Variation of Postprandial Plasma Glucose, Palatability, and Symptoms Associated With a Standardized Mixed Test Meal Versus 75 g Oral Glucose

THOMAS M.S. WOLEVER, DM, PHD
JEAN-LOUIS CHIASSON, MD
ADELE CSIMA, MSC
JOHN A. HUNT, MD
CAROL PALMASON, MSC
STUART A. ROSS, MD
EDMOND A. RYAN, MD

OBJECTIVE — To compare within-subject variability of plasma glucose measured 2 h after a glucose tolerance test (GTT) with that of plasma glucose measured 2 h after administration of a standardized test meal (diabetes screening product [DSP], Ceapro, Edmonton, Alberta, Canada) and to determine the relationship between the two sets of plasma glucose measurements.

RESEARCH DESIGN AND METHODS — Plasma glucose and insulin responses of 36 overnight-fasted subjects (10 lean normal, 9 obese normal, 9 with impaired glucose tolerance [IGT], and 8 with mild diabetes) were studied on eight different mornings after they consumed 75 g oral glucose or 50 g carbohydrate from the DSP. Each test meal was repeated four times by each subject. Within-subject coefficients of variation (CVs) (CV = 100 × SD/mean) of plasma glucose concentrations 2 h after administration of the GTT and DSP were compared by repeated measures ANOVA and linear regression analysis.

RESULTS — Mean plasma glucose 2 h after administration of the DSP (*D*) was linearly related to that 2 h after the GTT (*G*): $G = 1.5 \times D - 1.6$ ($r = 0.97$, $P < 0.0001$). The CV of 2-h plasma glucose was significantly lower after administration of the DSP, 10.5 ± 1.0%, than after the GTT, 12.7 ± 1.18% ($P = 0.025$). The effect of test meal on CV differed in different groups of subjects ($P = 0.018$), with the largest difference found in IGT subjects, in whom the CV after DSP administration was 47% less than after the GTT ($P = 0.0005$). The DSP was significantly more palatable and produced fewer adverse symptoms than the GTT.

CONCLUSIONS — Plasma glucose concentrations measured 2 h after DSP administration are closely related to those measured 2 h after the GTT but are more consistent than the 2-h post-GTT concentrations within the critical IGT range. This finding suggests that measurement of plasma glucose 2 h after administration of the DSP may allow more precise discrimination among normal glucose levels, IGT, and diabetes than measurement of plasma glucose 2 h after the GTT.

From the Departments of Nutritional Sciences (T.M.S.W.) and Public Health Sciences (A.C.), and St. Michael's Hospital (T.M.S.W.), University of Toronto, Toronto, Ontario; Research Centre (J.-L.C.), CHUM, Hôtel-Dieu de Montreal Hospital, Montreal, Quebec; Lion's Gate Hospital (J.A.H.), North Vancouver, British Columbia; Heritage Medical Research Centre (E.A.R.), University of Alberta, and Ceapro Inc. (C.P.), Edmonton; and Calgary Metabolic Education and Research Centre (S.A.R.), Calgary, Alberta, Canada.

Address correspondence and reprint requests to Dr. Thomas M.S. Wolever, Department of Nutritional Sciences, University of Toronto, Toronto, Ontario, Canada M5S 3E2. E-mail: thomas.wolever@utoronto.ca.

Received for publication 15 August 1997 and accepted in revised form 3 November 1997.

T.M.S.W. serves as president of Glycaemic Index Testing; holds stock in Ceapro and Merck; has received honoraria or consulting fees from Ceapro, Bayer, Procter & Gamble, and Quaker Oats; and has received laboratory funding from Ceapro, Bayer, Kellogg, and the International Olive Oil Council. J.A.H. is a member of an advisory panel for Ceapro. C.P. holds stock in Ceapro. S.A.R. is a member of the Medical Advisory Board for Ceapro.

Abbreviations: ANOVA, analysis of variance; CV, coefficient of variation; DSP, diabetes screening product; FPG, fasting plasma glucose; GTT, glucose tolerance test; IGT, impaired glucose tolerance; WHO, World Health Organization.

The prevalence of abnormal glucose tolerance in different populations varies from <2 to >50% (1). Diabetes is a major cause of blindness, end-stage renal disease, and peripheral vascular disease and is a significant risk factor for ischemic heart disease (2). Its importance as a public health problem is likely to increase substantially during the next 2 decades. In developed countries, this change will occur because diabetes prevalence increases markedly with age, and the proportion of the population >65 years of age is growing (3). In developing countries, diabetes prevalence is increasing rapidly in parallel with greater affluence and prevalence of obesity (4).

Interest in mass screening for diabetes to enable early diagnosis and prevent complications has been moderated by lack of proven benefit and the undesirable economic, social, physical, and psychological consequences of diagnosing diabetes (5). It is widely accepted that diabetes is present when plasma glucose is ≥11.1 mmol/l 2 h after a 75-g oral glucose tolerance test (GTT) (6). The GTT is a more sensitive test than fasting plasma glucose (FPG) (7) for detecting asymptomatic diabetes, even with the use of the newly recommended lower diagnostic cut point of 7.0 mmol/l (8). However, the value of the GTT is debated, because it is perceived as an expensive, complex, time-consuming, and difficult test (8–11) that is unpalatable and has poor reproducibility (12,13). To address some of these issues, a prototype diabetes screening product (DSP) (Ceapro, Edmonton, Alberta, Canada) was developed. A pilot study in 10 nondiabetic subjects showed that the DSP produced less variable capillary blood glucose responses than did the GTT (14). Thus, the primary objectives of this study were to compare the within-subject variability of plasma glucose concentrations measured 2 h after the GTT with that of plasma glucose concentrations measured 2 h after administration of the DSP and to determine the relationship between the two sets of plasma glucose measurements in subjects whose glucose tolerance status ranged from normal to diabetic.

RESEARCH DESIGN AND METHODS — We planned to study four groups of subjects in five centers: 10 lean normal subjects (BMI <27 kg/m²), termed lean; 10 obese normal subjects (BMI ≥27 kg/m²), termed obese; 10 subjects with impaired glucose tolerance (IGT); and 10 subjects with diabetes treated by diet alone. Each subject was studied after 12-h overnight fasts on 8 separate days over a period of 6–8 weeks. After a fasting blood sample was obtained, subjects were given a test meal of either 75 g oral glucose (the GTT) or 87 g of a solid standardized mixed test meal (the DSP) according to a randomized block design. Each subject underwent four blocks, with each block consisting of one GTT (Glucodex, Bougier, Chambly, Quebec, Canada) and one standardized mixed test meal administered in random order. The test meal was consumed within 10 min. Additional blood samples were obtained, using an indwelling catheter, at 15, 30, 45, 60, 90, and 120 min after subjects started the meal. The standardized mixed test meal consisted of 87 g of the DSP served with 250 ml water. The DSP is a solid test meal in the form of wafers containing oat-fractionation products, soy protein, and canola oil sweetened with honey. The 87-g portion (five wafers) contained 345 kcal, 10.7 g fat, 12.1 g protein, 8.9 g simple sugars, 41.1 g starch, and 3.8 g dietary fiber.

After the last blood sample was taken, the palatability and acceptability of the test meal were assessed using visual analog scales (15), and subjects indicated whether they experienced headache, dizziness, stomach discomfort, bloating, belching, flatulence, diarrhea, hunger, or other symptoms during the test.

A central laboratory measured plasma glucose using an automatic analyzer (Model 2300STAT, Yellow Springs Instruments, Yellow Springs, OH) and insulin using radioimmunoassay (Phamacia, Dorval, Quebec, Canada). The coefficients of variation (CVs) of 273 duplicate analyses of glucose (concentrations <4.9 to >14.9 mmol/l [<88 to >268 mg/dl]) were 3.1–4.9%, and the CVs of 118 duplicate analyses of insulin (concentrations <100 to >399 pmol/l [<16.7 to >66.5 μU/ml), were 5.7–8.0%.

Lean and obese normal subjects had no known history of diabetes and did not have to undergo a GTT before enrollment. Subjects with IGT and diabetes were recruited from a population of patients who had had abnormal results of the GTT or abnormal glycosylated hemoglobin within 12 months of the study. For the purpose of statistical analysis, subjects were classified according to World Health Organization (WHO) criteria (6) as having normal plasma glucose, IGT, or diabetes based on the average fasting and 2-h plasma glucose concentrations of the four GTTs performed during the study. Of the 17 subjects thought to be normal on enrollment, 1 was found to have IGT and 1 was found to have diabetes; of the 5 who had IGT before enrollment, 1 was found to be normal; and of the 14 subjects who had diabetes before enrollment, 3 were found to be normal and 4 were found to have IGT (the improvement in glucose tolerance was presumably due to weight loss). Thus, for statistical analysis, 10 subjects were classified as lean normal, 9 as obese normal, 9 as having IGT, and 8 as having diabetes. After completion of the study, the diagnostic criteria for diabetes were revised (8), with diabetes being defined as FPG ≥7.0 mmol/l (126 mg/dl). None of the subjects classified as normal had FPG ≥7.0 mmol/l; one of the nine subjects with IGT had FPG ≥7.0 mmol/l; and only two of the eight subjects classified by WHO criteria as having diabetes had FPG ≥7.0 mmol/l.

One primary objective was to compare the within-subject variability of plasma glucose 2 h after the GTT with that of plasma glucose 2 h after administration of the DSP. Variabilities of plasma glucose and insulin at other time points were determined as secondary end points. Variation within subjects was expressed as CV = 100 × SD/mean. The CV of plasma glucose and insulin concentrations at each time point were subjected to a three-factor, repeated measures analysis of variance (ANOVA) examining the effects of group, center, and test meal, and the interactions among these main effects, using the General Linear Model procedure of the SAS statistical program system (SAS Institute, Cary, NC). The other primary objective was to determine the relationship between the mean plasma glucose value obtained 2 h after the GTT with that obtained 2 h after the DSP, using linear regression analysis (16). Correlations between mean plasma insulin and glucose concentrations at other times were calculated as secondary end points. Mean ratings for palatability and acceptability were analyzed by repeated measures ANOVA (16). The numbers of symptoms experienced on the GTT and the DSP were compared by the χ^2 test (16).

The protocol of the study was approved by the ethics review committee at each participating institution, and informed consent was obtained from all subjects.

Table 1—*Subject characteristics*

	Lean	Obese	IGT	Diabetes	*P**
n	10	9	9	8	—
Sex (M/F)	2/8	5/4	4/5	4/4	NS
Age (years)	35 ± 4*	49 ± 3†	48 ± 5†	58 ± 5‡	0.004
BMI (kg/m²)	22.2 ± 0.5*	31.9 ± 1.3†	29.7 ± 2.2†‡	29.1 ± 1.3‡	<0.001
FPG (mmol/l)	4.6 ± 0.1*	4.9 ± 0.2*	5.7 ± 0.3†	7.3 ± 0.3‡	<0.001
FPIns (pmol/l)	37 ± 4	56 ± 10	71 ± 15	57 ± 13	NS

Data are means ± SE or *n*. *P* values represent significance of heterogeneity by ANOVA. Within rows, means appearing with different symbols are significantly different, $P < 0.05$. To convert glucose to milligrams per deciliter, multiply by 18; to convert insulin picomoles per liter to microunits per milliliter, divide by 6. FPIns, fasting plasma insulin.

RESULTS — Of the 36 subjects, 35 completed all eight tests, and 1 IGT subject withdrew from the study after completing five tests. Mean age, BMI, and FPG and fasting plasma insulin for the four groups are shown in Table 1. Mean plasma glucose and insulin concentrations after the GTT were significantly greater than those after the DSP at all time points except fasting (Fig. 1).

Between 0 and 1 h, plasma glucose CVs after the DSP were not significantly different from those after the GTT (Fig. 2). The overall mean plasma glucose CV after the DSP was less than after the GTT at 1.5 h (10.0 ± 0.7 vs. 13.8 ± 1.37%, $P = 0.002$) and 2 h (10.5 ± 1.0 vs. 12.7 ± 1.18%, $P = 0.025$). However, the effect of the test meal on the 2-h plasma glucose CV differed in the different groups of subjects ($P = 0.018$). In subjects with IGT, the CV of 2-h plasma glucose after the DSP was 47% less than that after the GTT (9.1 ± 1.5 vs. 15.9 ± 2.9%, $P = 0.008$). The difference between

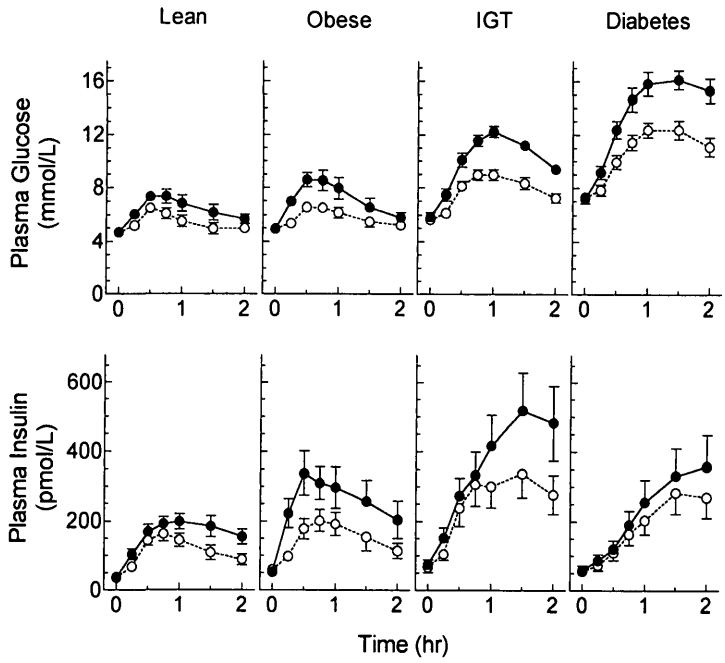

Figure 1—*Plasma glucose and insulin responses after the GTT (●) and the DSP (○) in 10 lean normal subjects, 9 obese normal subjects, 9 subjects with IGT, and 8 subjects with diabetes. Points represent means ± SE, and each subject repeated each test meal four times.*

the 2-h plasma glucose CVs of the DSP and the GTT, respectively, was not significant in lean (9.2 ± 1.9 vs. 13.1 ± 2.1%, $P = 0.10$), obese (9.0 ± 1.3 vs. 11.2 ± 1.9%, $P = 0.37$), or diabetic (15.3 ± 2.9 vs. 10.3 ± 2.3%, $P = 0.063$) subjects (Fig. 2). The CVs of plasma insulin concentrations followed a similar pattern, but were two to three times greater than those of plasma glucose (Fig. 2). The CV of plasma insulin after the DSP did not differ significantly from that after the GTT at any time point.

There was a very close correlation between mean plasma glucose values obtained 2 h after the DSP (D) and those obtained 2 h after GTT (G) for the 36 subjects ($r = 0.97$) (Fig. 3). The regression equation was as follows: $G = 1.5 \times D - 1.6$. The SD of the residuals (difference of y-axis values from the regression line) was 0.97 mmol/l (17.5 mg/dl). Mean values for plasma insulin 2 h after the DSP and 2 h after the GTT were closely related (Fig. 3). There was close correlation between mean FPG before the DSP and mean plasma glucose 2 h after the GTT ($r = 0.89$), and the correlation coefficient increased with time after the DSP, approaching a maximum value at 1 h. The correlation between plasma glucose 1 h after the DSP and plasma glucose 2 h after the GTT ($r = 0.96$) was better than that between plasma glucose 1 h after the GTT and plasma glucose 2 h after the GTT ($r = 0.91$).

Questionnaires on palatability and symptoms were completed by 31 subjects. The DSP was significantly more palatable and acceptable (scores were 65 ± 4 and 67 ± 4 mm, respectively) than the GTT (52 ± 5 and 56 ± 5 mm; $P = 0.048$). Occurrence of headache (15%), dizziness (7%), bloating (5%), flatulence (5%), and diarrhea (2.5%) was similar after both the DSP and the GTT. However, stomach discomfort, belching, hunger, and nausea occurred significantly less often after the DSP than after the GTT (Table 2).

CONCLUSIONS — The GTT was expected to elicit greater plasma glucose and insulin responses than the DSP because it contained more carbohydrate, and because glucose has a higher glycemic index than most starchy foods (17). The values for CV of plasma glucose 2 h after the GTT (11–15%) agree with those previously reported from our laboratory (12.9%) (14), and from a large Dutch population (n = 555) (16.7%) (13). The Dutch study had larger CVs for plasma insulin (34–44%) than our values (20–30%), possibly because in the Dutch study, only two GTTs were performed, with the second producing significantly different results from the first (13).

The present results are consistent with our preliminary conclusion (14) that starchy test meals produce less variable glycemic responses than the GTT in non-

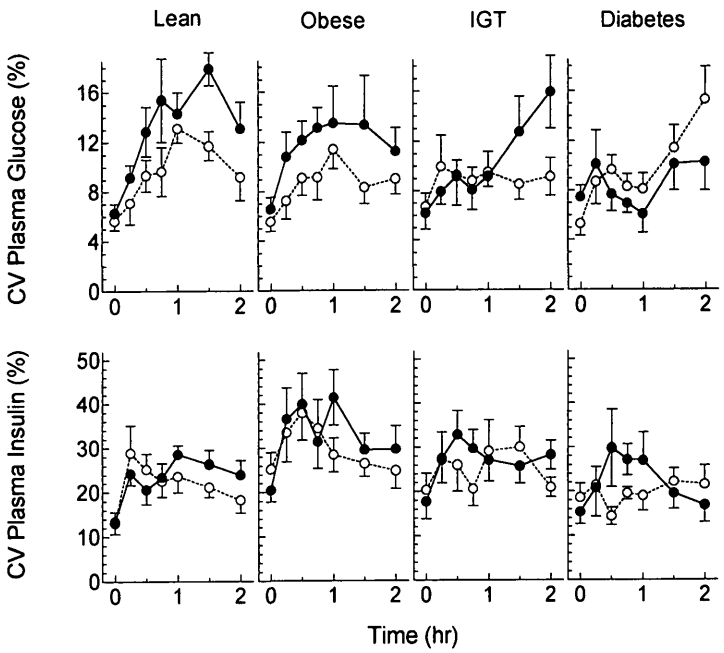

Figure 2—*CVs of plasma glucose and insulin concentrations at various times after the GTT (●) and the DSP (○) in 10 lean normal subjects, 9 obese normal subjects, 9 subjects with IGT, and 8 subjects with diabetes. Points represent means ± SE of the CVs calculated for the four repeated tests of each test meal consumed by each subject (CV = 100 × SD/mean).*

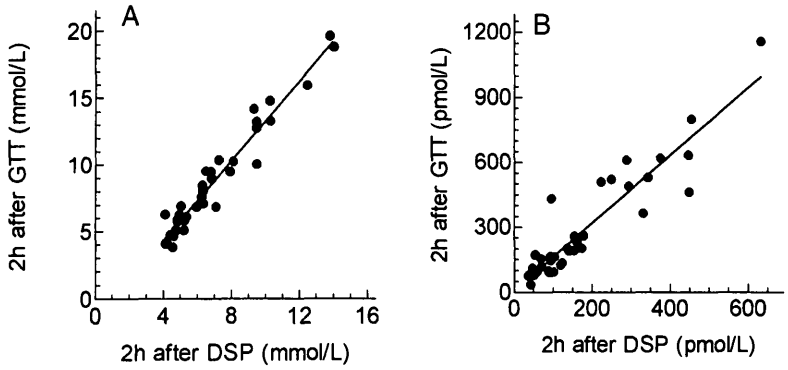

Figure 3—*Relationship of mean plasma concentrations of glucose* (A) *and insulin* (B) *of the 36 subjects measured 2 h after the DSP* (x-axis) *to those measured 2 h after the GTT* (y-axis). *Line represents regression equations. For plasma glucose,* r = *0.97; for plasma insulin,* r = *0.93.*

diabetic subjects, but we were surprised that the CV of 2-h plasma glucose after the DSP did not differ significantly from the GTT in diabetic subjects. Variability can be expressed in multiple ways; we chose CV instead of SD because SD is positively related to the mean, and we wished to avoid bias arising from the fact that mean plasma glucose was lower after the DSP than after the GTT. Indeed, the SD of 2-h glucose increased linearly with the mean but reached a maximum when the mean was 9 mmol/l (162 mg/dl; data not shown). Failure of the SD of 2-h plasma glucose to increase when the mean was >9 mmol/l is difficult to explain, but glucose loss in urine may have been the cause.

The values we report for day-to-day variation in postprandial plasma glucose and insulin concentrations include both analytic variability and true within-subject variation. However, the contribution of analytic variability is small and does not affect the conclusions; for example, excluding analytic variability (CV = 4%) would reduce plasma glucose CVs of 13 and 9% to 12.4 and 8.1%, respectively. True within-subject variation may be due, in part, to the fact that insulin is secreted in pulses (18), so that plasma concentrations of both glucose and insulin fluctuate minute to minute (19,20). The magnitudes of fasting insulin fluctuations, expressed as percentages of the mean, are two to three times greater than those for plasma glucose (20) and may explain why the CV of plasma insulin was two to three times that of plasma glucose.

The increase in variability of plasma glucose 2 h after the GTT versus the DSP may be due to differences in gastric emptying. Glycemic responses after the GTT are higher when the test is performed during a period of upper gastrointestinal motor activity as opposed to a period of quiescence (21). There is some evidence that the emptying of solids from the stomach is more consistent from day to day than is the emptying of liquids (22) and that coordinated gastroduodenal motor activity is stimulated more consistently by intragastric infusion of fat than by infusion of glucose (23). Thus, the physiological mix of nutrients in the DSP may stimulate gastric motor activity, resulting in more consistent gastric emptying and, hence, more consistent postprandial plasma glucose concentrations than the GTT.

The relationship between plasma glucose 2 h after the DSP and 2 h after the GTT was linear; 95% confidence limits of the residuals from the regression line were ±1.9 mmol/l (34 mg/dl). If the GTT is considered the "gold standard," then the deviation of the points from the regression line would be ascribed entirely to error in the DSP. However, both GTT and DSP test results vary from day to day, and deviation of the points from the regression line results from error attributable to both DSP and GTT. The present results show that in nondiabetic subjects, the error of the GTT is larger than that of the DSP, especially in subjects with IGT. This suggests that the DSP may be a more precise test than the GTT for detecting IGT.

IGT can be identified only by measuring postprandial plasma glucose. The usefulness of diagnosing IGT is suggested by evidence that lifestyle intervention reduces the rate of conversion of IGT to diabetes (24). If trials currently underway in North America, Europe, and Scandinavia show that pharmacological interventions have the same effect, there will be strong reasons to screen for IGT. In that case, a more precise test than the GTT might be useful. However, since glycemic responses after the DSP differ from those after the GTT, different diagnostic cut points would apply. The regression equation suggests that the range of plasma glucose 2 h after the DSP that corresponds to IGT is 6.3–8.4 mmol/l (113–151 mg/dl) (equivalent to 7.8–11.0 mmol/l [140–198 mg/dl] 2 h after the GTT), with normal values <6.3 mmol/l (113 mg/dl) and diabetic values >8.4 mmol/l (151 mg/dl). Using these cut points, the individual DSP tests correctly identified a proportion of cases of IGT and diabetes similar to that identified by the GTTs. In normal subjects, results were normal for 71 (93%) of 76 (95% CI 85–98%) individual GTTs and 70 (92%) of 76

Table 2—*Occurrence of symptoms*

Symptom and test	Symptom absent	Symptom present*	% tests with symptom present	P†
Stomach discomfort				
GTT	102	17 (7)	14	
DSP	114	7 (3)	6	0.028
Belching				
GTT	95	23 (11)	19	
DSP	113	8 (5)	7	0.003
Hunger				
GTT	90	29 (15)	24	
DSP	104	17 (10)	14	0.042
Nausea				
GTT	112	7 (3)	6	
DSP	121	0 (0)	0	0.007

Data are number of tests with or without symptoms or %. *Values in parentheses are number of subjects with symptoms. †Significance of difference in number of symptom occurrence between GTT and DSP.

(84–97%) DSP tests; in IGT subjects, results indicated IGT for 22 (65%) of 34 (46–80%) GTTs and 22 (63%) of 35 (45–79%) DSP tests; and in diabetic subjects, results indicated diabetes in 30 (94%) of 32 (79–99%) GTTs and 28 (88%) of 32 (71–96%) DSP tests. This study was not designed to compare the diagnostic accuracy of the DSP with that of the GTT, and the number of subjects is far too small to obtain reliable estimates of sensitivity, as shown by the wide 95% CIs. Although the results suggest that the DSP may be more accurate than the GTT in identifying subjects with IGT, designing a study to compare the diagnostic accuracy of the DSP with that of the GTT is difficult, since, by definition, the sensitivity and specificity of the GTT equal 100%. Greater precision in diagnosis could be demonstrated by showing a greater degree of concordance between repeated tests, but a different study design and a much larger number of subjects than used here would be required.

We conclude that plasma glucose concentrations 2 h after the DSP are closely related to those 2 h after the GTT, but that the results are more consistent after the DSP in the critical IGT range. This finding suggests that plasma glucose concentration 2 h after the DSP may discriminate among normal, IGT, and diabetic subjects more precisely than plasma glucose 2 h after the GTT.

Acknowledgments — This work was supported by a grant from Ceapro Inc., Edmonton, Alberta, Canada.

These results were presented in abstract form at the 57th Annual Meeting of the American Diabetes Association, Boston, Massachusetts, 19–24 June 1997.

References

1. King H, Rewers M, WHO Ad Hoc Diabetes Reporting Group: Global estimates for prevalence of diabetes mellitus and impaired glucose tolerance. *Diabetes Care* 16:157–177, 1993
2. National Diabetes Data Group: *Diabetes in America*. 2nd ed. Harris MI, Cowie CC, Stern MP, Boyko EJ, Reiber GE, Bennett PH, Eds. Washington, DC, U.S. Govt. Printing Office, 1995 (NIH publ. no. 95-1468)
3. Murray CLJ, Lopez AD: Mortality by cause for eight regions of the world: Global Burden of Disease Study. *Lancet* 349:1269–1276, 1997
4. Zimmet PZ: The pathogenesis and prevention of diabetes in adults: genes, autoimmunity, and demography. *Diabetes Care* 18:1050–1064, 1995
5. Singer DE, Samet JH, Coley CM, Nathan DM: Screening for diabetes mellitus. *Ann Int Med* 109:639–649, 1988
6. WHO Expert Committee: *Diabetes Mellitus*. Geneva, World Health Org., 1980 (Tech. Rep. Ser., no. 646)
7. Modan M, Harris MI: Fasting plasma glucose in screening for NIDDM in the U.S. and Israel. *Diabetes Care* 17:436–439, 1994
8. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 20:1183–1197, 1997
9. Drash AL: Is the oral glucose tolerance test obsolete? *Diabetes Care* 18:1072–1073, 1995
10. McCance DR, Hanson RL, Charles M-A, Jacobsson LTH, Pettitt DJ, Bennett PH, Knowler WC: Which test for diagnosing diabetes? *Diabetes Care* 18:1042–1044, 1995
11. Stolk RP, Orchard TJ, Grobbee DE: Why use the oral glucose tolerance test? *Diabetes Care* 18:1045–1049, 1995
12. McDonald GW, Fisher GF, Burnham C: Reproducibility of the oral glucose tolerance test. *Diabetes* 14:473–480, 1965
13. Mooy JM, Grootenhuis PA, de Vries H, Kostense PJ, Popp-Snijders C, Bouter LM, Heine RJ: Intra-individual variation of glucose, specific insulin and proinsulin concentrations measured by two oral glucose tolerance tests in a general Caucasian population: the Hoorn Study. *Diabetologia* 39:298–305, 1996
14. Wolever TMS, Vuksan V, Palmason C: Less variation of postprandial blood glucose after starchy test meals than oral glucose. *Nutr Res* 16:899–905, 1996
15. Rogers PJ, Carlyle J, Hill AJ, Blundell JE: Uncoupling sweet taste and calories: comparison of the effect of glucose and three intense sweeteners on hunger and food intake. *Physiol Behav* 43:547–552, 1988
16. Snedecor GW, Cochran WG: *Statistical Methods*, 7th ed. Ames, IA, Iowa State University Press, 1980
17. Wolever TMS, Bolognesi C: Source and amount of carbohydrate affect postprandial glucose and insulin in normal subjects. *J Nutr* 126:2798–2806, 1996
18. Matthews DR, Lang DA, Burnett M, Turner RC: Control of pulsatile insulin secretion in man. *Diabetologia* 24:231–237, 1983
19. Lang DA, Matthews DR, Burnett M, Turner RC: Brief, irregular oscillations of basal plasma insulin and glucose concentrations in diabetic man. *Diabetes* 30:435–439, 1981
20. Abdullah L, Chabert M, Louis-Sylvestre J: Cephalic phase responses to sweet taste. *Am J Clin Nutr* 65:737–743, 1997
21. Thompson DG, Wingate DL, Thomas M, Harrison D: Gastric emptying as a determinant of the oral glucose tolerance test. *Gastroenterology* 82:51–55, 1982
22. Collings PJ, Horowitz M, Cook DJ, Harding PE, Shearman DJC: Gastric emptying in normal subjects: a reproducible technique using a single scintillation camera and computer system. *Gut* 24:1117–1125, 1983
23. White CM, Poxon V, Alexander-Williams J: Effects of nutrient liquids on human gastroduodenal motor activity. *Gut* 24:1109–1116, 1983
24. Pan X, Li G, Hu Y-H, Wang J, Yang W, An Z, Hu Z, Lin J, Xiao J-Z, Cao H, Liu P-A, Jiang X, Wang J, Zheng H, Zhang H, Bennett PH, Howard BV: Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. *Diabetes Care* 20:537–544, 1997