sincerely apologize; however, this is in no way meant to be a retraction of my view that the medical profession involved in the research and development of new techniques must be cautious and careful in accepting any new technology. Articles or papers that espouse new techniques should be viewed cautiously if they are coauthored by someone associated with the commercial development of the new product or technology recommended in the article.

ROBERT EHRLICH, MD

From the Division of Endocrinology, The Hospital for Sick Children, Toronto, Ontario, Canada.
Address correspondence to Dr. Robert M. Ehrlich, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario, Canada M5G 1X8.

EDITOR'S NOTE

The distress expressed by Dr. Schiffrin is regrettable and totally unintended. The policy regarding letters and comments is purposely liberal to promote free exchange of ideas, but comments or innuendos regarding professional integrity are not permitted. As to the issue of potential conflict of interest, one of the authors of Dr. Schiffrin's article has a financial interest in the company that manufactures the device reported; this information was noted in the acknowledgments in that article. Dr. Ehrlich's letter was not circulated to any of the authors of the papers referenced (including one from this institution) because it did not occur to the editors that anything but a self-evident principle was being addressed. In publishing Dr. Ehrlich's letter, the editors had not the slightest intention of impugning the high academic standards and professional integrity of Dr. Schiffrin, who has been highly regarded by the journal for faithful support as a reviewer and editorial board member.

FJS, RAR, BRZ

Biphasic Patterns of Peripheral Insulin and Glucose Concentrations After Meals

I have read with interest the report by Robbins et al. (1). Their detailed analysis of post-meal glucose and insulin peaks is of interest, especially the emphasis on post-meal secondary peaks. However, I would like to point out that this observation is not new. In 1976, we published insulin and glucose profiles in normal subjects ingesting three identical mixed meals (43% carbohydrate, 48% fat, 9% protein) at 4-h intervals throughout the day (2). Post-meal secondary peaks in insulin and glucose concentrations were clearly identified after all three meals. This was particularly prominent among the male subjects. The presence of these peaks was commented on in the report. The correlation between the glucose and insulin peaks also was commented on but a statistical analysis of the correlation was not attempted. More recently, we also have demonstrated multiple post-meal insulin and glucose peaks in normal subjects ingesting high carbohydrate, high protein, and high fat meals (2). The lack of association of post-meal insulin peaks with alpha-amino nitrogen concentrations also was pointed out (3,4). This was particularly apparent in subjects ingesting three high protein meals throughout the day. The lack of change in glucagon concentration with the normal mixed meals also was demonstrated (2).

I am disappointed that the authors did not discuss or reference any of these studies.

FRANK Q. NUTTALL, MD, PhD

From the Veterans Administration Medical Center, Minneapolis, Minnesota.
Send correspondence and reprint requests to Dr. Frank Q. Nuttall, Veterans Administration Medical Center, 54th Street and 48th Avenue South, Minneapolis, MN 55417.

REFERENCES

1. Robbins DC, Jaspan J, Vasquez B, Van Cauter E: Biphasic patterns of peripheral insulin and glucose levels after lunch in normal subjects. *Diabetes Care* 10:293–99, 1987
2. Ahmed M, Gannon MC, Nuttall FQ: Postprandial plasma glucose, insulin, glucagon and triglyceride responses to a standard diet in normal subjects. *Diabetologia* 12:61–67, 1976
3. Nuttall FQ, Gannon MC, Wald JL, Ahmed M: Plasma glucose and insulin profiles in normal subjects ingesting diets of varying carbohydrate, fat and protein content. *J Am Coll Nutr* 4:437–50, 1985
4. Ahmed M, Nuttall FQ, Gannon MC, Lamusga RF: Plasma glucagon and alpha-amino nitrogen response to various diets in normal humans. *Am J Clin Nutr* 33:1917–24, 1980

BIPHASIC PATTERNS OF PERIPHERAL INSULIN AND GLUCOSE CONCENTRATIONS AFTER MEALS: A REPLY

Previous studies of substrate and hormone levels after mixed meals in nondiabetic volunteers (1–6) have generally failed to observe or mention the presence of the secondary, post-lunch peaks in serum insulin or plasma glucose or failed to validate the observations with appropriate statistical tests of hormone or substrate movement with time. In many of these investigations sampling was too infrequent to reliably detect such peaks, meals of different composition were served at variable

times of day, or data from several volunteers were pooled, thereby transforming the distinct secondary peaks of blood glucose and insulin into a vague descending "shoulder" on the graph of the post-meal response. Accordingly, the multiphasic nature of post-meal insulin secretion was not the focus of the discussions, nor was it even mentioned in the abstracts.

In the design of our study, these issues were carefully considered. To maximize the number of data points contributing to a peak we drew blood every 10 min. To minimize assay variability, all hormone and substrate samples were measured in single assays. To avoid the confounding consequences of different meal content on the time-of-day response, identical meals were served at breakfast and lunch. Finally, in an attempt to be rigorous in the designation of significant hormone and substrate peaks, strict and conservative statistical criteria were used in the analyses. Our inferences were supported by appropriate spectral analysis and statistical tests of probability.

We thank Dr. Nuttall for pointing out his studies on the response to mixed meals in normal subjects and apologize for inadvertanly overlooking his observations. We have extended these observations and hopefully put them on a more firm statistical footing by virtue of different study design and analysis.

JONATHAN B. JASPAN, MD
DAVID C. ROBBINS, MD
EVE VAN CAUTER, PhD
BARBARA VASQUEZ, PhD

From the Department of Medicine, University of Chicago Medical Center, Chicago, Illinois.
Address correspondence and reprint requests to Dr. Jonathan B. Jaspan, Department of Medicine, University of Chicago, 5841 S. Maryland Avenue, Box 435, Chicago, IL 60637.

REFERENCES

1. Alberti KGMM, Dornhorst A, Rowe AS: Metabolic rhythms in normal and diabetic man: studies in insulin-treated diabetes. *Isr J Med Sci* 11:571–80, 1974
2. Hansen AP, Johansen K: Diurnal patterns of blood glucose, serum free fatty acids, insulin, glucagon and growth hormone in normals and juvenile diabetics. *Diabetologia* 6:27–33, 1970
3. Hansen B, Jen K, Pek S, Wolfe R: Rapid oscillations in plasma insulin, glucagon and glucose in obese and normal weight humans. *J Clin Endocrinol Metab* 54:785–92, 1982
4. Lang DA, Matthews DR, Jeto J, Turner RC: Cyclic oscillations of basal plasma glucose and insulin concentrations in human beings. *N Engl J Med* 301:1023–27, 1979
5. Kraegen EW, Young JD, George EP, Lazarus L: Oscillations in blood glucose and insulin after oral glucose. *Horm Metab Res* 4:409–13, 1972
6. Rizza RA, Gerich JE, Haymond MW, Westland RE, Hall LD, Clemens AH, Service FJ: Control of blood sugar in insulin-dependent diabetes: comparisons of an artificial endocrine pancreas, continuous subcutaneous insulin infusion, and intensified conventional insulin therapy. *N Engl J Med* 303:1313–17, 1980

Does Pan-Pancreatic Involvement Occur in IDDM?

Many experimental models of virus-induced insulin-dependent (type I) diabetes mellitus (IDDM) revealed the inflammatory lesions of the exocrine pancreas (1). However, almost all IDDM patients with exceptional cases of mumps infection (2) lacked the evidence of the exocrine impairment. Recently developed highly sensitive radioimmunoassay for pancreatic elastase I (3) and trypsin (4) enabled us to evaluate the inflammatory lesion of the pancreas. We first documented the longitudinal changes of these enzymes in newly diagnosed IDDM patients.

A 45-yr-old male (case 1) was admitted to our hospital with blood glucose of 545 mg/dl and ketonuria on the day after sudden onset of diabetic symptoms including thirst, polydipsia, and polyuria. His urinary C-peptide excretion was 1.4–5.1 μg/day, indicating that he was in an insulin-dependent state. He was treated immediately with insulin. His serum elastase I, lipase, and trypsin levels were markedly elevated on admission, and decreased gradually, returning to normal ~120 days later (Fig. 1). Serum amylase level remained unchanged. Ultrasonographic examination and endoscopic retrograde

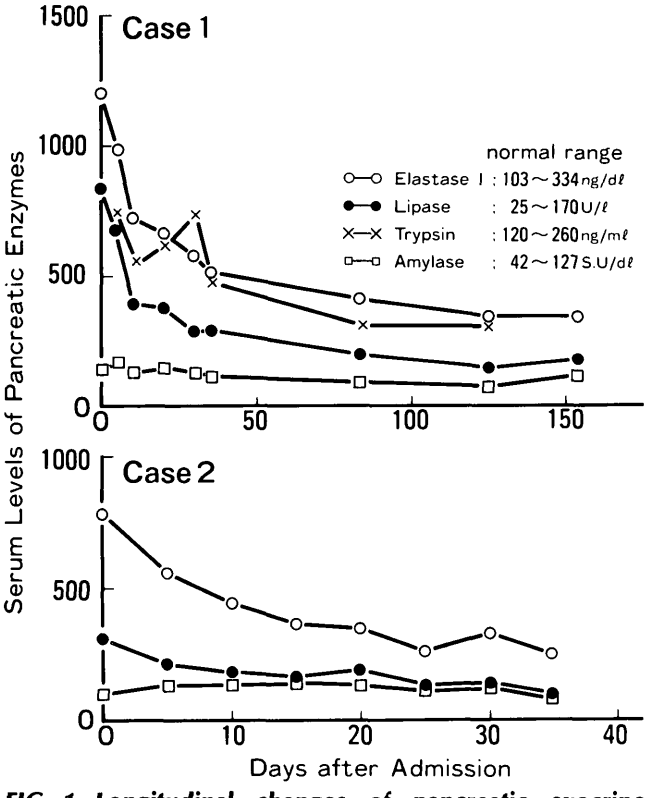

FIG. 1. Longitudinal changes of pancreatic exocrine enzymes in 2 newly diagnosed insulin-dependent diabetic patients.