Does control influence the growth of diabetic children?

S. K. M. JIVANI and P. H. W. RAYNER

*From the Institute of Child Health, University of Birmingham, and The Children's Hospital,
Ladywood Middleway, Birmingham*

Jivani, S. K. M., and Rayner, P. H. W. (1973). *Archives of Disease in Childhood*, **48**, 109. **Does control influence the growth of diabetic children?** Growth of 60 girls and 56 boys is analysed both in terms of linear growth and growth velocity. The children were of normal height at the onset of diabetes and were shorter when analysed 3 years or more after the onset of diabetes. The growth retardation was not related to the degree of control of diabetes but was related to the duration of diabetes before the onset of puberty and was due to retarded and delayed peak growth at puberty.

In the preinsulin era the growth of diabetic children who survived any length of time was severely retarded (Joslin, Root, and White, 1925). After the introduction of insulin the situation improved dramatically, but several authors have subsequently reported retarded growth in diabetic children (Wagner, White, and Bogan, 1942; Bergqvist, 1954; Danowski, 1957; Hamne, 1962; Sterky, 1963; Knowles *et al.*, 1965; Sterky, 1967; Craig, 1970; Pond, 1970).

Some authors have considered that growth is related to the degree of control of diabetes (Boyd and Nelson, 1928; Boyd and Kantrow, 1938; Jackson and Kelly, 1946; Bergqvist, 1954; Pond, 1970). However, others found no relation (Wagner *et al.*, 1942; Danowski, 1957; Sterky, 1963; Sterky, 1967; Craig, 1970). Despite these conflicting reports, normal growth has traditionally been accepted as a useful long-term index of satisfactory control. We have, therefore, undertaken this study to assess the value of this parameter.

Materials and methods

Children studied. The study was based on 116 children (60 girls and 56 boys) currently and previously attending the Birmingham Children's Hospital. Children with any other condition which might have affected growth were excluded.

Management. Management has remained essentially unchanged over the past 15 years. A regulated carbohydrate diet is given providing 40% of the total calorie intake. Calorie requirements in individual children vary but as a guide a 1-year-old child is given 100 g carbohydrate and this is increased by 10 g a year until puberty. Most children were given a once-daily injection of a mixture of amorphous and crystalline insulin zinc suspension in proportions adjusted at the

clinic and by the parents at home. Some were given a mixture of soluble and isophane insulins twice daily at adolescence.

Assessment of control. The criteria of control are shown in Table I. Records of diet, insulin requirements, physical examination, episodes of ketosis and hypoglycaemia, and blood sugar levels were available for each child. Each child at each clinic visit was graded on the basis of urine testing at home and clinic records of glycosuria, ketosis, blood sugar levels, and incidence of hypoglycaemia. For the purpose of this study two groups have been defined: those having on aggregate predominantly good control or predominantly poor control.

Growth assessment. The ages at onset of diabetic children are shown in Fig. 1a and 1b for girls and boys. The range was from 1 year to 13 years for girls and from 9 months to 13 years for boys. Only children followed up for more than 3 years are included in the series (range 3 years to 13 years with an average follow-up for girls of 7·17 years and for boys 6·64 years). Growth has been compared with the standards for British children of Tanner, Whitehouse, and Takaishi (1966) and has been analysed both in terms of linear growth and growth velocity. Centile channels I to VIII have been added to facilitate analysis of results. The height at onset of an additional group diagnosed in the past 5 years and currently attending the clinic has been analysed separately to detect any secular change in height.

Methods of analysis. A convenient and a reasonably accurate way of combining the heights for age of a group of subjects is to regard an individual's height in a particular channel (channels I–VIII on Tanner and Whitehouse growth charts) as being at the midpoint on that channel. Thus, if at the onset of diabetes there are 10 children in channel V, i.e. between the 50th and 75th centile, their heights are regarded as being at a centile value of 62·5. In this way a mean centile value (MPV) of a

TABLE I

Criteria used for assessment of diabetic control

| Category	Preprandial urine specimens for glycosuria			Occasional clinic blood sugar (mg/100 ml)	Hypoglycaemic reactions	Other
	Daily second-voided					
	a.m.	p.m.	Clinic visit			
Good	Mainly 0%, occasionally 0·5%	Mainly 0%, occasionally 1%; no ketonuria	Up to 1%	·150	Rare, mild only	Normal growth; normal school life
Fair	Mainly 0%, occasionally to to 1%	Variable, but only occasionally 2%; no ketonuria	Mainly 1%, occasionally 2%	150 to 250	Occasional, infrequent, mild to moderate	Normal or near normal growth; normal school life
Poor	Frequent 1–2%, only occasionally sugar free, any ketonuria		Up to 5%	7250	Severe and/or frequent	Disturbed growth; disturbed school attendance
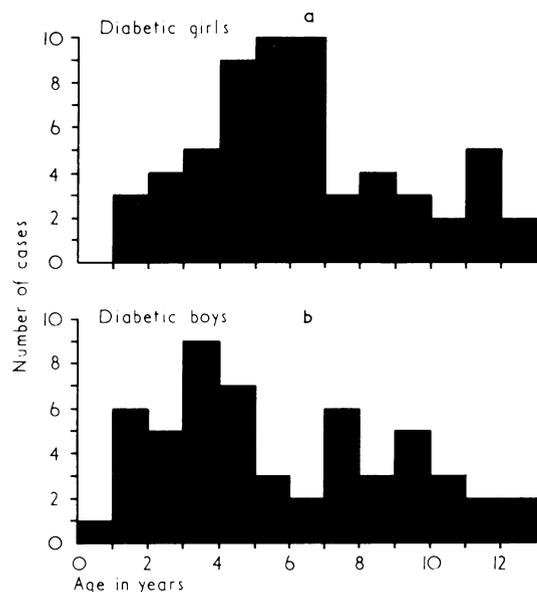
FIG. 1.—(a) *Age of onset of diabetes, 60 cases analysed (girls).* (b) *Age of onset of diabetes, 54 cases analysed (boys).*

group of children can be calculated. The expected MPV of a group of normal children can be taken as 50. Height velocities per year were calculated for each child and from this the mean was determined. The groups were divided into good control and poor control according to the criteria given above and their growth patterns separately analysed. Growth in childhood may be divided into three phases, (i) rapid growth during infancy, (ii) a midchildhood plateau, and (iii) the pubertal growth spurt. In order to assess whether diabetes affected growth differently in these separate phases, three further subgroups were also analysed. (1) Onset of diabetes before 6 years of age and analyses

at 9 years for girls and 10 years for boys. (2) Onset at or around 9 years for girls and 10 years for boys, and analysis after puberty had been completed. (3) Onset before 6 years, analysis after puberty.

Results

Height at onset and analysis. Fig. 2a and 2b show the heights at onset and analysis for girls and boys, respectively. At the onset of diabetes height lies close to the 50th centile, but at analysis there are more below than above it. Fig. 3a and 3b compare the expected number of children in each channel in a normal population and the actual number of children present in each channel at onset of diabetes and at analysis. A shift to the left at analysis is apparent indicating that their height is retarded.

Analysis for girls. Tables II and III show the mean centile value at onset and analysis for girls. It can be seen that height at onset of diabetes is not statistically different from the 50th centile. When analysed at varying periods of follow-up (range 3 to 13 years, with a mean of 7·1 years) they were, however, significantly shorter than the 50th centile ($0 \cdot 005 > P > 0 \cdot 001$) and their height centile had fallen significantly on a 'within patient' basis ($P < 0 \cdot 001$). When analysed by grade of control, both the well and poorly controlled girls were shorter than the 50th centile at analysis ($0 \cdot 05 > P > 0 \cdot 025$ for both groups) and their height centile had fallen significantly on a 'within patient' basis ($0 \cdot 005 > P > 0 \cdot 001$ and $0 \cdot 025 > P > 0 \cdot 02$ for well controlled and poorly controlled, respectively). The degree of the control of diabetes does not appear to have affected the pattern of growth. On analysing the subgroups there is no statistically significant retardation of
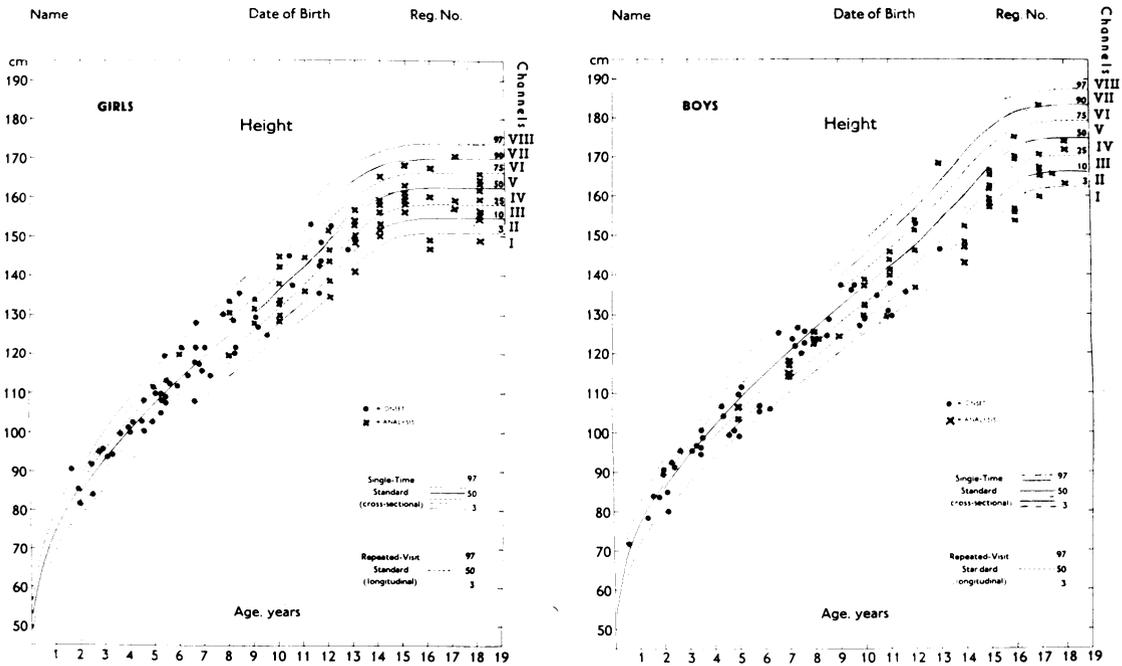
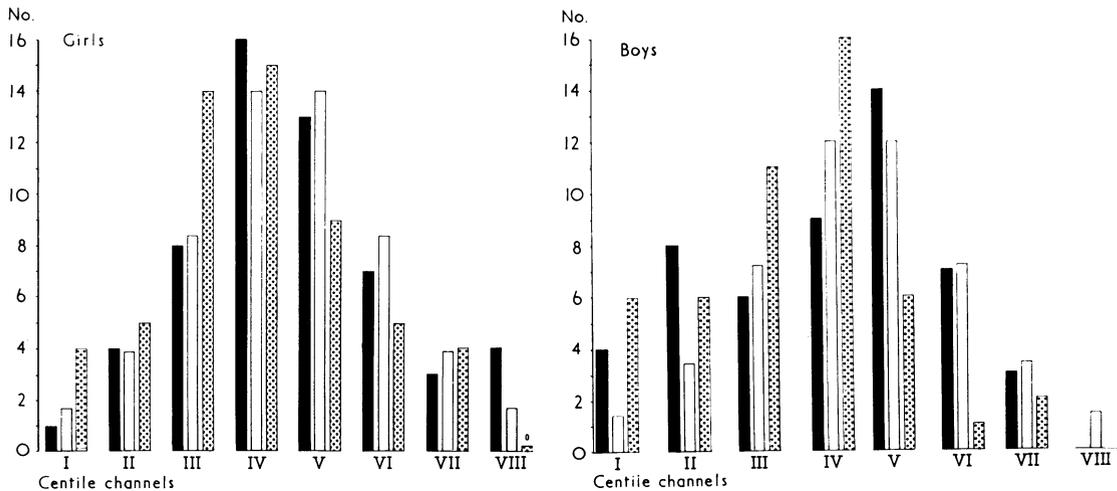FIG. 2.—(a) Height at onset (●) and analysis (×) (girls). (b) Height at onset (●) and analysis (×) (boys).

FIG. 3.—(a) Distribution of heights according to centile channels for girls. (b) Distribution of heights according to centile channels for boys.

Key: ■ Actual no. of children in each channel at onset of diabetes.
     □ Expected no. of children in each channel.
     ▦ Actual no. of children in each channel at analysis.

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TABLE II
Mean centile value (height) for girls

Category	No.	Onset	Sig. of diff. from mean (P)	Analysis	Sig. of diff. from mean (P)	Sig. of diff. 'within patient basis' (P)
Total girls	56	51·7	NS	38·7	0·005–0·001	<0·001
Good control	34	49·5	NS	39·94	0·05–0·025	0·005–0·001
Poor control	22	55·1	NS	38·4	0·05–0·025	0·025–0·02

NS, not significant.

TABLE III
Mean centile value (height) girls

Category	No.	Onset	Sign. of diff. from mean (P)	Analysis	Sig. of diff. from mean (P)	Sig. of diff. 'within patient basis' (P)
Group 1 Onset: before 6 years Analysis: at 9 years	25	53·94	NS	45·94	0·4–0·3	<0·05
Group 2 Onset: after 9 years Analysis after puberty	10	41·5	NS	41·9	0·3–0·4	0·9
Group 3 Onset: before 6 years Analysis: after puberty	11	55	NS	33·68	0·05–0·02	0·05–0·025

NS, not significant.

height in groups 1 and 2 (Table III). In group 3, however, there is a significant retardation in height when girls start their diabetes prepubertally ($0·05 > P > 0·025$).

Analysis for boys. Tables IV and V show the mean centile values at onset and analysis for boys. The boys tend to be shorter than the 50th centile but the difference is not statistically significant ($0·7 > P > 0·6$) except for boys who have their onset at or around puberty ($0·02 > P > 0·01$). The group when analysed at varying periods of follow-up (range 3 to 13 years with a mean of 6·64 years) was shorter than the 50th centile ($0·01 > P > 0·005$) and the height centile had fallen on a 'within patient' basis ($P = 0·001$). The well-controlled boys were shorter than the 50th centile at analysis ($P = 0·001$) and their height centile had fallen significantly on a 'within patient' basis ($0·01 > P > 0·005$). In the poorly controlled group, however, though shorter than the 50th centile at analysis ($0·025 > P > 0·02$), the fall in height centile on a 'within patient' basis just escapes statistical significance ($0·1 > P > 0·05$). Adequacy of control

TABLE IV
Mean centile value (height) for boys

Category	No.	Onset	Sig. of diff. from mean (P)	Analysis	Sig. of diff. from mean (P)	Sig. of diff. 'within patient basis' (P)
Total boys	48	43·58	NS	31·42	0·01–0·005	<0·001
Good control	29	41·65	NS	29·32	<0·001	0·01–0·005
Poor control	19	46·2	NS	34·63	0·025–0·02	0·1–0·05

NS, not significant.

TABLE V

Mean centile value (height) boys

Category	No.	Onset	Sig. of diff. from mean (P)	Analysis	Sig. of diff. from mean (P)	Sig. of diff. 'within patient basis' (P)
Group 1 Onset: before 6 years Analysis: at 10 years	18	51·0	NS	46·33	0·5–0·6	0·4–0·5
Group 2 Onset: after 10 Analysis: after puberty	7	25·42	0·02–0·01	21·2	0·025	0·4–0·3
Group 3 Onset: before 6 years Analysis: after puberty	6	42·16	NS	21·33	0·005–0·001	0·2–0·1

NS, not significant.

had not therefore affected their growth pattern. On analysing the subgroups (Table V) there is no statistically significant retardation in height in groups 1 and 2. In group 3 though there is no significant drop in height centile, on a 'within patient' basis it is significantly shorter than the 50th centile at analysis.

Separate analysis of the height at onset of diabetic children diagnosed in the last 5 years is shown in Table VI. This shows no significant difference from the normal population or from the patients studied.

TABLE VI

Mean centile value (MPV) for height
(Children diagnosed in past 5 years, 1966–1971)

	Boys	Girls
No.	32·0	40·0
MPV	43·8	53·75
SD	28·9	28·6
P	NS	NS

NS, not significant.

Girls' growth velocity. The mean velocity of the group is normal until puberty but their pubertal growth spurt is reduced and delayed. There is no significant difference between the well and poorly controlled diabetics. When the onset of diabetes occurs before puberty their growth velocity is normal until puberty but the pubertal growth spurt is again reduced and delayed. Girls whose onset of diabetes occurs at or around puberty have a normal growth velocity.

Boys' growth velocity. The mean velocity of the group is normal until puberty but their pubertal growth spurt is reduced and delayed. The well controlled and poorly controlled follow the same pattern until puberty but then a difference emerges. The pubertal growth spurt in the well controlled is lower and later than the group as a whole. The poorly controlled diabetics have a near normal pubertal growth spurt. When the onset of diabetes occurs before puberty, they have a growth velocity slightly below the 50th centile until puberty and at puberty there is a reduced pubertal growth spurt. Boys with onset of diabetes at or around puberty have a normal but slightly delayed pubertal growth spurt.

From the tables of growth velocities, weighted mean velocities were calculated and the difference between the well controlled and poorly controlled ascertained. There was no statistically significant difference between the two groups for girls or boys.

Weight for height analysis. Since at the onset of diabetes the majority of children are dehydrated and in a catabolic state, it was felt that it would be more meaningful to look at their weight/height ratio one year after the onset of diabetes The weight/height ratio of the girls is shown in Table VII. When analysed one year after the onset of diabetes they were significantly heavier than normal children (P <0·001) and became still heavier at analysis 3 years or more after onset ('within patient' basis 0·005>P>0·01). There is no significant difference in weight for height ratio between the well and poorly controlled groups. The boys' data for weight/height is

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TABLE VII

Mean centile value weight/height girls

Category	No.	Onset	Sig. of diff. from mean (P)	Analysis	Sig. of diff. from mean (P)	Sig. of diff. 'within patient basis' (P)
Total	53	67·4	<0·001	80·86	<0·001	0·005–0·001
Good control	33	68·75	<0·001	79·35	<0·001	0·02–0·01
Poor control	20	65·23	0·02–0·01	83·87	<0·001	0·05–0·025

given in Table VIII. They, like the girls, when analysed one year after the onset of diabetes are significantly heavier than normal children (P <0·001), and remain so at analysis (P <0·001), but in contrast to girls they do not significantly gain weight when analysed on a 'within patient' basis. The well controlled diabetic boys are heavier at 1 year after onset of diabetes (P=0·001) and remain so at analysis, but again do not significantly alter their height/weight at analysis. Poorly controlled boys, though heavier at 1 year after onset of diabetes, do not remain so at analysis (0·5>P>0·01).

Discussion

Height at onset. Joslin *et al.* (1925) first reported that diabetic children were taller than average at diagnosis and this has subsequently been reported by Boyd and Nelson (1928), Wagner *et al.* (1942), White (1960), Pond (1970), and Craig (1970). This is an attractive finding since insulin is an important anabolic hormone and the hyper-insulinism which precedes overt carbohydrate intolerance might be expected to result in advanced growth, as occurs in the fetuses of mothers with gestational diabetes. Other authors, however, have found no difference in the height of diabetic children at the time of diagnosis (Boyd, 1937; Jackson and Kelly, 1946; Danowski, 1957; Hamne, 1962). Our findings are in agreement with the latter workers. The children in our series are no taller than the standards for British children of Tanner *et al.* (1966); this still applies when we look at the height at onset of a group of children

presenting within the past 5 years. This discrepancy is hard to explain but may be due to regional variations in the height of British children. Craig's children were no taller than the standards of Tanner *et al.* (1966) for British children but were taller than local standards for Scottish children. No standards are available for the height of children in the Birmingham area, but as far as we are aware our local population does not differ from the national average.

Growth of the diabetic child. White (1960) comments that between 1922 and 1936 failure of linear growth characterized juvenile diabetes. Since the discovery of insulin and the use of intermediate and long-acting preparations, severe growth failure associated with infantilism and hepatomegaly (Mauriac syndrome) has been eliminated. Most diabetic children may now anticipate reaching an adult height within the normal range, but overall a slight but statistically significant degree of retardation of linear growth is present in our series in both sexes. Boyd and Kantrow (1938) suggested that the determining factor was an insufficient food intake but gave no precise details. The calorie intake of our children was reviewed annually. In so far as weight for height ratio gives an index of nutritional state, our children were not malnourished and we feel that calorie intake has not played any part in their growth retardation.

Control of diabetes and growth. Control of diabetes is difficult to define and good control

TABLE VIII

Mean centile value weight/height boys

Category	No.	Onset	Sig. of diff. from mean (P)	Analysis	Sig. of diff. from mean (P)	Sig. of diff. 'within pstient basis' (P)
Total	44	69·1	<0·001	67·0	<0·001	0·8–0·7
Good control	25	74·86	<0·001	71·24	<0·001	0·8–0·7
Poor control	19	61·68	0·05–0·025	61·5	0·1–0·5	0·8–0·7

even more so. The criteria used by various authors to define control vary widely and it may not therefore be meaningful to compare our results too closely with other series. On the basis of our criteria, however, control has no effect on growth. Danowski (1957), Sterky (1963, 1967), and Craig (1970) reached the same conclusion. Our series in fact shows a tendency, at least in boys, for growth to be better in the poorly controlled group. Wagner *et al.* (1942) analysing growth in relation to control found a slight predominance of very good control in favour of growth retarded children. It is not our intention to dispute the overall benefit of good control in the management of the diabetic child, but linear growth is not a satisfactory criterion by which control may be assessed.

Growth during puberty. When growth is analysed in relation to duration of diabetes before puberty it is apparent that the growth retardation of the group as a whole is chiefly due to a delayed and reduced pubertal growth spurt in those children who developed diabetes 3 years or more before puberty. The onset of diabetes shortly before or during puberty does not affect the peak velocity achieved. Wagner *et al.* (1942) found that the diabetic child was most susceptible to growth retardation between the twelfth and sixteenth years of life and from the second to sixteenth year of diabetes. Bergqvist (1954) followed 8 boys and 10 girls whose onset was between 10 and 15 years. Among boys he found a slight tendency to retardation of growth, though statistically not significant, and among girls there was no such tendency; whereas he found retarded growth in those with onset before 5 years and also in those with onset between 5 and 10 years. Knowles *et al.* (1965) found mean heights of adult diabetic men and women to be shorter than average and that the decrease in stature was mainly in those with diabetes diagnosed before the growth spurt.

In conclusion we feel that the growth of diabetic children is not severely retarded but when it occurs it is related to the duration of the disease before puberty and is principally due to a delayed and reduced pubertal growth spurt and is not related to adequacy of control.

Further studies to correlate the timing of pubertal changes and the skeletal maturation with the pubertal growth spurt of diabetic children are in progress in our department.

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Correspondence to Dr. P. H. W. Rayner, The Children's Hospital, Ladywood Middleway, Birmingham B16 8ET.