suggest, or an experimental artifact for which we compensate by the use of an internal standard. In addition, the data are difficult to interpret, since the authors do not report whether they measured total *chiro*-inositol (the sum of D and L optical isomers) or the desired D enantiomer. Both occur in urine.

Although not acknowledged in the paper (1), the reader should be aware that we have found increased D-*chiro*-inositol in urine from predominantly Caucasian non-insulin-dependent and insulin-dependent diabetes subjects using quantitative GC/MS techniques with an internal standard (3). Our finding is thus exactly the opposite of the authors, who reported decreased urinary levels in non-insulin-dependent diabetes patients (1,2). In our work, elevated urinary excretion of D-*chiro*-inositol by diabetic subjects was strongly related to urinary glucose, plasma glucose, and glycated hemoglobin levels. Diabetic urine contains greatly increased quantities of many polyols and sugars (4), making trace analyses very difficult without extensive prepurification and the use of an internal standard. Thus, it is possible that the reduced urinary levels of D-*chiro*-inositol reported by the authors in diabetic subjects from both Japanese (1) and Caucasian (2) populations may have resulted from a GC/MS artifact. It would be important to resolve this question by cross-comparison of results and validation of the authors' assays. Future work published in this area should include detailed documentation of the analytical methods used.

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The Effect of Hyperglycemia on Glipizide Absorption in NIDDM Patients

Recently, it has been described that glucose-induced hyperglycemia impairs the absorption of the sulfonylurea agent glipizide in healthy young subjects (1). Therefore, the absorption and therapeutic activity of this drug in diabetic patients could be affected by metabolic state. The current study examined whether the absorption rate of glipizide in non-insulin-dependent diabetes mellitus (NIDDM) subjects would be increased following insulin-induced euglycemia.

Seven patients (five female and two male) with NIDDM who started insulin therapy because of sulfonylurea failure were studied. Their mean age was 46.0 ± 3.0 years, duration of diabetes was 13.5 ± 4.2 years, body mass index (BMI) was 30.2 ± 1.9 kg/m^2, and HbA_{1c} was 10.1 ± 0.3%. The existence of upper gastrointestinal surgery, peptic ulcer disease, or autonomic neuropathy were considered exclusion criteria. No patient had clinical signs or symptoms of renal or hepatic disease, and serum creatinine and liver enzyme levels were normal in every case. Two patients presented background retinopathy, and one patient had microalbuminuria (urinary albumin excretion: 30–300 μg/min).

The study was initiated after subjects were hospitalized for two days and received an isocaloric diet as the only diabetic treatment. Glipizide absorption was measured on two consecutive days, in hyperglycemic and euglycemic conditions, respectively. On day 1, after a sample for measurement of baseline plasma glucose and glipizide was obtained, a 5-mg tablet of glipizide was given with 200 ml of water. Thereafter, samples for measurement of plasma glucose were taken every 15 min and for plasma glipizide at 15, 45, 90, and 150 min. When plasma glucose decreased to <250 mg/dl, a 20% glucose infusion was started through a contralateral antecubital venous catheter adjusted to maintain hyperglycemia (250–350 mg/dl). After the study, insulin infusion was started to maintain the euglycemic state for 24 h (80–120 mg/dl). With the subjects in this condition, the study was repeated on day 2. Serum glipizide concentration was measured by high-performance liquid chromatography (2).

On day 1, mean blood glucose during the study was 271 ± 18 mg/dl, and during the second day it was 94 ± 3 mg/dl ($P < 0.001$). Peak concentrations of glipizide were 0.59 ± 0.30 (hyperglycemia) and 0.77 ± 0.20 (euglycemia) μg/ml. During euglycemia, glipizide appeared earlier in serum (47 ± 8 vs. 90 ± 18 min, $P < 0.05$) (Table 1). In both glycemic conditions, a plateau of the glipizide level was achieved between 90 and 150 min after ingestion of the drug (Table 1). There was no relationship between age, duration of diabetes, HbA_{1c}, or BMI and glipizide absorption.

Our results indicate that hyper-

Table 1—*Peak concentration (C_{max}), time to peak concentration (t_{max}) and time detection (t_{det}) following a single dose of 5 mg glipizide in seven NIDDM patients, during hyperglycemia and normoglycemia*

	C_{max} (μg/ml)		t_{max} (min)		t_{det} (min)	
Patient	Hyperglycemia	Normoglycemia	Hyperglycemia	Normoglycemia	Hyperglycemia	Normoglycemia
1	542	139	150	90	150	90
2	399	1,572	90	90	90	45
3	239	484	90	150	90	45
4	99	415	150	45	150	45
5	397	780	90	45	45	45
6	224	446	150	150	90	45
7	1,747	1,475	150	90	15	15
Means ± SE	521 ± 211	758 ± 210	124 ± 12	94 ± 16	90 ± 18*	47 ± 8*

* $P < 0.05$.

glycemia may cause a delay in the absorption of sulfonylurea drugs. The glipizide absorption rate varies greatly between subjects, probably because of differences in the rate of gastric emptying and hence in glipizide dissolution rate (3). Hyperglycemia slows gastric emptying, and this factor can modify drug absorption (4,5). The mechanisms responsible for the inhibitory action of hyperglycemia on gastric motility are not known. Alterations in gastrointestinal hormone secretion (such as motilin, pancreatic polypeptide, somatostatin, glucagon, gastrin, and gastric inhibitory polypeptide) may be important (6–8). On the other hand, hyperglycemia stimulates pyloric motility (9) and may supress vagal nerve activity, producing an autonomic nerve dysfunction (10). According to our results, hyperglycemia per se could influence the therapeutic efficacy of the sulfonylureas, delaying their absorption and, therefore, their hypoglycemic effect in relation to the meal-induced increase of blood glucose.

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Impaired Glucose Tolerance of Pregnancy by WHO and NDDG Criteria

Pettitt et al.'s article "Comparison of World Health Organization and National Diabetes Data Group procedures to detect abnormalities of glucose tolerance during pregnancy" (17:1264, 1994), is an important paper to help rationalize the diagnostic approach to gestational diabetes. However, I feel the authors may be unduly harsh on the two-step procedure (1-h screening test and then an oral glucose tolerance test). Using the World Health Organization (WHO) criteria, there are three possible outcomes after diagnostic testing: normal, impaired glucose tolerance, or diabetes. Using the formal criteria of the National Diabetes Data Group for diabetes in pregnancy, it's an all or nothing result, either normal or diabetic. Previous studies have shown that one abnormal value is of some predictive value for neonatal morbidity (1,2), and thus I think that the data on the sub-