higher glycemic threshold), as recently suggested by Cryer (2) and others, seems to me to be both unnecessarily confusing and semantically incorrect. Lower may mean higher in golf and politics, but not in describing glycemic *thresholds* for counterregulatory responses.

WILLIAM V. TAMBORLANE, MD

FROM THE YALE UNIVERSITY SCHOOL OF MEDICINE, SECTION OF PEDIATRIC ENDOCRINOLOGY, NEW HAVEN, CONNECTICUT.

ADDRESS CORRESPONDENCE AND REPRINT REQUESTS TO WILLIAM V. TAMBORLANE, MD, PROFESSOR AND SECTION CHIEF, PEDIATRIC ENDOCRINOLOGY, YALE UNIVERSITY SCHOOL OF MEDICINE, P.O. BOX 3333, NEW HAVEN, CT 06510–8064.

References

1. Costello RB (Ed.): *Webster's New Collegiate Dictionary*. Springfield, MA, G&C Merriam, 1981, p. 1207
2. Cryer PE: Iatrogenic hypoglycemia as a cause of hypoglycemia—associated autonomic failure in IDDM: a vicious cycle. *Diabetes* 41:255–60, 1992

Reply

Blakiston's Gould Medical Dictionary defines *threshold* as "the lower limit of stimulus capable of . . . evoking a response" (1).

Thus, if a greater hypoglycemic stimulus (i.e., a lower plasma glucose concentration) is required to elicit a response, then the glycemic threshold for that response is higher or elevated. If a lesser hypoglycemic stimulus (i.e. a higher plasma glucose concentration) elicits a response, then the threshold is lower or reduced.

This is the rationale for my current use of the terms elevated or reduced glycemic thresholds (2). Unfortunately, it has not always been so (3). However, to paraphrase Confucius, a person who makes a mistake and fails to correct that mistake has made another mistake. The fundamental point, of course, is that all authors must define their terminology clearly when discussing glycemic thresholds.

PHILIP E. CRYER, MD

FROM THE WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, DIVISION OF ENDOCRINOLOGY, DIABETES AND METABOLISM, ST. LOUIS, MISSOURI. PHILIP E. CRYER IS THE EDITOR OF THE JOURNAL *DIABETES*.

ADDRESS CORRESPONDENCE AND REPRINT REQUESTS TO PHILIP E. CRYER, MD, EDITOR, *DIABETES*, DIVISION OF ENDOCRINOLOGY, DIABETES AND METABOLISM, BOX 8127, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, 660 S. EUCLID AVE., ST. LOUIS, MO, 63110.

References

1. *Blakiston's Gould Medical Dictionary*. Fourth Edition. New York, McGraw-Hill, 1979, p. 1372
2. Cryer PE: Iatrogenic hypoglycemia as a cause of hypoglycemia-associated autonomic failure in IDDM: a vicious cycle. *Diabetes* 41:255–60, 1992
3. Schwartz NS, Clutter WE, Shah SD, Cryer PE: The glycemic thresholds for activation of glucose counterregulatory systems are higher than the threshold for symptoms. *J Clin Invest* 79:777–81, 1987

Difference Between Islet Cell Antibodies and Autoantibodies to Glutamic Acid Decarboxylase–Containing Purkinje Cells in IDDM

The occurrence of autoantibodies to GABA-ergic neurons and pancreatic β-cells was reported in stiff-man syndrome and in several patients with IDDM (1). They were directed against GAD in β-cells and in a subpopulation of nerve cells (i.e., Purkinje cells), and they have been found to be identical to the 64K antibodies related to the development of IDDM (2). A new question was raised regarding the correspondence of the autoantibody against GAD (the 64K antibody) with ICA, which is another marker of active pancreatic β-cell damage in IDDM (3,4). This is because immunofluorescence studies demonstrated that the GAD antibody reacted homogenously to β-cell cytoplasm with a similar pattern to ICA (2). In this study, the possible differences between the target antigens of ICA and the autoantibodies to GABA-ergic neurons in IDDM were examined.

Seventy-five subjects were studied, including 14 with recent-onset (<3 mo) IDDM (8 men, 6 women, mean age 23 yr), 11 with ICA^+ NIDDM, (8 men, 3 women, mean age 48 yr, duration 2.3 yr), 23 with ICA^- NIDDM, (12 men, 11 women, mean age 45 yr, duration 2.5 yr), 1 with stiff-man syndrome (1 male, mean age 61 yr, duration 1 yr), and 26 normal control subjects (16 men, 10 women, mean age 32 yr). The titers of autoantibodies to GABA-ergic neurons were assayed by reactivity to unfixed human cerebellar GAD-containing Purkinje cells using indirect immunofluorescence. ICA was assayed by the sensitive method previously reported (5).

Positive immunostaining of GAD-containing Purkinje cells was observed in 29% (4 of 14) of recent-onset IDDM patients and in 18% (2 of 11) of ICA^+ NIDDM patients, with a titer ranging from 1:20–1:40 (Fig. 1). Purkinje cell autoantibody was positive in the stiff-man syndrome patient with a titer of 1:80, but was negative in the 23 ICA^- NIDDM patients and the 26 normal control subjects. All recent-onset IDDM patients were positive for ICA, with a titer ranging from 5 to 10,240 JDF U. The stiff-man syndrome patient was negative for ICA. The titers of Purkinje cell auto-

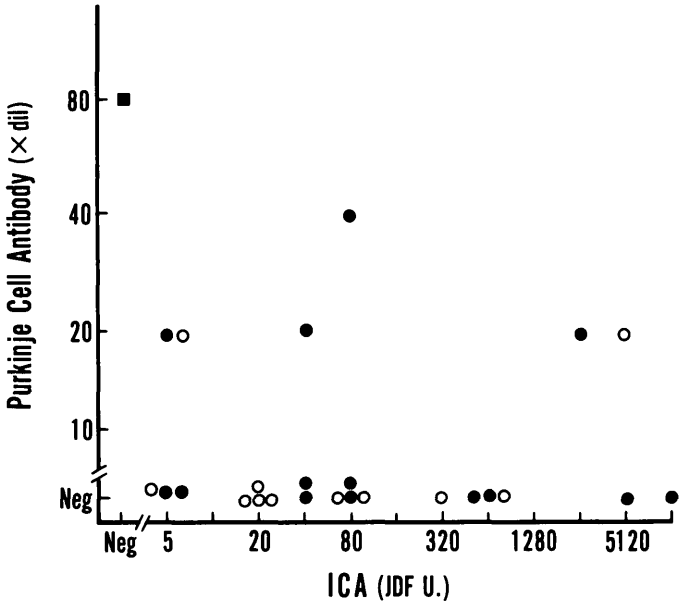

Figure 1—*Correlation between the titer of ICA and the titer of autoantibodies to glutamic acid decarboxylase–containing Purkinje cells in 14 patients with ICA$^+$ IDDM (●), 11 patients with ICA$^+$ NIDDM (○), and 1 patient with stiff-man syndrome (■).*

antibody and ICA did not show any positive correlation (Fig. 1).

In a previous report (2), anti-GAD antibodies (the 64K antibody) in IDDM patients, which reacted with GABA-ergic neurous, rarely recognized denatured GAD on Western blotting analysis. In this study, an immunohistochemical approach that used unfixed and undenatured specimens was adopted to examine the reactivity of anti-GAD antibody to its target antigens. No association between ICA and Purkinje cell autoantibody was observed in terms of positivity and titers in IDDM and stiff-man syndrome, suggesting that the two antibodies are distinct from each other.

TETSURO KOBAYASHI, MD
KOJI NAKANISHI, MD
TOSHIO MURASE, MD
KINORI KOSAKA, MD

FROM THE DEPARTMENT OF ENDOCRINOLOGY AND METABOLISM, TORANOMON HOSPITAL AND OKINAKA MEMORIAL INSTITUTE FOR MEDICAL RESEARCH, TORANOMON, MINATO-KU, TOKYO, JAPAN.

ADDRESS CORRESPONDENCE AND REPRINT REQUESTS TO TETSURO KOBAYASHI, MD, DEPARTMENT OF ENDOCRINOLOGY AND METABOLISM, TORANOMON HOSPITAL, 2-2-2 TORANOMON, MINATO-KU, TOKYO 105, JAPAN.

IDDM, INSULIN-DEPENDENT DIABETES MELLITUS; GAD, GLUTAMIC ACID DECARBOXYLASE; ICA, ISLET CELL CYTOPLASMIC ANTIBODIES.

Acknowledgments— Supported in part by a grant from the Ministry of Health and Welfare of Japan.

References

1. Solimena M, Folli F, Aparisi R, Pozza G, De Camilli P: Autoantibodies to GABA-ergic neurons and pancreatic beta cells in stiff-man syndrome. *N Engl J Med* 322: 1555–60, 1990
2. Baekkeskov S, Aanstoot HJ, Christgau S, Reetz A, Solimena M, Cascalho M, Folli F, Richter-Olesen H, De-Camilli P: Identification of the 64K autoantigen in insulin-dependent diabetes as the GABA-synthesizing enzyme glutamic acid decarboxylase. *Nature* 347:151–56, 1990
3. Bottazzo, GF: β-cell damage in diabetic insulitis: are we approaching a solution? *Diabetologia* 26:241–49, 1984
4. Kobayashi T, Itoh T, Kosaka K, Sato K, Tsuji K: Time course of islet cell antibodies and β-cell function in non-insulin-dependent stage of type I diabetes. *Diabetes* 36:510–17, 1987
5. Kobayashi T, Sugimoto T, Itoh T, Kosaka K, Tanaka T, Suwa S, Sato K, Tsuji K: The prevalence of islet cell antibodies in Japanese insulin-dependent and non-insulin-dependent diabetic patients studied by indirect immunofluorescence and by a new method. *Diabetes* 35:335–40, 1986

Glycemic Index Versus Glycemic Response

Nonsynonymous terms

Rasmussen et al. (1) found that most of the variation of glycemic responses in NIDDM subjects is attributable to between-subject variation. It was gratifying that the CVs of blood glucose responses within- and between-subjects that they observed in NIDDM patients treated with diet and oral agents—19 and 33%—respectively, were similar to those we found in 1985, for NIDDM patients on diet and oral agents—16 and 34%, respectively (2). These values also are similar to those for within- and between-subject variation of glycemic responses we found in 1985 for NIDDM patients on insulin—15 and 23% (2), and in 1989 for a mixed group of NIDDM patients (7 on insulin and 4 on diet or oral agents)—16 and 25% (3). Rasmussen et al. then expressed surprise about our report in 1990 that the within-subject variation of the glycemic index was much greater than that between subjects, with SDs of 16 and 6, respectively (4). However, far from being surprising,