these results are to be expected. It is important not to confuse the terms glycemic index and glycemic response; they mean different things and have different mathematical and statistical properties. The glycemic index standardizes glycemic response areas to each individual's response to a standard food, thus correcting for between-subject variation. The figure, drawn from our 1990 data, shows the percentage of the total variance of the glycemic responses and glycemic index values attributable to the order of testing, the different foods (bread, rice, and spaghetti), order-food interaction,[2] subject (between-subject variation), and error (within-subject variation) (4). Most of the variation of the blood glucose response areas was attributable to between-subject variation. However, expressing the results as glycemic indexes, the proportion of the total variance attributable to between-subject variability is reduced markedly. This is the purpose of the glycemic index.

It also should be pointed out that expressing results as the glycemic index reduces total variability by reducing only between-subject variation without affecting within-subject or between-food variation (Table 1). The between-subject variation of glycemic responses in this study is large because both IDDM and NIDDM subjects were studied and the subjects were selected to be dissimilar so as to increase between-subject variation (4).

Table 1—Sources of variation of glycemic response areas and glycemic index values expressed as SDs and CVs

	Glycemic response area		Glycemic index	
Source of variance	SD	CV (%)	SD	CV (%)
Food	262	31	22.9	30
Within-subject	210	25	15.9	21
Between-subject	408	49	5.8	8

Data from reference 4.

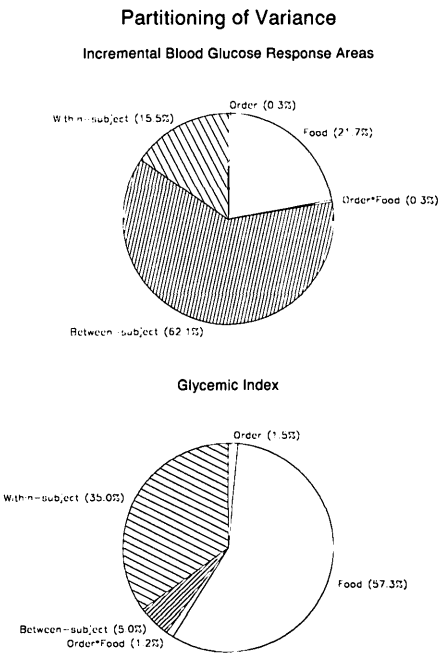

FIG. 1—*Sources of variance of glycemic responses and glycemic index values expressed as percentage of total variance. Data from (4).*

THOMAS M.S. WOLEVER, BM, BCH, PHD

FROM THE DEPARTMENT OF NUTRITIONAL SCIENCES AND THE CLINICAL NUTRITION AND RISK FACTOR MODIFICATION CENTRE, ST. MICHAEL'S HOSPITAL, UNIVERSITY OF TORONTO, TORONTO, ONTARIO, CANADA.

ADDRESS CORRESPONDENCE TO DR. T.M.S. WOLEVER, DEPARTMENT OF NUTRITIONAL SCIENCES, UNIVERSITY OF TORONTO, TORONTO, ONTARIO, CANADA M5S 1A8.

NIDDM, NON-INSULIN-DEPENDENT DIABETES MELLITUS; CV, COEFFICIENT OF VARIATION; IDDM, INSULIN-DEPENDENT DIABETES MELLITUS.

References

1. Rasmussen OW, Gregersen S, Dorup J, Hermansen K: Day-to-day variation of blood glucose and insulin responses in NIDDM subjects after starch-rich meal. *Diabetes Care* 15:522–24, 1992
2. Wolever TMS, Nuttall FQ, Lee R, Wong GS, Josse RG, Csima A, Jenkins DJA: Prediction of the relative blood glucose response of mixed meals using the white bread glycemic index. *Diabetes Care* 8:418–28, 1985
3. Wolever TMS, Csima A, Jenkins DJA, Wong GS, Josse RG: The glycemic index: variation between subjects and predictive difference. *J Am Coll Nutr* 8:235–47, 1989
4. Wolever TMS, Jenkins DJA, Vuksan V, Josse RG, Wong GS, Jenkins AL: Glycemic index of foods in individual subjects. *Diabetes Care* 13:126–32, 1990

Hazard of Glucagon Test in Diabetic Patients

Hypertensive crisis in asymptomatic pheochromocytoma

Plasma C-peptide response to glucagon has been widely applied for a measure of insulin secretory capacity or classification of insulin-requiring or non-insulin-requiring diabetic patients (1,2). On the other hand, glucagon has been used for the diagnosis of pheochromocytoma as provocative test, which can precipitate a severe pressor response and even a hypertensive crisis. Patients with pheochromocytoma are often associated with diabetes mellitus, indicating the danger of glucagon test in such cases. To the best of our knowledge, no such case has been reported. We present a case of asymptomatic pheochromocytoma, which was incidentally diagnosed because of the occurrence of hypertensive crisis during glucagon test for evaluation of β-cell function.

A 50-yr-old Japanese woman (1.64 m, 57 kg, body mass index 21.2 kg/m^2) was referred to our hospital in December 1990 for uncontrolled diabetes mellitus. She had been taking hypoglycemic agents for 6 yr and had no history of hypertension. On admission,

plasma glucose was 25.4 mM and HbA_1 was 12.8%. Diabetes was controlled eventually with 16 U Novolin 30R (Novo Nordisk, Bagsvaerd, Denmark), and she was discharged 5 January 1991. Her blood pressure had been quite normal (100–120/70 mmHg) during admission. In February 1991, her postprandial blood glucose increased to >16.8 mM (302 mg/dl), and urinary glucose was >100 g/day, despite increased insulin dosage. To assess the β-cell function, glucagon test was performed 5 March 1991. After a bolus injection of 1 mg glucagon, she complained of palpitation, chest discomfort, nausea, and throbbing headache. Her blood pressure rose to 180/100 mmHg followed by the development of generalized urticaria. Initial diagnosis was glucagon anaphylaxis, and the patient was treated with prompt administration of 100 mg hydrocortisone phosphate i.v. One hour later, her blood pressure fell to 156/96 mmHg, and skin eruptions disappeared. About 12 h later, she suddenly complained of headache, chest discomfort, and nausea. Because of continuous symptoms and frequent vomiting, she sought another consultation. Her blood pressure was 220/90 mmHg, pulse rate was 84 beats/min and regular, and blood glucose was 25.8 mM (464 mg/dl). The suspicion of pheochromocytoma prompted us to administer orally 1 mg doxazosin mesilate, a long-acting α-receptor blocking agent, and her blood pressure fell to 100/70 mmHg. Urinary norepinephrine and epinephrine were elevated (142 and 61.3 μg/day, respectively). In April, left adrenal pheochromocytoma (17 g) was removed, and her diabetes was controlled with 26 U insulin.

Asymptomatic pheochromocytomas incidentally discovered by new imaging techniques have been increasingly reported (3). The incidence of pheochromocytoma in the diabetic population is not so high compared with only 11 functional pheochromocytomas in >120,000 diabetic cases at the Joslin Clinic (Boston, MA) (4). In a 50-yr autopsy series of 40,078 patients at the Mayo Clinic, however, the prevalence of pheochromocytoma was 0.13%, suggesting more undiagnosed cases in diabetes (5). In our experience, the mean ± SD body mass index of 9 patients with pheochromocytoma was 19.1 ± 2.4 kg/m^2 (range 16.0–22.6 kg/m^2), significantly lower than those in untreated non-insulin-dependent diabetes mellitus (23.9 ± 3.0 kg/m^2, n = 109) and in nondiabetic (22.7 ± 3.5 kg/m^2, n = 79) subjects. Glucagon test should be performed in diabetic patients, particularly thin patients, under the precautionary measures with phentolamine or nifedipine for hypertensive attacks, although they may be asymptomatic and not hypertensive. Furthermore, this case suggests that glucagon may cause a paroxysmal hypertension even after several hours.

YOSHIAKI MINAMORI, MD
MAYUMI YAMMOTO, MD
ATSUKO TANAKA, MD
NORIYUKI TAKEDA, MD
KEIGO YASUDA, MD

FROM THE KANAYAMA MUNICIPAL HOSPITAL, INTERNAL MEDICINE, KANAYAMA, MASHITAGUN, GIFU; AND THE THIRD DEPARTMENT OF INTERNAL MEDICINE, GIFU, JAPAN.

ADDRESS CORRESPONDENCE AND REPRINT REQUESTS TO YOSHIAKI MINAMORI, MD, KANAYAMA MUNICIPAL HOSPITAL, KANAYAMA, MASHITA-GUN, GIFU, MZ 509–16, JAPAN.

References

1. Madsbad S, Krarup T, McNair P, Christiansen C, Faber OK, Transbol I, Binder C: Practical clinical value of the C-peptide response to glucagon stimulation in the choice of treatment in diabetes mellitus. *Acta Med Scand* 210:153–56, 1981
2. Hother-Nielsen O, Faber O, Sorensen NS, Beck-Nielsen H: Classification of newly diagnosed diabetic patients as insulin-requiring or non–insulin-requiring based on clinical and biochemical variables. *Diabetes Care* 11:531–37, 1988
3. Ross NS, Aron DC: Hormonal evaluation of the patients with an incidentally discovered adrenal mass. *N Engl J Med* 323: 1401–405, 1990
4. Kozak GP, Coopan R: Diabetes mellitus and other endocrine diseases. In *Clinical Diabetes Mellitus*. Kozak GP, Ed. Philadelphia, PA, Saunders, 1982, p. 342–52
5. Sutton MG, Sheps SG, Lie JT: Prevalence of clinically unsuspected pheochromocytoma: a review of a 50-year autopsy series. *Mayo Clin Proc* 56:354–60, 1981

Isolated Fatty Change of Liver as Marker of Glucose Intolerance

The hepatomegaly more commonly found in diabetic subjects is due to fat (1). Creutzfeldt et al. (2) pooled the data of >1750 liver biopsies and found that fatty infiltration of the liver in diabetic patients was 25–78%, with a higher prevalence in maturity-onset (non-insulin-dependent) diabetic patients with respect to juvenile-onset (insulin-dependent) diabetic patients (63 vs. 21%, respectively). The pathophysiology of this condition is complex but seems related to an increased fatty acid afflux to the liver, as a consequence of enhanced lipolysis by adipose tissue, which in turn may lead to increased formation of triglycerides and lipoprotein and hepatic accumulation of fat.

We examined 30 consecutive patients with an ultrasonography diagnosis of fatty liver (3) made by chance during a regular check-up. Subjects ranged in age from 31 to 68 yr, and mean ± SD body mass index was 27 + 1 kg/m^2. Common laboratory tests for liver functions were in the normal range: In particular, aspartate amino transferase was 23 ± 6 U/L (normal values 0–29), alanine amino transferase was 22 ± 6 U/L (0–29), and γ-GT was 31 ± 8 U/L (8–38). Erythrocyte sedimentation rate was also normal. None of the subjects gave a history of previously known hepatic ill-