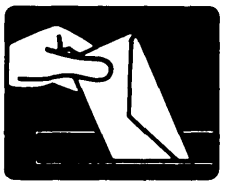
Letters and Comments



Pancreatic Polypeptide: Marker for Autonomic Neuropathy but Not for Lean NIDDM

We have several comments on a recent interesting article by Service et al. (1) about pancreatic polypeptide (PP) as a marker for lean non-insulin-dependent diabetes (NIDDM). The authors clearly showed twofold increases in basal and threefold in postprandial PP concentrations in lean NIDDM patients. However, because we were unable to agree with their results, we tried to determine whether elevated PP levels are indeed a characteristic of lean NIDDM patients in Japan.

Twenty-five NIDDM patients (15 men and 10 women) were studied after informed consent was obtained. The patients were 50.0 ± 0.9 yr old (range 40–58 yr), had body mass index of 21.9 ± 0.4 kg/m^2 (range 18.3–26.0), had diabetes for 6.7 ± 0.9 yr (range 0.5–17 yr), and were treated by diet or oral agents. No patient was ketotic, and all had taken oral glucose tolerance tests. Subjects had no sign of autonomic neuropathy, as evaluated by diminished deep tendon reflexes, decreased beat-to-beat variation in heart rate during deep breathing, or orthostatic hypotension. None had chronic pancreatitis or renal dysfunction. In addition, an age-matched group of 13 lean normal controls was selected.

Each subject was studied after an overnight fast before and for 2 h after consumption of a standard mixed meal (640 kcal) of 36% carbohydrate, 36% fat, and 28% protein distribution. All tests were conducted with subjects at bed rest. The composition of our test meal was different from that used by Service et al., with less carbohydrate but a higher caloric value. We also used a fixed nutrient load rather than one based on the subjects' ideal weights. PP and insulin were measured by double-antibody radioimmunoassay, and plasma glucose was measured by the glucose oxidase method (2).

As shown in Fig. 1, both basal and peak postprandial plasma glucose of the lean NIDDM patients exceeded ($P < .0005$) those of the age- and weight-matched controls. However, although basal plasma PP of the lean NIDDM patients tended to exceed that of the controls, peak postprandial plasma PP did not differ significantly. The degree of similarity of this PP response was best indicated by the integrated PP responses (IPPR), determined from the area under the curve of plasma levels above basal levels. The IPPR to mixed meal in the normal and NIDDM subjects was 99.0 ± 17.3 and 98.2 ± 10.5 ng · min · ml^{-1}, respectively. The postprandial plasma insulin response of our NIDDM patients did not differ significantly from the controls, thus suggesting residual β-cell function in NIDDM patients as reported by Service et al.

Previous studies have shown that impaired secretion of PP serves as a sign of autonomic neuropathy in both diabetic (3) and nondiabetic (4) patients. We previously reported that the postprandial plasma PP response, especially the first phase, is blunted in diabetics with autonomic neuropathy (5). Thus, we think that PP can be a clinical indicator for autonomic neuropathy but not for lean NIDDM subjects.

AKIO INUI, MD
NORIAKI SAKATANI, MD
TORU INOUE, MD
MANABU OYA, MD
HIDEKI MORIOKA, MD
NOBUHIKO MIZUNO, MD
SHIGEAKI BABA, MD

From the Department of Internal Medicine II, University of Kobe School of Medicine, Chuo-ku, Kobe 650, Japan.

Send correspondence and reprint requests to Akio Inui, MD, at the above address.

REFERENCES

1. Service FJ, Koch MB, Jay JM, Rizza RA, Go VLW: Pancreatic polypeptide: a marker for lean non-insulin-dependent diabetes mellitus? *Diabetes Care* 8:349–53, 1985
2. Mizuno N, Ishida M, Okada K, Baba S: Studies on the radioimmunoassay of human pancreatic polypeptide (hPP) and basal levels of plasma hPP in healthy subjects and diabetic patients (Abstract). *J Jpn Diabetes Soc* 22:895–905, 1979
3. Krarup T, Schwartz TW, Hilsted J, Madsbad S, Verlaege O, Sestoft L: Impaired response of pancreatic polypeptide to hypoglycaemia: an early sign of autonomic neuropathy in diabetics. *Br Med J* 2:1544–46, 1979
4. Polinsky RJ, Taylor IL, Chew P, Weise V, Kopin IJ: Pancreatic

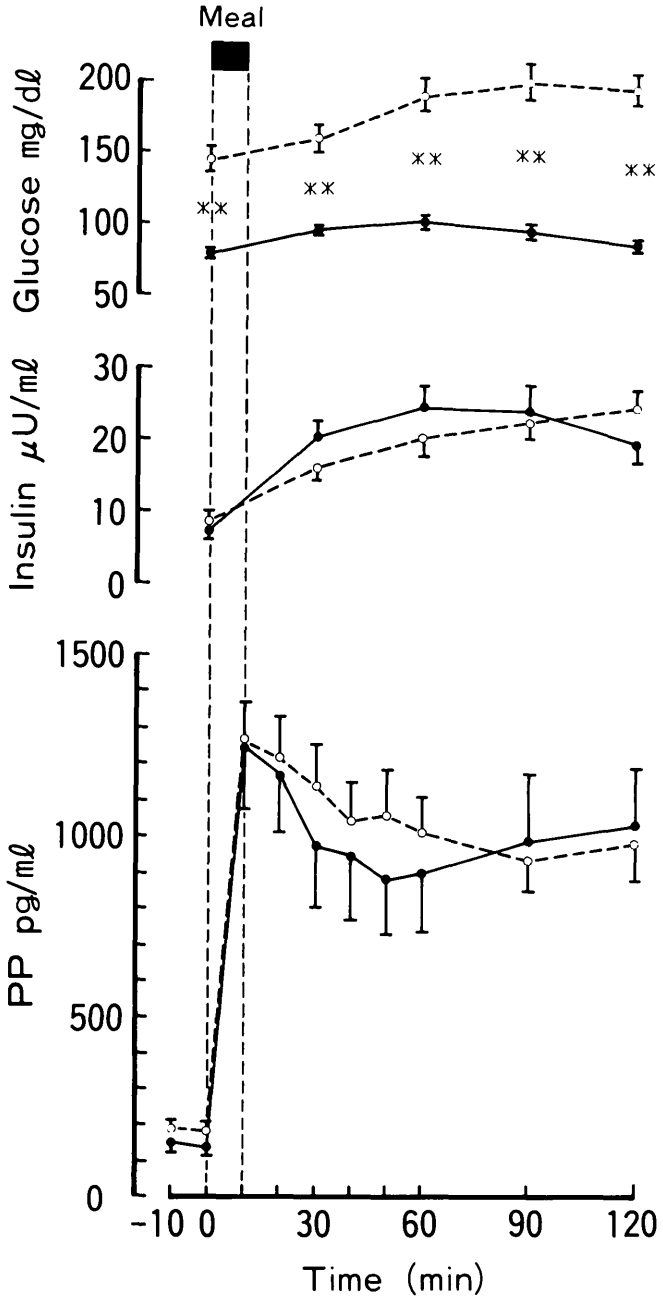


FIG. 1. Plasma glucose, insulin, and pancreatic polypeptide responses to mixed meal were measured in 25 lean NIDDM patients (○) and 13 controls (●). Results are means ± SE. **$P < .0005$, significant difference between NIDDM patients and controls, assessed by nonpaired Student's t test.

polypeptide responses to hypoglycemia in chronic autonomic failure. *J Clin Endocrinol Metab* 54:48–52, 1982

5. Ishida M, Mizuno N, Inui A, Ogawa T, Okada K, Taniguchi H, Baba S: Abnormal pancreatic polypeptide response in diabetic autonomic neuropathy (Abstract). In *Proc 11th Congr Int Diabetes Fed.* Amsterdam, Excerpta Med., 1982, p. 138

Pancreatic Polypeptide as Marker for Autonomic Neuropathy: Reply

An explanation for the disparity between Professor Baba's observations and ours with respect to pancreatic polypeptide responses in lean IDDM subjects is not readily apparent. There are several differences in conduct of the two studies, any of which may be implicated. Professor Baba's patients had mild diabetes treated with diet or oral hypoglycemic agents, whereas our patients, although NIDDM, were treated with insulin. The test meal was larger and was comprised of less carbohydrate but more fat and protein than ours. In addition, postprandial sampling was terminated at 120 min, whereas ours proceeded to 240 min. Both studies used patients of similar age and duration of diabetes and compared responses to age-matched controls. In addition, the degrees of basal and postprandial hyperglycemia and insulin secretory reserve were similar in both studies. Reconciliation of the discrepancies between the two studies may require mutual adoption of patient-selection methods and study design to determine whether those are the factors at play here.

F. J. SERVICE, MD
R. A. RIZZA, MD
V. L. W. GO, MD

From the Department of Internal Medicine, Division of Endocrinology and Metabolism, Mayo Clinic, 200 First Street, S.W., Rochester, Minnesota 55905.

Send correspondence to Dr. F. John Service at the above address.

Factitious Hypoglycemia Due to Administration of Human Synthetic Insulin: New Diagnostic Challenge

Diagnosis of factitious hypoglycemia in a nondiabetic patient with symptomatic hyperinsulinemic hypoglycemia is often elusive. It is based on the clinical setting, a high index of suspicion, and specific laboratory tests (1). We describe a health-care professional who covertly self-administered human synthetic insulin but who was subjected to a long, expensive, and potentially dangerous workup for an insulinoma. The delay in establishing the correct diagnosis was due, in part, to the inadequacy of certain laboratory tests (speciation of insulin and presence of serum insulin antibodies) that were heretofore critical in securing the diagnosis of surreptitious insulin administration. This case of factitious hypoglycemia, perhaps the first due to the administration of human insulin,