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Precision and costs of techniques for self-monitoring of serum glucose levels

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The poor correlation between serum and urine glucose measurements has led to the development of new techniques for monitoring the blood glucose level in diabetic patients. Either a nurse or the patient can perform these tests, which involve spreading a single drop of blood onto a reagent strip. A colour change that is proportional to the serum glucose level can be read visually or with a reflectance meter. Evaluated against simultaneous serum glucose levels determined by the hospital biochemistry laboratory, those of the new techniques employing reflectance meters all showed excellent correlation (r^2 = 0.85 to 0.96). Reagent strips used without meters showed poorer correlation (r^2 = 0.69 to 0.90). The instruction given to the patients and one nurse enabled them to obtain more accurate results with one of the meters than nurses not specially trained (r^2 = 0.94 and 0.92 v. 0.85 respectively). The mean cost per glucose determination with the new techniques was 75¢, compared with $1.45 for the laboratory determinations done with automated equipment. It was concluded that the new techniques compared well with the reference method, particularly when reflectance meters were used, and that they were easily applied by the patient, as well as the medical staff, at a reasonable cost.

La piètre corrélation qui existe entre les mesures du glucose sérique et celles du glucose urinaire ont provoqué le développement de nouvelles techniques de surveillance des taux sanguins du glucose chez les patients diabétiques. Les infirmières de même que les patients peuvent pratiquer ces épreuves en étendant une seule goutte de sang sur une bande de papier réactif. Un changement de couleur proportionnel à la concentration du glucose sérique peut être apprécié soit par lecture directe ou à l'aide d'un réflectomètre. Comparées aux taux de glucose mesurés simultanément au laboratoire de biochimie de l'hôpital, les concentrations obtenues par ces nouvelles techniques et utilisant un réflectomètre ont montré d'excellentes corrélations (r^2 = 0.85 à 0.96). Les bandes de papier réactif utilisées sans réflectomètre ont montré une faible corrélation (r^2 = 0.69 à 0.90). Les directives données aux patients et à une infirmière leur ont permis d'obtenir des résultats plus précis avec un des réflectomètres que les infirmières qui n'avaient pas reçu de formation particulière (r^2 = 0.94 et 0.92 contre 0.85 respectivement). Le coût moyen de chaque glycémie était de 75¢ avec les nouvelles techniques, comparativement à $1.45 pour les déterminations du laboratoire à l'aide d'équipement automatisé. On conclut que les nouvelles techniques se comparaient favorablement à la méthode de référence, particulièrement avec l'utilisation de réflectomètres, et que celles-ci ont pu être facilement appliquées par les patients et le personnel médical, à faible coût.

Recent observations seem to implicate hyperglycemia, the hallmark of uncontrolled diabetes mellitus, in the pathogenesis of the complications of chronic diabetes.[1] Short-term studies have suggested that control of blood glucose levels can result in the regression of such complications as peripheral neuropathy and peripheral vascular disease.[2] It is therefore reasonable that the aim of treatment for diabetes should be the achievement of consistently normal glucose levels.

However, this objective is not easily attained. Many factors, such as diet, exercise, hypoglycemic agents, and the dose and timing of insulin administration affect blood glucose levels throughout the day. Associated illnesses tend to increase the blood glucose concentration. It is unlikely, then, that a fasting blood glucose test done once every 2 or 3 months would be adequate for

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assessing the degree of glucose control and modifying the treatment. Even frequent monitoring of the urine glucose level is questionable as a method of monitoring blood glucose control.[3] Fortunately, there are new techniques that permit not only medical staff but also patients to measure the serum glucose level from a single drop of blood.

Several studies have already shown the feasibility of home monitoring in the self-management of diabetes.[4-6] This new approach has been successful in pregnant diabetic women.[4,7,8] Schiffrin and Belmonte[9] have even shown that frequent self-monitoring is essential for long-term control of blood glucose levels. In theory, home monitoring could decrease the risk of complications of diabetes.[2]

The purpose of the following study was to evaluate the accuracy and cost of some of the different techniques available for blood glucose monitoring.

Methods

Materials and procedures

To establish the level of reliability of urine glucose measurements the reactive end of a Diastix strip (Miles Laboratories, Inc., Rexdale, Ont.) was dipped into a urine specimen obtained from the second voiding of the morning and removed immediately. The excess urine was removed and the reagent strip compared with the standard colours on the bottle.

All the techniques for measuring serum glucose levels that we evaluated involved reactions with glucose oxidase, which is specific for glucose. A drop of either venous or capillary whole blood was applied to the reactive surface at one end of a rigid plastic reagent strip. There, chemicals react with the glucose in the blood and produce a change in colour that is proportional to the glucose concentration. However, because only the serum comes into contact with the strip's glucose oxidase,[10] the result indicates the serum level and not the whole blood level of glucose. After 60 seconds the blood on the reactive surface was washed away with tap water or wiped off with a cotton swab. The colour could then be compared with standard colours or, for some of the strips, read with a particular reflectance meter. A reflectance meter is a colorimeter that gives a digital readout of the new colour, in milligrams per decilitre. Standard strips or solutions are used for calibration.

The equipment and reagent strips assessed were the Reflomat meter and Chemstrip bG (Boehringer Mannheim Canada, Dorval, PQ); the Hypo-Count II reflectance meter and BM-strip (Clageno Medic Ltd., Montreal, PQ); and the Dextrometer, the Glucometer, Dextrostix and Visidex (Miles Laboratories).

The results obtained with the different reagent strips and meters were compared with reference values determined by the hexokinase method in the biochemistry laboratory at the Hôtel-Dieu de Montréal with Simultaneous Multiple Analysis, Computerized (SMAC) or the Auto-Analyzer II (AAII) (Technicon Instruments Corporation, Tarrytown, New York). The reproducibility of the hexokinase method was excellent, with coefficients of variation of 2.6% (low standard) and 1.7% (high standard) for the SMAC and 2% (low standard) and 0.9% (high standard) for the AAII.

Sampling and procedures

Over 100 patients, both diabetic and nondiabetic, at Hôtel-Dieu de Montréal and the Clinical Research Institute of Montreal participated in this study. The protocol was divided into three parts.

In part 1 blood sampling was done by members of a rotating staff of 18 nurses in the infectious disease unit of the hospital. Capillary blood glucose concentrations were measured by the nurses with the Chemstrip bG and with the Dextrometer and the Dextrostix strip, and urine glucose concentrations were assessed by Diastix for comparison with serum glucose measurements in samples obtained simultaneously for the biochemistry laboratory. Since all the patients were fasting when the samples were taken, the difference between venous and capillary glucose levels was negligible.

In part 2 a nurse trained for the task obtained venous blood and determined the blood glucose levels with Chemstrip bG, Dextrostix, Visidex, the Dextrometer–Dextrostix, the Glucometer–Dextrostix, the Reflomat–Reflotest and the Hypo-Count II–BM strip. Simultaneously, samples of venous blood were sent to the biochemistry laboratory for measurement of the serum glucose levels.

Table I—Precision of new techniques for measuring serum glucose levels

Type of reagent strip or combination with meter	Method of reading result	Person reading results; coefficient of variation, %* (and no. of determinations)		
		Member of rotating nursing staff	Trained nurse	Patient
Chemstrip bG	Visual	12.5 (78)	15.5 (105)	13.5 (63)
Dextrostix	Visual		11.2 (43)	13.9 (65)
Visidex	Visual		16.7 (55)	16.9 (25)
Dextrometer–Dextrostix	Meter	10.5 (69)	9.5 (119)	8.2 (40)
Glucometer–Dextrostix	Meter		5.7 (55)	
Reflomat–Reflotest	Meter		10.8 (63)	
Hypo-Count II–BM-strip	Meter		5.7 (52)	

*Coefficient of variation of the differences between each new technique and the reference method, the latter being automated analysis of venous blood by the hexokinase method in the hospital's biochemistry laboratory.

In part 3 the same kinds of procedures and readings were done by the patients themselves. At the clinical research unit of the hospital the patients sampled their own capillary blood using Autolet lancets (Owen Mumford Ltd., Oxford, England) while in the fasting state and again 1 hour after a meal and carried out the glucose determinations using the Dextrometer–Dextrostix. Simultaneously, venous samples were taken for measurement of the serum glucose levels by the biochemistry laboratory. At the Clinical Research Institute of Montreal the venous blood was sampled by a nurse, who also placed a drop of blood on a Chemstrip bG, Dextrostix or Visidex reagent strip; the patients read the results. Again, samples of venous blood were sent to the biochemistry laboratory.

Statistical analysis

The correlation between the new techniques and the reference method was assessed by linear regression analysis[11] and expressed as r^2. Each individual determination was compared with the reference method by computation of the coefficient of variation of the difference. Separate evaluations were done for the low (less than 70 mg/dL), normal (70 to 160 mg/dL) and high (more than 160 mg/dL) serum glucose values. Since the differences in results between the test and the reference methods did not themselves differ significantly between the three study groups, though, only the overall coefficient of variation for each test method has been included in Table I.

Retail costs

We also surveyed the cost of the reagent strips in 13 drugstores throughout metropolitan Montreal.

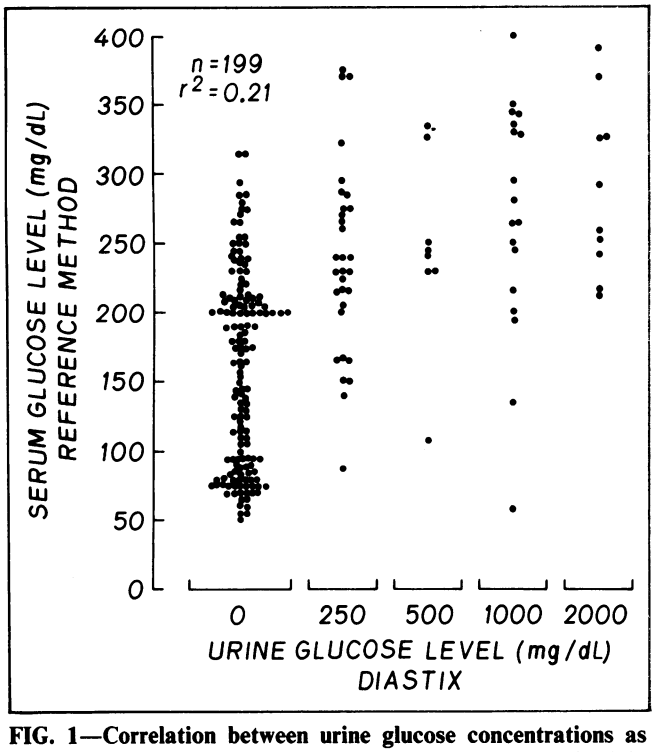

FIG. 1—Correlation between urine glucose concentrations as measured by Diastix and serum glucose levels determined in hospital laboratory.

Results

Urine glucose measurement

Over 400 urine glucose levels measured by Diastix were compared with serum glucose concentrations determined by the hexokinase method. The correlation was poor ($r^2 = 0.21$) (Fig. 1). Approximately 54% of the serum glucose determinations above 180 mg/dL were associated with negative results of urine tests for glucose, and 14% of the serum glucose determinations below that level were associated with urine glucose levels as high as 1000 mg/dL.

Serum glucose measurement

Part 1: When serum glucose levels were determined by the rotating nursing staff using the Chemstrip bG and capillary blood samples obtained with the patients fasting the correlation with the reference method was 0.69 (Fig. 2). When the Dextrometer–Dextrostix was used the correlation improved to 0.85. The coefficients of variation for the two techniques, however, were not significantly different (Table I).

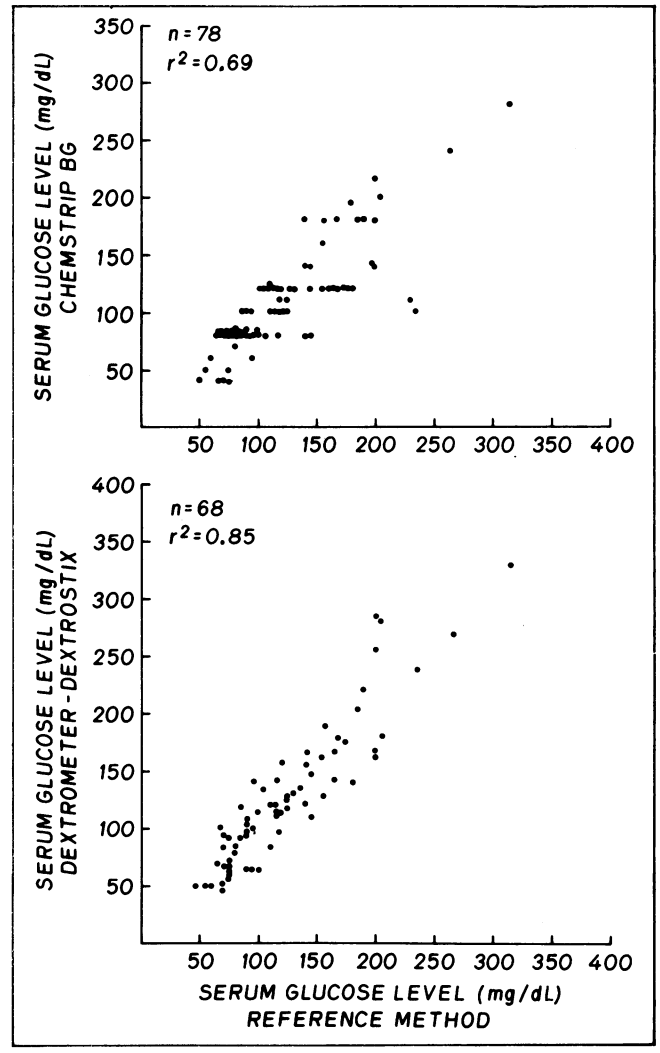

FIG. 2—Correlation between serum glucose levels determined in hospital laboratory by reference method and results obtained by members of rotating nursing staff using Chemstrip bG or Dextrometer–Dextrostix.

Part 2: When a trained nurse did the serum glucose determinations the correlation with the hexokinase method was better. Even the strips read visually showed relatively good correlation (r^2 = 0.86 to 0.90) (Fig. 3). Visidex (not illustrated) had an r^2 value of 0.89. The strips used with a reflectance meter showed slightly better correlation (r^2 = 0.92 to 0.96). The coefficients of variation showed that the techniques involving a reflectance meter were more precise.

Part 3: When the colour on the Chemstrip bG, Dextrostix or Visidex strip was read by the patients, the correlations with the reference method were 0.72, 0.71 (Fig. 4) and 0.78 (not illustrated) respectively. When the whole process (pin prick, spreading the drop of blood on a reagent strip, timing and reading) was performed by the patients with the Dextrometer–Dextrostix combination the correlation with the hexokinase method was 0.94. The coefficients of variation were better for the Dextrometer–Dextrostix than for the Chemstrip bG, Dextrostix and Visidex, which were read visually (Table I).

Comparative costs (Table II)

The reflectance meters used in these studies — the Reflomat, the Hypo-Count II, the Dextrometer and the Glucometer — are available on the Canadian market at retail prices of $565, $390, $365 and $290 respectively. In the long term, however, the major cost involved in the determination of serum glucose levels using the meters comes from the reagent strips.

For bottles of 25 reagent strips the cost ranged between $13 and $16.64 for Dextrostix, between $16.79 and $23.40 for Chemstrip bG and between $16.99 and $19.80 for Visidex. The reagent strips for the Reflomat and Hypo-Count II meters were not available at the drugstores surveyed, but according to the manufacturers the retail cost would be $17.50 and $12 respectively. The cost for each determination ranged from 46¢ to 99¢. Whichever of these techniques was used, though, it was still up to three times cheaper than the hexokinase method with the SMAC ($1.86) or the AAII ($1.04)

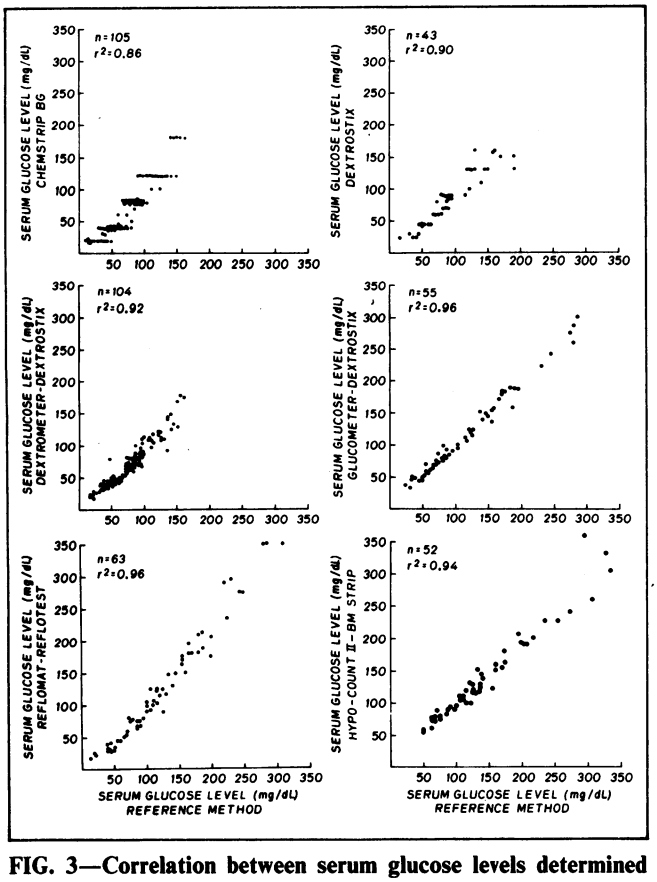

FIG. 3—Correlation between serum glucose levels determined by reference method and results obtained by trained nurse using Chemstrip bG, Dextrostix, Dextrometer–Dextrostix, Glucometer–Dextrostix, Reflomat–Reflotest or Hypo-Count II–BM strip.

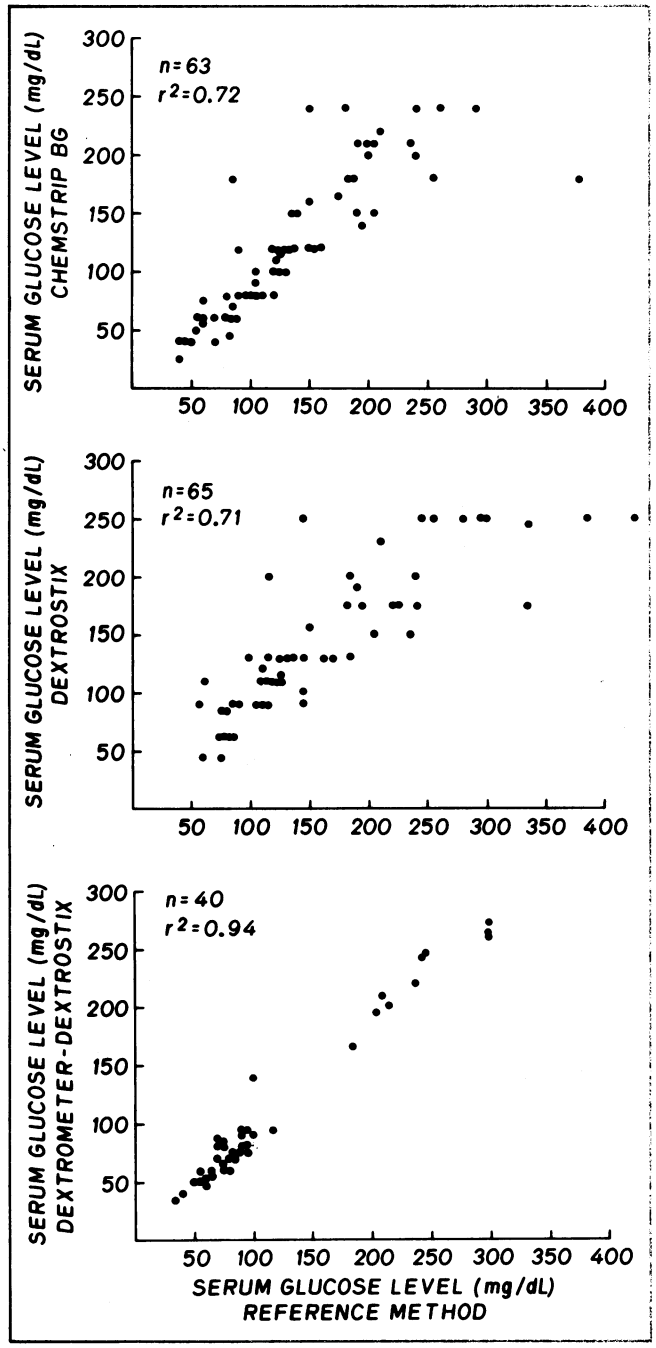

FIG. 4—Correlation between serum glucose levels determined by reference method and results obtained by patients using Chemstrip bG, Dextrostix or Dextrometer–Dextrostix.

(Mr. Guy Charbonneau, Montreal, for Technicon Instruments: personal communication, 1982).

Discussion

The poor correlation that we found between urine and serum glucose levels corroborates the reports of others.[3,12] More than half of the serum glucose levels above 180 mg/dL were associated with negative results of tests for glucose in the urine. Even if the urine tests were to be done four times a day, exclusive use of such an insensitive method would mean that many patients would not receive adequate treatment. If the dose of insulin were to be increased for the few patients with false-positive results, such as one with a 3+ urine glucose reading and a low serum glucose level, serious hypoglycemia would result.

Urine glucose measurements should be used to modify the treatment of diabetes only when other techniques are not available and the renal threshold is known, in the absence of renal or bladder complications and when the technique can be done properly. Furthermore, because the renal threshold is rarely below 180 mg/dL and can vary with the degree of hyperglycemia, glycosuria is usually a sign of poor control. Its absence does not necessarily reflect good control.

In contrast, all the techniques in which serum glucose levels were measured by means of a reflectance meter showed excellent correlation with the reference method. This was true whether the procedure was done by a member of the rotating nursing staff, by a specially trained nurse or by the patients. The coefficients of variation for the differences between test and reference methods were at or below 10% for each of the three groups. These techniques are, therefore, reliable and can be used by hospital staff or by the patient at home to adjust treatment. This conclusion is supported by the results of other studies.[10,13-15]

When the serum glucose level was assessed by using the reagent strips without a meter, the correlation was not as good, although a trained nurse could obtain better results. Similar observations have been made by others.[16-19] But when determinations were done by a member of the rotating nursing staff or the patient the correlations were around 0.70 owing to scattering of the data. The coefficient of variation for all three groups was above 11%.

The patients performed the test better than the rotating nursing staff and as well as the trained nurse when using the Dextrometer–Dextrostix. This is probably because the patients and the trained nurse had been instructed in the use of the apparatus and had had experience with it, while this was not the case for the members of the rotating nursing staff. Training, then, is essential if results are to be reliable. Special training sessions should be a prerequisite for the use of these techniques by the patients and medical staff. The use of reagent strips without a meter should be reserved for situations in which the insulin dose is not adjusted by the patients. It appears advisable to use a reflectance meter, whether at home or in the hospital, if the blood glucose level is to be finely controlled on the basis of these techniques.

Although the serum glucose levels measured from capillary blood samples obtained with the patient fasting correlated quite well with the venous glucose concentrations, observations in 12 of our patients showed that after meals there could be a difference as great as 25 mg/dL, depending mainly on the carbohydrate content of the meal. This difference, however, does not interfere with the use of these techniques for self-management of diabetes as long as it is taken into account.

All the participants in the study agreed on the simplicity of using the reagent strips and the reflectance meters. However, when only the reagent strips were used by the patients, most of them did not feel as confident as they did when using the meters, and a few complained of difficulty in reading the colours.

Another important factor in the application of these different techniques is the cost. Table II shows that the cost can vary considerably depending on the retail source. The cost of each determination (about 75¢ excluding the cost of the meter) is comparable to that reported by Shapiro and coworkers.[14] However, the cost is still less than that of the hexokinase method used by the hospital's biochemistry laboratory. Some insurance companies will pay for the patient's reagent strips and 80% of the cost of the meter. The tests cost about as much as one package of cigarettes a day.

All the new techniques evaluated here, which involve a glucose oxidase reagent strip with or without a reflectance meter, are relatively simple and easy to perform. The major advantages of these techniques over that used by the biochemistry laboratory in measuring serum glucose levels are the rapidity of the determination, the feasibility of the patient's performing the tests and the lower cost per determination.

We thank Normand Girard and the nursing staff of the infectious disease unit and Marie-Thérèse Caron of the division of endocrinology of Hôtel-Dieu de Montréal, as well as Francine Ducros and Danielle Bédard of the Clinical Research Institute of Montreal for their collaboration. We are also grateful to Dr. Michel Bourque for the statistical analysis. We thank Boehringer Mannheim Canada, Clageno Medic Ltd. and the Ames Division, Miles Laboratories Inc. for supplying the reflectance meters and some of the reagent strips.

Table II—Cost per blood glucose determination* in the hospital and in the patient's home

Technique	Location of testing; cost per determination ($)	
	Hospital	Home
SMAC†	1.86	
AAII‡	1.04	
Chemstrip bG	0.54	0.72–0.99
Dextrostix	0.46	0.57–0.72
Visidex	0.50	0.68–0.79
Reflomat–Reflotest	0.70	0.70
Hypo-Count II–BM-strip	0.53	0.53

*Excluding the cost of any apparatus or accessories.
†SMAC = Simultaneous Multiple Analysis, Computerized.
‡AAII = Auto-Analyzer II (Technicon Instruments Corporation, Tarrytown, New York).

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Leading a normal life

It is absurd to even suggest that a diabetic can lead a completely "normal" life. Is it normal to check your urine and monitor your blood sugar every day? Is it normal to inject insulin daily while also keeping an eye on what and when you eat? For diabetics, their families and friends, who have become accustomed to this sort of thing, day after day, it may become routine. But it is not "normal". The best we diabetics can do is adjust to the fact that we have diabetes; first by accepting it, then by working on it, constantly. *Exercise, diet, oral medication and when required, insulin, are only the tools with which we can combat a potential killer disease.*

—Dr. Peter H. Forsham, addressing the 1981 annual meeting and convention of the Canadian Diabetes Association in London, Ont.