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Intensive attention improves glycaemic control in insulin-dependent diabetes without further advantage from home blood glucose monitoring: results of a controlled trial

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Abstract

Forty-six diabetics treated with twice-daily insulin were seen every two weeks for six months in an intensive education programme aided by regular home urine glucose testing. Control was improved with a decrease in 24-hour urinary glucose excretion (median 138 mmol/24 h (24·8 g/24 h) falling to 70 mmol/24 h (12·6 g/24 h); $p < 0·002$), glycosylated haemoglobin concentration (mean 11·4 ± SD 2·3% falling to 10·4 ± 1·5%; $p < 0·001$), and Diastix score (median 3·0 falling to 1·3; $p < 0·001$). There was no reported increase in hypoglycaemia.

Thirty-eight of the diabetics proceeded to a nine-month randomised cross-over study of the effect on blood glucose control of monitoring urinary glucose or blood glucose measured visually or by a reflectance meter using appropriate reagent strips. No further improvement in control was observed after home blood glucose monitoring. Nevertheless, 29 out of 37 patients preferred blood to urine glucose monitoring.

During both the education and cross-over studies there was evidence of an initial improvement in control followed by deterioration. This was independent of the monitoring method used in the cross-over period and may have been due to waning enthusiasm.

Despite patient enthusiasm and other reports to the contrary, home blood glucose monitoring offered no improvement in control over intensive attention and conventional urine glucose monitoring.

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Introduction

Other studies have shown how poorly many diabetics understand their disease and its management[1-3] and how difficult it may be to obtain information and help from medical and nursing staff and dietitians.[4-7] Attempts to improve patient education and access to advice have been partially successful[3 4 7 8] but metabolic control as assessed by blood and urine glucose estimations remained unchanged.[8] A major problem is the inadequacy of the methods used to assess diabetic control, investigators relying at best on random blood or urine glucose estimations,[8] with their inherent drawbacks,[9 10] or even the frequency of admission to hospital.[4 7] Glycosylated haemoglobin assays, however, now permit the collection of more accurate information about glycaemic control.

Increasing awareness of the importance of good control of blood glucose values in diabetes[11-13] and acknowledgment of the limitations of urine testing[9 10] have led to the introduction of self-monitoring of blood glucose concentrations by the patient as a potential method of improving control.[14-19] The improved control attributed to home blood glucose monitoring in these reports has not been analysed to separate the effect of the inevitable increased attention by the patient and staff from the effect of monitoring alone.

To try to overcome this problem we studied a group of patients who took part in a six-month period of optimisation of diabetic control which included frequent clinic visits and regular conventional urine testing. This was followed by a nine-month

period when patients monitored and managed their own progress using home blood glucose or urine glucose estimations in a cross-over study. To investigate the importance of a reflectance meter as opposed to visual assessment of glucose reagent strips we included both procedures in the second part of the study. Throughout the 15 months objective measurements of diabetic control were recorded.

Patients and methods

A total of 154 patients on our diabetic clinic register aged 16-60 years and receiving twice-daily insulin were invited by letter to participate in a study of diabetic control. They were told that the study would include intensive efforts to improve their control, firstly with conventional urine testing and subsequently with home blood glucose monitoring as aids. Pregnant patients, those taking drugs known to alter carbohydrate metabolism (for example, oral contraceptives), and patients with renal disease (plasma creatinine concentration >200 μmol/l (>2·26 mg/100 ml)) or proliferative retinopathy were excluded.

Table I shows the design of the study. During the initial six-month optimisation period patients managed their diabetes solely with regular urine tests. They were then allocated at random to one of six groups to define the sequence of the subsequent monitoring methods. Monitoring of urine with glucose reagent strips continued throughout the nine-month cross-over period but was the only method used in the periods marked "urine." In the periods marked "visual" and "meter" self-monitoring of blood glucose values was performed in addition using, respectively, glucose reagent strips read by eye against a colour scale and strips read in a reflectance meter.

Fifty-four patients entered the study but eight were subsequently excluded (table II). Results are presented for 27 men and 19 women completing the six-month optimisation period (mean % ideal body weight[20] 104±SD 10, range 83-131; mean age 34±SD 9 years, range 16-51).

Two patients excluded from the initial six-month analysis rejoined at the beginning of the cross-over study (the patient taking once-daily insulin had returned to twice-daily injections, and one pregnant diabetic had a therapeutic abortion on social grounds, but she then withdrew again soon after rejoining). Thus 48 patients proceeded to the cross-over period but 10 were excluded (table II). Results are presented for the 38 patients completing this phase (24 male, 14 female; mean % ideal body weight 103±9, range 85-134; mean age 36±9 years, range 17-51). All patients began the cross-over study at the same time. Hence a few had less than 12 visits in the optimisation period because occasional visits were made at three-weekly intervals owing to other commitments. Thus all 46 patients completed nine visits, 45 completed 10, 44 completed 11, and 37 completed 12 visits before entering the cross-over period.

TABLE I—*Study design (method of monitoring diabetic control)*

Optimisation period	Cross-over period			
6 months	3 months	3 months	3 months	No of patients*
Urine	Urine	Visual	Meter	7
Urine	Urine	Meter	Visual	6
Urine	Visual	Urine	Meter	6
Urine	Visual	Meter	Urine	7
Urine	Meter	Urine	Visual	6
Urine	Meter	Visual	Urine	6

Urine = Semiquantitative urine tests (Diastix). Visual = BM-Glycemie 20-800 strips read visually. Meter = Reflotest-Glucose strips read with a reflectance meter.
*Number of patients shown for each subgroup in cross-over period.

TABLE II—*Reasons for withdrawal from study*

No entering optimisation period		54
Failure to return to clinic	4	
Pregnancy	2	
Moved from area	1	
Period on once-daily insulin	1	
No completing optimisation period		46
No entering cross-over period		48*
Pregnancy	3	
"Insufficient time"	2	
"Social problems"	2	
Non-compliance	2	
"Nerves"	1	
No completing cross-over period		38

*Two patients re-entered at beginning of cross-over period (see text).

PROTOCOL

Patients were seen fortnightly by either RW or PDH with 30 minutes available for each visit. Between visits patients were encouraged to telephone with problems, but they rarely did this. An initial assessment of dietary intake was obtained by an experienced dietitian, who was available for consultation throughout. At each visit patients were weighed, symptoms assessed, and a record made of current dietary intake and insulin dose. The number of symptomatic hypoglycaemic episodes in the preceding fortnight was noted (defined as any event necessitating additional carbohydrate to correct symptoms thought by the patient to be due to hypoglycaemia).

Patients were instructed on the importance of a regular carbohydrate intake and on modification to diet and insulin dosage, depending on changes in weight, physical activity, or diabetic control as assessed by home tests. Patients were instructed carefully in the performance and interpretation of urine and blood tests, and this was monitored frequently throughout the study. They were told to take their insulin 20-30 minutes before meals, and injection techniques and sites were periodically assessed. All subjects continued with twice-daily short-acting (Actrapid (Novo) or soluble (Wellcome)) and intermediate-acting insulins (Insulatard (Nordisk), isophane (Wellcome), or Monotard (Novo)).

Urine tests were performed by the patients using semiquantitative urine tests (Diastix, Ames) four times daily, before main meals and at bedtime. Results were recorded graphically. For later statistical analysis Diastix results were scored by the medical staff (0% = 1; 0·1% = 2; 0·25% = 3; 0·5% = 4; 1% = 5; 2% = 6) and median scores for each two-week period thus obtained.

Visual estimations of blood glucose concentrations were performed by patients using BM-Glycemie 20-800 reagent strips (Boehringer Mannheim).[21-24] A series of Glucochek meters (Medistron Ltd, Alpine Works, Crawley, Sussex) were modified to read Reflotest-Glucose reagent strips (Boehringer Mannheim) rather than Dextrostix (Ames), in view of the better overall performance characteristics of the former.[23] Estimations below 4 mmol/l (72 mg/100 ml) on the meter were repeated with visual reading of the Reflotest-Hypoglycemie reagent strip (Boehringer Mannheim) because the standard Reflotest-Glucose strips were not accurate at hypoglycaemic concentrations. The accuracy of the two systems within the first fortnight was assessed for each patient by taking simultaneous samples for laboratory analysis of blood glucose values and comparing patient and laboratory results. Correlation coefficients for visually read samples (n = 37) and meter-read samples (n = 35) were 0·79 ($p < 0·001$) and 0·78 ($p < 0·001$), respectively.

Visual readings were overestimated as often (17 times) and by the same amount (median error 1·4 mmol/l (25 mg/100 ml), range 0·2-7·0 mmol/l (4-126 mg/100 ml)) as they were underestimated (20 times, median error 1·4 mmol/l (25 mg/100 ml), range 0·1-8·1 mmol/l (2-146 mg/100 ml)). Meter-read samples, however, were overestimated (27 times, median error 2·2 mmol/l (40 mg/100 ml), range 0·1-8·0 mmol/l (2-144 mg/100 ml)) more than they were underestimated (eight times, median error 0·5 mmol/l (9 mg/100 ml), range 0·4-1·4 mmol/l (7-25 mg/100 ml)). Patients were asked to monitor their blood glucose values on at least two days each week with samples taken before and one hour after each main meal and before bedtime. They were also encouraged to perform intermittent estimations on intervening days, concentrating particularly on times known to be associated with problems with control. Sampling was aided using atraumatic lancets (Monolet, Sherwood) and a spring-loaded capillary puncture device (Autolet, Owen-Mumford). Advice on adjusting insulin dosage from results obtained was similar to the guidelines advocated by Skyler *et al*,[25] with adjustment of insulin dosage if a clear pattern arose in successive profiles. Compensation for variations in activity was usually dietary except for strenuous exercise, when a reduction in insulin dosage was also advised.

One or two days before each visit patients were asked to obtain a seven-point capillary blood glucose profile consisting of samples collected before and one hour after meals and before bedtime. Blood was collected into fluoride-oxalate containers for laboratory analysis. A single 24-hour urine collection was also obtained before each visit for subsequent glucose analysis.

At every clinic attendance venous blood samples were obtained for glycosylated haemoglobin estimation. At the beginning and end of

the optimisation period and at the end of each cross-over period blood (after a meal) was collected for analysis of serum total cholesterol and plasma urea and creatinine concentrations. Postprandial blood samples for plasma C-peptide estimation were obtained on one to three (median 3) occasions from each subject. C-peptide results were expressed as positive or negative.

At the first visit in the optimisation period patients were instructed in the collection of samples, and thus the first results for median Diastix and blood and urinary glucose measurements were obtained at visit 2.

Three months after the cross-over study patients completed a questionnaire asking about attitudes to the various methods of monitoring control.

CHEMICAL METHODS

Whole blood glucose was analysed by a standard automated glucose oxidase assay (Technicon AA II, Boehringer GOD-PAP). Urine glucose was estimated by a hexokinase method (Roche) with aqueous chlorhexidine (Hibitane, 20% vol/vol) as preservative (one volume to 100-400 volumes of urine). Glycosylated haemoglobin was analysed by a modification of the colorimetric method of Fluckiger *et al.*[26 27] Interassay variation for the glycosylated haemoglobin estimation was 3·8% and the reference range 5·0-8·2%. Autoanalyser techniques were used for estimating serum total cholesterol (Technicon AA II, fully enzymatic GOD-PAP) and plasma urea and creatinine concentrations (Technicon SMA 6/60). Plasma C-peptide was estimated with antibody M1230, which has a detection limit of 0·06 nmol/l.[28]

STATISTICAL METHODS

Statistical analyses were performed on an IBM computer (370/168) using programs from the Statistical Package for Social Sciences. Differences from baseline measurements were analysed with Student's paired *t* test (glycosylated haemoglobin, pre- and postprandial, and mean blood glucose, serum cholesterol, plasma urea and creatinine, dietary carbohydrate intake, insulin dose, and body weight) or Wilcoxon's matched pairs signed-rank test (24-hour urinary glucose excretion, frequency of hypoglycaemia, and Diastix scores). Differences between groups of patients at individual times were assessed by Student's unpaired *t* test or Wilcoxon's unpaired rank test. Correlations were sought by linear regression analysis or Spearman's ranking method as appropriate, and trends of change over the study period sought by analysis of variance or the Kruskal-Wallis test for differences between visits.

Values are expressed as the mean, mean ± SD, or median + range.

A mean preprandial blood glucose value was calculated for each individual blood glucose profile only if three or more capillary blood samples were provided (out of a possible four). Similarly, a mean overall blood glucose value (preprandial and postprandial samples) was determined only if six or more samples were obtained (out of a possible seven). For the group as a whole mean blood glucose represents the mean ± SD of the mean blood glucose concentrations in all subjects with a valid profile at a particular visit.

Results

OPTIMISATION PERIOD (SIX MONTHS)

24-Hour urinary glucose excretion

Urinary glucose excretion fell during the study (table III). Initial median 24-hour values (138 (range 1-591) mmol/24 h (24·8 (range 0·2 106·4) g/24 h) at visit 2) fell significantly using paired comparisons by visit 10 (70 (1-508) mmol/24 h (12·6 (0·2-91·4) g/24 h); $p < 0·002$) and visit 11 (52 (1-745) mmol/24 h (9·4 (0·2-134·1) g/24 h); $p < 0·02$). The correlation between median 24-hour urinary glucose excretion and visit number was significant ($n = 11$; $r_s = -0·79$; $p < 0·01$). Figure 1 shows the median change in median 24-hour urinary glucose excretion over the six months.

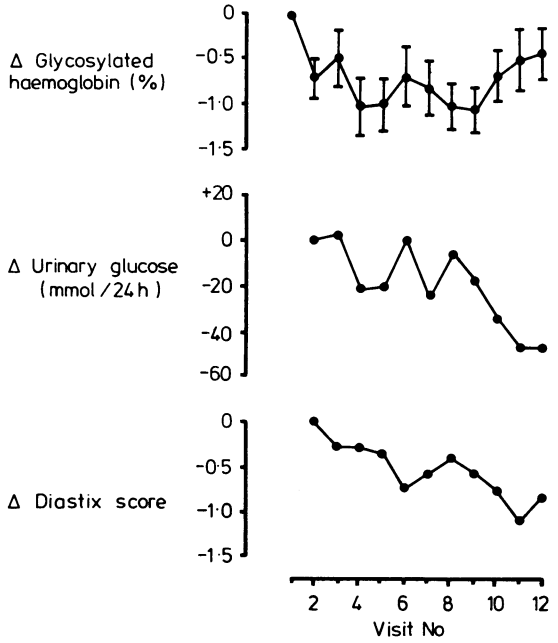

FIG 1—Changes in glycosylated haemoglobin, 24-hour urinary glucose excretion, and Diastix score over optimisation period. Results expressed as mean change (± SEM) in mean glycosylated haemoglobin, median change in median 24-hour urinary glucose, and median change in median Diastix score. Visits made two-weekly.

Conversion: SI to traditional units—Urinary glucose: 1 mmol/24 h ≈ 0·18 g/24 h.

TABLE III—*Twenty-four-hour urinary glucose excretion, Diastix scores, and glycosylated haemoglobin and mean blood glucose concentrations during initial six-month optimisation period*

Visit No	24-Hour urinary glucose (mmol/24 h)				Diastix score				Glycosylated haemoglobin (%)			Mean blood glucose (mmol/l)			
												Preprandial		Overall§	
	n	Median	Range	p†	n	Median	Range	p†	n	Mean ± SD	p‡	n	Mean ± SD	n	Mean ± SD
1	*	*	*	*	*	*	*	*	46	11·4 ± 2·3	—	*	*	*	*
2	45	138	1-591	—	45	3·0	1-6	—	44	10·7 ± 2·0	<0·01	26	8·1 ± 3·7	9	10·3 ± 4·1
3	45	108	1-934	NS	46	2·7	1-6	<0·05	45	11·0 ± 2·0	NS	33	8·6 ± 2·8	13	8·7 ± 2·7
4	42	82	2-823	NS	46	2·1	1-6	<0·02	46	10·4 ± 1·8	<0·005	33	8·7 ± 2·6	18	8·9 ± 2·0
5	43	95	1-747	NS	45	2·3	1-6	<0·05	41	10·4 ± 1·9	<0·005	39	9·0 ± 3·4	23	9·4 ± 3·2
6	43	106	3-659	NS	45	1·7	1-5	<0·001	34	10·8 ± 1·5	NS	41	8·8 ± 3·4	27	9·4 ± 3·3
7	44	88	2-959	NS	45	1·6	1-6	<0·002	40	10·7 ± 2·2	<0·02	43	8·4 ± 2·7	26	8·7 ± 2·5
8	42	118	1-624	NS	45	1·8	1-6	<0·002	46	10·4 ± 1·6	<0·001	44	8·6 ± 3·2	30	9·2 ± 2·4
9	44	65	1-937	NS	46	1·6	1-5	<0·001	46	10·4 ± 1·5	<0·001	41	7·7 ± 2·9	21	8·7 ± 3·4
10	43	70	1-508	<0·002	43	1·4	1-5	<0·001	45	10·7 ± 1·9	<0·05	39	9·2 ± 3·7	27	10·6 ± 4·1
11	40	52	1-745	<0·02	42	1·3	1-5	<0·001	44	10·9 ± 1·8	NS	40	8·2 ± 2·9	27	9·1 ± 3·3
12	33	46	1-685	NS	37	1·7	1-5	<0·001	37	11·0 ± 1·9	NS	28	8·5 ± 4·6	17	10·2 ± 4·7

*Patients instructed on sampling at visit 1 and therefore results available from visit 2 only. Visits made two-weekly.
†Differences from visit 2 tested for significance with Wilcoxon's matched pairs signed-rank test.
‡Differences from visit 1 tested for significance with Student's paired *t* test.
§Mean overall blood glucose includes preprandial and postprandial samples. By Student's paired *t* test no mean blood glucose value significantly different from visit 2.
Conversion: SI to traditional units—Urinary glucose: 1 mmol/24 h ≈ 0·18 g/24 h. Blood glucose: 1 mmol/l ≈ 18 mg/100 ml.

Diastix score

Median Diastix scores fell over the study period ($p < 0.001$ for the last four visits) (table III). Paired testing against visit 2 was significant at all subsequent times, and the correlation between Diastix scores and visit number was highly significant ($r_s = -0.82$; $p < 0.005$). This trend was confirmed by the Kruskal-Wallis test ($p < 0.005$). Figure 1 shows the median change in Diastix score during the study.

Glycosylated haemoglobin

During the education period glycosylated haemoglobin concentrations fell rapidly from visit 1 ($11.4 \pm 2.3\%$) to visit 2 ($10.7 \pm 2.0\%$: $p < 0.01$) and reached the nadir at visit 9 ($10.4 \pm 1.5\%$; $p < 0.001$) (table III). Thereafter, values rose and were not significantly different from baseline at visits 11 and 12. The rise at visit 12 (to $11.0 \pm 1.9\%$) was significant compared with values at visit 9 ($10.4 \pm 1.5\%$; $p < 0.005$) (fig 1).

Blood glucose

Mean blood glucose concentrations did not alter over the six months (table III). Values after lunch were significantly increased at visits 7, 9, and 11 compared with the initial assessment, whereas values after the evening meal showed a fall, achieving significance at visits 8-11 (table IV). Blood glucose concentrations did not change significantly at other times.

Serum cholesterol

Serum cholesterol concentrations fell over the six-month study period (initial value 6.3 ± 1.4 mmol/l (244 ± 54 mg/100 ml), final value 5.7 ± 1.3 mmol/l (221 ± 50 mg/100 ml); $p < 0.001$).

Plasma urea and creatinine, and urine creatinine

There was no significant change in either plasma urea (initial value 5.1 ± 1.1 mmol/l (31 ± 7 mg/100 ml), final value 5.4 ± 1.2 mmol/l (33 ± 7 mg/100 ml)) or plasma creatinine concentrations (initial 74 ± 12 μmol/l (0.84 ± 0.14 mg/100 ml), final 76 ± 13 μmol/l (0.86 ± 0.15 mg/100 ml)) over the six months. Mean 24-hour urinary creatinine excretion was also unchanged (initial 11.6 ± 3.3 mmol/24 h (1.3 ± 0.4 g/24 h), final 12.1 ± 3.0 mmol/24 h (1.4 ± 0.3 g/24 h)).

Duration of diabetes and plasma C-peptide values

The overall duration of diabetes in the group was 15 ± 8 years (range 1-32). Only six patients had measurable circulating C-peptide concentrations. In these patients the mean duration of diabetes was less than in the remainder of the group (6 ± 4 *v* 16 ± 7 years; $p < 0.001$). While measures of control were usually nearer normal in patients with positive C-peptide results, the small number in this group precluded meaningful statistical analysis. Trends were similar to those in patients with negative results. In particular, review of the data for glycosylated haemoglobin after removal of patients with positive C-peptide results showed no change from the pattern previously described for the whole group.

Frequency of symptomatic hypoglycaemia

There was no significant change in the number of hypoglycaemic episodes during the study (table V).

TABLE V—*Frequency of hypoglycaemia during optimisation period*

No of hypoglycaemic episodes reported over preceding two weeks	No of patients			
	Visit 1	Visit 5	Visit 9	Visit 12
0	24	24	26	17
1	10	14	9	9
2	7	3	3	7
3	0	1	2	0
4	1	0	2	0
5-10	1	1	1	1
>10	0	0	0	0
No of patients with record available	43	43	43	34

Body weight, insulin dose, and carbohydrate intake

For the group as a whole there was no significant change in body weight (initial weight 66.2 ± 10.7 kg, final weight 66.4 ± 9.9 kg) or mean total daily insulin dose (initial dose 53 ± 20 units, final dose 55 ± 17 units) over the study period. Nevertheless, significant changes did occur in the distribution of insulin dose through the day. Thus when initial and final visits were compared the mean dose of short-acting insulin fell in the morning (18 ± 9 units *v* 13 ± 6 units; $p < 0.001$), while the mean dose of intermediate-acting insulin rose both in the morning (9 ± 8 units *v* 15 ± 9 units; $p < 0.001$) and in the evening (14 ± 8 units *v* 17 ± 7 units; $p < 0.005$).

The mean estimated total dietary intake of carbohydrate fell slightly but significantly from 176 ± 45 g/day at the initial visit to 166 ± 48 g/day at the final visit ($p < 0.001$).

CROSS-OVER PERIOD (NINE MONTHS)

Comparisons between different methods of self-monitoring

Table VI gives the values for glycosylated haemoglobin, 24-hour urinary glucose excretion, median Diastix scores, and mean blood glucose estimations. Results were those at the end of the six-month "run-in" period of optimisation of control with urine tests and during the cross-over period after self-monitoring by semiquantitative urine tests, visual assessment of glucose strips, and assessment with reflectance meter, irrespective of their order during the cross-over study. There was no significant change from initial values (end of run-in period) in any of these estimates of control, and no differences were found among the individual methods of self-monitoring. Examination of values at individual clinic visits (fig 2) also showed no change in glycosylated haemoglobin or in urine glucose excretion during self-monitoring by any method over the cross-over period.

TABLE IV—*Blood glucose concentrations (mean ± SD) at each individual time-point during optimisation period. Values given in mmol/l*

Visit No	Fasting		Before lunch		Before evening meal		Before bed		After breakfast		After lunch		After evening meal	
	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD
2	23	10.0 ± 5.5	27	6.7 ± 5.4	34	9.5 ± 4.0	26	6.2 ± 3.4	14	14.1 ± 5.2	14	7.8 ± 2.1	11	13.5 ± 3.3
3	31	10.1 ± 4.7	36	6.4 ± 4.0	41	10.6 ± 4.9	36	7.3 ± 4.2	11	12.8 ± 4.6	18	9.5 ± 3.6	20	11.4 ± 6.0
4	34	10.1 ± 4.1	32	6.7 ± 3.7	34	9.9 ± 5.0	37	7.4 ± 4.5	22	11.1 ± 5.0	19	9.1 ± 3.0	15	9.9 ± 2.8
5	38	11.3 ± 6.0	39	7.0 ± 5.2	38	9.9 ± 4.6	37	7.3 ± 4.0	25	13.2 ± 5.5	28	8.4 ± 4.0	24	10.3 ± 4.3
6	41	11.2 ± 5.6	39	6.1 ± 4.5	43	10.1 ± 5.1	35	6.9 ± 4.2	27	13.0 ± 5.8	25	8.4 ± 3.4	26	10.4 ± 5.2
7	43	10.4 ± 4.5	41	6.3 ± 4.8	41	9.4 ± 4.8	42	7.0 ± 3.7	28	12.7 ± 5.5	31	9.3 ± 4.2*	24	9.4 ± 5.0
8	39	10.8 ± 5.3	44	6.9 ± 4.9	42	9.9 ± 4.5	42	7.6 ± 4.5	32	12.8 ± 5.7	33	9.8 ± 4.6	27	8.9 ± 4.6**
9	39	8.4 ± 4.0	40	6.9 ± 4.3	39	8.2 ± 4.6	41	7.2 ± 4.5	28	12.9 ± 4.5	25	9.6 ± 4.9*	24	8.7 ± 4.9***
10	41	10.3 ± 4.3	38	7.0 ± 5.2	38	10.3 ± 5.5	39	8.2 ± 5.3	30	12.4 ± 5.7	26	10.8 ± 4.8	28	11.4 ± 5.8*
11	41	9.2 ± 3.8	40	7.2 ± 5.5	38	9.0 ± 4.8	37	7.4 ± 4.8	29	11.3 ± 5.1	26	10.1 ± 3.9*	26	8.7 ± 5.7**
12	28	9.8 ± 5.5	29	7.3 ± 5.9	28	9.5 ± 5.8	28	7.9 ± 5.1	19	14.0 ± 6.7	20	10.0 ± 5.9	19	8.8 ± 5.9

Comparison with values at visit 2: *$p < 0.05$; **$p < 0.005$; ***$p < 0.001$ (Student's paired *t* test).
Conversion: SI to traditional units—Blood glucose: 1 mmol/l ≈ 18 mg/100 ml.

TABLE VI—*Results at induction to cross-over study and after 12 weeks of monitoring of control with urine tests, blood glucose values read visually, and blood glucose values read by meter. Values expressed as means ±SD or as medians (and range)*

	Induction to cross-over study	After 12 weeks of monitoring		
		Urine tests	Visual blood glucose	Meter blood glucose
Glycosylated haemoglobin (%)	10·8±1·8	10·5±2·0	10·6±2·1	10·4±1·9
Urinary glucose (mmol/24 h)	81·5 (0-685)	59 (1-903)	82 (0-680)	84 (0-1009)
Diastix score	1·5 (1-5)	1·4 (1-6)	1·4 (1-6)	1·5 (1-6)
Mean preprandial blood glucose (mmol/l)	7·9±2·9 (n=35)	8·6±3·6 (n=38)	8·0±2·9 (n=32)	8·0±3·6 (n=33)
Mean preprandial and postprandial blood glucose (mmol/l)	8·3±2·4 (n=24)	9·2±3·3 (n=25)	8·2±2·6 (n=23)	8·4±3·0 (n=21)
Serum total cholesterol (mmol/l)	5·6±1·2	5·5±1·1	5·6±1·1	5·5±1·1
Plasma urea (mmol/l)	5·5±1·2	5·3±1·2	5·5±1·1	5·4±1·2
Plasma creatinine (μmol/l)	76±13	82±13**	82±16**	82±13**
Frequency of hypoglycaemia per fortnight	0·5 (0-3)	0·4 (0-7)	0·4 (0-10)	0·7 (0-4)
Total insulin dose (units/day)	54±15	54±16	53±18	54±17
Body weight (kg)	66·7±9·4	67·2±10·7	67·7±10·2	67·2±10·8
Dietary carbohydrate (g/day)	173±49	171±50*	169±52*	170±50

Comparison with values at induction: *$p<0.05$; **$p<0.01$. All other comparisons not significant.
Conversion: SI to traditional units—Urinary glucose: 1 mmol/24 h ≈ 0·18 g/24 h. Blood glucose: 1 mmol/l ≈ 18 mg/100 ml. Cholesterol: 1 mmol/l ≈ 38·7 mg/100 ml. Urea: 1 mmol/l ≈ 6·02 mg/100 ml. Creatinine: 1 μmol/l ≈ 0·0113 mg/100 ml.

The design of the study produced six subgroups depending on the sequence of using the three monitoring methods (table I). Figure 3 shows the mean glycosylated haemoglobin values for each of these at each clinic visit. No monitoring method was associated with any particular trend in values. Past use of a meter did not improve results when using visual interpretation of strips.

Serum cholesterol concentration was not influenced by any method of self-monitoring (table VI). Plasma urea concentrations were also unchanged but plasma creatinine values rose slightly but significantly during the cross-over study, independently of the means of control ($p<0.01$) (table VI).

The frequency of symptomatic hypoglycaemia was low and not influenced by any method of self-monitoring (table VI).

There were no significant differences in total daily insulin dose, body weight, or dietary carbohydrate intake among the three different monitoring techniques. Dietary carbohydrate intake at induction to the cross-over study was 173±49 g/day and showed a slight fall with each monitoring method (urine testing 171±50 g/day ($p<0.05$), visual testing 169±52 g/day ($p<0.05$), meter testing 170±50 g/day (NS)).

Of the 38 patients, 37 completed the questionnaire. No patient thought that urine testing was ideal for monitoring control (table VII), in contrast to 21 patients (57%) who believed that blood testing alone was superior. Fifteen patients (40%) thought that blood and urine testing together was better. All but one of the patients (97%), therefore, thought blood testing, either alone or in combination with urine tests, was *ideal* for controlling their diabetes. Eight patients (22%), however, thought that urine tests were the most practical means of self-monitoring, blood tests alone were considered to be the most practical by 14 (38%), and a combination of both methods was preferred by 15 patients (40%). Thus 29 patients (78%) thought that blood testing was a useful, *practical* technique.

No clear preference was expressed for blood glucose monitoring by visual inspection of the strip (20 patients, 54%) as opposed to meter reading (16 patients, 43%). One patient was ambivalent.

Three months after the study, 31 patients (84%) were still regularly carrying out home blood glucose testing, though less frequently than during the study period, only 16 patients (43%) testing more than five samples a week.

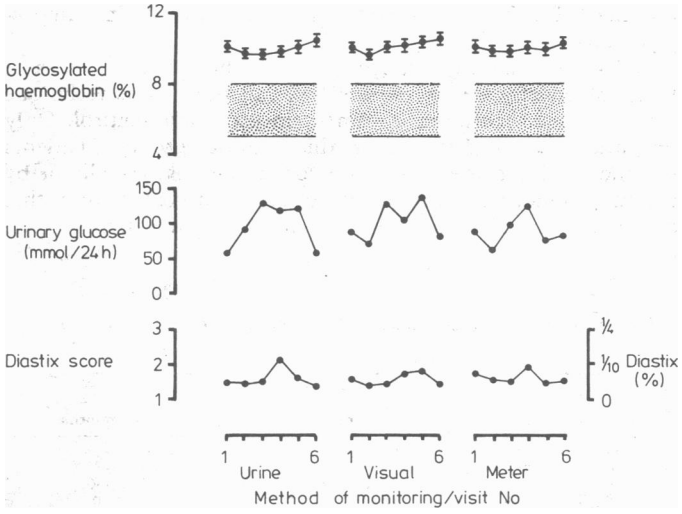

FIG 2—Results for glycosylated haemoglobin (mean±SEM), 24-hour urinary glucose excretion (median), and median Diastix score (median) at each visit in cross-over period, irrespective of sequence of using three methods of monitoring. Shaded area indicates normal range for glycosylated haemoglobin (5·0-8·2%). Visits made two-weekly.

Conversion: SI to traditional units—Urinary glucose: 1 mmol/24 h ≈ 0·18 g/24 h.

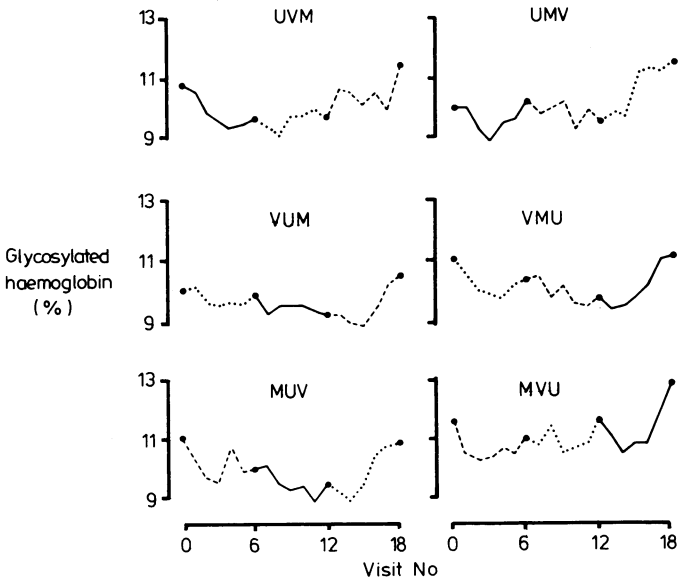

FIG 3—Results for mean glycosylated haemoglobin at every visit in each of six subgroups of patients showing method of monitoring control. Urine testing (U ●——●); visual monitoring of blood glucose (V ●. . . . . ●); meter monitoring of blood glucose (M ●— — — — — ●). Visits made two-weekly.

TABLE VII—*Patients' opinions of "best" and "most practical" methods of monitoring control of their diabetes. Results expressed as number (%) of patients (n=37)*

	"Best"	"Most practical"
Urine tests	0	8 (22)
Blood tests	21 (57)	14 (38)
Combination of urine and blood	15 (40)	15 (40)
None	1 (3)	0

Chronological analysis

Data from the study were also analysed chronologically independently of the method of monitoring. Table VIII gives the results for the end of each cross-over period—that is, three, six, and nine months.

Glycosylated haemoglobin values fell from 10·8±1·8% at induction to the study to 10·2±1·4% at three months ($p < 0·02$) and to 9·9±1·7% at six months ($p < 0·005$ *v* induction values). By the end of the study, at nine months, values had, however, risen to 11·4±2·4% ($p < 0·001$ *v* six-month value) (table VIII).

No significant changes occurred in 24-hour urinary glucose excretion, median Diastix score, or mean blood glucose or serum cholesterol concentrations (table VIII). Although the rise in glycosylated haemoglobin values at nine months was reflected in trends to increased 24-hour urinary glucose excretion and median Diastix score, these changes were not significant.

Daily dietary carbohydrate intakes were less than initial levels (173±49 g) at six months (169±50 g; $p < 0·05$) and nine months (169±51 g; $p < 0·05$). There were no significant differences in total daily insulin dose or body weight at any time point (table VIII).

Figure 4 shows the changes in mean glycosylated haemoglobin values, median 24-hour urinary glucose excretion, and median Diastix score for each of the individual visits analysed chronologically. No trends were evident between cross-over points.

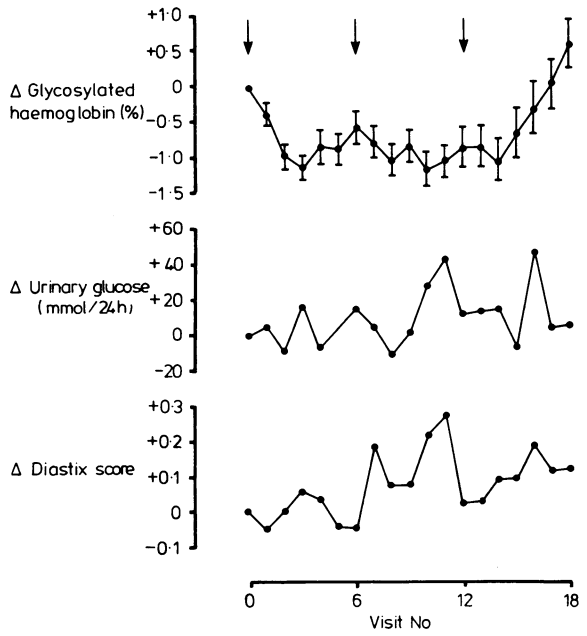

FIG 4—Results for mean change (±SEM) in glycosylated haemoglobin, median change in 24-hour urinary glucose excretion, and median change in median Diastix score over nine-month cross-over period (18 visits). Results shown chronologically irrespective of method of monitoring. Monitoring methods changed at visits 0, 6, and 12 (arrowed). Visits made two-weekly.

Conversion: SI to traditional units—Urinary glucose: 1 mmol/24 h ≈ 0·18 g/24 h.

Discussion

Assessing the quality of diabetic control in insulin-dependent outpatients is difficult,[29] and we therefore used multiple objective measurements. The inaccuracies associated with semiquantitative urine glucose analyses performed by the patient[9 29] may be offset considerably by measurement of multiple samples to provide an index of control. Twenty-four-hour urinary glucose excretion may be accurately measured and correlates well with mean blood glucose concentration assessed by continuous analysis,[10] but this provided only an intermittent index in this study. The unchanged urinary creatinine excretion confirmed that collections were consistent. Even frequent blood glucose samples may be relatively unreliable indices of overall control in insulin-dependent diabetes.[29-31] Estimation of glycosylated haemoglobin values provides a reliable measure of mean blood glucose concentration over the weeks before sampling, despite some difficulties with the method and interpretation of results.[32-36] Finally, since poor control may be associated with hyperlipidaemia,[37] measurement of blood lipid values may give further information on control.

Frequent outpatient visits and intensive education together with conventional urine glucose analysis were associated with significant improvements in quantitative and semiquantitative urinary glucose, glycosylated haemoglobin, and total serum cholesterol values. Other workers have failed to show objective improvements after such efforts.[7 8] This may have been due to the inadequacy of their methods of assessing control, since in our study frequent but intermittent blood glucose estimations also failed to reflect the change in control. Compliance in producing capillary blood for laboratory glucose analysis was never good, especially at the beginning of the study and after meals (table IV), so that some improvement may have gone unobserved. The change in serum cholesterol values was probably attributable to better diabetic control, since we did not attempt to change the nature or content of dietary fat.[38-40]

In the first six months of the study symptomatic hypoglycaemia before lunch and pronounced fasting glycosuria were commonly recorded, resulting in redistribution of the insulin dose with more emphasis on intermediate-acting insulin. Subsequently laboratory blood glucose values confirmed that these changes were appropriate (table IV), but the effect on blood glucose concentrations was disappointing. The deterioration noted after lunch and the improvement after the evening meal may have resulted from the change in insulin distribution. Others have noted the difficulty in controlling postprandial hyperglycaemia, even in diabetics in hospital.[41] Our results show the need for better methods of controlling fasting hyperglycaemia.

It has been strongly suggested from the earliest studies of home blood glucose monitoring[14-19] that use of this technique results in a dramatic improvement in glycaemic control. Only one study has failed to support this.[42] In our group of patients self-monitoring of blood glucose concentrations, visually or by meter, produced no further improvement in control than that achieved by regular urine tests and intensive education.

TABLE VIII—*Results at induction to cross-over study and after three, six, and nine months, irrespective of monitoring method used. Values expressed as means ±SD or as medians (and range)*

	Induction to cross-over study	Three months	Six months	Nine months
Glycosylated haemoglobin (%)	10·8±1·8	10·2±1·4**†	9·9±1·7††***	11·4±2·4
24-Hour urinary glucose (mmol/24 h)	81·5 (0-685)	72·5 (0-1009)	76·5 (0-903)	105 (1-809)
Diastix score	1·5 (1-5)	1·3 (1-6)	1·4 (1-6)	1·8 (1-6)
Mean preprandial blood glucose (mmol/l)	7·9±2·9 (n=35)	8·8±3·2 (n=34)	7·3±2·9 (n=35)	8·5±3·8 (n=34)
Mean preprandial and postprandial blood glucose (mmol/l)	8·3±2·4 (n=24)	8·8±2·7 (n=24)	8·0±2·8 (n=25)	9·2±3·5 (n=20)
Serum total cholesterol (mmol/l)	5·6±1·2	5·6±1·2	5·6±1·1	5·4±1·0
Total insulin dose (units/day)	54±15	53±15	55±17	53±19
Body weight (kg)	66·7±9·4	67·0±10·1	67·2±10·9	67·8±10·8
Dietary carbohydrate (g/day)	173±49	172±51	169±50*	169±51*

Comparison with values at induction: *$p < 0·05$; **$p < 0·02$; ***$p < 0·005$.
Comparison with values at nine months: †$p < 0·002$; ‡$p < 0·001$. All other comparisons not significant.
Conversion: SI to traditional units—Urinary glucose: 1 mmol/24 h ≈ 0·18 g/24 h. Blood glucose: 1 mmol/l ≈ 18 mg/100 ml. Cholesterol: 1 mmol/l ≈ 38·7 mg/100 ml.

There are several possible reasons for the discrepancies between our own and earlier results. Our subjects were recruited by letter without prior knowledge of the patient or his quality of control, and medical reasons for exclusion (pregnancy, renal failure, etc) were clearly defined at the outset. Before starting home blood glucose monitoring all of our patients had their control optimised so far as possible by conventional means with intensive education and regular home urine testing; this is particularly important in view of the improvements noted in our run-in period. In the cross-over period each patient served as his own control. In contrast, other investigators have selected their patients for specified (or unspecified) reasons but, perhaps more important, not made intensive efforts to optimise control by conventional means and not included control groups.[43]

There may be other reasons for the disparity between this and other reports. Though our patients were well motivated, they did not monitor blood glucose values *every* day as in certain previous studies, and this intensity of monitoring may be necessary for full benefits to accrue.[44 45] Some workers[14 44] have also used multiple (more than two) injections of insulin daily, whereas our patients were receiving twice-daily injections. Also all but six of our patients gave negative C-peptide results and thus may have been less responsive to the benefits of home blood glucose monitoring. The small number of patients with positive C-peptide results did not permit meaningful comparisons but we could see no obvious differences in trend between those with positive and negative results. Work by Seigler *et al*[46] suggests that in the short term (two months) excellent control may be achieved in patients with negative C-peptide results taking twice-daily insulin provided intensive monitoring and education is used.

Schiffrin and Belmonte, who used four injections daily *and* obtained seven capillary blood glucose samples *every* day, achieved excellent glycaemic control over six months in a group of 16 patients with negative C-peptide results.[47] Unfortunately they did not define their selection procedure. They also showed that reducing the frequency of capillary blood glucose sampling to twice daily resulted in a deterioration in control. We specifically tried to place only realistic demands on our patients, since we have not been able to persuade patients to adopt the intensity of management used by Schiffrin and Belmonte.

Though home blood glucose monitoring did not appear to improve control in our patients, certain selected groups may find it helpful. Real benefit may, for example, occur in pregnancy (though this is contrary to the findings of one study[42]) in the presence of altered renal threshold for glucose or unstable control with recurrent hypoglycaemia.

Our patients greatly preferred home blood glucose measurements to urine tests alone. The importance of this should not be underestimated. Most of our patients, as in other studies,[14-19 44-47] derived a considerable amount of confidence and knowledge from the ability to measure their own blood glucose concentrations whenever required. This was particularly true with testing before bedtime. In the long term the preference for blood as opposed to urine tests might lead to a greater awareness and understanding of the importance of control by the patient, though this requires confirmation in long-term studies. The use of a meter, however, appears unnecessary, since it produced no better control and was not preferred by our patients when compared with visual readings.

In both the optimisation and cross-over periods there was evidence for an initial improvement in control with a subsequent deterioration. We cannot exclude the possibility of a seasonal variation[48] in the control of our diabetics but think it more likely to have been due to an initial enthusiasm under study conditions which subsequently waned. The crossover nature of the home blood glucose monitoring period prevented this from influencing our results and is lacking in other studies. Our experience shows the difficulty in maintaining enthusiasm over prolonged periods, which has been noted by others.[3] The short-term improvement but long-term deterioration in control shown in our chronological analysis emphasises the need for studies to be adequately controlled and of sufficient duration to allow for this problem.

Opponents of the policy of striving for improved control of blood glucose concentrations have pointed out the possibility of increased morbidity associated with hypoglycaemia.[13] The improved control with education and regular urine tests was not obtained at the price of more frequent hypoglycaemia, though episodes may have gone unrecognised. In the cross-over period urine and blood glucose monitoring resulted in similar incidences of hypoglycaemia.

The highly subjective nature of dietary assessment makes interpretation of such data speculative. The surprising levels of statistical significance for dietary changes, particularly in the cross-over period, were most unlikely to be of clinical importance and simply reflect the powerful nature of paired testing.

We conclude that in unselected insulin-dependent subjects intensive education associated with regular urine glucose monitoring can improve diabetic control. The addition of home blood glucose monitoring, though popular with patients, does not necessarily result in improved control. Results may be different with more intensive monitoring methods or in different groups of patients. The main benefit of home blood glucose monitoring probably lies in its use as an educational modality, the increased contact time with staff that automatically ensues, and the improved motivation that results from introducing any new technique. Enthusiasm for any method of self-assessment, however, diminishes with time. Future studies should concentrate on long-term results and must incorporate appropriate control groups.

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References

1 Beaser SM. Teaching the diabetic patient. *Diabetes* 1956;**5**:146-9.
2 Collier BN, Etzwiler DD. Comparative study of diabetes knowledge among juvenile diabetics and their parents. *Diabetes* 1971;**20**:51-7.
3 Whitehouse FW, Whitehouse IJ, Smith J, Hohl RD. Teaching the person with diabetes: experience with a follow-up session. *Diabetes Care* 1979; **2**:35-8.
4 Miller LV, Goldstein J. More efficient care of diabetic patients in a county-hospital setting. *N Engl J Med* 1972;**286**:1388-91.
5 Etzwiler DD. Who's teaching the diabetic? *Diabetes* 1967;**16**:111-7.
6 Graber AL, Christman BG, Alogna MT, Davidson JK. Evaluation of diabetes patient-education programs. *Diabetes* 1977;**26**:61-4.
7 Dudley JD. The diabetes educator's role in teaching the diabetic patient. *Diabetes Care* 1980;**3**:127-33.
8 Etzwiler DD, Robb JR. Evaluation of programmed education among juvenile diabetics and their families. *Diabetes* 1972;**21**:967-71.
9 James RC, Chase GR. Evaluation of some commonly used semi-quantitative methods for urinary glucose and ketone determination. *Diabetes* 1974;**23**:474-9.
10 Service FJ, Molnar GD, Taylor WF. Urine glucose analyses during continuous blood glucose monitoring. *JAMA* 1972;**222**:294-8.
11 Tchobroutsky G. Relation of diabetic control to the development of microvascular complications. *Diabetologia* 1978;**15**:143-52.
12 Pirart J. Diabetes mellitus and its degenerative complications: a prospective study of 4400 patients observed between 1947 and 1973. *Diabetes Care* 1978;**1**:168-88, 252-63.
13 Cahill GF, Etzwiler DD, Freinkel N. "Control" and diabetes. *N Engl J Med* 1976;**294**:1004-5.
14 Danowski TS, Sunder JH. Jet injection of insulin during self-monitoring of blood glucose. *Diabetes Care* 1978;**1**:27-33.
15 Sonksen PH, Judd LS, Lowy C. Home monitoring of blood glucose. Method for improving diabetic control. *Lancet* 1978;i:729-32.
16 Walford S, Gale EAM, Allison SP, Tattersall RB. Self-monitoring of blood glucose. Improvement of diabetic control. *Lancet* 1978;i:732-5.

[17] Skyler JS, Lasky IA, Skyler DL, Robertson EG, Mintz DH. Home blood glucose monitoring as an aid in diabetic management. *Diabetes Care* 1978;**1**:150-7.
[18] Tattersall RB. Home blood glucose monitoring. *Diabetologia* 1979;**16**:71-4.
[19] Symposium on home blood glucose monitoring. *Diabetes Care* 1980;**3**: 57-186.
[20] Metropolitan Life Insurance Company. Desirable weights of adults. In: *Documenta Geigy: scientific tables*. 7th ed. Basle: Ciba-Geigy, 1970:712.
[21] Shapiro B, Savage PJ, Lomatch D, *et al.* A comparison of accuracy and estimated costs of methods for home blood glucose monitoring. *Diabetes Care* 1981;**4**:396-403.
[22] Reeves ML, Forhan SE, Skyler JS, Peterson CM. Comparison of methods for blood glucose monitoring. *Diabetes Care* 1981;**4**:404-6.
[23] Worth RC, Harrison K, Anderson J, Johnson DG, Alberti KGMM. A comparative study of blood glucose test strips. *Diabetes Care* 1981;**4**: 407-11.
[24] Kubilis P, Rosenbloom AL, Lezotte D, *et al.* Comparison of blood glucose testing using reagent strips with and without a meter. *Diabetes Care* 1981;**4**:417-9.
[25] Skyler JS, Skyler DL, Seigler DE, O'Sullivan MJ. Algorithms for adjustments of insulin dosage by patients who monitor blood glucose. *Diabetes Care* 1981;**4**:311-8.
[26] Fluckiger R, Winterhalter KH. In vitro synthesis of hemoglobin $A1_c$. *FEBS Lett* 1976;**71**:356-60.
[27] Fluckiger R, Berger W, Winterhalter KH. Haemoglobin $A1_c$, a reliable index of diabetic control. *Diabetologia* 1977;**13**:393.
[28] Faber OK, Markussen J, Naithani VK, Binder C. Production of antisera to synthetic benzyloxycarbonyl-C-peptide of human pro-insulin. *Hoppe-Seylers Z Physiol Chem* 1976;**357**:751-7.
[29] Molnar GD, Marien GJ, Hunter AN, Harley CH. Methods of assessing diabetic control. *Diabetologia* 1979;**17**:5-16.
[30] Schlichtkrull J, Munck O, Jersild M. The M-value, an index of blood sugar control in diabetes. *Acta Med Scand* 1965;**177**:95-102.
[31] Service FJ, Molnar GD, Rosevear JW, Ackerman E, Gatewood LC, Taylor WF. Mean amplitude of glycemic excursions, a measure of diabetic instability. *Diabetes* 1970;**19**:644-55.
[32] Gonen B, Rochman H, Horwitz DL, Rubenstein AH, Tanega SP. Haemoglobin A1: an indicator of the metabolic control of diabetic patients. *Lancet* 1977;ii:734-6.
[33] Gabbay KH, Hasty K, Breslow JL, Ellison RC, Bunn HF, Gallop PM. Glycosylated hemoglobins and long-term blood glucose control in diabetes mellitus. *J Clin Endocrinol Metab* 1977;**44**:859-64.
[34] Koenig RJ, Peterson CM, Jones RL, Saudek C, Lehrman M, Cerami A. Correlation of glucose regulation and hemoglobin $A1_c$ in diabetes mellitus. *N Engl J Med* 1976;**295**:417-20.
[35] Svendsen PAa, Christiansen JS, Soegard U, Weldinder BS, Nerup J. Rapid changes in chromatographically determined haemoglobin $A1_c$ induced by short-term changes in glucose concentration. *Diabetologia* 1980;**19**:130-6.
[36] Jovanovic L, Peterson CM. The clinical utility of glycosylated hemoglobin. *Am J Med* 1981;**70**:331-8.
[37] Shafrir E. Hyperlipidemia in diabetes. In: Sussman KE, Metz RJS, eds. *Diabetes mellitus*. Vol 4. New York: American Diabetes Association, 1975:221-8.
[38] Jarrett RJ, Keen H, eds. Diabetes and atherosclerosis. In: *Complications of diabetes*. London: Edward Arnold, 1975:179-203.
[39] Sterky GCG, Persson BEH, Larsson YAA. Dietary fats, the diurnal blood lipids and ketones in juvenile diabetes. *Diabetologia* 1966;**2**:14-9.
[40] Kaufman RL, Assal JP, Soeldner JS, *et al.* Plasma lipid levels in diabetic children. Effect of diet restricted in cholesterol and saturated fats. *Diabetes* 1975;**24**:672-9.
[41] Raskin P. Diabetic regulation and its relationship to microangiopathy. *Metabolism* 1978;**27**:235-52.
[42] Stubbs SM, Pyke DA, Brudenell JM, Watkins PJ, Stubbs WA, Alberti KGMM. Management of the pregnant diabetic: home or hospital with or without glucose meters? *Lancet* 1980;i:1122-4.
[43] Anonymous. Home blood glucose monitoring: revolution, revelation or rip-off? *Lancet* 1980;ii:187-8.
[44] Bernstein RK. Virtually continuous euglycemia for 5 years in a labile juvenile-onset diabetic patient under non-invasive closed loop control. *Diabetes Care* 1980;**3**:140-3.
[45] Barbosa J, Menth L, Schumacher G, Johnson S, Najarian J. Feasibility of blood glucose self-monitoring in unstable insulin-dependent diabetes. *Diabetes Care* 1980;**3**:155-9.
[46] Seigler DE, Reeves M, Ryan E, Goldberg RB, Skyler JS. Glycaemic control with intensified conventional therapy. *Diabetologia* 1981;**21**:326-7.
[47] Schiffrin A, Belmonte MM. Comparison between continuous subcutaneous insulin infusion and multiple injections of insulin. *Diabetes* 1982;**31**:255-64.
[48] Suarez L, Barrett-Connor E. Seasonal variation in fasting plasma glucose levels in man. *Diabetologia* 1982;**22**:250-3.

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SHORT REPORTS

Congenital syphilis as an unusual cause of abnormal cardiotocogram

Prelabour fetal heart monitoring is widely used to monitor the wellbeing of babies at risk of intrauterine growth retardation. We describe an unusual case of intrauterine growth retardation presenting with diminished fetal movements. Fetal distress was shown by cardiotocography and confirmed at caesarean section.

Case report

An unmarried 32-year-old multigravida presented to the antenatal clinic on 8 April 1981. Her last menstrual period had been on 3 July 1980 and the expected date of delivery was 10 April. She was a somewhat unreliable historian but a letter of referral dated September 1980 summarised her medical history. She had had four previous full-term normal deliveries, all the babies weighing over 3700 g, and had been a heroin addict for several years. In 1979 she had developed septicaemia and subacute bacterial endocarditis, which had damaged the mitral valve. During two months as an inpatient she had been weaned off drugs of addiction. She had been in Germany since September 1980 and as she had felt well had not sought antenatal care. Two weeks earlier she had noted decreased fetal movements and had returned to England for delivery.

At examination she looked well. She had a heart murmur consistent with mitral incompetence. There was no evidence of heart failure or pre-eclamptic toxaemia. The uterus was compatible with a gestation of 36 weeks. The fetal heart was heard and the rate noted to be 60 beats/min after abdominal palpation but rising to 130 beats/min. Fetal weight was estimated as less than 3000 g.

She was admitted direct from the clinic after undergoing routine antenatal blood tests and testing for Australia antigen. The first cardiotocogram on 8 April showed deep type II decelerations with uterine contractions, but the rate and baseline variability were within the normal range. A fetal movement chart was started and confirmed little activity. On 9 April the cardiotocogram showed loss of baseline variability and several decelerations. Elective caesarean section was performed. A live female infant in very poor condition, weighing 2800 g, and with Apgar scores of one at one minute and six at 10 minutes was delivered covered in thick meconium. After resuscitation the baby was noted to have a fine petechial rash, hepatosplenomegaly, and ascites. Intrauterine infection was diagnosed and the baby transferred to the neonatal intensive care unit.

Routine investigations were begun to determine the nature of the infection, but syphilis was diagnosed when treponemes were seen in the refrigerated ascitic fluid examined two days after birth. Serological tests for syphilis were positive on both the mother's blood and cord blood. Both mother and baby were treated with penicillin with good results, though the infant was seriously ill with thrombocytopenic purpura, haemolytic anaemia, and disseminated intravascular coagulation and was jaundiced for several weeks. She was discharged on 2 July and taken into care. She did not have any skin lesions apart from the petechial rash, nor were there the expected radiological bony changes of congenital syphilis. The mother had been treated for early syphilis and gonorrhoea in February 1980, but a new infection had probably been acquired in December 1980, when she would have been about 24 weeks pregnant.

Comment

Congenital syphilis is now uncommon in Britain, only 19 cases having been reported in 1979 and eight in 1980.[1] This is probably largely due to antenatal screening, though penicillin has made a contribution. Treponemes cross the placenta even in the first trimester, but the fetus does not seem to react to this process until after the fourth month.[2] Intrauterine death may result or a child may be born with or soon develop signs of syphilis. Intrauterine growth retardation may precede the intrauterine death, and without fetal monitoring, prompt intervention, and skilled paediatric intensive care this baby would probably have died. We have been unable to find a report of congenital syphilis presenting with diminished movements or fetal distress detected by monitoring before labour.

As syphilis becomes less common it will be considered less often.