boys

YEARS BEFORE ONSET	SDS			
	<9 YR AT DIAGNOSIS (N)	>9 YR AT DIAGNOSIS (N)	BOYS (N)	GIRLS (N)
0	0.84 ± 0.22 (21)	0.66 ± 0.19 (32)	0.78 ± 0.22 (26)	0.67 ± 0.19 (27)
1–2	1.11 ± 0.27 (14)	0.94 ± 0.24 (16)	1.03 ± 0.24 (18)	1.00 ± 0.25 (12)
>3	0.81 ± 0.25 (21)	0.78 ± 0.34 (12)	0.86 ± 0.23 (19)	0.71 ± 0.37 (14)

Table 3—Height SDS of diabetic patients, siblings, and control subjects (2 for each diabetic or sibling)

AGE (YR)	N	SDS		N	SDS	
		DIABETIC	CONTROL		SIBLING	CONTROL
3.5	23	1.05 ± .18	0.53 ± .14	18	0.67 ± 0.19	0.28 ± 0.15
6	30	0.81 ± .21	0.10 ± .12	28	0.05 ± 0.21	0.14 ± 0.12
11	40	0.90 ± .18	0.04 ± .10	26	-0.05 ± 0.14	-0.05 ± 0.15
13	10	0.79 ± .41	0.11 ± .23	24	-0.18 ± 0.24	-0.12 ± 0.19

dren, we should look for etiological factors at least 3 yr before the onset of the disease.

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