CONDENSED REPORT

Does "afternoon diabetes" predict diabetes?

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Summary and conclusions

Twenty-eight men were given morning and afternoon oral glucose tolerance tests in 1969 and again in 1975. According to British Diabetic Association criteria all 28 had normal morning values in 1969 but seven had "afternoon diabetes." Four men had diabetic values in the morning in 1975 but only two of these had had afternoon diabetes in 1969. Better prediction of subsequent diabetes was obtained by calculating the area under the morning glucose tolerance curve in 1969. All four men who progressed to diabetes had areas exceeding 1000 units, which distinguished them absolutely from the other 24. They also tended to be more obese, but this was less predictive of subsequent diabetes.

Introduction

Diurnal variation in oral glucose tolerance is a well established phenomenon,[1] with blood sugar concentrations after a glucose load reaching higher values in the afternoon than in the morning. Roberts[2] suggested that impaired glucose tolerance in the afternoon ("afternoon diabetes") was an early sign or a forerunner of diabetes, and we also speculated that enhanced diurnal variation might be a stage in the evolution of maturity-onset diabetes.[3] The single follow-up study of the phenomenon[4] supported Roberts's thesis.

In 1975 we repeated the morning and afternoon oral glucose tolerance tests in a group of men who had served as normal controls in our 1969 study.[3]

Subjects and methods

Initially 40 men participated as controls in the Whitehall survey of civil servants[5] and had normal screening blood sugar concentrations (< 6·1 mmol/l (< 110 mg/100 ml)) two hours after a 50 g oral glucose load taken in the morning after an overnight fast. According to the British Diabetic Association criteria,[6] however, though all had normal values in the morning, 10 gave an abnormal ("diabetic") result in the afternoon. Six years later two of the men had died and 10 were either unable or unwilling to participate in the follow-up study. We retested the remaining 28 using exactly the same procedures as in the initial investigation. On both occasions all blood samples were taken by RJJ and blood sugar concentrations estimated by the same technician using the same method and apparatus. Blood samples were taken from an ear lobe, and 0·1 ml was added to 0·9 ml 1% potassium fluoride for blood sugar estimation on an autoanalyser; Technicon method N-9a was used. Height, weight, and blood pressure were recorded during the first test on both occasions, and plasma cholesterol was estimated in a venous sample at the original visit. Morning and afternoon tests were carried out in random order. During the test the subjects sat and did not smoke. The oral glucose load was given as 235 ml Lucozade, which was drunk within two minutes under supervision. Unless otherwise stated statistical analyses were performed with Student's *t* test for paired and unpaired data. Correlation coefficients were calculated by a least-squares method.

Results

Of the 28 men who participated in the follow-up study, seven had afternoon diabetes in 1969, the same proportion (25%) as in the original 40 subjects. The mean morning and afternoon test results at baseline and follow-up are shown in fig 1. There was an increase in the fasting and post-glucose blood sugar concentrations in the morning, which was significant at each point in the test. In contrast the mean results of the afternoon tests were closely similar, significantly higher values in the second test being recorded only at 30 and 60 minutes. Interestingly the mean fasting concentration in the morning was significantly higher ($P < 0.02$) than that in the afternoon at the follow-up investigation.

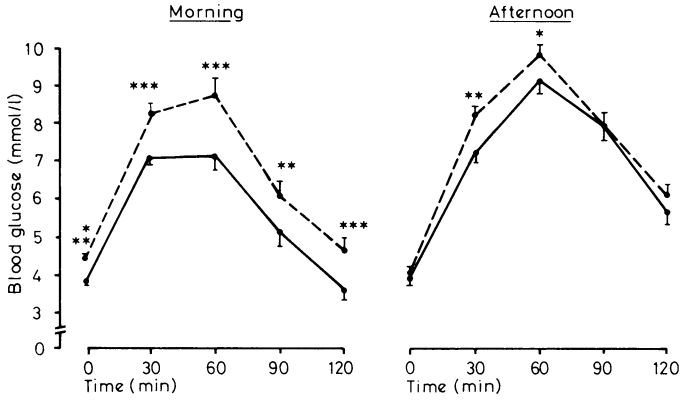

FIG 1—Mean (±SE of mean) blood glucose concentrations in morning and afternoon oral glucose tolerance tests in 28 men seen in 1969 (solid line) and 1975 (broken line). *P<0·05. **P<0·01. ***P<0·001.

Conversion: SI to traditional units—Blood glucose: 1 mmol/l ≈ 18 mg/100 ml.

The individual test results are given in tables A and B.* Of the seven men with afternoon diabetes in 1969, two had progressed to morning diabetes in 1975. Two others had normal afternoon values at follow-up, however, while three had afternoon diabetes at follow-up but continued to have normal morning values. The other two men with morning diabetes at follow-up had had normal afternoon values in 1969. Thus afternoon diabetes did not prove to be a good predictor of morning diabetes. We therefore looked at other variables to see if better prediction could be obtained.

Figure 2 shows the correlation between the area under the 1969 morning glucose tolerance curve (calculated as described[7]) and the degree of obesity expressed as the body mass index (BMI; calculated as (weight/height)^2). The four men who had developed morning diabetes in 1975 were in the fatter end of the range, but the remarkable

*Copies of tables A-C may be obtained from the authors.

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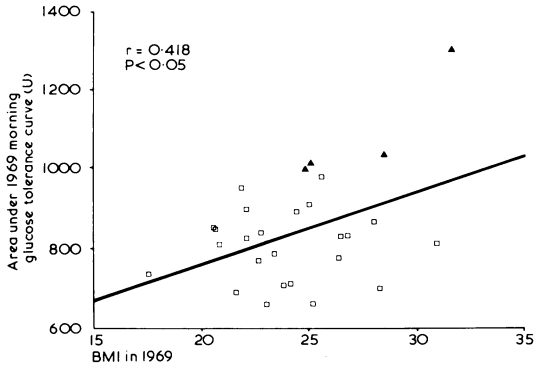

FIG 2—Correlation between area under morning glucose tolerance curve in 1969 and body mass index (BMI). ▲ = Men whose 1975 morning test values were diabetic according to British Diabetic Association criteria.

feature was that they were the only four with glucose tolerance areas exceeding 1000 units. Furthermore, the only man who developed fasting hyperglycaemia (subject 9) had the highest glucose tolerance area as well as the highest BMI.

The table gives the mean values for age, BMI, area under the morning glucose tolerance curve, plasma cholesterol concentration, and systolic blood pressure at the first test for those who did and did not become diabetic. Only glucose tolerance area and BMI differed significantly. We further analysed the data on 25 subjects (data were missing for the other three) using a multiple regression procedure (table C). With progression to morning diabetes as the dependent variable the calculated t value for area under the glucose tolerance curve was much greater than the others. To exclude the possibility that other variables might nevertheless have accounted for the considerable differences in the glucose tolerance areas (see table) a partial F test[8] was carried out. This showed that the glucose tolerance area was still significantly different even when linear relationships with the other variables were allowed for ($F(1, 19) = 12{\cdot}06$; $P < 0{\cdot}01$).

Mean values for age, area under glucose tolerance curve, body mass index (BMI), plasma cholesterol concentration, and systolic blood pressure in men who did and did not develop diabetes. Means expressed ± SE of mean

	Men who developed diabetes (n = 4)	Men who did not develop diabetes (n = 24)	t values	Significance
Age (years)	55 ± 1·78	58 ± 1·33	−0·95	NS
Area under curve (U)	1086·25 ± 72·16	801·21 ± 17·92	5·60	P<0·001
BMI	27·59 ± 1·60	23·91 ± 0·61	2·30	P<0·05
Systolic BP (mm Hg)	147 ± 9·44	132·9 ± 3·41	1·59	NS
Plasma cholesterol mmol/l	5·73 ± 0·45	5·24 ± 0·28	0·71	NS

NS = Not significant.
Conversion: SI to traditional units—Plasma cholesterol: 1 mmol/l ≈ 38·6 mg/100 ml.

When the area under the glucose tolerance curve was excluded from the multiple regression analysis no subgroup of two or more variables provided a significant discriminant function.

Discussion

Our suggestion[3] that an exaggerated diurnal variation in glucose tolerance might be a stage in the evolution of maturity-onset diabetes was based on a cross-sectional study of men with varying degrees of glucose intolerance in the morning. In that group the difference between morning and afternoon blood sugar concentrations after oral glucose diminished with increasing morning blood sugar values. In addition, men with greater degrees of impaired morning glucose tolerance had higher mean values for their overnight fasting blood sugar concentrations than for their afternoon fasting concentrations—a rediscovery of the circadian variation of blood sugar concentrations in diabetics originally described in 1924.[9] This phenomenon was seen again at the follow-up examination of subject 9, who developed overnight fasting hyperglycaemia. It was also seen in the mean values for the whole group. Whereas in 1969 the mean overnight fasting blood sugar concentration was lower than the afternoon fasting value, in 1975 the position was reversed in association with the mean worsening of the morning glucose tolerance.

The results of the afternoon glucose tolerance test, however, did not prove to be an entirely satisfactory predictor of subsequent impairment of morning glucose tolerance when the criteria of the British Diabetic Association were used as guidelines. Two of the seven men with afternoon diabetes (28·6%) compared with two of the 21 with normal afternoon values (9·5%) became both morning and afternoon diabetics, a difference that did not reach significance with Fisher's exact test ($P > 0{\cdot}05$). Much better prediction was obtained by calculating the area under the original morning glucose tolerance curve.

Extrapolation of our results may be warranted but it must be emphasised that the glucose tolerance tests were done under standardised conditions and that blood sugar concentrations were measured in *capillary* blood samples. Glucose tolerance tests are widely believed to show considerable intraindividual variability. This is certainly true when conditions are not standardised, and particularly when venous blood is sampled, for capillary and venous—that is, arteriovenous—blood sugar differences may be considerable and are unpredictable. Nevertheless, under rigidly standardised conditions and with capillary blood samples, Carlström *et al*[10] obtained good reproducibility in oral glucose tolerance tests. This was in a group of borderline diabetics who might have been expected to show more rather than less biological variation.

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Tables A-C may be obtained from Dr R J Jarrett, Unit for Metabolic Medicine, Department of Medicine, Guy's Hospital Medical School, London Bridge, London SE1 9RT.

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