Standardization of IVGTT

Importance of method used to calculate glucose disappearance

Bingley et al. (1) correctly identified the importance to comparative (as well as longitudinal) research of consistent standardization of the protocol for the IVGTT. Their recommendations are reasonable and should receive further discussion followed by either modification or formal adoption by the ADA. We would, however, urge that the protocol be further amended to include identification of the samples to be used in determining the glucose disappearance rate (K_G) and the method of its calculation.

We previously examined IVGTTs from a wide range of rhesus monkeys (lean normal, insulin resistant, IGT, and overt type II diabetic) and have shown that significant and important differences can result simply from the means used to calculate the K_G (2). For monkeys, we established a recommended method for calculating the K_G based on two factors: *1*) the most linear portion of the glucose curve after a sufficient period for equilibration, and 2) ability to use the same time points in animals ranging from absolutely normal to severely diabetic. For monkeys, this is the 5–20-min time period. We urge that a similar analysis be conducted using consistently obtained data from humans who range widely in glucose tolerance in order to determine the optimum K_G calculation method for clinical studies.

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ADA, AMERICAN DIABETES ASSOCIATION; IVGTT, INTRAVENOUS GLUCOSE TOLERANCE TEST; K_G, GLUCOSE DISAPPEARANCE RATE; IGT, IMPAIRED GLUCOSE TOLERANCE; TYPE II DIABETES, NON-INSULIN-DEPENDENT DIABETES MELLITUS.

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Depression in Adults With Diabetes

A recent article in this journal (1) stated that ". . . data to support convincingly a theory that prolonged depressive episodes result from glucose dysregulation are yet unavailable." I agree that convincing data indeed has not yet appeared. My experience with diabetic individuals who have been taught to achieve virtually normal blood glucose suggests to me, however, that for at least a significant subset of IDDM patients, glucose dysregulation can indirectly cause depression.

An analysis of interviews with previously depressed patients who were able to attain essentially normal blood glucose has been described in my previous publication (2). Abstracts of some of their comments follow:

"I became a person again. I am now in control of my life."

"I am coming to life again. . . and I'm not afraid of insulin reactions."

"For me, the pain came. . . from not knowing what my body was doing, or how to treat it correctly."

"The fatigue, frustration, and all the problems that went with it are gone."

"For 25 years, I felt as if I were on a rudderless ship, allowing my body to deteriorate. I'm truly better now both mentally and physically. For the first time, I feel in command of my life."

Virtually all of the individuals interviewed cited at least two of the DSM III-R(3) criteria for a diagnosis of depressive neurosis before achieving blood glucose control.

In summarizing these and other comments, the 1984 article cites the major concerns of patients before regulation of their blood glucose as "the fear of the unknown (hypoglycemia, long-term complications, impaired offspring, never knowing blood glucose level, etc.) and the total inability to control it. . ."

In 1980, Oehler-Giarratana and Fitzgerald listed the 25 topics most commonly discussed by diabetic individuals who were going blind and had entered group psychotherapy (4). Blindness was the second most frequently discussed topic. Diabetic control was number one.

In summary, it seems reasonable, but certainly not proven, that chronic exposure to the seemingly random metabolic fluctuations of IDDM plus the ominous threat of long-term sequelae invite depressive neurosis when combined with helplessness. Controlled studies of the long-term effect on depression of giving patients the knowledge and tools to normalize their glycemic states are certainly warranted.

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IDDM, INSULIN-DEPENDENT DIABETES MELLITUS;

DSM-III R, DIAGNOSTIC AND STATISTICAL MANUAL, THIRD EDITION, REVISED.

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Autonomic Neuropathy in Newly Diagnosed Diabetes Mellitus

Two papers in the July 1992 issue of *Diabetes Care* (1,2) discuss neuropathy in patients with newly diagnosed diabetes. Recently, severe early-onset polyneuropathy has been reported in IDDM (3). We examined autonomic function in 50 newly diagnosed diabetic patients in four groups: 21 had IDDM (group 1), 14 had NIDDM (group 2), 10 had GDM (group 3; 9 of the patients had NIDDM on retyping after delivery), 5 newly diagnosed diabetic patients (group 4) had chronic alcoholic liver disease, another risk factor for autonomic failure (4). We evaluated heart rate responses to deep breathing, Valsalva maneuver, and standing up, and blood pressure responses to standing up and sustained handgrip (5,6). Cardiovascular reflex testing was performed within 10 days after diabetes diagnosis in groups 1, 2, and 4 and in the period starting insulin therapy in group 3.

In our study, 3 patients (14%) with IDDM, 6 (43%) with NIDDM, 4 (40%) with GDM, and all 5 diabetic patients with alcoholic liver disease (100%) had at least one abnormal parameter. Table 1 shows the results in the five tests. In the 3 IDDM patients with autonomic dysfunction, the interval between the onset of symptoms (polyuria, polydipsia, weight loss) and the diagnosis of diabetes was >4 mo, rising to 1.5 yr. Symptoms were not present in the other groups; in these subjects, diabetes was diagnosed by laboratory screening. Among GDM patients with autonomic damage, 1 had IDDM and 3 had NIDDM on retyping. In these 3 patients the duration of untreated hyperglycaemia—identified by past medical records—was 3 mo in 2 subjects and 5 mo in the third patient (mean value, 3.66 mo), whereas the mean value of this period was 1.4 mo in GDM patients with normal autonomic function. The mean duration of pregnancy was 26 wk in the 3 patients with autonomic dysfunction and 16 wk in patients without autonomic neuropathy when cardiovascular testing were performed. Among GDM patients with NIDDM on retyping, a big baby (>4500 g) was present in the history in 2 of 3 patients with autonomic failure and in 1 of 6 patients with normal reflex tests. Positive familial history—diabetes in parents—occurred in these two subgroups in 2 of 3 and in 2 of 6 patients, respectively. Even though as a result of the small number of GDM patients a statistical significance could not be proved, our data suggest that some inequality may exist between GDM patients with and without autonomic neuropathy.

Metabolic factors seem to have a dominant role in the progression of neuropathy (1,3). Similarly, long-lasting unrecognized or untreated metabolic disturbances are the most probable causes of autonomic neuropathy in newly diagnosed diabetic patients. Autonomic neuropathy may be present even in GDM—although this has not been studied, to our knowledge. To prevent it, early adequate treatment of GDM seems to be very important. Therefore, general screening of diabetes in pregnancy would be desirable—as early as possible in patients at higher risk.

Alcoholism, liver disease, and other etiological factors of autonomic neuropathy also should be taken into

Table 1—*Cardiovascular reflex test results*

		Abnormal test results (*n*)				
	N	Deep breathing test	30/15 Ratio	Valsalva ratio	Sustained handgrip test	Blood pressure response to standing
IDDM	21	2	2	0	0	0
NIDDM	14	4	2	0	2	1
Diabetes plus ALD	5	4	5	3	4	1
GDM	10	1	3	0	0	0