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SHORT COMMUNICATIONS

Growth in Juvenile Diabetes Mellitus

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Summary. Height, weight, height velocity and skeletal maturity information was collected on a group of 94 juvenile diabetics in a mixed longitudinal study, and compared to a control population. Familial growth trends were taken into consideration where possible. Although the hormonal environment in the juvenile diabetic is probably unusual and fluctuating, there is no evidence that juvenile diabetes is likely to interfere with growth provided that a reasonable degree of control is maintained.

Key words: Growth, juvenile diabetic, maturation, height, weight, bone age.

Introduction

That chronic disease tends to interfere with growth is a widely accepted fact, although often the evidence for such belief is meagre. Juvenile diabetes mellitus may be considered a chronic metabolic disease; however it differs from such conditions as congenital cardiac disease or chronic renal disease in that the abnormalities involve endocrine-metabolic relationships which are central to growth processes.

In the literature of the early insulin era, references on growth and juvenile diabetes are numerous, and generally suggest subnormal growth is to be expected, although a few suggest "good control" will result in normal growth. However in more recent years, since current modes of management have been adopted, references are rare, and further equally divided between the opinions that juvenile diabetes, even if well controlled, is, [1—4] or is not, [5, 6] associated with growth disturbances. The object of the present mixed longitudinal study was to investigate whether growth disturbances were usually associated with controlled diabetes.

Material and Methods

The study population consists of a total of 94 juvenile diabetics ranging from three to twenty years of age at the present time. Duration of diabetic state varied from 1 to 15 years. All subjects have been followed longitudinally over a period of at least one year, and some as long as four or five years. Subjects are normally seen three or four times a year.

The great majority of heights have been recorded with a Harpenden stadiometer. Skeletal maturity was determined from posteroanterior films of the left hand and wrist. Maturity is rated by the method of Tanner [7].

Growth velocity was obtained from measurements over periods of at least one year. This is essential to eliminate the seasonal effects on growth rate [8]. Unfortunately it is not usually possible to schedule visits at exact intervals, and thus the seasonal effect has not been entirely excluded but at least minimized.

Height and weight have been compared with the standards (3rd, 50th and 97th centiles) reported by Tanner *et al.* (1966) [8]. In a previous paper [9] we have reported the height and weight of healthy Vancouver school children using the same standards. Skeletal maturity has been plotted and compared with the same control population. Skeletal maturity films were available in 74 subjects.

Information regarding growth patterns, final height, and age of menarche was sought on close relatives (siblings, parents and parent siblings). Useful data were obtained in forty subjects.

Discrepancies (of any sign and magnitude) between apparent skeletal maturity and chronological age were examined in the light of family data. In view of its greater precision and reliability, only menarchial age in female relatives was utilized.

"Good control" is herein defined as absent or minimal glucosuria at most times; absence of ketosis or prolonged heavy glucosuria, except when infection is present; infrequent hypoglycemic episodes; and evidence of satisfactory adherence to a measured (but not weighed) dietary regimen, and urine testing. Insulin therapy should have been adjusted appropriate to urine testing findings.

Results

Achieved stature. Figs. 1 and 2 show achieved stature of all subjects at their most recent measurement. This cross-sectional method has been used by almost all previous workers. It will be seen from Table

1 that compared to the standards used, the skewing to the higher centiles seen in our control population is fully reflected in our female subjects, but not in our male subjects. This apparent excess of shorter males will be discussed below.

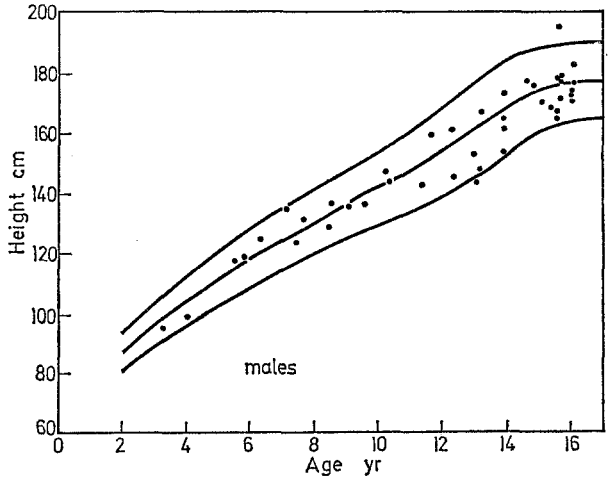

Fig. 1. Achieved stature, male diabetics

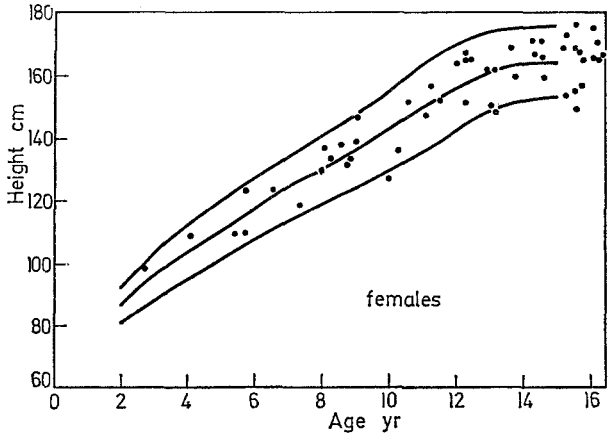

Fig. 2. Achieved stature, female diabetics

Table 1. *Achieved height and weight of diabetic subjects*

	Below 3rd centile	3—50 centile	50—97 centile	Above 97 centile	n
Height					
Males	1	21	19	1	42
Control males	1	15	24	3	
Females	3	16	33	0	52
Control females	1	18	30	2	
Weight					
Males	3	13	24	2	42
Control males	1	14	25	2	
Females	2	21	28	1	52
Control females	1	23	26	2	

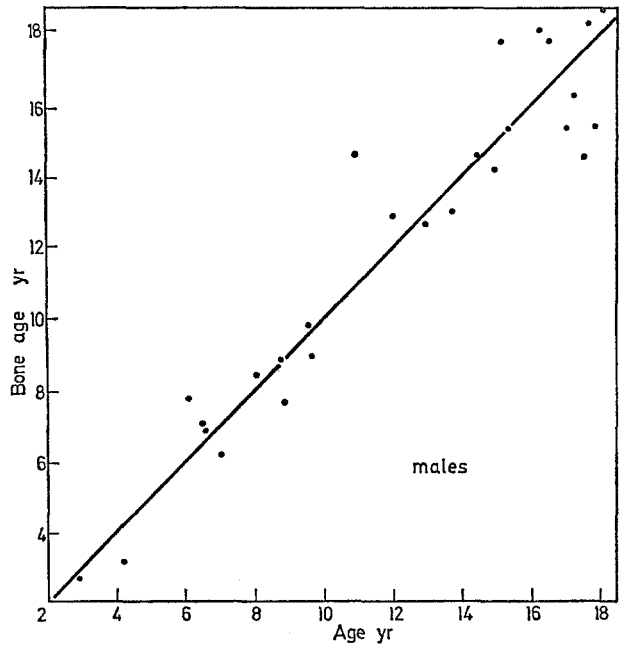

Fig. 3. Skeletal maturity, male diabetics

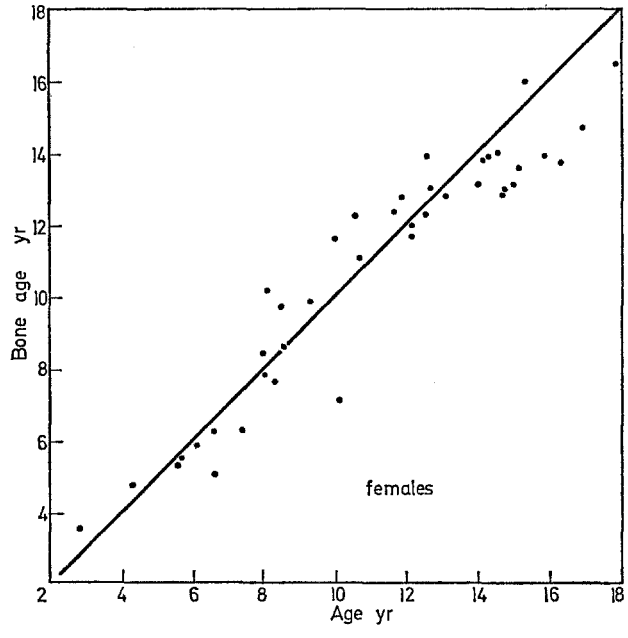

Fig. 4. Skeletal maturity, female diabetics

Achieved weight. Weight distribution is compared with the control subjects in Table 1. Here no difference between the two groups can be found.

Skeletal maturity. Figs. 3 and 4 show skeletal maturity in terms of skeletal age equivalent to the Tanner score, compared to their chronological age. An arbitrary range of one year on either side of the equivalence line has been utilized.

The summary in Table 2 shows that female but not male diabetics show a modest skewing to the left

compared to the standards. However our control subjects of both sexes showed a similar skewing, and we conclude that the diabetic children show no significant abnormalities of skeletal maturation.

Height velocity. We compared the height velocity in 76 subjects with the appropriate standard of Tanner *et al.* [8], and recorded the average centile status of the individual over the period of observation in Table 3. Some subjects showed considerable variation in their actual centile position from year to year. This may be due to natural variations or measurement errors; it might also be due to fluctuations in diabetic control, although we have been unable to show any such correlation from our clinical records.

Table 2. *Skeletal maturity distribution*

	Over 1 year delay	−1 to 0 delay	No delay	0 to +1 advance	Over 1 year advance	n
Males	5	7	1	10	7	30
Females	11	14	1	10	8	44
Both	16	21	2	20	15	74

Table 3. *Average growth velocity centile data*

	Much below	Below average	Average	Above average	Much above	n	Mean obs./ subject
Males	3	5	16	8	3	35	3.1
Females	1	12	15	11	2	41	3.1

Table 4. *Family stature data*

	Below 3rd centile	3—50 centile	50—97 centile	Above 97 centile	n
Males					
Immature sibs	4	9	18	3	34
Mature sibs	0	3	5	1	9
Fathers	1	15	27	2	45
Females					
Immature sibs	3	10	11	4	28
Mature sibs	0	7	9	2	18
Mothers	1	13	29	2	45

Table 5. *Skeletal maturity and family trend*

Maturity discrepancy compatible with family trend	21
Maturity discrepancy not compatible:	19
Delay less than in family	13
Delay greater than in family	6

Family data. The reliability of family stature data is open to question, as in few cases was it measured by us. Stature of close relatives is described in Table 4. All male relatives and females, except for immature siblings, show distributions similar to the control population.

As will be seen from Table 5, in about half the instances the bone age discrepancy of the diabetic is compatible with the family trend. In those where the difference was not compatible, in the majority it was better than (i.e. less than) the family trend.

Discussion

Serum growth hormone levels, which are high in untreated or inadequately treated juvenile diabetics, fall when control is established [10, 11]. However in longstanding diabetes, good control is often associated with higher growth hormone levels [11]. Recent reports demonstrate that sleep-related plasma growth hormone elevation is normal in juvenile diabetics even in the presence of hyperglycemia [12].

Insulin also fulfills the criteria of a growth hormone; it is anabolic, promotes cell growth, and an insufficiency leads to growth stunting. Like somatotropin itself, we face the paradox that the secretion and circulating levels of a major growth-promoting hormone are so variable, depending on the nutritional status of the individual at the moment. It is clear that insulin levels achieved in the therapy of juvenile diabetes are "unphysiological", in the sense that they cannot reflect rapidly changing metabolic needs. It is likely that the *mean* level of plasma insulin in a juvenile diabetic is usually less than in a non-diabetic, since to avoid periods of incapacitating hypoglycemia during the post-absorptive phase, we accept a degree of hyperglycemia, and thus of hypoinsulinemia. Growth failure is certainly a feature of uncontrolled juvenile diabetes, this being part of the "Mauriac syndrome" [13, 14].

At present the possible interplay of these, at times, conflicting hormonal patterns on growth cannot be perceived. The problem is whether "good" control will prevent the growth retardation characteristic of undertreated juvenile diabetes.

Nutritional factors are prominent among the requirements for optimal growth. The diabetic diet, with emphasis on variety, adequate caloric intake, and with its relatively high protein content (typically 20% of calories compared to the usual 12—15%) should also favour growth.

The data on achieved stature are not in favour of poor growth in our subjects. Examination of individuals shorter than expected reveals familial factors in most instances. Height velocity data, although more difficult to interpret, are much more valuable than single determinations. Again no obviously abnormal trend is evident. We were not able to correlate fluctuations in height velocity with variation in diabetic control.

Skeletal maturity patterns, allowing for familial trends, were again comparable to our control population.

Included in this series were 11 subjects (7 male, 4 female), whose diabetic control status, even by our moderate standards, was for prolonged periods judged unacceptable by the criteria noted above. Of these, 8 were unusually short, and 7 markedly underweight. Only 4 had radiography, and while one showed much delay in bone maturation, two were normal and one was accelerated for age. None of these subjects had hepatomegaly.

The apparent excess of shorter diabetic males compared to the control population must be contrasted with the growth rates of these males, which are normal when compared to the controls. Thus the shorter stature was not due to diminished growth rates during the period of observation. Familial factors certainly were responsible in some instances. Contrary to the observation of Bergqvist [1], there was no relationship between shorter stature and early onset of diabetes in our series. The poorly controlled short subjects noted above were also included in the series and affected the distribution of stature.

It is concluded that diabetes mellitus, with adequate therapy, is not usually associated with growth delay or short stature.

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