supportive evidence for the presence of the former mechanism.[4]

We are well aware of the reported antidiuretic action of tolbutamide.[5] In the article, however, we stressed the fact that a much higher incidence of hyponatremia (serum sodium ≤ 129 meq/L) existed in chlorpropamide-treated patients (6.3%) than in tolbutamide- or glibenclamide-treated patients (0.9% and 0.0%, respectively).

TAKASHI KADOWAKI, M.D.

From the Institute for Adult Diseases, Asahi Life Foundation, Tokyo, Japan.

Address reprint requests to Takashi Kadowaki, M.D., The Third Department of Internal Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan.

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The Potential Usefulness of Postprandial Urine C-Peptide Measurement in Classifying Diabetic Patients

Measurement of 24-h urine C-peptide excretion has proven to be a useful means of distinguishing patients with insulin-dependent (IDDM) and non-insulin-dependent (NIDDM) diabetes mellitus.[1,2] However, data evaluating the utility of shorter, more easily obtained urine collections for C-peptide have not been reported. We therefore wish to present our experience in using 4-h, postprandial urinary C-peptide to confirm the classification of typical IDDM and NIDDM patients.

Ten healthy subjects (mean age, 39; range, 22–69 yr), 12 subjects with IDDM (mean age, 26; range, 19–35 yr), and nine subjects with NIDDM (mean age, 63; range, 44–82 yr) were evaluated. All IDDM subjects were taking daily or twice-daily insulin injections. Their mean duration of diabetes was 10 yr (range, 1–27 yr). Nine of the IDDM subjects had experienced at least one episode of ketoacidosis or were ketotic at the time of diagnosis of diabetes. The remaining three IDDM subjects developed diabetes before the age of 20, had taken insulin continuously since the time of diagnosis of diabetes, and demonstrated labile plasma glucose concentrations. The nine NIDDM subjects all had fasting plasma glucose concentrations greater than 140 mg/dl on more than one occasion. Their mean duration of diabetes was 7 yr (range, 2 mo to 17 yr). None of the NIDDM subjects was taking insulin or oral hypoglycemic agents. All subjects had normal renal function as determined by a normal serum creatinine and the absence of proteinuria.

Research subjects were asked to fast overnight and report to the General Clinical Research at 8:00 a.m. At approximately 8:30 a.m., a 700-kcal mixed meal composed of 48% carbohydrate, 20% protein, and 32% fat was served. Subjects voided before eating and all urine output during the following 240-min period was collected. Plasma glucose and serum insulin concentrations were determined after the meal and are the subject of a separate report.[3] On study mornings, IDDM subjects administered their usual dose of insulin 30 min before the test meal. Urine C-peptide was determined by radioimmunoassay as previously described.[4]

Mean postprandial urinary C-peptide excretion was 7.8 ± 2.9 (±SD) nmol/4 h in healthy subjects, 0.4 ± 0.4 nmol/4 h in IDDM subjects, and 11.1 ± 2.8 nmol/4 h in NIDDM subjects (Figure 1). C-peptide excretion was significantly less in IDDM subjects than in either healthy or NIDDM subjects. Urinary creatinine excretion was greater than 1.7 mg/kg

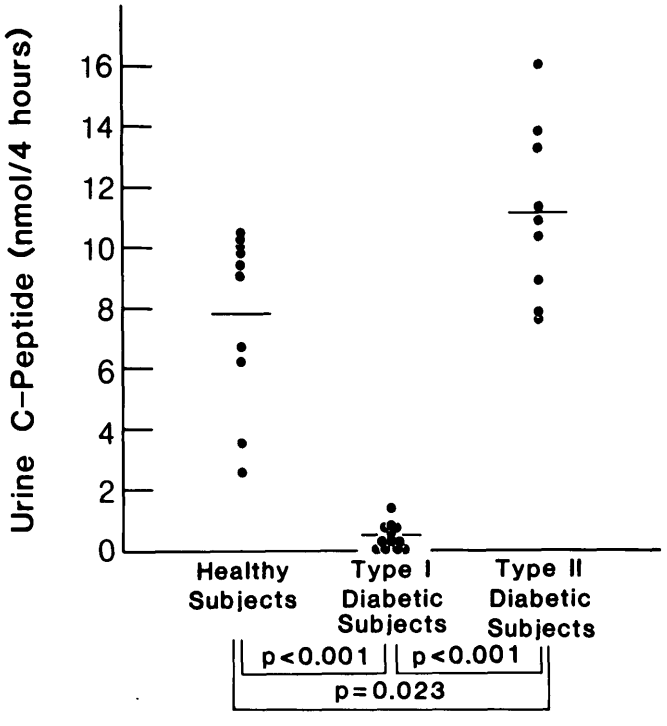

FIG. 1. Urinary C-peptide excretion during a 4-h postprandial period in healthy, IDDM (type I), and NIDDM (type II) subjects. Lines indicate the group means.

body wt/4 h in all female subjects and was greater than 2.5 mg/kg body wt/4 h in all male subjects, suggesting that the urine collections were complete.

In many clinical situations, it is difficult to be certain whether or not an insulin-taking diabetic patient is truly insulin dependent. Measurement of stimulated serum C-peptide is useful in making this distinction as is the determination of 24-h urinary C-peptide excretion. Our data suggest that the distinction can also be made with a 4-h postprandial urine collection, as all of our subjects with IDDM excreted less than 1.4 nmol C-peptide/4 h, whereas all subjects with NIDDM excreted more than 7.5 nmol C-peptide/4 h. However, until more subjects are studied, we cannot classify diabetic individuals whose C-peptide excretion is between 1.4 and 7.5 nmol/4 h.

JOHN P. BANTLE, M.D.
DAWN C. LAINE, R.D.
BYRON J. HOOGWERF, M.D.
FREDERICK C. GOETZ, M.D.

From the Division of Endocrinology and Metabolism, Department of Medicine, and the General Clinical Research Center, University of Minnesota, Minneapolis, Minnesota 55455.

Address reprint requests to John P. Bantle, M.D., at the above address.

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Relaxation-induced Improvement in Glucose Tolerance Is Associated with Decreased Plasma Cortisol

In a recent issue of this journal (March-April 1983) we reported that relaxation training significantly improved glucose tolerance in patients with non-insulin-dependent diabetes.[1] Twelve patients with non-insulin-dependent diabetes were hospitalized in a clinical research ward under identical conditions. A 3-h glucose tolerance test and intravenous insulin tolerance test were performed on each patient. Half of the patients were then given 5 days of progressive relaxation training after which all patients were retested while treated patients practiced relaxation. Relaxation was found to significantly improve glucose tolerance without affecting insulin sensitivity or glucose-stimulated insulin secretory activity. We now report that these changes were associated with a decrease in plasma cortisol in patients receiving relaxation.

TABLE 1
Means and standard errors of plasma cortisol (μg/dl) in six treated and six control subjects

	Pretreatment	Posttreatment	Difference
Relaxation	21.5 ± 5.6	12.3 ± 2.6	−9.4 ± 4.1
Control	13.2 ± 2.5	16.8 ± 3.2	+3.6 ± 4.7

Three blood samples collected at 5-min intervals before the administration of oral glucose on both the first and second glucose tolerance test were assayed for catecholamines and cortisol. The radioenzymatic technique developed by Passon and Peuler[2] was used to assay catecholamines, and plasma cortisol was determined by a commercially available radioimmunoassay kit (New England Nuclear, Boston, Massachusetts). Difference scores representing changes in epinephrine, norepinephrine, and cortisol were derived by subtracting values obtained from averages of the first set of samples from values in the second. These values were then analyzed by analysis of variance.

As shown in Table 1, patients receiving progressive relaxation training averaged a 9.4 μg/dl decrease in plasma cortisol in the posttreatment assessment. At the same time, control patients demonstrated a 3.6 μg/dl increase in plasma cortisol. These differences were significant ($P < 0.03$). Plasma levels of epinephrine and norepinephrine were within normal limits in all subjects and did not change with relaxation.

These data are consistent with previous reports showing that relaxation training is associated with a decrease in adrenal cortical activity.[3,4] To date, there have been no reports of relaxation-induced decreases in plasma catecholamine levels. Although there are no previous data reporting the effect of variations of plasma cortisol, within the physiologic range, on glucose tolerance, the effects of cortisol on glucose transport and metabolism are well known. It is also possible that small changes in plasma cortisol could affect adrenergic receptor sensitivity to circulating catecholamines,[5] thus modulating glucose tolerance. Further research into the mechanisms by which stress and relaxation affect glucose tolerance is currently in progress in our laboratory.

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RICHARD S. SURWIT, Ph.D.
MARK N. FEINGLOS, M.D.