

Sterile water alone induced no reaction. In a separate test performed the next day, diphenhydramine was injected into the same site as the insulin and hydrocortisone mixture. This combination prevented both immediate and delayed reactions. In conclusion, the results clearly demonstrate that our patient displayed both immediate and delayed hypersensitivity to human insulin, which could be prevented by simultaneous administration of local antihistamine and corticosteroid, respectively.

DISCUSSION

Based on these clinical observations, it was decided that optimally a mixture containing adjusted proportions of insulin, diphenhydramine, and hydrocortisone could be injected together to prevent local reactions. However, although this simple set of skin tests both defines the types of allergic reactions and suggests a mode of treatment, management of these reactions is beset by numerous complicating factors. It has been suggested that a solution of diphenhydramine and insulin is incompatible due to precipitation of insulin probably related to lowering the pH (2,6). Moreover, hydrocortisone is not stable for >3 days in aqueous solution and is even less stable when mixed with diphenhydramine (7). Thus, the patient was sent home with instructions to apply a high-potency topical corticosteroid preparation (0.05% fluocinonide) to her injection site 30 min before injection and to take terfenadine (60 mg), an oral antihistamine lacking the side effects of drowsiness characteristic of other antihistamines. Although providing considerable relief, this regimen was not completely effective, presumably because of lower local concentrations of antihistamine and corticosteroid attained at the injection site and variability in the application of the corticosteroid cream. We subsequently have been able to overcome some of these problems by the administration of a stable mixture containing insulin and dexamethasone at a concentration of 1 µg dexamethasone/1 U insulin. This preparation prevents the more disturbing delayed reaction, but systemic antihistamines are still required to minimize the immediate hypersensitivity reaction. With this treatment protocol, our patient has been able to achieve good

diabetic control on insulin, free of bothersome side effects. After 6 mo on this therapeutic program, her glycohemoglobin level was 6.6% (normal range 4–6.3%). This suggests that the addition of dexamethasone to insulin does not affect the bioavailability and efficacy of insulin.

Glucose 1 mM = 18 mg/dl

From the Section of Endocrinology, Department of Medicine, University of Chicago, Chicago, Illinois.

Address correspondence and reprint requests to Jonathan Jaspan, MD, Department of Medicine, University of Chicago, 5841 Maryland Avenue, Box 435, Chicago, IL 60637.

ACKNOWLEDGMENTS

This work was supported by The University of Chicago Diabetes Research and Training Center Grant DK-20595. J.A.L. was supported by Medical Scientist Training Program Grant GM-07281 from the National Institutes of Health. K.C.H. is the recipient of a Career Development Award from the Juvenile Diabetes Foundation International.

REFERENCES

1. Anderson JA, Adkinson NF Jr: Allergic reactions to drugs and biologic agents. *JAMA* 258:2891–99, 1987
2. Galloway JA, deShazo RD: The clinical use of insulin and the complications of insulin therapy. In *Diabetes Mellitus: Theory and Practice*. Ellenberg M, Rifkin H, Eds. New Hyde Park, NY, Med. Exam., 1983, p. 519–38
3. DeShazo RD, Levinsbom AI, Boehm T, Evans R III, Ward G Jr: Severe persistent biphasic local (immediate and late) skin reactions to insulin. *J Allergy Clin Immunol* 59:161–64, 1977
4. Wurzbarger MI, Gordana MP, Despotovic N, Vuckovic S, Brkic S, Bozovic M, Nastic-Miric D: Delayed-type allergy against various insulin preparations including human semisynthetic insulin. *Ann Allergy* 59:44–47, 1987
5. DeShazo RD, Boehm TM, Kumar D, Galloway JA, Dvorak HF: Dermal hypersensitivity reactions to insulin: correlations of three patterns to their histopathology. *J Allergy Clin Immunol* 69:229–37, 1982
6. Lamkin N, Lieberman P, Hashimoto K, Morohashi M, Sullivan P: Allergic reactions to insulin. *J Allergy Clin Immunol* 58:213–23, 1976
7. Trissel LA: *Handbook of Injectable Drugs*. Bethesda, MD, Am. Soc. Hosp. Pharm., 1988, p. 358–61

Effect of Sucrose-Containing Snacks on Blood Glucose Control

To determine whether ingestion of sucrose-containing snacks would affect blood glucose (BG) control, 16 subjects with insulin-dependent diabetes mellitus participated in a 5-day double-blind study at a diabetes camp. Eight subjects in the sucrose group ate sucrose-

sweetened snacks twice a day, and 8 subjects in the control group ingested snacks that were sweetened with aspartame. The percentage of total daily calories derived from added sucrose was 7% for the sucrose group and 1% for the control group. Metabolic control

Joyce E. Wise, MD
Kathryn S. Keim, PhD
Jacqueline L. Huisinga, RD
Pamela A. Willmann, BS

was assessed by daily capillary BG measurements obtained before meals and the bedtime snack and by determination of serum fructosamine (F) concentrations on arrival at camp (day 0) and after 5 days on the study protocol (day 5). No significant difference was seen between the groups on day 0 (sucrose group [mean \pm SD]: BG 9.9 \pm 3.6 mM, F 3.54 \pm 0.38 mM; control group: BG 9.1 \pm 2.8 mM, F 3.74 \pm 0.71 mM) or day 5 (sucrose group: BG 8.8 \pm 2.6 mM, F 2.94 \pm 0.32 mM; control group: BG 7.4 \pm 2.8 mM, F 2.92 \pm 0.59 mM). We conclude that ingestion of sucrose, added to snacks in an amount up to 7% of total energy intake, does not adversely affect short-term BG control. *Diabetes Care* 12:423-26, 1989

Sucrose has been traditionally excluded from the diet of patients with insulin-dependent diabetes mellitus (IDDM), based on the belief that sucrose is more rapidly absorbed from the gastrointestinal tract and causes a greater rise in blood glucose concentrations than that seen after ingestion of more complex carbohydrates. Several recent clinical investigations have not supported this hypothesis (1-8). In a well-controlled study by Bantle et al. (1), patients with IDDM were able to consume 23% of their total calories as sucrose for 8 days without adversely affecting blood glucose control or serum lipids. In a study by Peterson et al. (8), 12 subjects with IDDM ingested 45 g of sucrose with each meal for a period of 6 wk. Again, blood glucose and serum lipid concentrations were unaffected.

Despite these studies, there is still a reluctance on the part of physicians, dietitians, and patients to accept sucrose as a normal component of the diabetic diet. One reason may be that previous studies may not be completely applicable to the typical patient with IDDM. The subjects studied by Bantle et al. (1) were all in good metabolic control, and the study was performed in a clinical research unit. Other investigations have examined the response to eating just one meal or snack or have been performed during modes of therapy that are not used by most patients with IDDM, such as the artificial pancreas or subcutaneous insulin pumps (2-7). Finally, the study of Peterson et al. (8) has been criti-

cized because it was performed in an outpatient setting where dietary intake was not controlled (9).

In an effort to evaluate this question further, we examined the effect of ingesting sucrose-containing snacks on blood glucose concentrations in a group of conventionally treated subjects who were in varying degrees of metabolic control for 5 days in a closely monitored outpatient setting.

MATERIALS AND METHODS

Sixteen staff members (3 dietitians, 12 counselors, and 1 camp director) with IDDM at Camp GranADA, a summer camp for children with diabetes mellitus sponsored by the American Diabetes Association Downstate Illinois Affiliate, were randomly assigned to the control or sucrose group. The membership of each group was unknown to the subjects, camp dietitians, and camp physicians. Baseline characteristics of the two groups are shown in Table 1. All subjects were within 10% of ideal body weight. This project was reviewed and approved by the Institutional Review Board, University of Illinois College of Medicine, and written informed consent was obtained from all subjects.

Subjects in both groups ate the standard camp diet except for the midmorning and midafternoon snacks, which were sweetened with sucrose for the sucrose group and with aspartame for the control group (Table 2). The snacks were prepared and divided into portions equivalent to one bread exchange and color-coded before the study by one of the investigators (P.A.W.) who did not attend the camp. Camp meal plans were standardized according to calorie level, and the number of snack portions ingested at a given time depended on the subject's calorie level. Similar types of snacks were ingested by the two groups on different days so that portion size and texture could not be compared. Food intake was recorded on a flow sheet, and actual nutritional composition for both groups was calculated after the camp session (Table 3; 10). Because the subjects were more physically active at camp than at home, their baseline calorie intake was increased by 5-10%, and their baseline insulin doses were decreased by 5-10% on arrival

TABLE 1
Baseline characteristics of study subjects

	Groups	
	Control	Sucrose
n (M/F)	4/4	5/3
Age (yr)	24 \pm 8 (16-39)	20 \pm 5 (16-31)
Duration of IDDM (yr)	16 \pm 7 (4-25)	10 \pm 2 (5-12)
Glycosylated hemoglobin, normal <7.5 (%)	11.5 \pm 3.1 (7.9-18.4)	12.2 \pm 1.9 (8.3-13.7)
Insulin (U/day)	59 \pm 42 (20-156)	73 \pm 21 (48-112)
Diet (cal/day)	2200 \pm 800 (1400-3500)	2500 \pm 600 (1800-3200)

Values are means \pm SD; ranges are in parentheses.

TABLE 2
Composition of control- and sucrose-group snacks

	Groups													
	Control						Sucrose							
	Carbohydrate (g)				Protein (g)	Fat (g)	Calories	Carbohydrate (g)				Protein (g)	Fat (g)	Calories
	Added sucrose	Other sugars*	Starch	Lactose				Added sucrose	Other sugars*	Starch	Lactose			
Oatmeal fudge														
cookie	0	0.6	10.2	0.4	3.6	9.5	145	9.8	0.3	5.0	0.2	1.8	4.8	112
Fudgesicle	0	0	7.2	9.2	6.4	3.6	124	8.0	0	2.8	4.6	3.6	2.3	97
Fudge cookie	3.5	0.2	4.8	5.8	5.4	7.8	149	8.7	0.1	3.4	1.9	2.1	4.2	103
Granola bar	0	8.4	5.6	0	3.7	7.3	137	7.4	4.0	2.7	0	1.8	3.5	95
Banana bar	0	2.8	9.8	1.1	2.8	4.9	110	10.5	1.0	5.1	0	1.1	2.6	94
Coconut bar	0	7.5	9.5	0	2.2	11.7	182	9.6	0.3	5.2	0	1.2	5.9	118
Cereal bar	3.7	0.6	10.3	0	2.5	11.8	175	11.7	0.7	5.8	0	0.8	0.1	77

*Glucose, maltose, fructose, and sucrose contained in fruits and prepared foods (10).

at camp. Total daily calorie intake was then altered by camp dietitians depending on the subject's appetite.

Capillary blood glucose was measured four times per day (before meals and the bedtime snack) with Accu-Chek blood glucose monitors (Boehringer Mannheim, Indianapolis, IN). Blood glucose results were reviewed daily by camp physicians, and insulin doses were adjusted to maintain optimal blood glucose control. Metabolic control was evaluated by daily capillary blood glucose measurements and by serum fructosamine determinations that were drawn on arrival at camp (day 0) and after 5 days on the study protocol (day 5). Serum fructosamine was determined colorimetrically (Glyco-PROBE GSP, Isolab, Akron, OH) (11). Samples were stored at -70°C , and both samples from each subject were analyzed in the same assay.

The Mann-Whitney *U* test for two independent samples was used to compare blood glucose (daily mean and specific preprandial and bedtime measurements) and serum fructosamine concentrations between the control and sucrose groups. Differences within the groups on

days 0 and 5 were determined by Wilcoxon's *T* test for two dependent samples. Results are expressed as means \pm SD.

RESULTS

No significant difference was seen between the control or sucrose group for daily capillary blood glucose levels or fructosamine concentrations on days 0 and 5. Both groups had an improvement in metabolic control, as indicated by a decrease in mean daily blood glucose and fructosamine concentrations, by day 5 (Table 4). Changes in insulin dose and daily energy requirements from baseline were similar in both groups: control group decreased 9 ± 11 U/day (15%), increased 112 ± 125 cal/day (5%); sucrose group decreased 10 ± 13 U/day (14%), increased 150 ± 278 cal/day (6%). The number of hypoglycemic episodes per subject, defined as typical symptoms of neuroglycopenia and/or a capillary blood

TABLE 3
Nutrient composition of study diets

	Groups	
	Control	Sucrose
Energy intake (cal/day)	2312 \pm 882	2650 \pm 692
Carbohydrates (%)	43 \pm 2	47 \pm 2
Sucrose	1 \pm 1	7 \pm 2
Other sugars	12 \pm 1	12 \pm 2
Starch	23 \pm 3	21 \pm 3
Lactose	7 \pm 2	7 \pm 1
Protein (%)	21 \pm 3	20 \pm 1
Fat (%)	36 \pm 3	33 \pm 2

Values are means \pm SD.

TABLE 4
Blood glucose and fructosamine concentrations at baseline (day 0) and after 5 days on study protocol (day 5)

	Groups	
	Control	Sucrose
Blood glucose (mM)		
Day 0	9.1 \pm 2.8	9.9 \pm 3.6
Day 5	7.4 \pm 2.8	8.8 \pm 2.6
Fructosamine (mM)		
Day 0	3.74 \pm 0.71	3.54 \pm 0.38
Day 5	2.92 \pm 0.59*	2.94 \pm 0.32*

Values are means \pm SD.

**P* < .01 vs. day 0.

glucose concentration of <3.9 mM, did not vary between the two groups (control group 2.6 ± 2.1 and sucrose group 2.6 ± 1.8). No significant change in weight occurred in any of the subjects.

DISCUSSION

Several aspects of our study are unique. All subjects received conventional therapy with two injections of insulin per day. Metabolic control at the beginning of the study ranged from excellent to very poor. The camp was an excellent outpatient setting in which the subjects could exercise and where their food intake was closely monitored and controlled.

Under these conditions, no deterioration in glucose control was seen when subjects in the sucrose group ate sucrose-sweetened snacks twice a day for 5 days. Serum fructosamine, a measurement of glycosylated serum proteins that reflects mean glycemia over the preceding 1–3 wk, fell in all subjects (11). The improvement in glycemic control was probably due to increased frequency of blood testing, careful adjustment of insulin doses, and increased exercise. More important, no significant difference in glucose control was seen between the group that ate the standard camp diet and the group that ingested sucrose-sweetened snacks.

These results pertain only to short-term metabolic control, because the length of the camp session prevented observation over a longer period. Further studies during longer camp sessions would be needed before the results of this study could be generalized to chronic situations. A longer study period would also allow subjects to adapt to the increased exercise at camp. However, it is unlikely that the additional physical activity compensated for the hyperglycemic effect of the sucrose, because both groups engaged in the same activities and had comparable numbers of hypoglycemic reactions and changes in insulin and calorie requirements.

The average American is reported to consume ~18% of his total daily calories as sucrose (12). Although subjects in the sucrose group ate less than that amount, the average amount of sucrose ingested at one time was 24 g, which is equivalent to the amount contained in 2 fudge brownies, 1½ iced cupcakes, or a slice of apple pie (13). Inclusion of these foods in the diet would help to lessen the feeling of deprivation experienced by many patients with IDDM. The results of this study suggest that up to 7% of total calories can be ingested as sucrose and added to snacks for as long as 5 days without adversely affecting metabolic control in patients with IDDM.

Glucose 1 mM = 18 mg/dl Fructosamine 1 mM = 24.93 mg/dl

From the Department of Pediatrics, University of Illinois College of Medicine, and the Diabetes Resource Center, Saint Francis Medical Center, Peoria; and the Department of Foods and Nutrition, University of Illinois, Champaign, Illinois.

Address correspondence and reprint requests to Joyce E. Wise, MD, One Illini Drive, Box 1649, Peoria, IL 61656.

ACKNOWLEDGMENTS

We thank Elsie Kolb for technical assistance and Debbie Batey for help in the preparation of the manuscript.

This work was partially funded by Illinois Agricultural Experiment Station Project Grant 60345.

REFERENCES

- Bantle JP, Laine DC, Thomas JW: Metabolic effects of dietary fructose and sucrose in types I & II diabetic subjects. *JAMA* 256:3241–46, 1986
- Bantle JP, Laine DC, Castle GW, Thomas JW, Hoogwerf BJ, Goetz FC: Postprandial glucose and insulin responses to meals containing different carbohydrates in normal and diabetic subjects. *N Engl J Med* 309:7–12, 1983
- Slama G, Jean-Joseph P, Goicolea I, Elgrably F, Haardt MJ, Costagliola D, Bornet F, Tchobroutsky G: Sucrose taken during mixed meal has no additional hyperglycemic action over isocaloric amounts of starch in well-controlled diabetics. *Lancet* 2:122–24, 1984
- Chantelau EA, Gosseringer G, Sonnenberg GE, Berger M: Moderate intake of sucrose does not impair metabolic control in pump-treated diabetic out-patients. *Diabetologia* 28:204–207, 1985
- Lenner RA: Studies of glycemia and glucosuria in diabetics after breakfast meals of different composition. *Am J Clin Nutr* 29:716–25, 1976
- Steel JM, Mitchell D, Prescott RL: Comparison of the glycemic effect of fructose, sucrose and starch-containing mid-morning snacks in insulin-dependent diabetics. *Hum Nutr Appl Nutr* 37A:3–8, 1983
- Lean MEJ, Tennison BR, Williams DRR: Glycemic effects of bread and marmalade in insulin-dependent diabetes. *Diabetic Med* 2:117–20, 1985
- Peterson DB, Lambert J, Gerring S, Darling P, Carter RD, Jelfs R, Mann JI: Sucrose in the diet of diabetic patients—just another carbohydrate? *Diabetologia* 29:216–20, 1986
- Reaven GM, Hollenbeck C, Coulston A: Sucrose in the diabetic diet: a reply (Letter). *Diabetes Care* 10:668–69, 1987
- Paul AA, Southgate DAT: *McCance & Widdowson's The Composition of Foods*. 4th ed. London, HMSO, 1978
- Johnson RN, Metcalf PA, Baker JR: Fructosamine: a new approach to the estimation of serum glycosylprotein: an index of diabetic control. *Clin Chim Acta* 127:87–95, 1982
- Anderson TA: Recent trends in carbohydrate consumption. *Annu Rev Nutr* 2:113–32, 1982
- Better Homes and Gardens New Cookbook*. Des Moines, IA, Meredith, 1981