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Effects of Dietary Carbohydrate on Fasting Levels of Human Growth Hormone and Cortisol[1] (41303)

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Abstract. Ten men and nine women aged 35–55 years consumed two diets for 6 weeks each in a crossover design. Diets provided identical foods with 30% of the kilocalories (kcal) as either sucrose or cooked wheat starch. Of the total kcal 43% was supplied as carbohydrate, 42% as fat, and 15% as protein. The dietary pattern consisted of two meals divided so as to provide 10% of the kcal at breakfast (0700–0830 hr) and 90% of the kcal at dinner (1630–1830 hr). Initial body weights were essentially maintained. Fasting human growth hormone (HGH) level decreased significantly as a function of time on diets. Fasting cortisol level differed significantly between Periods I and II regardless of whether or not diets contained starch or sucrose and was also affected by time on the study. The consumption of diets containing 30% of the kcal as either starch or sucrose in a gorging pattern apparently promoted changes in levels of HGH and cortisol in the direction that would favor lipid formation.

The sucrose intake in urbanized societies such as that in the United States is believed to contribute 15–20% of the daily total kcal (1, 2). A tendency to ingest the bulk of the day's kilocalories (kcal) in large and infrequent meals (gorging) has also been noted in urbanized societies (3, 4). Although neither sucrose nor eating pattern has been positively shown to promote coronary heart disease, diabetes, or obesity, the combination of the two factors might potentiate the development of these conditions (5).

A human study conducted by Reiser *et al.* (6, 7) and designed to investigate the role of sucrose gorging on indices of glucose tolerance indicated that the replacement of starch by sucrose promoted elevations in levels of fasting serum insulin and glucose. In the normal individual with adequate supplies of carbohydrate as a precursor, insulin, glucagon, and epinephrine play major roles in the minute-by-minute control of glucose concentration. Two other hormones (human growth hormone and cortisol) also influence blood glucose regulation but in an indirect manner. Due to the nature of their action, their regulatory roles are difficult to assess when compared to those of insulin and glucagon. Even so, it is highly likely that dietary carbohydrates that promote changes in serum concentrations of the acute regulatory hormones also promote changes in concentrations of human growth hormone (HGH) and cortisol.

In an attempt to provide insight into the possible effect of sucrose on HGH and cortisol, subjects were given diets of identical foods plus 30% of the kcal as either sucrose or wheat starch. Subjects ate 10% of the kcal at breakfast and 90% at dinner.

The 30% level of sucrose was not considered greatly excessive when compared to the 15–20% level currently consumed in the United States. A 6-week experimental period was considered adequate for adaptation to the diets. The composition of the experimental diets also approximated that of the average United States diet in 1974 (8).

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Materials and Methods. Candidates were medically examined to determine that they were free of overt disease, and 19 subjects, 10 males and 9 females aged 35–55 (average 42 years) and weighing 53.0–99.5 kg (average 71.7 kg), were selected to participate in a split-plot crossover design study. Initial weight of the males was 76.6 kg and of the females was 66.2 kg. Each subject submitted dietary and activity records for the 7 days prior to each dietary period. Individuals were then matched for weight and age and divided into two groups. Group I comprised five males and five females averaging 71.9 kg and 42 years. Group II comprised five males and four females averaging 71.3 kg and 42 years. Menus closely resembling those consumed in the United States were fed for two 6-week periods separated by a 4-week break during which subjects consumed self-selected diets. Diets followed 3-day rotating menus and food was eaten in two unequal meals (10% of the kcal at breakfast; 90% of the kcal at dinner). The only difference in the menus between groups was the addition of 30% of the kcal as either a sucrose patty or a wheat starch (purified gelatinized food grade wheat starch, Midwest Solvents Co., Atchinson, Kans.) wafer. Each patty and wafer contained 210 g of the respective carbohydrate, 23 g Crisco, and 42 g butter. The subjects in Group I ate the sucrose diet during the first 6-week period. Following a 4-week rest period, they ate the starch diet during the second 6-week period. Group II ate the diets in the reverse order.

The nutrient contents of the experimental diets are given in Table I. The diet for an average 70-kg subject was made up of about 2700 kcal of which 43% was from carbohydrate, 42% from fat, and 15% from protein. Nutrients in both the experimental and the self-selected diets recorded on 7-day dietary records were calculated from data in Agricultural Handbooks No. 8 (9) and No. 456 (10). The levels of sucrose and starch were calculated from the data of Hardinge *et al.* (11) and from Kellogg's Purchasing Guide NV-3 15M 9-76. Vitamin and mineral levels were determined from data in Agricultural Experiment Station Bulletin No. 435 (12), Home Economics Research Report No. 36 (13), Perloff and Butrum (14), and Murphy *et al.* (15). Diets of subjects weighing less than 70 kg were supplemented with vitamins and minerals in order to meet the Recommended Dietary Allowances of the National Research Council (16). Kilocalories consumed were adjusted to maintain individual initial weights of the subjects during the study.

TABLE. 1. NUTRIENT CONTENT OF EXPERIMENTAL DIETS[a]

Constituent	Average daily intake/70 kg body wt	
Energy (kcal)	2737.0	
Total carbohydrate (g)	294.0	
% of kcal	43.0	
Starch[b] (g)	229.1,[c]	19.1[d]
% of kcal	35.5,[c]	2.8[d]
Sucrose[b] (g)	16.8,[c]	226.8[d]
% of kcal	2.5,[c]	33.1[d]
Crude fiber (g)	4.2	
Total fat (g)	127.5	
% of kcal	41.9	
Saturated fat (g)	57.2	
% of kcal	18.8	
Polyunsaturated fat (g)	14.7	
% of kcal	4.8	
P/S ratio	0.26	
Cholesterol (mg)	562.0	
Protein (g)	103.3	
% of kcal	15.1	

[a] Calculated from data in Agricultural Handbook No. 8 (9) and No. 456 (10). Vitamins and minerals calculated to meet RDA allowances (12–16).

[b] Calculated from data of Hardinge *et al.* (11) and Kellogg's Food Service Products Nutritive Values and Purchasing Guide NV-3 15M 9-76.

[c] During starch period.

[d] During sucrose period.

Blood samples were drawn by venapuncture after a 12-hr fast 1 week before each dietary period and then weekly for 6 weeks. The blood was centrifuged at 5°C for 20–30 min at 1500*g*. Serum HGH was determined by a double-antibody radioimmunoassay method of Morgan (17). Serum cortisol was assayed by competitive protein binding (18).

The data (Data Systems Application Division, U.S. Department of Agriculture, Beltsville, Md.) were treated by analysis of variance and correlation coefficients were calculated. Duncan's multiple range test

(19) was used to determine which means were significantly different.

Results. Analysis of the dietary records submitted by subjects indicated that they consumed a mean of 3.8 ± 0.3 meals per day 1 week prior to Period I and 3.6 ± 0.3 meals 1 week prior to Period II. A meal was considered as the intake of more than 100 kcal within a 1-hr period. While the number of meals eaten was not different for the two periods, significantly fewer kcal were consumed between 0800 and 1600 hr during the week prior to Period II than during the week prior to Period I (32.6 ± 2.4% versus 24.7 ± 2.2%) ($P < 0.01$). The reverse was true between 1600 and 2400 hr (49.7 ± 2.2% versus 55.6 ± 1.8%) ($P < 0.05$). Patterns did not differ in kcal taken between 2400 and 0800 hr (17.3 ± 2.1% versus 19.7 ± 2.2%). Analysis of the daily consumption of the self-selected diets is presented in Table II.

Because the levels of fasting HGH did not differ significantly between Periods I and II, data from subjects consuming sucrose and starch during the two periods were combined for statistical analysis. Pretest fasting levels of HGH were similar to those reported in previous human studies (20, 21). The level of fasting HGH was significantly affected by time on the study ($P < 0.01$) (Table III). A time and sex interaction was also significant ($P < 0.01$); females exhibited a greater unit decrease than males over the 6-week period. The effect of dietary treatment on HGH was not highly significant, but levels tended to be affected by diet ($P < 0.25$); mean levels of all subjects were 21% higher on the sucrose diet than on the starch diet.

TABLE II. AVERAGE DAILY COMPOSITION OF SELF-SELECTED DIETS OF SUBJECTS 1 WEEK PRIOR TO EACH EXPERIMENTAL PERIOD

Dietary constituent	Period I	Period II
Carbohydrate (% kcal)	40.4 ± 3.3[a]	39.9 ± 3.8
Protein (% kcal)	16.7 ± 1.1	16.4 ± 1.2
Fat (% kcal)	43.9 ± 3.3	43.7 ± 4.4
P/S ratio	0.35 ± 0.35	0.40 ± 0.36
Cholesterol (mg)	420 ± 46	475 ± 40
Crude fiber (g)	3.6 ± 0.3	3.6 ± 0.3

[a] Mean daily values ± SEM from 19 subjects during the week prior to each experimental period.

Table IV shows that fasting cortisol levels differed significantly ($P < 0.01$) for the two dietary periods. Unlike HGH, cortisol levels were similar for males and females prior to and throughout the 6 weeks of treatment. Six-week means for Period I for males and females were: males fed sucrose, 16.27 ± 3.06 μg/dl; females fed sucrose, 15.5 ± 3.55 μg/dl; males fed starch, 10.64 ± 2.28 μg/dl; females fed starch, 15.57 ± 4.08 μg/dl. For Period II, means were: males fed sucrose, 16.48 ± 4.18 μg/dl; females fed sucrose, 20.85 ± 3.62 μg/dl; males fed starch, 17.17 ± 3.42 μg/dl; females fed starch, 18.95 ± 2.67 μg/dl. Cortisol levels tended to be elevated in subjects fed the sucrose diet ($P < 0.25$). The apparent decline in weekly levels at Weeks 5 and 6 might indicate that the elevation of cortisol in subjects fed sucrose is transient. Cortisol values pretest and during the dietary periods were within the range of 5–25 μg/100 ml reported for normal humans (22).

Discussion. Meal feeding human subjects commercially available foods in diets containing 30% of the daily kcal allowance as sucrose for comparatively short periods promoted elevated levels of fasting serum insulin, triglycerides, glucose, and cholesterol (6, 7). A direct relationship also was established between meal size and serum insulin response (23). Our study further suggests that fasting levels of serum HGH and cortisol are also influenced by the interrelationship of adaptation to feeding frequency and type of dietary carbohydrate. HGH levels, independent of diet, decreased significantly with time and returned to pretest levels after a 4-week rest period. Female subjects exhibited a greater unit decrease than males over the 6-week treatment period. This time and sex interaction might have been due to the fact that HGH was higher in females than in males early in the treatment periods. Higher fasting levels of HGH in females than in males have been reported (24) but not fully explained. While the subtle interrelationships between the various metabolites (i.e., fatty acids and glucose) that regulate HGH secretion make

TABLE III. FASTING SERUM HUMAN GROWTH HORMONE LEVELS (ng/ml) OF 10 MALES AND 9 FEMALES CONSUMING THE STARCH AND SUCROSE DIETS IN A GORGING PATTERN[a]

Weeks on diet	Males		Females		Weekly means[b]
	Starch	Sucrose	Starch	Sucrose	
Pretest	1.89 ± 0.35[c]	1.91 ± 0.27	5.17 ± 1.35	5.23 ± 1.13	3.46[1]
1	1.53 ± 0.30	1.95 ± 0.25	4.58 ± 1.06	6.21 ± 1.50	3.54[1]
2	1.80 ± 0.27	2.21 ± 0.35	3.22 ± 0.64	4.45 ± 0.69	2.86[1,2]
3	1.50 ± 0.22	1.49 ± 0.32	2.30 ± 0.41	4.40 ± 1.22	2.50[2,3]
4	0.80 ± 0.17	1.31 ± 0.28	2.64 ± 0.63	2.19 ± 0.78	1.74[3]
5	1.00 ± 0.13	1.20 ± 0.18	2.47 ± 0.65	2.28 ± 0.33	1.70[3]
6	1.26 ± 0.16	1.04 ± 0.26	1.33 ± 0.21	1.65 ± 0.52	1.39[3]
6-Week mean	1.35	1.53	2.86	3.59	

[a] Split plot crossover analysis of variance showed diet effect ($P < 0.25$); significant week effect ($P < 0.01$); significant week × sex interaction ($P < 0.01$).

[b] Values within weekly means column are significantly different ($P < 0.05$) if they do not share a common superscript number according to Duncan's multiple-range test; standard error = 0.28.

[c] Mean ± SEM.

it difficult to attribute this decrease to a single experimental factor (20), the meal pattern in this experiment apparently was primarily responsible for the decrease. Since the major events influenced by HGH include fatty acid mobilization and increased oxygen consumption (25), the decline in HGH levels during the gorging periods would enable the subjects to achieve a biologically useful adaptation to the extended periods between meals. When HGH levels are suppressed, the balance between lipogenesis and the liberation of fatty acids from adipose tissue remains markedly in favor of the formation of fat reserves (25).

The decline in HGH levels during the 6 weeks of dietary treatment is also in keeping with the findings that triglycerides, total lipids and glucose, and insulin and glucagon are significantly elevated in subjects fed starch or sucrose in a gorging pattern (6, 7). Inhibitory effects of lipids (i.e., triglycerides and free fatty acids) on HGH secretion were observed in both Rhesus monkeys (26) and human subjects (20). This inhibition seems logical from information available on insulin and HGH homeostasis. With the exception of amino acids, which stimulate secretion of both insulin and HGH, many of the regulatory factors for insulin

TABLE IV. FASTING SERUM CORTISOL (μg/100 ml) OF 10 MALES AND 9 FEMALES CONSUMING THE STARCH AND SUCROSE DIETS IN A GORGING PATTERN[a]

Weeks on diet	Period I		Period II		Weekly means[b]
	Starch	Sucrose	Starch	Sucrose	
Pretest	8.52 ± 1.02[c]	11.10 ± 1.61	14.10 ± 1.96	15.41 ± 2.26	12.85[1]
1	13.17 ± 2.63	16.92 ± 3.00	16.75 ± 2.80	10.08 ± 3.83	16.48[2,3]
2	12.35 ± 2.18	16.51 ± 1.51	16.12 ± 1.52	13.89 ± 2.39	14.72[3]
3	11.26 ± 1.01	14.70 ± 0.85	14.00 ± 1.77	18.28 ± 2.60	14.56[3]
4	12.83 ± 1.64	17.90 ± 2.82	22.05 ± 1.84	21.85 ± 2.01	18.85[2]
5	15.56 ± 2.59	15.48 ± 1.59	22.92 ± 2.69	17.46 ± 2.03	17.89[2,3]
6	13.70 ± 2.98	12.77 ± 2.11	16.48 ± 2.74	21.36 ± 2.31	16.08[2,3]
6-Week means	14.37		18.22		

Diet means: starch, 15.60; sucrose, 16.99

[a] Split plot crossover analysis of variance showed diet effect ($P < 0.25$); significant period difference ($P < 0.01$); significant week difference ($P < 0.05$).

[b] Values within weekly means column are significantly different ($P < 0.05$) if they do not share a common superscript number according to Duncan's multiple-range test; standard error = 1.17183.

[c] Mean ± SEM.

secretion affect HGH secretion in a reciprocal fashion (20).

Unlike HGH, fasting serum levels of cortisol did not return to pretest levels after the subjects consumed self-selected diets for 4 weeks. Apparently cortisol levels were modified by changes in the antecedent diet. Possibly the failure of cortisol level to return to pretest level after 4 weeks on a self-selected diet was due to the tendency by subjects to maintain a meal pattern more like that of Period I than like that prior to Period I. Cortisol levels, independent of time, were moderately higher ($P < 0.25$) in subjects fed the sucrose than in subjects fed the starch diet. This finding is similar to that noted by Yudkin (27) in young males fed high-sugar diets for 2 weeks.

By enhancing the activity of enzymes involved in gluconeogenesis (28, 29) as well as of enzymes involved in glucose catabolism (30), glucocorticoids, may act to efficiently regulate fuel supply over a 24-hr period (31). In this gorging situation an increase in cortisol, a decrease in HGH, and an excess of kcal could enhance lipid production and, over an extended period, lead to excessive fat accumulation.

In the present study, gorging diets containing 30% of the kcal as either starch- or sucrose-promoted changes in levels of HGH and cortisol in the direction favoring lipid formation. These findings are in keeping with those of Fabry and Tepperman (3), Cohen (23), and others who found that a dietary pattern with a small number of large meals promoted overweight and the deposition of fat reserves. In individuals on a relatively high intake of kcal and refined carbohydrate and engaged in low physical activity (such as in advanced civilizations), the consumption of large infrequent meals might favor the formation and deposition of body fat and the development of certain metabolic disorders.

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