a true placebo powder that can be applied to wounds. Even a chemically or biologically inert powder may have irritant effects in an ulcer that could promote or hinder healing. Some have argued that dermatologic bases could serve as inert comparisons, but they are not necessarily inert either, and they can interfere with the action of the agent to be tested.

Finally, we should point out that we said in our paper that "Phenytoin should prove especially useful in rural areas where daily attendance at clinic or hospital is not possible." The emphasis is on the "should." We quite agree that proper preventive foot care is important for diabetic patients, and we do not make the claim that phenytoin replaces the need for antibiotics, as the letter implies. Both preventive care and ulcer treatment need to be available in rural, poor areas. Consistent with this, we do state that phenytoin's low cost, ease of use, and safety are important features for use in rural areas where poverty is a constant companion—and indeed they are. Rather substantial experience with phenytoin in different parts of the world, as documented in some of the references in our paper, as well as others (personal communications) since, indicates that neither strict bedrest nor daily dressing changes are necessary with topical phenytoin therapy. We feel that our "should" merits further evaluation in the rural setting.

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Measuring Subjective Symptoms

We read with interest the article by Tandan et al. (1) on the subject of topical capsaicin in painful diabetic neuropathy. They reported that no difference was found in visual analogue pain scores between the capsaicin- and placebo-treated groups, but those who applied capsaicin received a more favorable evaluation by their physicians. They also reported improvement or cure of painful symptoms in almost half the patients who subsequently took part in an open-label study. Despite the lack of subjective improvement, and based on the physician's evaluation of the patients and the results from the open-label study, the authors concluded that capsaicin may be of value in treating patients with painful diabetic neuropathy.

According to Huskisson (2), "Pain is a personal psychological experience and an observer can play no legitimate part in its direct measurement." Prospective double-blind studies using visual analogue pain or symptom score scales have been suggested as the appropriate methods to evaluate new treatments (3,4). In view of these recommendations, failure of subjective improvement should be interpreted as a negative finding, and the physician's global evaluation should not be considered as a valid endpoint. Similarly, results from open-label studies, given the placebo effect and the lack of proper control, cannot be regarded as surrogates for positive efficacy of new treatments of highly subjective symptoms—such as pain.

Therefore, we think that the conclusions of this otherwise interesting study are not supported by the results, and, in agreement with the authors, we believe that further studies are needed to clarify the efficacy of capsaicin in painful diabetic neuropathy.

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Semantics of Plasma Glucose Thresholds for Counterregulatory Responses

Webster's dictionary defines *threshold* as "the point at which a physiologic or psychologic effect begins to be produced" (1).

Thus, if during decrements in plasma glucose, a lower than normal glucose level is required to cause a response, then the plasma glucose (or glycemic) threshold for that response is lowered or reduced. Conversely, if higher than normal glucose levels are required to elicit a response, then the glucose threshold for that response is higher or increased. Therefore, use of the opposite terminology (e.g., lower glucose level equals

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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.

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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.

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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-

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