The Effects of Oral Fructose, Sucrose, and Glucose in Subjects with Reactive Hypoglycemia

PHYLLIS A. CRAPO, JOHN A. SCARLETT, ORVILLE G. KOLTERMAN, LEONARD R. SANDERS, FRED D. HOFELDT, AND JERROLD M. OLEFSKY

We have evaluated the acute effects of orally administered 100-g loads of fructose, sucrose, or glucose given as drinks and of 100-g loads of fructose and sucrose given in cakes on the postprandial serum glucose, insulin, and cortisol responses in seven subjects with reactive hypoglycemia. We defined reactive hypoglycemia as a serum glucose nadir of 65 mg/dl or less, symptoms compatible with hypoglycemia occurring at or after the serum glucose nadir, a hypoglycemic index of greater than 1.0, and a rise in serum cortisol to greater than 20 μg/dl after the serum glucose nadir. The data demonstrated that (1) pure fructose given as a drink resulted in relatively flat serum glucose and insulin responses and did not cause a hypoglycemic reaction in any of the subjects, compared with the glucose drink, which caused a hypoglycemic reaction in all subjects; (2) ingestion of pure sucrose as a drink elicited significantly flatter serum glucose and insulin responses than did the glucose drink and was associated with some episodes of chemical hypoglycemia and symptoms, but did not result in a hypoglycemic reaction by our definition in any patient; and (3) ingestion of fructose cake led to serum glucose and insulin responses that were lower than those caused by ingestion of sucrose cake, but ingestion of neither fructose nor sucrose cake led to a hypoglycemic reaction by our definition in any patient. In conclusion, the use of fructose as a sweetening agent given either alone, in a drink, or with other nutrients in a cake resulted in markedly flatter serum glucose and insulin responses in subjects with reactive hypoglycemia. Fructose may thus prove useful as a sweetening agent in the dietary treatment of selected patients with reactive hypoglycemia.

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There is considerable controversy regarding the pathogenesis, diagnostic criteria, and treatment for the syndrome known as reactive hypoglycemia.[1–5] The hallmarks of this disorder appear to be the presence of symptoms or signs compatible with hypoglycemia occurring 2–5 h after meals and low blood glucose levels after the ingestion of glucose during an oral glucose tolerance test, which are associated with similar symptoms. Since many otherwise normal individuals have blood glucose nadirs of less than 60 mg/dl during oral glucose tolerance tests and yet remain asymptomatic,[6] chemical criteria for hypoglycemia after ingestion of oral glucose have not been standardized or widely accepted.[7] Therefore, other suggestions of criteria for the objective diagnosis of this disorder have included the occurrence of a rise in cortisol after symptomatic, chemical hypoglycemia[1–4] and the use of a hypoglycemic index that quantitates the rate of fall of the blood glucose after oral administration of glucose.[5] Still, the diagnosis of this disease remains fraught with difficulties.

Both the ability to diagnose this disease and the ability to treat it are difficult. In general, the cornerstone of therapy is diet.[3,7,8] Dietary therapy usually involves some combination of frequent feedings of low carbohydrate content, high-fat and protein intake, abstinence from refined or simple sugars, abstinence from caffeine,[9–13] and reduced alcohol consumption.[10,12] This can be a difficult dietary regimen to follow, since long-held food habits are difficult to change. In addition, the frequent feedings can potentially result in unacceptable weight gain, while the high-fat intake may be contraindicated because of its potentially adverse effects on serum lipid levels. Furthermore, diets that completely eliminate sweeteners may lead to poor compliance,[14] and the safety of saccharin, the primary non-nutritive sweetener presently available in the United States, has been ques-

tioned. Fructose is a naturally occurring sugar that is more slowly absorbed from the gastrointestinal tract than glucose and is rapidly taken up by the liver.[15] Consequently, when fructose is substituted for either glucose or sucrose in normal individuals,[16] a marked flattening of postprandial glucose levels occurs. This results in very little initial rise and little, if any, fall in blood glucose levels below baseline at later time points. It has been previously suggested that the postprandial fall in plasma glucose level, which usually occurs between 3 and 5 h in patients referred for reactive hypoglycemia, is prevented when fructose is consumed instead of glucose or sucrose.[17]

Thus, fructose would appear to be a potentially excellent choice of sweetener for patients with this disease. Therefore, we have studied the postprandial effects of fructose drinks and fructose cakes on serum glucose, insulin, and cortisol levels in seven subjects with reactive hypoglycemia of varying etiology, who met strict criteria for the diagnosis of this disorder, and have compared these results with the effects of glucose drinks, sucrose drinks, and sucrose cakes.

MATERIALS AND METHODS

Subjects. Seven subjects with the syndrome of reactive hypoglycemia were studied. The subjects had either been followed by one of the authors (F.H.) for symptomatic reactive hypoglycemia, or were identified through referral for symptoms of hypoglycemia. Referral subjects were pretested for documentation of reactive hypoglycemia before entrance to the study. Two subjects (nos. 3 and 4) met the criteria for impaired glucose tolerance as defined by the National Diabetes Data Group standards;[18] one subject (no. 7) had alimentary reactive hypoglycemia, presumably as a result of a partial gastrectomy 10 yr previously for peptic ulcer disease; and the remaining four subjects (nos. 1, 2, 5, and 6) were classified as having idiopathic postabsorptive hypoglycemia. The mean age (± SEM) of the subjects was 43 ± 6 yr, and the mean relative weight (± SEM) was 0.99 ± 0.04, with a range of 0.82–1.14.[19] Two subjects (nos. 4 and 5) were women. No subject was taking any drug known to affect glucose or insulin metabolism during the course of the study, and endocrine deficiency syndromes were ruled out with standard clinical and laboratory tests. To limit the effects of previous carbohydrate restriction on the occurrence of hypoglycemia,[20] each person consumed a weight maintenance solid food diet that contained a minimum of 200 g of carbohydrate for 2 wk before testing and for each day throughout the period of investigation.

Diagnosis of reactive hypoglycemia. Before enrollment in the study, each subject was prescreened with an oral glucose tolerance test, using a 100-g glucose drink as the glucose challenge. The diagnostic criteria used during this test to define acceptability for the study were the following: (1) a serum glucose nadir of 65 mg/dl or less[5] (It should be noted that Hadji-Georgopoulos et al.[5] measured blood glucose levels in their work and we have measured serum glucose levels, which yield values higher than blood glucose determinations. Consequently, our subjects are actually more hypoglycemic than they would appear in comparison.); (2) a hypoglycemic index of greater than 1.0;[5] (3) a rise in serum cortisol to greater than 20 μg/dl;[1] and (4) symptoms compatible with hypoglycemia occurring at or after the serum glucose nadir. These symptoms include tremor, lightheadedness, diaphoresis, thirst, dizziness, nervousness, weakness, tingling in fingers, sleepiness, mental lethargy, irritability, headache, and increased respiration rate. All patients also reported a history of symptoms compatible with postprandial hypoglycemia after mixed meals in the free living state.

Test meals. The subjects were given the following test meals in random order after an overnight fast: glucose, sucrose, and fructose tolerance tests, referred to as drinks, and sucrose and fructose cake tolerance tests. The compositions of these test meals are outlined in Table 1. Studies were performed using an indwelling intravenous catheter inserted ½ h before the onset of testing. A heparin lock was placed and the catheter was flushed with a heparin-containing solution after each blood sample. At 8 a.m. the subject was given one of the test meals to consume over a 15-min period of time. Blood samples were timed from the initiation of consumption of the meal and were drawn at 30-min intervals for 5 h. Both the subject and the nurse drawing the blood samples kept a diary of symptoms observed during the test. If symptoms of hypoglycemia occurred at any time during the test period, additional blood samples were drawn at that time.

Analytic methods. Samples for serum glucose were measured by the glucose-oxidase method using a Beckman Glucose Analyzer (Beckman Instruments, Fullerton, California). This method measures glucose specifically and is not affected by increases in serum fructose levels. Serum immunoreactive insulin was measured by the method of Desbuquois and Aurbach.[21] Serum cortisols were determined by radioimmunoassay (Solid-Phase Cortisol Kit, Beckman Instruments). Statistical analysis was carried out using the Student's *t* test for dependent means and is reported as the mean ± SEM.

TABLE 1
Composition of test meals

	Sugar composition		
	Glucose (g)	Sucrose (g)	Fructose (g)
Glucose drink*	100		
Sucrose drink*		100	
Fructose drink*			100
Sucrose cake†		104	
Fructose cake†			104

* The drinks also contained 15 ml of lemon flavoring and the total volume of each was 500 ml.

† The cakes were 63% (152 g) carbohydrate, 4% (11 g) protein, and 33% (35 g) fat, and a total of 967 kcal. Sucrose or fructose made up 68% (104 g) of total carbohydrate; the remainder was predominantly starch (22%), with small amounts of dextrins and lactose.

RESULTS

Diagnosis of reactive hypoglycemia (glucose drinks). All subjects met the criteria for diagnosis of reactive hypoglycemia, as demonstrated by glucose nadirs of 65 mg/dl or less (Table 2), hypoglycemic indices of greater than 1.0 (Table 3), cortisol rises to greater than 20 μg/dl (Table 4), and symptoms compatible with hypoglycemia during the oral glucose tolerance test (glucose drink). Each subject had a history of symptoms compatible with postprandial hypoglycemia after mixed meals for at least 1 yr before inclusion in the study.

Fructose drinks. No subject had changes compatible with hypoglycemia after ingestion of pure fructose as a drink. The serum glucose and insulin responses to the fructose drinks (Figure 1) were flattened and were significantly lower than after the other drinks at the time points shown in the legend for Figure 1. The mean glucose nadir was the highest for all the test meals and no subject, including the subject with alimentary hypoglycemia (no. 7), had a high hypoglycemic index, a significant cortisol rise after the serum glucose nadir, or symptoms compatible with hypoglycemia.

Sucrose drinks. The serum glucose and insulin responses to the sucrose drinks were intermediate between the responses to glucose and fructose drinks, as seen in Figure 1. These differences were statistically significant at the times shown in the legend for Figure 1. Two subjects experienced hypoglycemic symptoms after the sucrose drink (nos. 3 and 7) and in both cases the hypoglycemic index was elevated as well. The corresponding glucose nadirs were also decreased, but in neither case did the serum cortisol rise to greater than 20 μg/dl. Interestingly, subject no. 6 had a glucose nadir of 20 mg/dl after the sucrose drink, accompanied by an elevated hypoglycemic index, but unaccompanied by a significant rise in serum cortisol or symptoms.

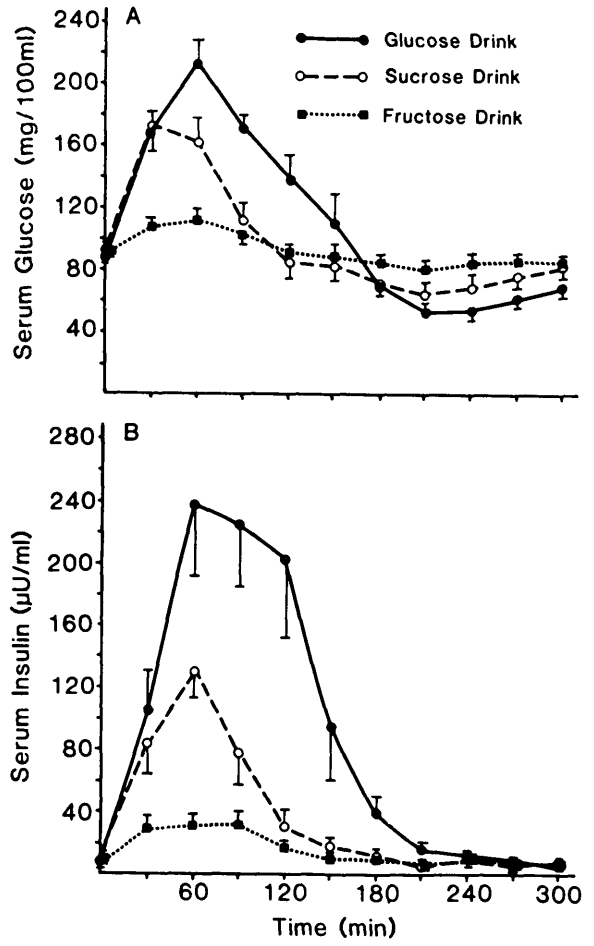

FIG. 1. Mean (±SEM) serum glucose (A) and insulin (B) responses to glucose (●), sucrose (○), and fructose (■) drinks. Serum glucose: glucose:sucrose, $P < 0.05$ at 60, 90, 120, 150, 240, and 300 min; glucose:fructose, $P < 0.05$ at 30, 60, 90, 120, 210, 240, 270, and 300 min; and sucrose:fructose, $P < 0.05$ at 30, 60, 180, 210, and 240 min. Serum insulins: glucose:sucrose, $P < 0.05$ at 60, 90, 120, 150, 180, and 210 min; glucose:fructose, $P < 0.05$ at 30, 60, 90, 120, 150, 180, and 210 min; and sucrose:fructose, $P < 0.05$ at 30, 60, 90, 120, and 150 min.

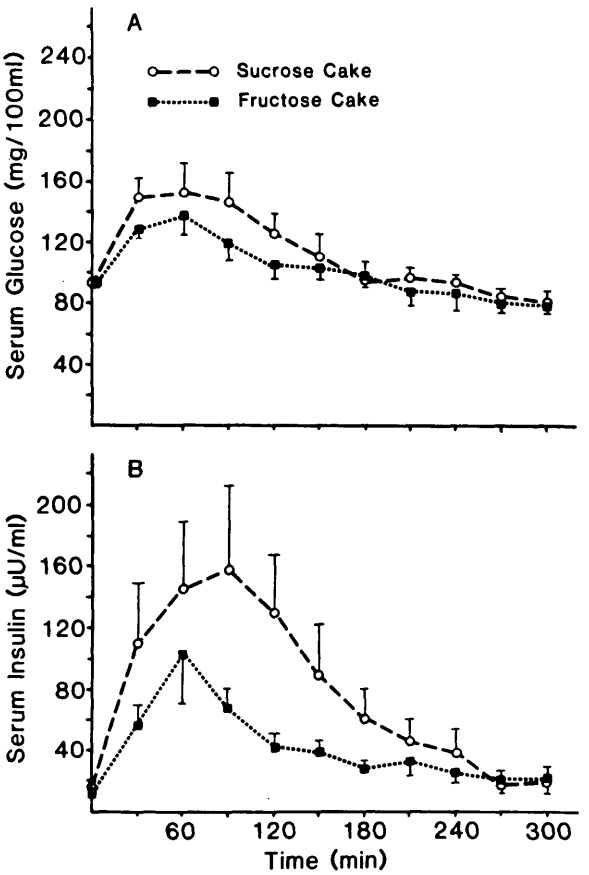

FIG. 2. Mean (±SEM) serum glucose (A) and insulin (B) responses to sucrose (○) and fructose (■) cakes. The serum glucose responses were significantly different at 120 min, $P < 0.02$. The serum insulin responses were significantly different at 60 min, $P < 0.02$; 90 min, $P < 0.05$; and 120 min, $P < 0.02$.

TABLE 2
Serum glucose nadirs (mg/dl) and time of glucose nadir (min) after ingestion of glucose, sucrose, fructose, sucrose cake, and fructose cake in patients with reactive hypoglycemia*

	Glucose drink		Sucrose drink		Fructose drink		Sucrose cake		Fructose cake	
Subjects	mg/dl	min	mg/dl	min	mg/dl	min	mg/dl	min	mg/dl	min
1	61	210	70	210	88	210	61	240	72	300
2	34	240	69	210	65	240	59	240	66	300
3	54	202	62	210	73	180	70	300	70	270
4	60	210	71	180	87	270	71	270	77	300
5	50	225	77	240	85	210	105	180	94	210
6	36	240	20	210	64	210	89	180	82	180
7	36	180	45	120	93	150	40	150	62	150
Mean (± SEM)	47 ± 4	215 ± 8	59 ± 8	197 ± 14	79 ± 4	210 ± 15	71 ± 8	223 ± 21	75 ± 4	244 ± 24

* Statistical comparisons as carried out by the use of the paired *t* test for dependent means indicate the following: glucose drink:sucrose drink = $P < 0.05$; glucose drink:fructose drink = $P < 0.001$; sucrose drink:fructose drink = $P < 0.02$; sucrose cake:fructose cake = NS.

Sucrose cake. As seen in Figure 2, the sucrose cake elicited a slightly higher mean serum glucose response (A) and a higher serum insulin response (B) than the fructose cake, although the differences were statistically significant at only a few points (see legend). Two subjects (nos. 2 and 7) had symptoms of hypoglycemia, both accompanied by low serum glucose nadirs but unaccompanied by a significant rise in the hypoglycemic index in subject no. 2 or by significant rises in cortisol levels. One subject (no. 4) had a peak cortisol level of 20 μg/dl, but a serum glucose nadir of only 71 mg/dl, a normal hypoglycemic index, and a lack of hypoglycemic symptoms.

Fructose cakes. Figure 2 demonstrates the mean serum glucose (A) and insulin (B) responses to sucrose and fructose cakes in all subjects. As with the drinks, the fructose-sweetened cake elicited a lower mean serum glucose and insulin response than did the corresponding sucrose-sweetened cake, although the differences were statistically significant at only a few points. The mean serum glucose nadir after fructose cake was 75 ± 4 mg/dl, and no subject experienced significant postprandial elevations of serum cortisol. The one subject with alimentary hypoglycemia (no. 7) did have slight symptoms and an elevated hypoglycemic index.

TABLE 3
Hypoglycemic index*

Subjects	Glucose drink	Sucrose drink	Fructose drink	Sucrose cake	Fructose cake
1	1.17	0.25	0.14	0.89	0.52
2	3.65	0.74	0.25	0.78	0.40
3	2.26	1.42	0.31	0.50	0.39
4	1.99	0.91	0.05	0.88	0.55
5	1.20	0.06	0.16	0.06	0.05
6	1.03	2.05	0.44	0.08	0.24
7	3.48	4.03	0.20	3.75	1.60

* The hypoglycemic index is obtained by the formula $(BG_N - 90 - BG_N)/BG_N$, where $BG_N - 90$ is the blood glucose 90 min before the nadir, and BG_N is the blood glucose nadir. It has been demonstrated[5] that when the hypoglycemic index is greater than 1.0, subjects are symptomatic; when it is less than 1.0, they are asymptomatic.

DISCUSSION

We have studied the effects of orally administered 100-g loads of glucose, sucrose, and fructose, and cakes prepared with approximately 100 g of either sucrose or fructose, on the postprandial serum glucose, insulin, and cortisol responses of subjects with reactive hypoglycemia as defined by four strict criteria. The subjects had reactive hypoglycemia due to a variety of etiologies, but the results were nevertheless striking. They show that the serum glucose responses to oral fructose were significantly flatter than the responses to glucose and sucrose when these substances were given alone as drinks. Serum insulin responses were also dramatically flatter after oral fructose ingestion when compared with levels after oral sucrose or glucose ingestion. In no case did any of the subjects have symptoms of hypoglycemia, a significant rise in serum cortisol level, or an elevated hypoglycemic index after ingestion of the fructose drink. These results after fructose drinks correspond to other recent preliminary studies of fructose consumption in subjects with reactive hypoglycemia.[17] When sucrose and fructose were ingested in comparable amounts in cakes, the differences in mean serum glucose responses between these two sugars were less striking, although the mean serum glucose and insulin responses were lower after ingestion of fructose cake than they were after ingestion of sucrose cake. None of the subjects with impaired glucose tolerance or idiopathic postabsorptive hypoglycemia experienced signs, symptoms, or chemical evidence of hypoglycemia after ingestion of the fructose-sweetened cake.

In contrast, several subjects became symptomatic, had elevated hypoglycemic indices, or had serum glucose nadirs

TABLE 4
Cortisol (μg/dl) changes to glucose nadir

	Glucose drink		Sucrose drink		Fructose drink		Sucrose cake		Fructose cake	
Subjects	Basal*	Peak	Basal	Peak	Basal	Peak	Basal	Peak	Basal	Peak
1	7.5	28.5	8.5	14.6	9.1	10.7	6.4	13.4	4.9	5.1
2	6.9	22.2	5.5	10.4	8.5	13.9	5.7	12.5	8.1	8.5
3	6.5	21.2	2.1	7.1	4.3	6.9	5.6	6.5	4.5	10.4
4	13.2	27.0	8.8	9.2	5.8	5.8	8.0	21.0	8.8	8.8
5	8.6	23.8	5.6	7.8	7.0	7.0	7.4	12.1	6.3	16.4
6	9.2	21.0	8.9	15.9	7.5	12.4	4.8	15.8	6.5	14.3
7	14.3	26.6	7.9	10.8	8.5	8.5	10.8	12.8	10.8	10.8

* Basal cortisol was the cortisol value obtained immediately before the glucose nadir. Cortisol peaks > 20 μg/dl after the hypoglycemic nadir and symptoms were considered evidence of pathophysiologic stress at the glucose nadir.

below 65 mg/dl after ingestion of either the sucrose drink or the sucrose-sweetened cake. Thus, the responses of these various parameters to sucrose-containing meals were, like the serum insulin and serum glucose responses, intermediate between the responses noted during the glucose- and fructose-sweetened meals.

The reason that fructose is not associated with postprandial hypoglycemia most likely relates to its unique mode of metabolism. Fructose is primarily metabolized by the liver, where it is rapidly phosphorylated to fructose-1-phosphate by fructokinase and then cleaved into trioses by liver aldolase. The trioses produced can be used for the synthesis of glycogen and triglyceride, or can enter the glycolytic pathway. In normal human beings, most of the absorbed fructose is used for synthesis of glucose and is stored as glycogen, with only a modest release of glucose from the liver. Consequently, there is only a slight increase in the serum glucose or insulin concentrations immediately after ingestion of pure fructose. The reason that fructose ingestion is not associated with the late drop in serum glucose is therefore most likely due to the fact that fructose ingestion does not cause glucose or insulin levels to rise as high as they do after glucose or sucrose ingestion.

It has been suggested[22] that the oral glucose tolerance test is an unphysiologic test since free glucose is not present in usual food, and ingestion of 50–100 g of pure carbohydrate without accompanying protein and fat is rare in normal life. Since the cakes we used in this study were composed of a variety of nutrients (simple and complex carbohydrate, protein, and fat), they could be likened to the ingestion of a mixed meal. In a recent study of the response of patients with idiopathic postabsorptive hypoglycemia to mixed meals, Charles et al.[4] found no chemical hypoglycemia; however, symptoms of hypoglycemia were present in 78% of the subjects after ingestion of the mixed meal. In our study we did not find this same result. Thus, we found symptoms of hypoglycemia to always be associated with chemical hypoglycemia. Our data confirm that hypoglycemia is probably far less frequent in patients with this disorder after mixed meals than previously appreciated. However, while it is true that free glucose is seldom encountered in usual foods unaccompanied by protein or fat, this is not as true for sucrose or mixtures of glucose and fructose. For example, sucrose, invert sugar (hydrolyzed sucrose), or similar amounts of glucose and fructose are commonly encountered in usual foods, such as soft drinks, juice, fruits, and some candies, with or without small amounts of protein and fat. In addition, we have recently shown that ingestion of at least one food, the potato, elicits serum glucose and insulin responses similar to those caused by ingestion of free glucose.[23] Thus, it is possible that individuals can create a glucose or sucrose tolerance test situation for themselves in the free living state.

Thus, our results suggest that fructose can be appropriately employed as a nutritive sweetener in the diet of selected individuals with reactive hypoglycemia. The use of fructose as a sugar substitute may obviate the need for other significant changes in the diets of these individuals. This sugar has excellent properties of palatability and sweetness, and can be readily incorporated into many food products. In addition, the use of fructose in the diets of these individuals could provide other benefits. The traditional dietary treatment of reactive hypoglycemia involves frequent feedings of a low-carbohydrate (avoidance of simple sugars), high-protein, high-fat diet, which often means excessive saturated fat and cholesterol intake, as well as increased caloric ingestion with weight gain. The use of fructose as a sweetener could allow a more normal dietary regimen, avoiding the nutritive penalties of the traditional reactive hypoglycemia diet. However, it should be cautioned that pure, refined fructose is devoid of nutrients other than carbohydrate calories, and its use should be limited to the amount that is sufficient for sweetening purposes only.

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From the Department of Medicine, University of Colorado Health Sciences Center, The Veterans Administration Hospital, and the Fitzsimons Army Hospital, Denver, Colorado.

Address reprint requests to Phyllis A. Crapo, University of Colorado Health Sciences Center, Department of Medicine, B151, 4200 East Ninth Avenue, Denver, Colorado 80262.

REFERENCES

[1] Hofeldt, F. D., Dippe, S., and Forsham, P. H.: Diagnosis and classification of reactive hypoglycemia based on hormonal changes in response to oral and intravenous glucose administration. Am. J. Clin. Nutr. *25*: 1193–201, 1972.

[2] Hofeldt, F. D., Adler, R. A., and Herman, R. H.: Postprandial hypoglycemia. Fact or fiction? JAMA *233*: 1309–10, 1975.

[3] Hofeldt, F. D.: Progress in endocrinology and metabolism. Reactive hypoglycemia. Metabolism *24*: 1193–208, 1975.

[4] Charles, M. A., Hofeldt, F., Shackelford, A., Waldeck, N., Dodson, L. E., Jr., Bunker, D., Coggins, J. T., and Eichner, H.: Comparison of oral glucose tolerance tests and mixed meals in patients with apparent idiopathic postabsorptive hypoglycemia. Absence of hypoglycemia after meals. Diabetes *20*: 465–70, 1981.

[5] Hadji-Georgopoulos, A., Schmidt, M. I., Margolis, S., and Kowarski, A. A.: Elevated hypoglycemic index and late hyperinsulinism in symptomatic postprandial hypoglycemia. J. Clin. Endocrinol. Metab. *50*: 371–76, 1980.

[6] Freinkel, N., and Metzger, M. E.: Oral glucose tolerance curve and hypoglycemia in the fed state. N. Engl. J. Med. *280*: 820–28, 1969.

[7] Ad Hoc Committee on Hypoglycemia: Statement on Hypoglycemia. Arch. Intern. Med. *131*: 591, 1973.

[8] Foster, D. W., and Rubenstein, A. H.: Hypoglycemia, insulinoma, and other hormone-secreting tumors of the pancreas. *In* Harrison's Principles of Internal Medicine, 9th edit. Isselbacher, K. J., Adams, R. D., Braunwald, E., Petersdorf, R. G., and Wilson, J. D., Eds. New York, McGraw-Hill, 1978, p. 1762.

[9] Harris, S.: The diagnosis and treatment of hyperinsulinism. Ann. Intern. Med. *10*: 514–33, 1936.

[10] Tato, J. C. D.: Investigations of a treatment method: relative hypoglycemia. Hawaii Med. J. *31*: 14–18, 1972.

[11] DeCastro, O. A. P., Sandberg, H., Feinberg, L. J., and Bellet, S.: Effects of various routes of caffeine administration on oral and intravenous glucose tolerance tests in dogs. Metabolism *18*: 163–71, 1969.

[12] Lovell, H. W., and Tintera, J. W.: Hypoadrenocorticism in alcoholism and drug addiction. Geriatrics *6*: 1–11, 1951.

[13] Phillips, K.: Clinical studies on the hypoglycemic syndrome. Am. Pract. Digest Treatment *10*: 971–78, 1959.

[14] The Need for Special Foods and Sugar Substitutes of Individuals with Diabetes Mellitus. Bethesda, Md., Life Sciences Research Office, FASEB, 1978.

[15] Dehmel, K. H., Forster, H., and Mehnert, H.: Absorption of xylitol. *In* International Symposium on the Metabolism, Physiology, and Clinical Use of Pentoses and Pentitols. Horecker, B. L., Lang, K., and Takagi, Y., Eds. New York, Springer-Verlag, 1969, pp. 177–81.

[16] Crapo, P. A., Kolterman, O. G., and Olefsky, J. M.: Effects of oral fructose in normal, diabetic, and impaired glucose tolerance subjects. Diabetes Care *3*: 575–82, 1980.

[17] Bohannon, N. V., Karam, J. H., and Forsham, P. H.: Advantages of fructose ingestion (FTT) over sucrose (STT) and glucose (GTT) in humans. Diabetes *27* (Suppl. 2): 438, 1978.

[18] National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes *28*: 1039–57, 1979.

[19] Society of Actuaries: Build and Blood Pressure Study *1*: 16, 1959.

[20] Permutt, M. A., Delmez, J., and Stenin, W.: Effects of carbohydrate restriction on the hypoglycemic phase of the glucose tolerance test. J. Clin. Endocrinol. Metab. *43*: 1088–93, 1976.

[21] Desbuquois, B., and Aurbach, D. F.: Use of polyethylene glycol to separate free and antibody bound peptide hormones in radioimmunoassays. J. Clin. Endocrinol. Metab. *33*: 732–38, 1971.

[22] Lefebvre, P. J., and Luyckx, A. S.: The breakfast tolerance test: a return to physiology. Diabete Metab. *2*: 15–19, 1976.

[23] Crapo, P. A., Reaven, G. M., and Olefsky, J. M.: Postprandial glucose and insulin responses to different complex carbohydrates. Diabetes *26*: 1178–83, 1977.